Urologic Diseases in America

2007

National Institute of Diabetes & Digestive & Kidney Diseases

NATIONAL INSTITUTES OF HEALTH

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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UROLOGIC DISEASES IN AMERICA

2007

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This book is dedicated to the memory of Dr. Dalia Spektor, 1944–2002.

UROLOGIC DISEASES IN AMERICA

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Introduction

Mark S. Litwin, MD, MPH
Christopher S. Saigal, MD, MPH

The burden of urologic diseases on the American public is immense in both human and financial terms and until now has remained largely unquantified. Urologic diseases encompass a wide scope of illnesses of the genitourinary tract, including conditions that are congenital and acquired, malignant and benign, male and female, medical and surgical. They can occur at any point in the course of human development, from hydronephrosis *in utero* to urinary incontinence in the elderly. They may be acute and self-limited or chronic and debilitating, may primarily affect quality or quantity of life, and may be financially insignificant or catastrophic. Some urologic diseases present with complex signs and symptoms and require extensive evaluation, while others present with classical symptoms and are easily diagnosed. Still others occur without any symptoms at all and are discovered incidentally or during screening.

The economic impact of urologic diseases is often substantial for patients and families, employers, payors, and society at large. Physician practice and patient care-seeking behavior in urology have changed dramatically in response to a variety of financial and non-financial incentives in recent years. In order to develop thoughtful public policy responses to these changes, we must have a thorough understanding of the healthcare resource utilization and clinical epidemiology that are relevant to urologic diseases in America.

Accurate information on the epidemiology and impact of urologic diseases is critical to the equitable allocation of scarce resources at the national, state, and local levels. Indeed, as the American population ages, there is a growing need for information about the urologic health problems facing older adults. In conjunction with findings from clinical studies and basic research on biological mechanisms, an epidemiologic approach offers insights into the prevalence, etiology, and impact of urologic conditions. Translational findings from clinical and basic science research must be considered in the context of epidemiologic observations in urology.

Until this project, no authoritative omnibus had compiled a comprehensive set of data analyses that synthesized information available from myriad national and regional sources across the public and private sectors in the United States. Despite the need, reliable and valid health services data about urologic diseases have been scattered, inconsistent, and not readily available. The capabilities of the information age highlight this deficiency. There is no national surveillance system describing prevalence and incidence across all urologic diseases. Instead, various governmental and non-governmental agencies in the United States maintain a patchwork of population-based studies, observational cohorts, national interview surveys, reviews of physician practice patterns, hospital system databases, regional cancer registries, state health department health information systems, and federal, state, and private insurance claims-based datasets that can provide useful health statistics. These sources contain a wealth of epidemiologic and health services information about healthcare costs, access, and quality, as well as trends in the diagnosis and management of urologic diseases; however, the information sources were prodigiously untapped for this project.

The overall objective of this project, *Urologic Diseases in America*, is to quantify the burden of urologic diseases on the American public. We undertook this effort with the aid of sophisticated research methodologies and experienced analytic and administrative staff. Our team included epidemiologists, health economists, statisticians, programmers, and urologists trained in health services research. We searched all potential data sources for relevant information and health statistics in order to gather current and retrospective data on all aspects of the epidemiology, practice patterns, costs, and impact of urologic diseases in the United States. This volume is intended to convey meaningful information to users at various levels of medical sophistication, including the public, elected leaders, government officials, non-governmental organizations, media outlets, physicians, nurses, allied healthcare personnel, and academic researchers.

We began our work by conducting an exhaustive nationwide search for all possible sources of health data for urologic diseases in America. This search included data sources such as the large population surveys maintained by the federal government (e.g., National Center for Health Statistics), healthcare financing agencies (e.g., Centers for Medicare and Medicaid Services), hospital consortia, insurers, physician groups, state and county medical associations, physician specialty societies, private healthcare foundations, private sources, and the published literature. After defining a universe of potential data sources, we assessed each one on the basis of relevance, reliability, validity, quality assurance mechanisms, accessibility, cost, user-friendliness, and other factors determined to be important to researchers and the public. With guidance from the National Institute of Diabetes and Digestive and Kidney Diseases, we selected the datasets most likely to provide useful information (Appendix A). These included datasets from the Center for Medicare and Medicaid Services, population-based datasets, datasets with information about healthcare utilization and costs, and those with unique features or populations of interest that added dimension to the project.

We stratified the scope of urologic practice into discrete clinical areas for analysis. Because resources were limited, we were able to address only the most frequent urologic diagnoses. Table 1 lists the conditions selected for inclusion in this *Urologic Diseases in America* compendium.

For each condition, clinical and coding experts developed a set of codes from the National Center for Health Statistics' International Classification of Diseases, 9th revision (ICD-9), the American Medical Association's Current Procedural Terminology (CPT), and the Healthcare Common Procedure Coding System (HCPCS) to define relevant diagnoses, diagnostic procedures, and therapeutic interventions.

Table 1. Conditions analyzed in *Urologic Diseases in America*

Prostate
Prostatitis
Benign Prostatic Hyperplasia
Prostate Cancer
Bladder
Interstitial Cystitis and Painful Bladder Syndrome
Urinary Incontinence
Female Adult
Male Adult
Bladder Cancer
Lower Tract Transitional Cell Carcinoma
Upper Tract Transitional Cell Carcinoma
Kidney
Urolithiasis
Ureteropelvic Junction Obstruction
Kidney Cancer
Pediatric
Vesicoureteral Reflux
Undescended Testis
Hypospadias
Ureterocele
Posterior Urethral Valves
Urinary Incontinence in Children
Urinary Tract Infection in Children
Male Health
Male Infertility
Erectile Dysfunction and Peyronie's Disease
Urethral Stricture
Testicular Cancer
Infections
Urinary Tract Infection
Female Adult
Male Adult
Sexually Transmitted Diseases

Table 2. The burden of urologic diseases in America in 2000

	Visits to Office-Based Physicians[1] and Hospital Outpatient Clinics[2]		Visits to Emergency Rooms[2]	Hospital Stays[3]	Total Expenditures[1–4]
	Primary Diagnosis	*Any Diagnosis*			
Prostate					
Prostatitis	*	1,841,066	*	7,390	$84,452,000
Benign Prostatic Hyperplasia	4,418,425	7,797,781	117,413	105,185	$1,099,500,000
Prostate Cancer	3,330,196	*	*	94,620	$1,295,800,312
Bladder					
Interstitial Cystitis/Painful Bladder Syndrome	*	4,137,000	*	*	$65,927,937
Urinary Incontinence					
Female Adult	1,159,877[a]	2,130,929	*	46,470	$452,800,000
Male Adult	207,595	353,065	*	1,332	$10,300,000
Bladder Cancer					
Lower Tract Transitional Cell Carcinoma	*	832,416	*	72,776	$1,073,803,094
Upper Tract Transitional Cell Carcinoma	*	*	*	5,184	$64,309,807
Kidney					
Urolithiasis	1,996,907	2,682,290	617,647	177,496	$2,067,400,000
Ureteropelvic Junction Obstruction	*	*	*	2,215	$11,747,477
Kidney Cancer	*	279,564	*	30,045	$401,390,672
Pediatric					
Vesicoureteral Reflux	83,791[a]	140,098[a]	*	5,675	$41,725,663
Undescended Testis	148,551	215,482	*	1,298	*
Hypospadias	*	17,364[b]	*	849	$16,563,330
Ureterocele	*	*	*	2,818	$16,803,712
Posterior Urethral Valves	*	*	*	148	*
Urinary Incontinence in Children	*	*	*	*	
Urinary Tract Infection in Children	*	*	*	*	
Male Reproductive Health					
Male Infertility	*	158,413[a]	*	*	$17,046,404
Erectile Dysfunction	*	2,904,896	*	8,158	$327,626,849
Peyronie's Disease	*	*	*	*	*
Urethral Stricture	*	364,389	*	5,035	$191,074,350
Testicular Cancer	*	14,790	*	1,907	$21,745,500
Infections					
Urinary Tract Infection					
Female Adult	6,860,160	8,966,738	1,311,359	245,879	$2,474,000,000
Male Adult	1,409,963	2,049,232	424,705	121,367	$1,027,900,000
Sexually Transmitted Diseases	*	*	*	*	*

*Counts too low to produce reliable estimate.

[a]Physician office vistis only; counts not available for hospital outpatient clinics.

[b]Hospital outpatient visits only; counts not available for pyhsician office visits.

SOURCES:[1]National Ambulatory Medical Care Survey; [2]National Hospital Ambulatory Medical Care Survey; [3]Healthcare Cost and Utilization Project; [4]Medical Expenditure Panel Survey.

Table 3. Annual expenditures for Medicare beneficiaries with urologic diseases

	Inpatient	Outpatient	Emergency Room	Total
Prostate				
Prostatitis	$8,500,240	$20,557,960	$1,283,440	$30,341,640
Benign Prostatic Hyperplasia	$315,000,000	$441,200,000	$19,800,000	$776,000,000
Prostate Cancer	$264,414,460	$660,791,840	$2,218,220	$927,424,520
Bladder				
Interstitial Cystitis/Painful Bladder Syndrome	$47,859,680	$65,050,680	$5,832,640	$118,743,000
Urinary Incontinence				
Female Adult	$110,100,000	$123,700,000	$600,000	$234,400,000
Male Adult	$11,300,000	$27,100,000	$600,000	$39,000,000
Bladder Cancer				
Lower Tract Transitional Cell Carcinoma	$446,062,440	$239,802,080	$1,139,600	$687,004,120
Upper Tract Transitional Cell Carcinoma	$24,814,400	$7,625,900	*	$32,440,300
Kidney				
Urolithiasis	$518,900,000	$296,100,000	$19,400,000	$834,400,000
Ureteropelvic Junction Obstruction				
Kidney Cancer	$104,869,840	$24,348,960	*	$129,218,800
Pediatric				
Vesicoureteral Reflux	*	*	*	*
Undescended Testis	*	*	*	*
Hypospadias	*	*	*	*
Ureterocele	$4,658,400	$1,849,720	*	$6,508,120
Posterior Urethral Valves	*	*	*	*
Urinary Incontinence in Children	*	*	*	*
Urinary Tract Infection in Children	*	*	*	*
Male Reproductive Health				
Male Infertility	*	*	*	*
Erectile Dysfunction	$36,310,280	$39,337,720	$604,340	$76,252,340
Peyronies's Disease	*	*	*	*
Urethral Stricture	$6,713,200	$28,102,060	$538,360	$35,353,620
Testicular Cancer	*	*	*	*
Infections				
Urinary Tract Infection				
Female Adult	$687,600,000	$210,500,000	$58,400,000	$956,500,000
Male Adult	$376,400,000	$81,400,000	$22,400,000	$480,200,000
Sexually Transmitted Diseases	*	*	*	*

*Figure does not meet standard for reliability or precision.
SOURCE: Centers for Medicare and Medicaid Services.

These codes appear in the first table of each chapter. We applied these codes to analytic files from each dataset. Wherever possible, we stratified results into major demographic groups, usually by age group, gender, race/ethnicity, geographic region, and rural/urban status. We age-adjusted certain tables at the discretion of each chapter author (so indicated in those tables). For certain economic analyses, we constructed multivariate models. Pediatric urologic disorders were selected based on the availability of data. Urinary incontinence and urinary tract infection are each divided into three chapters—female, male, and children. The chapters on urinary tract infection are complemented by a special chapter on sexually transmitted diseases, which was prepared by staff at the Centers for Disease Control. All analytic techniques and further information on the datasets are presented in great detail in the methods chapter.

After completing initial data analyses and constructing draft tables to present information on trends in incidence, prevalence, practice patterns, resource utilization, and costs, we convened writing

Table 4. Estimated annual cost to an individual with urologic diagnosis

Diagnosis	Individual annual cost*
Kidney Cancer	$12,155
Bladder Cancer	$9,585
Prostate Cancer	$7,019
Testicular Cancer	$6,236
Urinary Incontinence	$4,498
Urolithiasis	$4,472
Painful Bladder Syndrome	$4,396
Interstitial Cystitis	$4,251
Male Urinary Tract Infection	$2,829
Prostatitis	$1,759
Female Urinary Tract Infection	$1,574
Benign Prostatic Hyperplasia	$1,536
Erectile Dysfunction	$1,101

*Privately-insured patients 18 to 64 years of age.

committees of academic physicians with experience in health services research and detailed clinical knowledge of the conditions. At these meeting, we also shared with them detailed literature reviews that included all pertinent population-based epidemiological and economic studies in the urologic conditions of interest. These individuals provided expert feedback and subsequent input on the execution of additional analyses and refinement of the previous ones. After completing a final set of tables and figures for each condition, we asked the writing committee members to provide insight, elaboration, and interpretation—to draw qualitative meaning from—the quantitative findings. The essays they submitted on each clinical topic were subjected to three rounds of formal peer review. The resulting chapters fill this compendium.

Although the chapter authors have worked hard to identify and summarize principal findings for the urologic conditions of interest, we encourage both casual and formal readers of the compendium to roll up their sleeves and wander leisurely through the data tables and figures. The chapters are rife with large and small results, some annotated in the text and others waiting to be discovered in the myriad rows and columns. Interested readers could explore any of these findings in more detailed, multivariate analyses. Tables 2 and 3 recapitulate a few of the most salient observations regarding outpatient visits, inpatient hospitalizations, and costs per year. Table 4 summarizes the differential per-patient cost of each urologic condition.

We faced important challenges in our analytic endeavors. Foremost among these was the limited amount of data available for conditions in pediatric urology, particularly the lack of information on the costs of pharmaceutical and medical services. Other methodological limitations are listed in the methods chapter. Furthermore, each chapter concludes with specific recommendations for improving the available datasets to support more thorough descriptions of the impact of each condition.

By any measure, the burden of urologic disease on the American public is immense and deserves further attention, in terms of clinical investigation, epidemiologic analysis, and health services research.

Accurately describing the burden of urologic disease on the American public is one of the most important efforts undertaken by the NIDDK at the dawn of the new millennium. Documenting trends in epidemiology, practice patterns, resource utilization, technology diffusion, and costs for urologic disease has broad implications for quality of healthcare, access to care, and the equitable allocation of scarce resources, both in terms of medical services and research budgets. The *Urologic Diseases in America* project represents a major step toward accomplishing those goals.

CHAPTER 1

Prostatitis

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Prostatitis

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INTRODUCTION

Prostatitis refers to several clinical syndromes, including well-defined acute and chronic bacterial infections, poorly defined chronic pelvic pain syndrome, and asymptomatic inflammation in the prostate gland found in pathology specimens. Although in recent years researchers have made an effort to classify patients as having a specific type of prostatitis, for the purposes of this chapter we use *prostatitis* as an umbrella term, including both acute and chronic, because clinical practice and ICD-9 codes are generally limited by more traditional definitions (Table 1).

The symptoms associated with prostatitis are common, bothersome, and burdensome in terms of both their health-related quality-of-life implications (1, 2) and their economic impact (3).

DEFINITION AND DIAGNOSIS

The traditional definition of prostatitis included acute prostatitis, chronic bacterial prostatitis, chronic nonbacterial prostatitis, and prostatodynia (4). In 1995, following an NIH-sponsored workshop on prostatitis, a revised classification (5) included the term *chronic pelvic pain syndrome* to reflect the uncertainty about whether the discomfort in chronic nonbacterial prostatitis and prostatodynia in fact originates in the prostate gland (Table 2).

In the current classification system, Categories I and II refer to acute and chronic bacterial prostatitis, respectively. Together, these conditions account for approximately 5% to 10% of all cases. They are clearly associated with bacterial infection and a urine culture that grows uropathogens. Acute prostatitis is characterized by the sudden onset of fever and dysuria, whereas chronic bacterial prostatitis typically involves relapsing episodes of urinary tract infections, usually with the same organism seen on urine cultures. Patients with chronic bacterial prostatitis are usually asymptomatic between infections.

Category III, known as chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), comprises the vast majority (> 90%) of cases and is further divided, depending on the presence (Type IIIA) or absence (Type IIIB) of white blood cells in semen, post-prostate-massage urine specimens (VB3), or expressed prostatic secretions (EPS). Because there appears to be no correlation between the presence of leukocytes and symptoms, classification into Types IIIA and IIIB is controversial (6).

Category IV refers to asymptomatic inflammatory prostatitis that is diagnosed incidentally during a workup for infertility, an elevated prostate specific antigen (PSA) test, or other disorders.

Diagnosis of Category I prostatitis is primarily based on clinical findings and a positive urine culture. Prostate massage is not recommended because of fear of bacteremia. For the toxemic patient, other measures may include blood cultures and an evaluation, usually by ultrasound, of the patient's ability to empty his bladder. Imaging studies include computed tomography (CT) scans to look for a prostatic abscess in patients who do not respond to initial antibiotic therapy.

Table 1. Codes used in the diagnosis of prostatitis

Males 18 years or older with one or more of the following:	
ICD-9 diagnosis codes	
601.0	Acute prostatitis
601.1	Chronic prostatitis
601.2	Abscess of prostate
601.3	Prostatocystitis
601.4	Prostatitis in diseases classified elsewhere
601.8	Other specified inflammatory diseases of prostate
601.9	Prostatitis, unspecified

Categories II and III prostatitis were traditionally diagnosed using the four-glass test. This segmented, quantitative technique involves culturing initial-stream urine (so-called, voided bladder 1, VB1), mid-stream urine (VB2), expressed prostatic secretions after massage (EPS), and post-massage urine (VB3) (7). The simplified two-glass test involves culture and microscopic examination of urine obtained before and after prostatic massage; it is easier for all concerned and has operating characteristics similar to those of the four-glass test (8). While Category II prostatitis is characterized by the presence of uropathogenic bacteria, Category III prostatitis is defined by their absence in the setting of genitourinary pain. The symptom that often distinguishes CP/CPPS from other voiding dysfunction is the presence of pain.

Because there is no gold standard diagnostic test for CP/CPPS, and because its etiology and much of its pathogenesis are unknown, CP/CPPS is a diagnosis of exclusion. The main goal of the evaluation of patients with CP/CPPS is to find a treatable cause of the symptoms. Unfortunately, in the vast majority of men, no such cause is identified. A thorough discussion and detailed description of the recommended and optional tests for the evaluation of CP/CPPS has recently been published (9), and the assessment of symptoms has been greatly facilitated by the development of the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) (10), a self-administered, validated symptom index that measures pain and urinary symptoms and their impact on daily life (Table 3).

Category IV prostatitis is usually diagnosed incidentally by prostate biopsy or by finding leukocytes in semen samples collected for infertility evaluations.

RISK FACTORS

Categories I and II prostatitis are caused by bacteria, including *E.coli, Klebsiella*, *Enterobacter*, and *Pseudomonas*. Therefore, risk factors for these conditions are those that contribute to urinary tract infection, such as difficulty emptying the bladder. Prostatic abscess may also be facilitated by immunosuppressed states. Risk factors for CP/CPPS may include prior infection despite the lack of identifiable ongoing infection. In a comparison study, men with CP/CPPS were significantly more likely to report a history of nonspecific urethritis than men in a large group of asymptomatic controls. The men with CP/CPPS were also significantly more likely to report a history of cardiovascular disease such as hypertension; neurologic disease including vertebral or disc disease; sinusitis; and anxiety or depression (11). However, it is unclear whether these conditions are risk factors for CP/CPPS or may share some as-yet-undetermined common underlying physiologic abnormality. An article by Pontari et al. presents a detailed discussion of the possible mechanisms underlying CP/CPPS (12).

Table 2. NIDDK classification[a] of prostatitis

Category		Definition
I.	Acute Bacterial Prostatitis	Acute infection of the prostate
II.	Chronic Bacterial Prostatitis	Recurrent infection of the prostate
III.	Chronic Abacterial Prostatitis/Chronic Pelvic Pain Syndrome (CPPS)	No demonstrable infection
IIIA.	Inflammatory CPPS	White cells in semen, expressed prostatic secretions or post-prostatic massage urine
IIIB.	Non-Inflammatory CPPS	No white cells in semen, expressed prostatic secretions or post-prostatic massage urine
IV.	Asymptomatic Inflammatory Prostatitis	No symptoms; detected either by prostate biopsy, or the presence of white cells in semen samples during evaluation for other disorders

Source: Reprinted from Journal of Urology, 162, Litwin MS, McNaughton-Collins M, Fowler FJ, Nickel, JC, Calhoun EA, Pontari MA, Alexander RB, Farrar JT, O'Leary MP, and the Chronic Prostatitis Collaborative Research Network, The National Institutes of Health Chronic Prostatitis Symptom Index: Development and validation of a new outcome measure, 369–375, Copyright 1999, with permission from American Urological Association.

Table 3. NIH-Chronic Prostatitis Symptom Index (NIH-CPSI)

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?

	Yes	No
a. Area between rectum and testicles (perineum)	❑1	❑0
b. Testicles	❑1	❑0
c. Tip of the penis (not related to urination)	❑1	❑0
d. Below your waist, in your pubic or bladder area	❑1	❑0

2. In the last week, have you experienced:

	Yes	No
a. Pain or burning during urination?	❑1	❑0
b. Pain or discomfort during or after sexual climax (ejaculation)?	❑1	❑0

3. How often have you had pain or discomfort in any of these areas over the last week?

❑0 Never
❑1 Rarely
❑2 Sometimes
❑3 Often
❑4 Usually
❑5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?

❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑
0	1	2	3	4	5	6	7	8	9	10
NO PAIN										PAIN AS BAD AS YOU CAN IMAGINE

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

❑0 Not at all
❑1 Less than 1 time in 5
❑2 Less than half the time
❑3 About half the time
❑4 More than half the time
❑5 Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?

❑0 Not at all
❑1 Less than 1 time in 5
❑2 Less than half the time
❑3 About half the time
❑4 More than half the time
❑5 Almost always

Impact of Symptoms

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?

❑0 None
❑1 Only a little
❑2 Some
❑3 A lot

8. How much did you think about your symptoms, over the last week?

❑0 None
❑1 Only a little
❑2 Some
❑3 A lot

Quality of Life

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

❑0 Delighted
❑1 Pleased
❑2 Mostly satisfied
❑3 Mixed (about equally satisfied and dissatisfied)
❑4 Mostly dissatisfied
❑5 Unhappy
❑6 Terrible

Scoring the NIH-Chronic Prostatitis Symptom Index Domains

Pain: Total of items 1a, 1b, 1c,1d, 2a, 2b, 3, and 4 = ______

Urinary Symptoms: Total of items 5 and 6 = ______

Quality of Life Impact: Total of items 7, 8, and 9 = ______

Source: Reprinted from Journal of Urology, 162, Litwin MS, McNaughton-Collins M, Fowler FJ, Nickel, JC, Calhoun EA, Pontari MA, Alexander RB, Farrar JT, O'Leary MP, and the Chronic Prostatitis Collaborative Research Network, The National Institutes of Health Chronic Prostatitis Symptom Index: Development and validation of a new outcome measure, 369–375, Copyright 1999, with permission from American Urological Association.

TREATMENT

Treatment of Category I (acute bacterial) prostatitis begins with antibiotic therapy to eradicate the infection. Patients are sometimes hospitalized, and supportive measures such as intravenous hydration and analgesics may be needed. For patients unable to empty their bladders, suprapubic drainage is preferred over an indwelling urethral catheter. Following initial therapy, a two- to four-week course of an oral antibiotic with good prostate penetration is recommended (13).

Treatment of Category II (chronic bacterial) prostatitis also involves antibiotics to eliminate the organism producing the infection. Patients with frequent recurrences may be placed on antibiotic prophylaxis for three to six months and their clinical course reassessed. Treatment of bladder outlet obstruction, which may impair bladder emptying, is also important.

Since the cause of Category III prostatitis (CP/CPPS) is unknown, affected men receive various empirical therapies. The common practice of using antibiotics for chronic nonbacterial prostatitis is not supported by the existing evidence (14, 15). The effectiveness of alpha-blocker therapy, another common empirical treatment, also remains uncertain. A 2004 trial of six weeks of tamsulosin did not show symptom improvement (14); however, previous trials did show a benefit (16, 17). Further research is needed to test longer durations of alpha-blocker therapy, as well as alpha-blocker therapy in men naïve to previous treatments. In small trials, quercetin (18), finasteride (19), pentosan polysulfate sodium (20), and pelvic floor electromagnetic therapy (21) have appeared to show possible benefit, and further evaluation is merited. Other empiric treatments for CP/CPPS range from medications to treat neuropathic pain, anticholinergic medications, phytotherapies, physical therapy, and, in rare cases, surgery to treat bladder neck obstruction (22, 23). For Category IV prostatitis, no treatment is recommended.

PREVALENCE AND INCIDENCE

Unlike benign prostatic hyperplasia (BPH) and prostate cancer, which are predominantly diseases of older men, prostatitis affects men of all ages. The histologic prevalence of prostatitis was found to range from 6% to 44% in a study by Roberts et al. (24) and from 35% to 98% in a study by Bennett et al. (25). The discrepancy is due in part to the fact that Roberts et al. used only autopsy studies, whereas Bennett et al. used both autopsy and surgical specimens. Although these reviews provide compelling evidence that histologic prostatitis is common, the prevalence of clinically evident or symptomatic prostatitis is of greater importance to the patient and physician. Because of the varying definitions used, the literature contains a number of different prevalence estimates: The prevalence of medically diagnosed prostatitis is estimated to be 9% (26); the overall lifetime prevalence of prostatitis, 14% (27); the prevalence of a self-reported history of prostatitis, from 4% to 16% (28, 29, 30); and the prevalence of chronic prostatitis-like symptoms, from 10% to 12% (31, 32). The incidence of physician-diagnosed CP/CPPS is estimated to be 3.3 per 1,000 person-years (33).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Hospital admission for prostatitis is usually necessary only for men who are septic from a bout of acute bacterial prostatitis. Occasionally, older men with chronic bacterial prostatitis may also require hospitalization for the management of urosepsis. In rare instances, men with CP/CPPS are admitted for pain control.

According to the Healthcare Cost and Utilization Project (HCUP), the age-adjusted rate of inpatient hospitalizations for prostatitis in 2000 was 7.7 per 100,000, and the total number of admissions was 7,390—a 21% decrease since 1994, when the age-adjusted hospitalization rate was 9.8 per 100,000 and the total number of admissions was 8,666 (Table 4). The steady decline in the age-adjusted rate of hospitalization between 1994 and 2000 may reflect a change in medical practice—physicians now have higher thresholds for hospitalizing patients for infections, especially since some oral antibiotics, such as fluoroquinolones, can achieve blood levels comparable to those achieved with antibiotics administered intravenously. Patients with painful urinary symptoms who have high fever, hypotension, tachycardia, and leukocytosis will likely

Table 4. Inpatient stays for prostatitis listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	8,666	9.8 (9.0–11)	9.8	7,851	8.5 (7.9–9.2)	8.5	8,146	8.6 (8.0–9.3)	8.6	7,390	7.7 (7.2–8.2)	7.7
Age												
18–24	*	*		*	*		*	*		*	*	
25–34	534	2.7 (2.1–3.2)		525	2.6 (2.1–3.2)		499	2.6 (2.0–3.1)		389	2.1 (1.7–2.6)	
35–44	886	4.5 (3.7–5.2)		954	4.5 (3.7–5.3)		707	3.2 (2.6–3.8)		609	2.8 (2.2–3.3)	
45–54	1,282	9.1 (7.8–11)		1,351	8.7 (7.4–10)		1,299	7.8 (6.7–8.9)		1,218	6.8 (5.9–7.8)	
55–64	1,794	19 (16–21)		1,311	13 (11–15)		1,619	15 (13–17)		1,529	14 (12–15)	
65–74	2,374	30 (26–34)		1,901	23 (20–26)		2,029	25 (22–29)		1,918	24 (21–26)	
75–84	1,399	37 (31–42)		1,330	32 (26–37)		1,524	34 (29–38)		1,324	27 (24–31)	
85+	269	30 (19–41)		320	37 (26–48)		387	39 (29–49)		314	31 (23–38)	
Race/ethnicity												
White	5,542	8.2 (7.4–9.0)	7.6	4,804	6.9 (6.2–7.6)	6.4	5,110	7.3 (6.5–8.0)	6.7	4,271	6.0 (5.5–6.5)	5.5
Black	689	7.5 (5.8–9.2)	9.0	598	6.2 (4.7–7.7)	7.5	492	4.9 (3.7–6.2)	5.8	520	5.1 (3.9–6.3)	6.1
Hispanic	232	2.8 (2.0–3.7)	4.5	444	4.9 (3.6–6.2)	7.5	537	5.3 (4.0–6.7)	8.4	560	5.4 (4.2–6.7)	8.1
Region												
Midwest	2,148	10 (8.6–12)	10	1,715	8.0 (6.7–9.2)	7.9	1,692	7.8 (6.5–9.0)	7.7	1,517	6.8 (5.8–7.7)	6.9
Northeast	1,908	11 (8.9–12)	10	1,778	9.8 (8.2–12)	9.5	1,533	8.5 (7.0–10)	8.2	1,385	7.6 (6.4–8.9)	7.3
South	3,489	12 (10–13)	12	3,334	10 (9.1–12)	10	3,794	11 (10–13)	11	3,448	10 (9.0–11)	9.9
West	1,121	5.7 (4.7–6.7)	6.0	1,024	5.0 (4.1–5.9)	5.4	1,127	5.3 (4.4–6.2)	5.6	1,040	4.8 (4.0–5.6)	5.1
MSA												
Rural	2,357	11 (8.8–12)	9.4	2,195	11 (8.7–13)	9.8	2,457	12 (9.6–14)	11	1,953	9.2 (7.9–10)	8.5
Urban	6,277	9.5 (8.7–10)	9.9	5,604	7.9 (7.2–8.5)	8.1	5,648	7.7 (7.0–8.4)	8.0	5,423	7.2 (6.7–7.8)	7.5

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project, 1994, 1996, 1998, 2000.

Table 5. Inpatient stays by male Medicare beneficiaries with prostatitis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	3,460	23 (20–27)		2,400	16 (13–19)		2,340	16 (13–19)		2,040	13 (11–16)	
Total < 65	500	16 (9.7–22)		280	8.1 (3.9–12)		420	12 (7.0–18)		320	8.4 (4.3–12)	
Total 65+	2,960	28 (21–29)	26	2,120	18 (15–21)	19	1,920	17 (14–21)	18	1,720	15 (12–18)	15
Age												
65–69	920	23 (16–29)		520	13 (8.3–19)		560	17 (10–23)		280	7.9 (3.8–12)	
70–74	780	24 (16–32)		600	18 (12–24)		420	14 (7.9–20)		340	11 (5.8–16)	
75–79	460	20 (12–29)		420	19 (11–26)		520	23 (14–32)		500	20 (12–28)	
80–84	420	32 (18–46)		260	19 (8.6–29)		220	16 (6.5–25)		320	21 (11–32)	
85–89	260	44 (20–67)		280	44 (21–67)		160	25 (7.5–42)		160	22 (6.8–38)	
90–94	100	49 (5.9–93)		40	19 (0–45)		40	19 (0–44)		120	52 (10–93)	
95–97	20	50 (0–146)		0	0		0	0		0	0	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	2,980	24 (20–28)	23	2,180	17 (14–20)	17	2,080	17 (14–20)	17	1,720	13 (10–16)	13
Black	340	27 (14–39)	27	140	10 (2.6–18)	8.7	200	15 (5.7–24)	12	220	15 (6.1–24)	15
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	20	10 (0–30)	10	40	12 (0–28)	12	80	21 (0.5–42)	21
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	720	19 (13–26)	20	380	9.9 (5.4–14)	12	520	14 (8.7–20)	14	500	13 (8.0–18)	14
Northeast	580	18 (12–25)	20	560	18 (11–24)	16	180	6.5 (2.2–10)	6.5	380	13 (7.2–19)	11
South	1,700	32 (26–39)	31	1,260	23 (17–29)	22	1,420	26 (20–33)	27	840	14 (10–19)	14
West	420	17 (9.9–25)	17	160	6.9 (2.1–12)	6.0	180	8.0 (2.8–13)	7.2	240	9.7 (4.2–15)	8.1

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 6. Inpatient visits for males with prostatitis having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	31	8.6	31	5.6	37	4.2	35	3.5	31	3.5
As Any Diagnosis										
Total	82	23	137	25	191	22	178	18	162	18

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

continue to be admitted, but patients with mild to moderate symptoms may be more likely to be treated as outpatients.

HCUP data show that hospitalization rates for prostatitis increased with age in 1994, 1996, 1998, and 2000 (Table 4). The higher rate for the older age groups likely represents the lower threshold for their admission, probably due, in part, to a greater number of comorbid illnesses in older men. Hospitalization rates stratified by race/ethnicity showed that Hispanic men had the highest age-adjusted rates in 2000. Throughout the periods of observation, age-adjusted admission rates declined for Caucasian and African American men and increased for Hispanic men. Little regional variation was observed, with the exception of the West, where age-adjusted hospitalization rates were consistently lower than in the other geographic areas (Northeast, Midwest, and South). Age-adjusted admission rates were generally similar in urban and rural areas.

Medicare data for 1992, 1995, 1998, and 2001 (Table 5) indicate that age-adjusted inpatient hospitalization rates for prostatitis were 2 to 2.5 times higher in the Medicare patient population than in the broader population studied in HCUP. Total age-adjusted admission rates for men 65 years of age and older decreased substantially over time, from 26 per 100,000 in 1992 to 15 per 100,000 in 2001, a 42% reduction, compared with a 21% decrease from 1994 to 2000 in the HCUP population. The geographic distribution in the Medicare data was similar to that in the HCUP data, with the highest age-adjusted rates of hospitalization in the South and the lowest in the West. In 1995, when Medicare racial categories were modified, the age-adjusted admission rates were highest for Caucasian men. As in the HCUP database,

Table 7. Hospital outpatient visits for prostatitis listed as any diagnosis, 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000			
	Count	4- Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[d]	181,693	196 (126–266)	49	195
Age				
18–54	92,916	135 (62–207)	34	
55+	88,777	375 (201–550)	94	

*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area.
[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.
[b]Average annualized rate per year.
[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.
[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.
NOTE: Counts may not sum to total due to rounding.
SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

Table 8. Hospital outpatient visits by male Medicare beneficiaries with prostatitis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995				1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	12,140	82	(75–88)		18,400	121	(113–129)		17,500	121	(113–129)		17,100	111	(103–118)	
Total < 65	1,860	60	(47–72)		3,320	96	(82–111)		3,780	110	(94–126)		3,660	96	(82–110)	
Total 65+	10,280	87	(80–95)	88	15,080	239	(119–137)	129	13,720	124	(115–134)	125	13,440	116	(107–124)	117
Age																
65–69	3,240	80	(67–92)		4,880	127	(111–143)		4,180	124	(107–141)		3,660	103	(88–118)	
70–74	3,440	106	(90–122)		4,160	125	(108–142)		3,880	127	(109–145)		3,920	127	(110–145)	
75–79	1,920	85	(68–102)		2,880	127	(106–148)		2,520	110	(91–130)		2,820	115	(96–134)	
80–84	1,160	89	(66–111)		2,040	147	(118–175)		2,040	148	(119–177)		1,880	126	(100–151)	
85–89	220	37	(15–59)		920	144	(103–186)		840	129	(90–168)		900	124	(88–161)	
90–94	300	148	(73–223)		140	66	(17–115)		240	112	(48–175)		220	95	(39–151)	
95–97	0	0			60	159	(0–340)		20	51	(0–149)		20	52	(0–154)	
98+	0	0			0	0			0	0			20	37	(0–109)	
Race/ethnicity																
White	8,880	71	(64–77)	70	13,880	107	(99–115)	106	13,780	113	(104–121)	112	13,840	106	(98–114)	106
Black	2,260	177	(145–210)	177	2,840	205	(171–239)	196	2,280	171	(140–202)	174	2,020	138	(111–164)	138
Asian	…	...		…	40	55	(0–130)	55	180	131	(45–217)	102	0	0		0
Hispanic	…	...		…	800	403	(279–527)	463	460	137	(81–193)	149	600	160	(102–217)	154
N. American Native	…	...		…	20	99	(0–293)	99	160	572	(175–969)	572	80	240	(6.0–474)	240
Region																
Midwest	3,080	83	(70–96)	83	3,760	98	(84–111)	95	4,060	110	(95–125)	107	4,700	124	(108–140)	123
Northeast	2,620	83	(68–97)	80	3,240	102	(86–118)	104	2,080	75	(60–89)	74	1,800	62	(49–74)	60
South	4,120	79	(68–89)	79	8,640	157	(143–172)	156	8,940	167	(151–182)	170	7,480	129	(116–142)	132
West	2,200	91	(74–108)	92	2,540	110	(90–129)	111	2,140	96	(78–114)	93	2,840	115	(96–134)	109

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 9. Physician office visits for prostatitis listed as any diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1992			1994			1996		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total	2,176,818	2,477 (1,820–3,135)	2,477	1,406,750	1,594 (1,206–1,981)	1,594	1,602,700	1,743 (1,212–2,274)	1,743

	1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total	1,039,485	1,102 (680–1,525)	1,102	1,795,643	1,867 (1,339–2,396)	1,867

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 10. Physician office visits for prostatitis listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), age-adjusted rate[b], annualized rate[c]

	1992–2000			
	Count	5-Year Rate	Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	8,021,396	8,746 (7,599–9,893)	1,749	8,721
Age				
18–34	856,903	2,673 (1,733–3,614)	535	
35–44	1,593,750	7,671 (5,110–10,233)	1,534	
45–54	1,479,699	9,606 (6,914–12,297)	1,921	
55–64	1,792,593	17,464 (12,509–22,419)	3,493	
65–74	1,517,649	18,781 (13,499–24,062)	3,756	
75+	780,802	15,204 (8,468–21,940)	3,041	
Race/ethnicity				
White	6,758,464	9,727 (8,317–11,138)	1,945	9,306
Black	653,969	6,776 (4,017–9,535)	1,355	7,736
Hispanic	534,130	5,959 (2,935–8,983)	1,192	8,542
Region				
Midwest	1,809,245	8,399 (5,915–10,883)	1,680	8,284
Northeast	1,363,681	7,553 (5,345–9,761)	1,511	7,400
South	2,978,887	9,384 (7,448–11,320)	1,877	9,217
West	1,869,583	9,175 (6,560–11,791)	1,835	9,617
MSA				
MSA	6,286,413	8,974 (7,673–10,275)	1,795	8,985
Non-MSA	1,734,983	8,010 (5,584–10,435)	1,602	7,831

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[c]Average annualized age-adjusted rate.

[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

those rates declined over time for Caucasian men and increased for Hispanic men. In contrast to the HCUP data, the Medicare data showed that age-adjusted hospitalization rates for African American men increased over time.

According to data from the Center for Health Care Policy and Evaluation (CHCPE) for 1994, 1996, 1998, 2000, and 2002, the unadjusted rates for inpatient hospitalization for men with prostatitis who have commercial health insurance decreased over time, from 8.6 per 100,000 in 1994 to 3.5 per 100,000 in 2002, a 59% reduction (Table 6).

Overall, the three sets of data (HCUP, Medicare, and CHCPE) consistently demonstrated a decline over time in rates of inpatient hospitalization for men with prostatitis.

Outpatient Care

An individual may be seen in the outpatient setting for diagnosis, treatment, or follow-up of prostatitis. We focus on visits for which prostatitis was the primary diagnosis, except where noted.

Hospital Outpatient Visits

The rates of hospital outpatient visits by patients with prostatitis listed as any diagnosis for the visit, based on National Hospital Ambulatory Medical Care Survey (NHAMCS) data for 1994, 1996, 1998, and 2000, are presented in aggregate in Table 7. The age-adjusted rate for 1994–2000 was 195 per 100,000, for an annualized rate of 49. The estimated rate for men aged 55 and over was approximately 2.5 times higher than that for men aged 18–54 (375 per 100,000 vs 135 per 100,000). The finding that prostatitis is a relatively

Table 11. Frequency of benign prostatic hyperplasia diagnosis (ICD-9 600.XX) when prostatitis is listed as primary or any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b]

	1992–2000		
	Count	5-Year Rate	Annualized Rate
Primary Diagnosis of Prostatitis			
Total	5,430,681	5,921 (4,995–6,848)	1,184
with associated Dx 600.XX	342,889	374 (207–541)	75
Any Diagnosis of Prostatitis			
Total	8,021,396	8,746 (7,599–9,893)	1,749
with associated Dx 600.XX	781,963	853 (586–1,119)	171

[a]Rate per 100,000 is based on 1992–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

common urologic condition in older men is clinically important because all too often, physicians focus only on BPH and prostate cancer in these patients.

Information on hospital outpatient visits is also available from Medicare data for 1992, 1995, 1998, and 2001 (Table 8). The age-adjusted visit rate in Medicare patients 65 and older increased dramatically between 1992 and 1995, from 88 per 100,000 to 129 per 100,000; the rate declined slightly, to 125 per 100,000 in 1998 and to 117 per 100,000 in 2001, but still remained higher than the rate in 1992. The age group with the highest visit rate varied by year; the highest visit rates were for men aged 90–94 in 1992, men 95–97 in 1995, men 80–84 in 1998, and men 70–74 in 2001. Age-adjusted visit rates were highest in the West in 1992 and highest in the South in 1995, 1998, and 2001. Age-adjusted visit rates were highest for Hispanics in 1995. In 1998 and 2001, North American Natives appeared to have substantially higher rates, but this difference is so dramatic it must be interpreted with extreme caution, given the very low counts for this group.

Physician Office Visits

Rates of physician office visit by patients with prostatitis listed as any diagnosis were determined from National Ambulatory Medical Care Survey (NAMCS) data for the even years between 1992 and 2000 (Table 9). The age-adjusted visit rate in 2000 was 1,867 per 100,000, with a total of 1,795,643 physician office visits—a 25% decrease since 1992, when the age-adjusted rate was 2,477 per 100,000 population, and the total number of visits was 2,176,818. The aggregate age-adjusted rate for 1992–2000 was 8,746 per 100,000, for an annualized rate of 1,749 per 100,000 (Table 10). In general, the annualized rates increased with age, from a low of 535 per 100,000 by men aged 18–34 to a high of 3,756 per 100,00 by men 65–74. The rate tapered off to 3,041 per 100,000 for men 75 and older, although it remained over five times higher than the rate for men 18–34. Age-adjusted, annualized visit rates were highest for Caucasians; the next-highest rates were for African Americans and then Hispanics. Rates were highest in the South and lowest in the Northeast, and they were generally similar in urban and rural areas.

Some older men with lower urinary tract symptoms may be incorrectly diagnosed with BPH simply because of their symptoms and older age, yet the findings from various datasets have demonstrated that prostatitis is a common condition in older men as well as younger men. It is also possible for men to have both prostatitis and BPH. We examined the overlap of prostatitis and BPH diagnoses for 1992–2000, using the NAMCS database to assess the frequency of a BPH diagnosis when prostatitis was listed as the primary diagnosis for the visit. More than 6% of visits with a primary diagnosis of prostatitis had a concomitant diagnosis of BPH. However, when prostatitis was listed as any diagnosis, the overlap was 10% of visits with both conditions (Table 11). These findings are consistent with those of the Health Professionals Follow-Up Study database (29), which showed that

Table 12. Physician office visits by male Medicare beneficiaries with prostatitis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	387,400	2,601 (2,565–2,637)		356,840	2,345 (2,311–2,379)	
Total < 65	36,720	1,176 (1,122–1,229)		42,720	1,240 (1,188–1,292)	
Total 65+	350,680	2,979 (2,935–3,022)	2,981	314,120	2,668 (2,627–2,709)	2,667
Age						
65–69	115,560	2,839 (2,767–2,911)		100,180	2,601 (2,530–2,672)	
70–74	106,600	3,279 (3,192–3,365)		94,880	2,845 (2,766–2,925)	
75–79	72,360	3,197 (3,094–3,299)		65,020	2,866 (2,769–2,963)	
80–84	38,440	2,934 (2,805–3,063)		36,700	2,641 (2,522–2,761)	
85–89	13,840	2,321 (2,150–2,492)		13,700	2,151 (1,992–2,310)	
90–94	3,500	1,728 (1,474–1,982)		2,980	1,410 (1,185–1,634)	
95–97	340	842 (443–1,240)		480	1,273 (767–1,780)	
98+	40	105 (0–250)		180	406 (142–670)	
Race/ethnicity						
White	340,620	2,712 (2,672–2,752)	2,709	316,400	2,434 (2,396–2,471)	2,431
Black	25,320	1,984 (1,876–2,093)	1,917	25,160	1,817 (1,717–1,917)	1,818
Asian	…	…	…	1,520	2,086 (1,622–2,549)	2,195
Hispanic	…	…	…	4,480	2,256 (1,964–2,549)	2,287
N. American Native	…	…	…	120	596 (119–1,074)	696
Region						
Midwest	78,660	2,121 (2,055–2,186)	2,114	68,020	1,765 (1,706–1,823)	1,770
Northeast	58,780	1,854 (1,787–1,920)	1,835	56,140	1,765 (1,700–1,830)	1,763
South	191,980	3,665 (3,593–3,737)	3,684	176,440	3,216 (3,150–3,282)	3,225
West	53,380	2,210 (2,127–2,293)	2,208	49,800	2,148 (2,064–2,231)	2,125

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	281,900	1,947 (1,915–1,979)		244,520	1,586 (1,558–1,614)	
Total < 65	35,080	1,021 (973–1,068)		32,440	852 (811–894)	
Total 65+	246,820	2,235 (2,196–2,274)	2,244	212,080	1,826 (1,792–1,860)	1,828
Age						
65–69	72,660	2,152 (2,083–2,221)		63,900	1,806 (1,744–1,868)	
70–74	71,280	2,337 (2,261–2,413)		62,780	2,039 (1,969–2,110)	
75–79	58,900	2,579 (2,487–2,671)		45,240	1,844 (1,769–1,919)	
80–84	27,780	2,016 (1,911–2,121)		27,200	1,817 (1,722–1,913)	
85–89	12,680	1,949 (1,799–2,099)		9,960	1,377 (1,257–1,497)	
90–94	3,140	1,460 (1,233–1,687)		2,480	1,070 (883–1,258)	
95–97	340	859 (452–1,266)		440	1,145 (669–1,622)	
98+	40	84 (0–199)		80	147 (3.7–291)	
Race/ethnicity						
White	247,680	2,025 (1,990–2,061)	2,024	210,600	1,610 (1,580–1,641)	1,607
Black	18,300	1,371 (1,283–1,459)	1,379	17,920	1,221 (1,142–1,301)	1,240
Asian	2,580	1,881 (1,560–2,203)	1,765	2,300	1,122 (918–1,326)	1,054
Hispanic	6,780	2,020 (1,807–2,233)	1,990	6,120	1,629 (1,448–1,810)	1,544
N. American Native	180	644 (225–1,062)	644	320	961 (492–1,429)	841
Region						
Midwest	53,540	1,448 (1,393–1,502)	1,464	45,060	1,186 (1,138–1,235)	1,190
Northeast	39,640	1,426 (1,364–1,489)	1,411	36,480	1,248 (1,191–1,305)	1,235
South	140,100	2,610 (2,550–2,671)	2,634	113,040	1,947 (1,896–1,997)	1,959
West	41,680	1,864 (1,784–1,943)	1,807	40,360	1,631 (1,560–1,701)	1,610

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 13. Physician outpatient visits for males with prostatitis having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	1,615	450	2,197	397	3,411	386	3,584	357	2,605	296
Age										
18–24	53	112	57	82	112	100	125	97	89	83
25–34	225	258	334	246	537	260	507	230	367	198
35–44	481	473	593	378	969	388	1,002	363	672	285
45–54	514	685	662	558	992	509	1,069	460	766	370
55–64	270	711	431	733	672	667	698	572	572	483
65–74	63	754	103	853	110	634	154	699	117	532
75–84	8	*	16	*	18	*	27	*	21	*
85+	1	*	1	*	1	*	2	*	1	*
Region										
Midwest	1,028	474	1,307	419	1,630	382	1,656	337	1,316	283
Northeast	153	296	162	289	223	307	169	285	110	292
Southeast	353	530	635	407	1,436	413	1,619	395	1,136	320
West	81	342	93	315	122	340	140	312	43	185
As Any Diagnosis										
Total	2,160	602	3,141	567	4,846	549	5,330	530	3,968	451
Age										
18–24	60	127	77	111	137	123	148	115	107	100
25–34	275	316	411	303	680	330	666	302	502	271
35–44	583	573	789	503	1280	513	1,375	498	944	400
45–54	703	936	945	796	1459	749	1,605	691	1,162	561
55–64	415	1,092	688	1,170	1060	1,051	1,200	983	971	819
65–74	102	1,221	199	1,648	189	1,090	282	1,279	245	1,115
75–84	20	*	28	*	39	1,445	52	1,551	33	936
85+	2	*	4	*	2	*	2	*	4	*
Region										
Midwest	1,360	628	1,841	590	2,312	542	2,471	503	2,006	432
Northeast	199	385	213	380	297	409	249	420	178	473
Southeast	487	732	963	617	2,069	595	2,398	586	1,715	484
West	114	481	124	420	168	468	212	472	69	296

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

more than 50% of men with prostatitis reported BPH, and more than one-third of those with BPH reported prostatitis. The distinction between the two conditions may be blurred because each is a clinical diagnosis with no gold standard or specific diagnostic test.

Medicare data for 1992, 1995, 1998, and 2001 show that the age-adjusted physician office visit rates for prostatitis for men aged 65 and over decreased steadily between 1992 and 2001, from a rate of 2,981 per 100,000 population (a total of 350,680 visits) to 1,828 per 100,000 population (a total of 212,080 visits)—an almost 40% reduction (Table 12). Rates were highest for men aged 70–74 in 1992 and 2001 and highest for men aged 75–79 in 1995 and 1998. Age-adjusted physician office visit rates across all the years were highest in the South and lowest in the Northeast, and they were highest for Caucasian men.

Center for Health Care Policy and Evaluation (CHCPE) data for 1994, 1996, 1998, 2000, and 2002 show that unadjusted physician outpatient visit rates for men with prostatitis who have commercial health insurance steadily decreased over time, from 450 per 100,000 in 1994 to 296 per 100,000 in 2002, a 34% reduction (Table 13). Within each year studied,

Table 14. Secondary diagnoses associated with number of visits for a primary diagnosis of prostatitis in individuals having commercial health insurance, regardless of site of service, count, percent

	BPH		Depression		STD		Substance Abuse		Urinary Tract Infection		Erectile Dysfunction		Incontinence		Total	
	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent
Age																
18–24	3	0.6%	3	0.6%	…		…		9	1.9%	5	1.1%	…		20	4.3%
25–34	39	1.9%	32	1.6%	2	0.1%	13	0.6%	84	4.1%	19	2.4%	6	0.3%	195	9.5%
35–44	101	2.7%	52	1.4%	4	0.1%	16	0.4%	143	3.9%	57	1.5%	8	0.2%	381	10.3%
45–54	203	5.2%	62	1.6%	3	0.1%	14	0.4%	145	3.7%	91	2.3%	9	0.2%	527	13.4%
55–64	214	8.3%	23	0.9%	1	0%	10	0.4%	97	3.8%	58	2.2%	10	0.4%	413	16.0%
65–74	65	12.1%	5	0.9%	1	0.2%	1	0.2%	14	2.6%	10	1.9%	7	1.3%	103	19.2%
75–84	15	15.8%	1	1.1%	…		…		4	4.2%	2	2.1%	1	1.1%	23	24.2%
85+	1	16.7%	…		…		…		…		…		…		1	16.7%
Total	641	4.8%	178	1.3%	11	0.1%	54	0.4%	496	3.7%	242	1.8%	41	0.3%	1663	12.4%

… data not available.

BPH, benign prostatic hyperplasia; STD, sexually transmitted disease.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 15. Medication use associated with visits for prostatitis listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], rate per 100,000 visits[c] (95% CI)

	1992–2000			
	Count	5-Year Rate	Annualized Rate	5-Year Rate Per 100,000 Visits for Prostatitis
Chronic or infectious prostatitis				
Total	8,021,396	8,746 (7,599–9,893)	1,749	100,000 (86,885–113,115)
Quinolones ordered/provided at visit	1,464,487	1,597 (1,148–2,046)	319	18,257 (13,127–23,388)
TMP-SMX/Sulfa ordered/provided at visit	1,315,221	1,434 (925–1,943)	287	16,396 (10,578–22,215)
BPH medications ordered/provided at visit	415,493	453 (227–679)	91	5,180 (2,594–7,766)
Chronic prostatitis				
Total	7,384,915	8,052 (6,960–9,144)	1,610	100,000 (86,440–113,560)
Quinolones ordered/provided at visit	1,353,675	1,476 (1,034–1,918)	295	18,330 (12,837–23,823)
TMP-SMX/Sulfa ordered/provided at visit	1,176,772	1,283 (794–1,773)	257	15,935 (9,856–22,014)

BPH, benign prostatic hyperplasia.

[a]Rate per 100,000 is based on 1992–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Rate per 100,000 adult male visits is based to 1992–2000 estimated number of visits for prostatitis in NAMCS.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 16. Male VA users with diagnosis of prostatitis in 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	19,604	597	19,288	101	18,792	511	19,676	482	18,403	82	18,932	398
Age-adjusted Total	22,402	604	20,481	552	18,792	511	17,842	481	15,288	412	14,725	397
Age												
< 25	48	165	44	150	54	184	41	141	37	127	46	158
25–34	477	288	486	294	452	273	443	268	422	255	397	240
35–44	1,644	449	1,552	424	1,508	412	1,466	401	1,313	359	1,184	324
45–54	4,955	605	4,631	565	4,411	538	4,181	510	3,801	464	3,651	445
55–64	4,874	781	4,350	697	3,977	637	3,803	609	3,411	546	3,395	544
65–74	6,485	673	5,978	621	5,508	572	5,117	531	4,135	429	4,099	425
75–84	3,688	541	3,257	478	2,860	420	2,619	384	2,032	298	1,847	271
85+	231	373	183	296	202	327	171	279	138	223	107	173
Race/ethnicity												
White	13,391	638	13,408	589	13,052	524	13,530	485	12,325	406	12,157	394
Black	3,714	786	3,444	719	3,316	683	3,168	649	2,815	576	2,634	553
Hispanic	772	851	686	713	749	778	810	806	683	662	650	643
Other	235	552	239	549	214	460	203	416	191	382	166	339
Unknown	1,492	257	1,511	246	1,641	276	1,965	298	2,389	299	3,325	318
Insurance Status												
No insurance/self-pay	14,605	585	13,608	540	12,501	507	11,839	780	10,583	418	10,582	420
Medicare	1,603	628	2,224	569	3,257	500	4,742	780	4,796	384	5,280	354
Medicaid	22	1003	18	660	14	365	22	354	26	300	39	409
Private Insurance/HMO	3,892	626	3,336	577	3,071	540	2,902	488	2,844	438	2,862	410
Other Insurance	71	634	101	587	128	545	167	619	143	469	164	458
Unknown	0	0	1	328	1	115	4	210	11	390	5	290
Region												
Eastern	1,625	339	1,679	326	1,585	284	1,677	246	1,758	226	1,863	233
Central	2,576	446	2,645	422	2,658	411	2,731	376	2,870	320	3,492	332
Southern	9,632	787	9,646	721	9,363	648	9,857	607	9,555	529	9,709	500
Western	5,571	568	5,318	516	5,366	506	5,411	513	4,220	424	3,868	401

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

the visit rates increased with age. These findings are similar to those from the NAMCS and Medicare databases.

We also examined the frequency of various secondary diagnoses, which we expected to be associated with the primary diagnosis of prostatitis, based on the experience of the NIH Chronic Prostatitis Collaborative Research Network (11). We assessed seven conditions and found that the most common secondary diagnosis associated with the primary diagnosis of prostatitis in these individuals was BPH. This finding is not surprising given the substantial overlap of the diagnoses for prostatitis and BPH found in the NAMCS database. Across all age groups, the next most common secondary diagnosis was urinary infection, followed by erectile dysfunction, depression, substance abuse, incontinence, and sexually transmitted disease (STD) (Table 14).

According to the NAMCS database, in 1992–2000, the most common medications associated with any visits for prostatitis were quinolones (an annualized rate of 319 per 100,000), followed by sulfa medications (an annualized rate of 287 per 100,000), then BPH medications (an annualized rate of 91 per 100,000) (Table 15). When visits for "infectious prostatitis" were removed from the data, the rate of prescribing quinolones and sulfa medications remained essentially the same (Table 15). These findings reveal that large amounts of antibiotics are prescribed in association with the diagnosis of prostatitis, even though the vast majority of prostatitis is noninfectious. Given the overlap of BPH and prostatitis diagnoses, it is not possible to determine whether BPH medications were being prescribed for the prostatitis or for the BPH that may have been a concomitant condition.

A few general comments are in order before we discuss the Veterans Affairs (VA) data. Despite the clear differences indicated in rates by age and race, the data have not been age- or race-standardized (see Methods chapter in this compendium), except where indicated. Although we use the term rate, the VA data present the number of cases seen for the specified condition per 100,000 unique VA patients; 95% confidence intervals are not available for the VA rates reported here.

The rates for visits by VA patients with a primary diagnosis of prostatitis steadily decreased between 1998 and 2003 (Table 16). The age-adjusted visit rate was 604 per 100,000 population in 1998, declining to 397 per 100,000 in 2003—a 34% reduction. The visit rate peaked at ages 55–64 in each of the years. The visit rate was highest for men with race/ethnicity listed as Hispanic or African American as compared with Caucasian in most years analyzed. Visit rates were significantly higher in the Southern region in all years studied.

According to data from the Pharmacy Benefits Management of the Department of Veterans Affairs, the rates of alpha-blocker use for men with a primary diagnosis of prostatitis increased slightly over time, from 39,491 per 100,000 in 1999 to 41,675 per 100,000 in 2003 (Table 17). Use of alpha-blockers generally peaked in older age groups, i.e., men 65 and older. There was no clear racial/ethnic pattern in use. They were routinely prescribed in the East at about one-third lower the rates in the Central, Southern, and Western regions. Rates of use of cephalosporins, penicillins, and sulfonamides for men with prostatitis steadily declined over time from 1999 to 2003 (Table 18); however, the rate of use of flouroquinolones increased over time. The use of tetracylines was variable but generally stable across the years.

Ambulatory Surgery Procedures

Visits to an ambulatory surgery centers by individuals with commercial insurance who had a primary diagnosis of prostatitis were tabulated for 1994, 1996, 1998, 2000, and 2002 from the CHCPE database (Table 19). The rate of visits decreased steadily between 1994 and 2002, from 11 per 100,000 to 6.5 per 100,000, a decrease of 41%.

Procedures associated with a primary diagnosis of prostatitis in individuals having commercial health insurance included ablative surgery, cystoscopy, hydrodistention, urethral procedures, urine studies, and urodynamic studies (Table 20).

The Medicare database shows that the rate of age-adjusted ambulatory surgery visits by Medicare patients 65 and older with a primary diagnosis of prostatitis remained stable over time, at 31 to 33 per 100,000 (Table 21). Of note, the rate of visits by patients in the Medicare database was about five times the rate in the CHCPE database. The peak age for visits in the Medicare database was generally either 70–74 or 75–79 across the period of study. The age-adjusted visit rate was dramatically lower in the West than in the

Table 17. Use of alpha blockers in men with prostatitis listed as primary diagnosis, count, rate[a] (95% CI)

	1999			2000			2001		
	Count	Rate		Count	Rate		Count	Rate	
Total	7,617	39,491	(38,604–40,378)	7,693	40,549	(39,643–41,455)	8,223	41,792	(40,889–42,695)
Age									
< 25	5	10,204	(1,260–19,148)	4	7,407	(148–14,667)	6	15,385	(3,074–27,695)
25–34	69	13,093	(10,004–16,182)	53	11,726	(8,569–14,833)	51	12,349	(8,960–15,738)
35–44	308	18,678	(16,592–20,764)	330	21,883	(19,522–24,244)	285	20,757	(18,348–23,167)
45–54	1,386	30,800	(29,178–32,422)	1,367	30,991	(29,348–32,634)	1,418	32,538	(30,844–34,231)
55–64	1,733	42,737	(40,725–44,750)	1,705	42,872	(40,837–44,907)	1,822	42,293	(40,351–44,235)
65–74	2,741	48,938	(47,106–50,770)	2,732	49,601	(47,741–51,461)	2,888	50,270	(48,436–52,103)
75–84	1,300	47,221	(44,654–49,788)	1,404	49,091	(46,523–51,659)	1,658	51,459	(48,982–53,936)
85+	75	48,701	(37,679–59,723)	98	48,515	(38,909–58,120)	95	43,578	(34,815–52,341)
Race/ethnicity									
White	5,527	41,395	(40,303–42,486)	5,491	42,385	(41,264–43,506)	5,893	44,040	(42,916–45,164)
Black	1,375	40,181	(38,057–42,305)	1,395	42,337	(40,115–44,559)	1,377	43,784	(41,471–46,096)
Hispanic	269	37,887	(33,360–42,415)	296	38,144	(33,799–42,490)	321	37,720	(33,594–41,847)
Other	96	41,739	(33,390–50,089)	79	38,916	(30,335–47,498)	83	42,784	(33,579–51,988)
Unknown	350	22,236	(19,907–24,566)	432	24,785	(22,448–27,122)	549	26,081	(23,899–28,262)
Insurance Status									
No insurance/self-pay	5,091	37,412	(36,384–38,440)	4,795	38,357	(37,271–39,443)	4,603	38,880	(37,757–40,003)
Medicare	1,049	47,167	(44,313–50,022)	1,600	49,125	(46,718–51,532)	2,345	49,452	(47,450–51,453)
Medicaid	7	38,889	(10,080–67,698)	7	50,000	(12,959–87,041)	10	45,455	(17,282–73,628)
Private Insurance/HMO	1,421	42,596	(40,381–44,811)	1,242	40,443	(38,194–42,692)	1,208	41,626	(39,279–43,974)
Other Insurance	48	47,525	(34,080–60,970)	49	38,281	(27,563–49,000)	57	34,132	(25,271–42,993)
Unknown	1	100,000	(96,000–296,000)	…	…		…	…	
Region									
Eastern	452	26,921	(24,439–29,403)	368	23,218	(20,845–25,590)	401	23,912	(21,571–26,252)
Central	1,096	41,437	(38,983–43,890	1,140	42,889	(40,400–45,379)	1,205	44,123	(41,632–46,614)
Southern	3,983	41,292	(40,009–42,574)	4,032	43,063	(41,734–44,392)	4,450	45,146	(43,819–46,472)
Western	2,086	39,225	(37,542–40,909)	2,153	40,123	(38,428–41,818)	2,167	40,048	(38,362–41,734)

Continued on next page

Table 17 (continued). Use of alpha blockers in men with prostatitis listed as primary diagnosis, count, rate[a] (95% CI)

	2002			2003		
	Count	Rate		Count	Rate	
Total	7,670	41,678	(40,745–42,611)	7,890	41,675	(40,756–42,595)
Age						
< 25	2	5,714	(-2,205–13,634)	4	9,091	(182–18,000)
25–34	48	12,766	(9,154–16,377)	44	12,644	(8,908–16,380)
35–44	223	19,060	(16,558–21,561)	189	18,602	(15,950–21,254)
45–54	1,319	32,147	(30,412–33,882)	1,272	33,386	(31,551–35,221)
55–64	1,906	42,187	(40,293–44,081)	2,230	41,038	(39,335-42,741)
65–74	2,510	49,911	(47,958–51,863)	2,517	49,189	(47,267–51,111)
75–84	1,543	52,358	(49,746–54,971)	1,512	51,411	(48,820-54002)
85+	119	52,889	(43,386–62,392)	122	54,955	(45,203–64,707)
Race/ethnicity						
White	5,309	44,007	(42,823–45,191)	5,065	44,074	(42,860–45,288)
Black	1,250	44,996	(42,502–47,491)	1,185	45,895	(43,282–48,508)
Hispanic	284	39,065	(34,521–43,608)	288	42,291	(37,406–47,175)
Other	77	43,503	(33,786–53,220)	71	46,104	(35,380–56,828)
Unknown	750	28,227	(26,207–30,248)	1,281	31,842	(30,098–33,586)
Insurance Status						
No insurance/self-pay	3,983	37,636	(36,467–38,805)	4,064	38,405	(37,224–39,586)
Medicare	2,442	50,917	(48,898–52,937)	2,633	49,867	(47,963–51,772)
Medicaid	12	46,154	(20,040–72,268)	17	43,590	(22,868–64,311)
Private Insurance/HMO	1,177	41,385	(39,021–43,750)	1,105	38,609	(36,333–40,886)
Other Insurance	52	36,364	(26,480–46,247)	70	42,683	(32,684–52,682)
Unknown	4	36,364	(727–72,000)	1	20,000	(0–59,200)
Region						
Eastern	429	24,403	(22,094–26,712)	491	26,355	(24,024–28,687)
Central	1,214	42,300	(39,920–44,679)	1,461	41,838	(39,693–43,984)
Southern	4,281	44,804	(43,462–46,146)	4,263	43,908	(42,590–45,226)
Western	1,746	41,374	(39,434–43,315)	1,675	43,304	(41,230–45,378)

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Pharmacy Benefits Management Version 3.0 (PBM), Department of Veterans Affairs.

Table 18. Use of antimicrobials in men with prostatitis, count, rate[a] (95% CI)

	1999			2000			2001		
	Count	Rate		Count	Rate		Count	Rate	
Cephalosporins	1,629	8,446	(8,036–8,856)	1,542	8,128	(7,722–8,533)	1,442	7,329	(6,950–7,707)
Penicillins	2,733	14,169	(13,638–14,701)	2,678	14,116	(13,581–14,650)	2,618	13,306	(12,796–13,815)
Fluoroquinolones	9,310	48,268	(47,288–49,249)	9,884	52,098	(51,071–53,125)	10,870	55,245	(54,206–56,284)
Sulfonamides	6,978	36,178	(35,329–37,027)	6,267	33,033	(32,215–33,851)	5,743	29,188	(28,433–29,943)
Tetracyclines	2,003	10,385	(9,930–10,839)	1,997	10,526	(10,064–10,988)	1,914	9,728	(9,292–10,163)

	2002			2003		
	Count	Rate		Count	Rate	
Cephalosporins	1,213	6,591	(6,220–6,962)	1,293	6,830	(6,457–7,202)
Penicillins	2,110	11,466	(10,976–11,955)	2,165	11,436	(10,954–11,917)
Fluoroquinolones	10,342	56,197	(55,114–57,280)	10,736	56,708	(55,636–57,781)
Sulfonamides	4,928	26,778	(26,031–27,526)	4,507	23,806	(23,111–24,501)
Tetracyclines	2,012	10,933	(10,455–11,411)	1,919	10,136	(9,683–10,590)

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Pharmacy Benefits Management Version 3.0 (PBM), Department of Veterans Affairs.

Table 19. Ambulatory surgery visits for males with prostatitis having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	38	11	51	9	74	8	64	6	1	7
As Any Diagnosis										
Total	54	15	84	15	132	15	129	13	111	13

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for individuals in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 20. Procedures associated with primary diagnosis of prostatitis in males having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	28	685	35	650	40	467	37	412	29	457
Procedure										
Ablative procedure	2	49	2	37	8	93	10	111	2	32
Cytoscopy	17	416	20	371	19	221	19	212	23	363
Hydrodistension	…	…	…	…	…	…	1	11	…	…
Urethral procedure	6	147	8	149	10	117	4	45	1	16
Urine studies	…	…	3	56	…	…	…	…	1	16
Urodynamic studies	3	73	2	37	3	35	3	33	2	32

…data not available.

[a]Rate per 100,000 based on member months of enrollment in calendar years for individuals in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 21. Ambulatory surgery visits by male Medicare beneficiaries with prostatitis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	4,460	30 (26–34)		4,040	27 (23–30)		3,900	27 (23–31)		4,120	27 (23–30)	
Total < 65	540	17 (11–24)		440	13 (7.4–18)		460	13 (7.9–19)		480	13 (7.6–18)	
Total 65+	3,920	33 (29–38)	33	3,600	31 (26–35)	31	3,440	31 (26–36)	31	3,640	31 (27–36)	31
Age												
65–69	1,300	32 (24–40)		980	25 (18–33)		800	24 (16–31)		1,120	32 (23–40)	
70–74	1,220	38 (28–47)		1,080	32 (24–41)		1,240	41 (31–51)		1,160	38 (28–47)	
75–79	860	38 (27–49)		960	42 (30–54)		960	42 (30–54)		900	37 (26–47)	
80–84	320	24 (12–36)		440	32 (18–45)		340	25 (13–36)		340	23 (12–34)	
85–89	180	30 (10–50)		100	16 (1.9–30)		60	9.2 (0–20)		80	11 (0.3–22)	
90+	40	20 (0–47)		40	19 (0–50)		40	19 (0–44)		40	17 (0–41)	
Race/ethnicity												
White	4,020	32 (28–36)	32	3,520	27 (23–31)	27	3,520	29 (25–33)	29	3,400	26 (22–30)	26
Black	320	25 (13–37)	24	360	26 (14–38)	27	300	22 (11–34)	21	560	38 (24–52)	41
Asian	…	…	…	20	27 (0–81)	27	0	0	0	0	0	0
Hispanic	…	…	…	60	30 (0–64)	30	20	6.0 (0–18)	6.0	80	21 (0.5–42)	21
N. American Native	…	…	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	1,400	38 (29–47)	37	1,280	33 (25–41)	33	1,300	35 (27–44)	35	1,200	32 (24–40)	32
Northeast	960	30 (22–39)	30	1,080	34 (25–43)	35	800	29 (20–38)	30	780	27 (18–35)	25
South	1,780	34 (27–41)	35	1,440	26 (20–32)	26	1,460	27 (21–33)	26	1,760	30 (24–37)	31
West	320	13 (6.7–20)	12	240	10 (4.5–16)	10	340	15 (8.0–22)	16	380	15 (8.4–22)	15

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 22. Male Medicare beneficiaries with prostatitis receiving ablative surgery, percent[a] (95% CI), antibiotic injection, percent[b] (95% CI), cystoscopy, percent[c] (95% CI), urethral procedure, percent[d] (95% CI), and urodynamic studies, percent[e]

	1992	1995	1998	2001
	Percent (CI)	Percent (CI)	Percent (CI)	Percent (CI)
Ablative surgery	0.28 (0.27–0.28)	0.31 (0.31–0.32)	0.48 (0.48–0.48)	0.49 (0.49–0.49)
Antibiotic injection	2.1 2.1–2.1)	1.8 (1.8–1.8)	1.7 (1.7–1.7)	1.6 (1.6–1.6)
Cytoscopy	1.6 (1.6–1.6)	1.4 (1.4–1.5)	1.4 (1.4–1.4)	1.2 (1.2–1.2)
Urethral procedures	0.15 (0.15–0.15)	0.17 (0.16–0.17)	0.08 (0.08–0.08)	0.11 (0.11–0.12)
Urodynamics	1.0 (1.0–1.0)	0.76 (0.75–0.76)	0.74 (0.74–0.74)	0.76 (0.75–0.76)

[a]Percent of male Medicare beneficiaries 65 years and older with prostatitis who had ablative surgery.
[b]Percent of male Medicare beneficiaries 65 years and older with prostatitis who had antibiotic injection.
[c]Percent of male Medicare beneficiaries with prostatitis who had cystoscopy.
[d]Percent of male Medicare beneficiaries 65 years and older with prostatitis who had urethral procedure.
[e]Percent of male Medicare beneficiaries with prostatitis who had urodynamic studies.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

other regions, and this finding was consistent within each of the years studied. There were no apparent trends by race/ethnicity between 1995 and 2001. The percentage of male Medicare beneficiaries 65 years and older with prostatitis who had ablative surgery remained small at 0.28% in 1992 and 0.49% in 2001 (Table 22). The counts were not high enough to allow observations based on race/ethnicity or region. While prostatic abscess has been reported as a complication of prostatitis, there were no documented visits for prostatitis associated with surgical abscess drainage in 1992–2001 in the 5% Medicare sample studied. The percentage of male Medicare beneficiaries 65 years and older with prostatitis who had antibiotic injections declined from 2.1% in 1992 to 1.6% in 2001 (Table 22), possibly reflecting the decline in hospitalizations, as noted above. The percentage of male Medicare beneficiaries 65 and older with prostatitis who had bacterial culture and urinalysis remained steady (15% to 17%) from 1992 to 2001, which is not surprising, since the diagnostic approach to prostatitis has not changed over the years. The percentage of male Medicare beneficiaries 65 and older with prostatitis who had cystoscopy also remained steady (1.6% in 1992 to 1.2% in 2001) (Table 22). The percentage of those with prostatitis who had STD cultures was very low over the years, from 0.03% in 1992 to 0% in 2001 (Table 23). Part of the explanation for this low rate may be that STD testing is typically performed in younger, unmarried individuals. The percentage of those receiving urethral procedures also remained low over time, from 0.15% in 1992 to 0.11% in 2001 (Table 22). Finally, the percentage of those receiving urodynamic studies also remained low over time, from 1.0% in 1992 to 0.76% in 2001 (Table 22).

According to the National Survey of Ambulatory Surgery database, visit rates were essentially stable between 1994 and 1996, with an annualized rate of 33 per 100,000 for prostatitis listed as any diagnosis (Table 24). Visit rates were highest in the 55–74 age group (216 per 100,000), followed closely by the 75 and over group (201 per 100,000); men aged 35–54 and 18–34 had much lower rates (91 per 100,000 and 24 per 100,000, respectively). Three procedures were associated with ambulatory surgery visits for prostatitis—cystoscopy, prostatic biopsy, and urethral dilation. The annualized visit rate was highest for cystoscopy, followed by prostatic biopsy, then urethral dilation (Table 25).

All the outpatient databases indicated a slight decrease in visits for prostatitis over time. This trend may reflect an actual decline or simply a change in how physicians coded visits for prostatitis. The variety of diagnostic studies associated with prostatitis probably reflects the absence of a gold standard diagnostic test, and the variety of therapeutic procedures probably reflects the absence of an effective therapy for most cases of prostatitis.

Table 23. Male Medicare beneficiaries with prostatitis receiving STD culture, percent[a] (95% CI), age-adjusted percent[b]

	1992		1995		1998		2001	
	Percent (CI)	Age-Adjusted Percent	Percent (CI)	Age-Adjusted Percent	Percent (CI)	Age-Adjusted Percent	Percent (CI)	Age-Adjusted Percent
Total	0.03 (0.03–0.03)		0.02 (0.02–0.02)		0.01 (0.01–0.01)		0	
Age								
65–69	0.05 (0.05–0.06)		0		0		0	
70–74	0		0		0		0	
75–79	0		0		0		0	
80–84	0.08 (0.07–0.08)		0		0.09 (0.08–0.11)		0	
85–89	0		0.41 (0.36–0.46)		0		0	
90–94	0		0		0		0	
95+	0		0		0		0	
Race/ethnicity								
White	0.01 (0.01–0.01)	0.01	0.02 (0.02–0.02)	0.02	0	0	0	0
Black	0.27 (0.25–0.30)	0.28	0	0	0.18 (0.15–0.22)	0.17	0	0
Other	0	0	0	0	0	0	0	0
Asian	...	…	0	0	0	0	0	0
Hispanic	...	…	0	0	0	0	0	0
N. American Native	...	…	0	0	0	0	0	0
Region								
Midwest	0	0	0	0	0	0	0	0
Northeast	0.05 (0.05–0.06)	0.05	0.11 (0.11–0.12)	0.12	0.08 (0.07–0.08)	0.08	0	0
South	0.04 (0.04–0.04)	0.04	0	0	0	0	0	0
West	0	0	0	0	0	0	0	0

…data not available.

STD, sexually transmitted disease.

[a]Percent of male Medicare beneficiaries 65 years and older with prostatitis who had STD culture.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 24. Ambulatory surgery visits for prostatitis listed as any diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996			
	Count	3-Year Rate	Annualized Rate	3- Year Age-Adjusted Rate
Total	88,261	98 (84–111)	33	97
Age				
18–34	7,647	24 (14–34)	8.0	
35–54	32,225	91 (69–113)	30	
55–74	38,523	216 (169–263)	72	
75+	9,866	201 (127–275)	67	
Region				
Midwest	29,754	140 (112–168)	47	140
Northeast	23,218	129 (84–173)	43	127
South	30,288	97 (75–120)	32	96
West	*	*	*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey(CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Table 25. Procedure use during ambulatory surgery visits for prostatitis listed as any diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), annualized rate[b], rate per 100,000 visit[c] (95% CI)

	Count	3- Year Rate	Annualized Rate	3-Year Rate Per 100,000 visits for Prostatitis
Total	88,261	98 (84–111)	33	100,000 (85,800–114,200)
With associated cystoscopy (ICD-9 57.32)	58,932	65 (54–76)	22	66,770 (55,259–78,281)
With associated prostatic biopsy (ICD-9 60.11)	22,845	25 (19–32)	8.3	25,883 (19,404–32,363)
With associated urethral dilation (ICD-9 58.6)	13,387	15 (10–20)	5.0	15,168 (10,161–20,174)

[a]Rate per 100,000 is based on 1994–1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Rate per 100,000 men is based on average annualized rate per year.

[c]Rate per 100,000 is based on estimated number of visits for prostatitis in NSAS 1994–1996.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996

Table 26. Emergency room visits for males with prostatitis having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	41	11	52	9	106	12	132	13	104	12
As Any Diagnosis										
Total	63	18	72	13	165	19	218	22	165	19

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Emergency Room Care

Between 1994 and 2002, emergency room visits by individuals with commercial insurance who had a primary diagnosis of prostatitis remained relatively stable; according to the CHCPE database (Table 26), the rate of emergency room visits in 2002 was 12 per 100,000 population. While emergency room visits were nearly three times more common in the Medicare population than in the CHCPE population, the Medicare rates decreased over time (Table 27). In 2001, the age-adjusted emergency room visit rate for men 65 and older was 34 per 100,000, a 29% decline from 1992, when the rate was 48 per 100,000. The highest rates within each year tended to be in the older age groups, peaking each year in the 85+ group. The higher rate among older men likely reflects the lower threshold for referring older men with prostatitis to the emergency room for evaluation. The highest rates were in the South across all the years studied. The highest rates of emergency room visits were for African Americans in each of the years of study except 1995, when the rate was highest for North American Natives; however, the low counts make this estimate unreliable. According to NHAMCS data for 1994–2000 (Table 28), the annualized age-adjusted emergency room visit rate was 91 per 100,000, which is much higher than the rates noted in the CHCPE and Medicare databases. Because the years were aggregated to create an adequate sample size, we do not know if the rates declined with time in the NHAMCS data as they did in the other two databases.

ECONOMIC IMPACT

The economic impact of prostatitis includes the direct medical costs of treating the condition and the indirect costs associated with lost work time. Each inpatient or outpatient encounter may involve a variety of cost sources, including physician professional fees; radiographic studies; room and board; and laboratory, pharmacy, and operating room costs. We use the terms *costs* and *expenditures* to refer to total payments made by patients (co-insurance, co-payments, deductibles, and uncovered expenses) and by all third-party payors (primary and secondary coverage, when available).

Overall spending in the United States for diagnosis and management of prostatitis totaled $84 million in 2000 (Table 29). This estimate is exclusive of pharmaceuticals, which can play a significant role in initial management. Increases in expenditures for hospital outpatient services and physician office visits were 31% and 62%, respectively, from 1994 to 2000, while spending on ambulatory surgery and inpatient expenditures peaked in 1998. Inpatient services accounted for the greatest proportion of expenditures in 2000, but ambulatory surgery and emergency room visits combined accounted for almost half of the total expenditures.

Expenditures among Medicare enrollees 65 and over were $27 million in 2001 and have remained level since 1992, indicating a decrease in real spending over time (Table 30). The lack of a secular trend in expenditures was a function of slight decreases in inpatient expenditures and slight increases in physician office visit expenditures. Physician office visits accounted for more than half of the expenditures in 2001 in this population. Expenditures among Medicare enrollees under 65 were substantially less, totaling only $3 million in 2001. Physician office visits accounted for more than three-quarters of the expenditures in this group in 2001.

The incremental costs associated with prostatitis were estimated using risk-adjusted regression models

Table 27. Emergency room visits by male Medicare beneficiaries with prostatitis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995				1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	7,340	49	(44–54)		6,600	43	(39–48)		7,160	49	(44–55)		5,680	37	(33–41)	
Total < 65	1,800	58	(46–70)		1,880	55	(44–66)		2,200	64	(52–76)		1,780	47	(37–56)	
Total 65+	5,540	47	(42–53)	48	4,720	40	(35–45)	40	4,960	45	(39–51)	47	3,900	34	(29–38)	34
Age																
65–69	1,620	40	(31–48)		1,500	39	(30–48)		1,140	34	(25–43)		1,160	33	(24–41)	
70–74	1,500	46	(36–57)		1,320	40	(30–49)		1,340	44	(33–54)		1,040	34	(25–43)	
75–79	1,320	58	(44–72)		900	40	(28–51)		860	38	(26–49)		860	35	(25–46)	
80–84	680	52	(34–69)		620	45	(29–60)		520	38	(23–52)		460	31	(18–43)	
85–89	380	64	(35–92)		300	47	(23–71)		940	144	(103–186)		240	33	(14–52)	
90–94	0	0			40	19	(0–45)		160	74	(23–126)		120	52	(10–93)	
95–97	20	50	(0–146)		40	106	(0–252)		0	0			0	0		
98+	20	53	(0–155)		0	0			0	0			20	37	(0–109)	
Race/ethnicity																
White	5,820	46	(41–52)	46	5,260	40	(36–45)	40	5,220	43	(38–48)	45	4,400	34	(29–38)	33
Black	1,120	86	(65–111)	86	1,020	74	(53–94)	74	1,560	117	(91–143)	90	900	61	(43–79)	63
Asian	…	...		…	0			0	20	15	(0–43)	15	20	9.8	(0–29)	9.8
Hispanic	…	...		…	120	60	(12–109)	60	140	42	(11–73)	36	200	53	(20–86)	48
N. American Native	…	...		…	20	99	(0–293)	99	0	0		0	0	0		0
Region																
Midwest	1,500	40	(31–50)	39	1,620	42	(33–51)	39	2,060	56	(45–66)	48	1,180	31	(23–39)	31
Northeast	1,200	38	(28–47)	37	640	20	(13–27)	19	680	24	(16–33)	24	680	23	(15–31)	24
South	3,760	72	(62–82)	70	3,620	66	(56–76)	68	3,840	72	(61–82)	78	2,860	49	(41–57)	50
West	800	33	(23–43)	36	660	28	(19–38)	28	520	23	(14–32)	22	860	35	(24–45)	34

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 28. Emergency room visits for prostatitis listed as any diagnosis, 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000		
	Count	Annualized Rate	4–Year Age-Adjusted Rate
Total	336,915	91	361

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

that control for age, work status, income, urban or rural residence, and health plan characteristics (Table 31). Among 18- to 64-year-old males with employer-provided insurance, average annual expenditures were $5,464 for those treated for prostatitis, compared with $3,705 for similar men not treated for the condition; thus an incremental cost of $1,759 was associated with a diagnosis of prostatitis. Pharmaceuticals make up an important part of treatment costs (26%), which is consistent with the clinical management of the condition. Surgical removal of affected portions of the prostate is rare and is typically reserved for the most severe cases of prostatitis. Excess costs were found to vary substantially by age: treatment costs for 35- to 44-year-old men with prostatitis were $4,690 more than those for similar men of the same age without prostatitis. A diagnosis of prostatitis was associated with modest increases in medical expenditures overall, although excess costs were relatively higher among younger men, i.e., those 35 to 44 years of age.

In addition to the direct medical costs of treatment, the economic burden of prostatitis includes indirect costs associated with absenteeism and work limitations. Among 334 privately insured men with a medical claim for prostatitis in 2002, 14% missed some work related to the condition (Table 32). This proportion did not vary by age or region of the country, except in the Northeast, where only 3% of men treated for prostatitis missed work. The average annual amount of work missed by a patient with one or more claims for prostatitis was 4.4 hours. This low number is likely a result of most patients being treated with drugs rather than procedures. These estimates of work loss are modestly smaller than those of prior studies—the NIH Chronic Prostatitis Cohort Study reported that 26% of men experienced work loss over a three-month period, with an average, estimated value of $551 (3).

CONCLUSIONS

Prostatitis is a relatively common condition in the US male population. It affects adult men of all ages, unlike BPH and prostate cancer, which are mainly

Table 29. Expenditures for prostatitis, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$3,199,401	4.0%	$3,484,259	4.1%	$3,225,051	3.5%	$4,203,769	5.0%
Physician Office	$3,206,854	4.0%	$3,492,375	4.1%	$4,295,666	4.7%	$5,223,512	6.2%
Ambulatory Surgery	$23,560,902	29.6%	$27,425,839	32.4%	$31,669,599	34.4%	$23,831,205	28.2%
Emergency Room	$13,941,447	17.5%	$15,182,719	17.9%	$15,784,644	17.2%	$16,348,869	19.4%
Inpatient	$35,633,726	44.8%	$35,156,792	41.5%	$37,048,008	40.3%	$34,844,645	41.3%
TOTAL	$79,542,330		$84,741,984		$92,022,968		$84,452,000	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 30. Expenditures for Medicare beneficiaries for treatment of prostatitis (% of total)

	Age 65 and over							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$956,040	3.5%	$1,115,920	4.1%	$974,120	3.6%	$1,303,680	4.7%
Physician Office	$11,923,120	44.0%	$12,564,800	46.7%	$12,587,820	46.7%	$13,785,200	50.2%
Ambulatory Surgery	$2,649,920	9.8%	$3,088,800	11.5%	$3,532,880	13.1%	$2,948,400	10.7%
Emergency Room	$908,560	3.4%	$972,320	3.6%	$1,101,120	4.1%	$939,900	3.4%
Inpatient	$10,670,800	39.4%	$9,158,400	34.0%	$8,732,160	32.4%	$8,500,240	30.9%
TOTAL	$27,108,440		$26,900,240		$26,928,100		$27,477,420	

	Under 65							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$152,520	9.2%	$265,600	11.8%	$283,500	11.3%	$314,760	11.0%
Physician Office	$1,248,480	75.1%	$1,708,800	76.1%	$1,789,080	71.1%	$2,205,920	77.0%
Ambulatory Surgery	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Emergency Room	$261,000	15.7%	$270,720	12.1%	$444,400	17.7%	$343,540	12.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$1,662,000		$2,245,120		$2,516,980		$2,864,220	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 31. Estimated annual expenditures of privately insured employees with and without a medical claim for prostatitis in 2002[a]

	Annual Expenditures (per person)					
	Males without Prostatitis (N=281,633)			Males with Prostatitis (N=3,698)		
	Medical	**Rx Drugs**	**Total**	**Medical**	**Rx Drugs**	**Total**
Total	$2,669	$1,036	$3,705	$4,038	$1,426	$5,464
Age						
18–34	$1,288	$691	$1,979	$2,430	$1,345	$3,775
35–44	$2,120	$875	$2,995	$6,299	$1,386	$7,685
45–54	$3,061	$1,214	$4,275	$3,631	$1,442	$5,073
55–64	$3,208	$1,131	$4,339	$3,706	$1,458	$5,164
Region						
Midwest	$2,591	$1,021	$3,612	$3,916	$1,419	$5,335
Northeast	$2,616	$1,117	$3,733	$3,955	$1,544	$5,499
South	$2,717	$969	$3,686	$4,107	$1,322	$5,429
West	$2,879	$1,062	$3,941	$4,351	$1,495	$5,846

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions.

SOURCE: Ingenix, 2002.

Table 32. Average annual work loss of males treated for prostatitis, 1999 (95%CI)

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs) Inpatient[b]	Outpatient[b]	Total
Total	334	14%	0.4 (0–0.9)	4.0 (2.4–5.7)	4.4 (2.7–6.2)
Age					
18–29	7	14%	0	0.3 (0–0.9)	0.3 (0–0.9)
30–39	71	20%	0	4.7 (0.1–9.2)	4.7 (0.1–9.2)
40–49	104	13%	0.5 (0–1.4)	3.7 (1.1–6.3)	4.1 (1.1–7.1)
50–64	152	12%	0.6 (0–1.4)	4.1 (1.7–6.5)	4.7 (2.2–7.3)
Region					
Northeast	34	3%	0	0.9 (0–2.9)	0.9 (0–2.9)
Midwest	65	15%	0.5 (0–1.5)	2.7 (0–6.2)	3.2 (0–6.8)
South	174	16%	0.6 (0–1.4)	5.2 (2.5–7.8)	5.8 (2.9–8.7)
West	30	17%	0	5.5 (0–11.6)	5.5 (0–11.6)
Unknown	31	10%	0	2.1 (0–4.9)	2.1 (0–4.9)

[a]Individuals with an inpatient or outpatient claim for prostatitis and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

conditions of older men. *Prostatitis* is an umbrella term that refers to several types of prostatitis; however, coding schemes limit the ability to obtain detailed information on the individual types. Other conditions are commonly associated with prostatitis, especially BPH, and this may reflect misclassification or misdiagnosis, although it is also possible for an older man to have both conditions. Prostatitis is generally treated in the outpatient setting; inpatient hospitalizations have declined over time. There are various diagnostic and treatment procedures, but the variety likely reflects the absence of a definitive diagnostic test and the absence of effective therapies for prostatitis. The cost of prostatitis, exclusive of pharmaceutical spending, is about $84 million annually and appears to be increasing over time, despite the shift from inpatient to outpatient care. Given the extensive gaps in our understanding of the diagnosis and treatment of prostatitis, many of these expenditures may represent a waste of resources.

RECOMMENDATIONS

The Urologic Diseases in America project expended a great deal of effort to obtain the best data available on prostatitis and identified a number of knowledge gaps that need to be filled. We propose the following topics for investigation to improve the understanding of prostatitis:

- Explore the relationship between prostatitis and BPH.
- Explore differences in epidemiology, pathogenesis, and treatment response in men with pelvic pain and voiding symptoms and men with voiding symptoms but no pain.
- The relationship between inflammation and acute urinary retention, already noted in the Medical Treatment of Prostate Symptoms (MTOPS) study (34), needs to be characterized further.
- Given the expenditures on procedures for a clinical condition without a clear etiology, further basic research to identify the etiology and pathogenesis of male chronic pelvic pain is needed.
- A specific diagnostic code for Category III prostatitis would be beneficial in several ways: standardized coding would lead to more specific and therefore more useful estimates of the incidence, prevalence, and resource utilization of this condition and would necessitate education for clinicians on the criteria for using this diagnosis. This would likely raise awareness of CPP/CPPS, which would in turn lead to more-accurate diagnosis and coding of this condition.

REFERENCES

1. McNaughton Collins M, Pontari MA, O'Leary MP, et al. Quality of life is impaired in men with chronic prostatitis: the Chronic Prostatitis Collaborative Research Network. J Gen Intern Med 2001;16:656-62.
2. Turner JA, Ciol MA, Von Korff M, et al. Health concerns of patients with nonbacterial prostatitis/pelvic pain. Arch Intern Med 2005;165:1054-59.
3. Calhoun EA, McNaughton-Collins M, Pontari MA, et al. The economic impact of chronic prostatitis. Arch Intern Med 2004; 164:1231-6.
4. Drach GW, Fair WR, Meares EM, et al. Classification of benign diseases associated with prostatic pain: prostatitis or prostatodynia? J Urol 1978;120: 266.
5. Krieger JN, Nyberg L, Nickel JC. NIH consensus definition and classification of prostatitis. JAMA 1999;282: 236-7.
6. Schaeffer AJ, Knauss JS, Landis JR, et al. Leukocyte and bacterial counts do not correlate with severity of symptoms in men with chronic prostatitis: the National Institutes of Health Chronic Prostatitis Cohort Study. J Urol. 2002;168:1048-53.
7. Meares EM, Stamey TA. Bacteriologic localization patterns in bacterial prostatitis and urethritis. Invest Urol 1968;5:492-518.
8. Nickel JC. The Pre and Post Massage Test (PPMT): a simple screen for prostatitis. Tech Urol 1997;3:38-43.
9. Nickel JC. Clinical evaluation of the man with chronic prostatitis/chronic pelvic pain syndrome. Urology 2002;60:20-23.
10. Litwin MS, McNaughton-Collins M, Fowler JF, et al. The National Institutes of Health chronic prostatitis symptom index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. J Urol 1999;162: 369-75.
11. Pontari MA, McNaughton-Collins M, O'Leary MP, et al. A case-control study of risk factors in men with chronic pelvic pain syndrome. BJU Int. In press (2005).
12. Pontari MA, Ruggieri MR. Mechanisms in prostatitis/chronic pelvic pain syndrome. J Urol 2004;172:839-845.
13. Schaeffer AJ. Diagnosis and treatment of prostatic infections. Urol 1990;36:13-7.
14. Alexander RB, Propert KJ, Schaeffer AJ, et al. Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. Ann Intern Med 2004;141:581-9.
15. Nickel JC, Downey J, Clark J, et al. Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo-controlled multicenter trial. Urol 2003:62:614-7.
16. Cheah PY, Liong ML, Yuen KH, et al. Terazosin therapy for chronic prostatitis/chronic pelvic pain syndrome: a randomized, placebo-controlled trial. J Urol 2003;169:592-6.
17. Mehik A, Alas P, Nickel JC, et al. Alfuzosin treatment for chronic prostatitis/chronic pelvic pain syndrome: a prospective, randomized, double-blind, placebo-controlled, pilot study. Urol 2003;62:425-9.
18. Shoskes DA, Zeitlin SJ, Shahed A, et al. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. Urol 1999;54:960-3.
19. Nickel JC, Downey J, Pontari MA, et al. A randomized placebo-controlled multicentre study to evaluate the safety and efficacy of finasteride for male chronic pelvic pain syndrome (category IIIA chronic nonbacterial prostatitis). BJU Int 2004;93:991-5.
20. Nickel JC, Forrest J, Tomera KM, et al. Effects of pentosan polysulfate sodium in men with chronic pelvic pain syndrome: a multi-center, randomized, placebo-controlled study. J Urol 2005;173:1252-5.
21. Rowe E, Smith C, Laverick L, et al. A prospective, randomized, placebo-controlled, double-blind study of pelvic electromagnetic therapy for the treatment of chronic pelvic pain syndrome with 1 year of follow-up. J Urol 2005;173:2044-7
22. Shoskes DA, Hakim L,Ghoniem G, et al.. Long-term results of multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome. J Urol 2003;169:1406-10.
23. Nickel JC, Downey J, Ardern D, et al.. Failure of a monotherapy strategy for difficult chronic prostatitis/chronic pelvic pain syndrome. J Urol 2004; 172:551-4.
24. 24. Roberts RO, Lieber MM, Bostwick DG, Jacobsen SJ. A review of clinical and pathological prostatitis syndromes. Urol 1997;49:809-21.
25. 25. Bennett B, Richardson P, Gardner WJ. Histopathology and cytology of prostatitis. In: Lepor H, Lawson R, editors. Prostate Diseases. Philadelphia: WB Saunders Co. 1993. pp 399-413.
26. 26. Roberts RO, Lieber MM, Rhodes T, Girman CJ, Bostwick DG, Jacobsen SJ. Prevalence of a physician-assigned diagnosis of prostatitis: the Olmsted County Study of Urinary Symptoms and Health Status Among Men. Urol 1998;51:578-84.
27. Mehik A, Hellstrom P, Lukkarinen O, Sarpola A, Jarvelin M. Epidemiology of prostatitis in Finnish men: a population-based cross- sectional study. BJU Int 2000;86:443-8.
28. McNaughton Collins M, O'Leary M, Barry M. Prevalence of bothersome genitourinary symptoms and diagnoses in younger men on routine primary care visits. Urol 1998;52:422-27.
29. McNaughton Collins M, Meigs JB, Barry MJ, Walker Corkery E, Giovannucci E, Kawachi I. Prevalence and correlates of prostatitis in the health professionals follow-up study cohort. J Urol 2002;167:1363-6.
30. Moon TD. Questionnaire survey of urologists and primary care physicians' diagnostic and treatment practices for prostatitis. Urol 1997;50:543-7.

31. Nickel JC, Downey J, Hunter D, Clark J. Prevalence of prostatitis-like symptoms in a population based study using the National Institutes of Health chronic prostatitis symptom index. J Urol 2001;165:842-5.
32. Roberts RO, Jacobson DJ, Girman CJ, et al. Prevalence of prostatitis-like symptoms in a community based cohort of older men. J Urol 2002;168:2467-2471.
33. Clemens JQ, Meenan RT, O'Keeffe MC, et al. Incidence and clinical characteristics of NIH type III prostatitis in the community. J Urol 2005;174:2319-22.
34. Roehrborn CG, Kaplan SA, Noble WD, et al. The impact of acute or chronic inflammation in baseline biopsy on the risk of clinical progression of BPH: results from the MTOPS study. J Urol 173(suppl): p. 346, abstract #1277.

CHAPTER 2

Benign Prostatic Hyperplasia

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Benign Prostatic Hyperplasia

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INTRODUCTION

Benign prostatic hyperplasia (BPH), the most common benign neoplasm in American men, is a chronic condition that increases in both incidence and prevalence with age. It is associated with progressive lower urinary tract symptoms and affects nearly three out of four men during the seventh decade of life. Using definitions in the Agency for Health Care Policy and Research (AHCPR) Diagnostic and Treatment Guidelines for BPH (1), it is estimated that approximately 6.5 million of the 27 million Caucasian men 50 to 79 years of age in the United States in 2000 were expected to meet the criteria for discussing treatment options for BPH (2). In 2000, approximately 4.5 million visits were made to physicians' offices to for a primary diagnosis of BPH, and nearly 8 million visits were made with either a primary or secondary diagnosis of BPH. In the same year, approximately 87,400 prostatectomies for BPH were performed on inpatients in nonfederal hospitals in the United States. While the number of outpatient visits for BPH climbed consistently during the 1990s, there was a dramatic decline in the utilization of transurethral prostatectomy, inpatient hospitalization, and length of hospital stay for this condition. These trends reflect the changing face of medical management for BPH, i.e., increasing utilization of pharmacological agents and minimally invasive therapies. In 2000, the direct cost of BPH treatment was estimated to be $1.1 billion, exclusive of outpatient pharmaceuticals. Given the impact that BPH can have on quality of life and the cost of medical care for millions of American men, investigations into risk factors, diagnostic and therapeutic resource utilization, and outcomes related to BPH are warranted.

DEFINITION AND DIAGNOSIS

Benign prostatic hyperplasia is characterized pathologically by a cellular proliferation of the epithelial and stromal elements within the prostate gland. These changes, which begin histologically in the third decade of life and clinically in the fifth decade of life, are mediated primarily by tissue levels of dihydrotestosterone within the prostate and result in the gland's continued growth throughout life. When prostatic enlargement occurs, increased resistance in the proximal urethra may limit urinary flow during micturition, often resulting in pathophysiologic changes in the bladder wall. Consequently, lower urinary tract symptoms (LUTS) due to prostatic obstruction are inseparable from symptoms due to bladder detrusor dysfunction. Moreover, bladder dysfunction for reasons other than prostatic obstruction, such as aging or diabetic neuropathy, may occur independently; such cases are often misclassified as BPH.

Clinically, BPH is distinguished by progressive development of LUTS. These symptoms are variable and range from nocturia, incomplete emptying, urinary hesitancy, weak stream, frequency, and urgency to the development of acute urinary retention. Such symptoms can have a significant negative impact on quality of life, leading many men to seek treatment (3).

Table 1. Codes used in the diagnosis and management of benign prostatic hyperplasia

Males 40 years or older with:	
ICD-9 diagnosis codes	
599.6	Urinary obstruction, unspecified
600.0	Hypertrophy (benign) of prostate
600.9	Unspecified hyperplasia of prostate
ICD-9 procedure codes	
60.2	Transurethral prostatectomy
60.21	Transurethral (ultrasound) guided laser induced prostatectomy (TULIP)
60.29	Other transurethral prostatectomy
60.3	Suprapubic prostatectomy
60.4	Retropubic prostatectomy
60.94	Control of (postoperative) hemorrhage of prostate
60.95	Transurethral balloon dilation of prostatic urethra
60.96	Transurethral destruction of prostate tissue by microwave thermotherapy
60.97	Other transurethral destruction of prostatic tissue by other thermotherapy
CPT procedure codes	
52450	Transurethral incision of prostate
52510	Transurethral balloon dilation of the prostatic urethra
52601	Transurethral electrosurgical resection of prostate, including control of postoperative bleeding, complete (vasectomy, meatomy, cystourethroscopy, urethral calibration, and/or dilation, and internal urethrotomy are included)
52606	Transurethral fulguration for postoperative bleeding occurring after the usual follow-up time
52612	Transurethral resection of prostate; first stage of two-stage resection (partial resection)
52614	Transurethral resection of prostate; second stage of two-stage resection (resection completed)
52620	Transurethral resection of residual obstructive tissue after 90 days postoperative
52630	Transurethral resection of regrowth of obstructive tissue longer than one year postoperative
52640	Transurethral resection of postoperative bladder neck contracture
52647	Noncontact laser coagulation of prostate, including control of postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included)
52648	Contact laser vaporization with or without transurethral resection of prostate, including control of postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included)
53850	Transurethral destruction of prostate tissue by microwave thermotherapy
53852	Transurethral destruction of prostate tissue by radiofrequency thermotherapy
55801	Prostatectomy, perineal, subtotal (including control of postoperative bleeding, vasectomy, meatotomy, urethral calibration and/or dilation, and internal urethrotomy)
55821	Prostatectomy (including control of postoperative bleeding, vasectomy, meatotomy, urethral calibration and/or dilation, and internal urethrotomy); suprapubic, subtotal, one or two stages
55831	Prostatectomy (including control of postoperative bleeding, vasectomy, meatotomy, urethral calibration and/or dilation, and internal urethrotomy); retropubic, subtotal
Males 40 years or older with one of the following ICD-9 codes, but not carrying diagnosis code 185 (malignant neoplasm of prostate) as another diagnosis	
594.1	Other calculus in bladder
788.20	Retention of urine, unspecified
788.21	Incomplete bladder emptying
788.29	Other specified retention of urine
788.41	Urinary frequency
788.42	Polyuria
788.43	Nocturia
788.61	Splitting of urinary stream
788.62	Slowing of urinary system

Continued on next page

Table 1 (continued). Codes used in the diagnosis and management of benign prostatic hyperplasia

Any of the following ICD-9 codes and any of the procedure or BPH medication codes	
600.1	Nodular prostate
600.2	Benign localized hyperplasia (eg adenoma of prostate, adenofibramatous hypertrophy of prostate) of prostate

While no standard definition of BPH exists, clinically significant BPH is heralded by the onset of LUTS; therefore, LUTS are usually presumed to be due to BPH in the absence of another obvious cause. The International Classification of Diseases (ICD-9-CM) coding system is frequently used to identify cases in studies of BPH prevalence; other approaches include using codes for specific pharmacological or surgical interventions as surrogates for BPH cases.

In this chapter, the burden of illness attributable to BPH and its associated medical care is characterized from a variety of data sources, including administrative datasets using ICD-9 and Current Procedural Terminology (CPT) codes, large national health surveys, and community-based studies. Table 1 lists the codes used in the diagnosis and management of BPH. Although most BPH cases are coded as 600.0, this diagnostic code usually reflects a clinical diagnosis ranging from abnormal digital rectal examination to invasive therapy for symptoms. Although these administrative data provide for concrete estimates of resource utilization, they probably underestimate the number of men affected by BPH. In the National Health and Nutrition Examination Survey (NHANES-III), four items were used to identify symptomatic men:

- number of times a night the man gets up to urinate;
- feeling that the bladder is not empty;
- trouble starting urination; and
- in men older than 60 years, decreased urinary stream.

While NHANES-III data are nationally representative, they fail to capture the full range of BPH-related voiding symptoms. Methodological differences in data collection among the datasets used result in great variability in estimates of BPH prevalence, incidence, and resource utilization. National surveys such as NHANES-III are essential for ascertaining population-based estimates, but they are limited in the quantity of information available from each subject.

In 1994, the Agency for Health Care Policy and Research (AHCPR), since renamed the Agency for Healthcare Research and Quality (AHRQ), released a set of diagnostic and treatment guidelines for BPH tailored to symptom severity (1). The potential impact of BPH can be estimated by applying these guidelines to the proportion of symptomatic males in populations-based studies (Figure 1). As underscored by the AHCPR BPH Guidelines panel, BPH actually comprises four interrelated conditions (2):

- histologic BPH;
- symptomatic BPH;
- bladder outlet obstruction, as evidenced by symptomatic BPH;
- detrusor decompensation.

The AHCPR BPH Guidelines also outline the basic evaluation and stratification of patients for treatment decision making, whereby men are stratified on the presence of mild, moderate, or severe LUTS. The guidelines recommend using the American Urological Association Symptom Index (AUASI), a validated patient-reported measure of LUTS that captures both obstructive and irritative symptoms (4). The AUASI was developed by the American Urological Association (AUA) in collaboration with the Patient Outcomes Research Team for Prostate Disease (4). The self-administered instrument includes seven questions rated on 0-to-5 Likert scales; scores can range from 0 to 35 points. Nearly 60% of urologists reported documenting the AUASI for men with LUTS (5), and the vast majority report following the AHCPR guidelines by using an AUASI score higher than 7 as an indication of moderate-to-severe symptoms. Several large community-based cohort studies, including the Olmsted County Study of Urinary Symptoms and Health Status Among Men and the Flint Men's Health Study, have adopted the AUASI as their measure of disease severity in men with LUTS. Nevertheless,

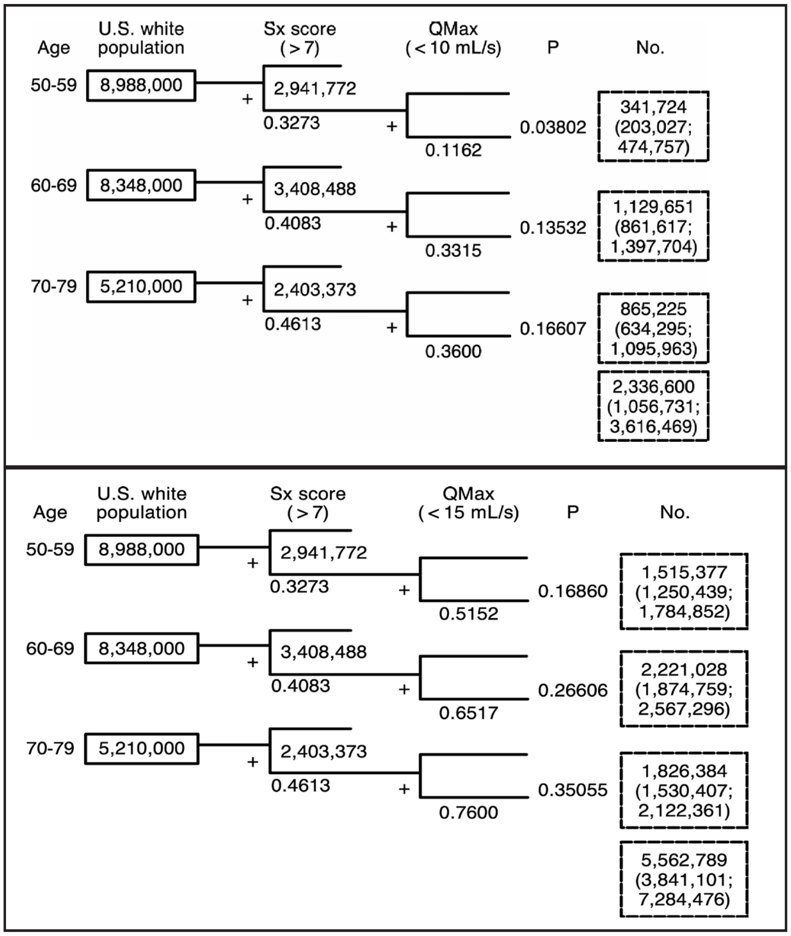

Figure 1. Potential impact of new benign prostatic hyperplasia guidelines on the 1990 US white male population aged 50 to 79 years. Top, Guideline criteria of American Urological Association Symptom Index (AUASI) greater than 7 and peak urinary flow rate (Qmax) less than 15 mL/s. Bottom, Guideline criteria of AUASI greater than 7 and Qmax less than 10 mL/s. P indicates the proportion of men within each age group meeting both criteria; No., number of men meeting both criteria (95% confidence interval). All proportions (decimal figures) are derived from the Olmsted County (Minnesota) Study of Urinary Symptoms and Health Status Among Men.

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a limitation of these datasets is that histological confirmation of BPH is universally absent. Despite the widespread acceptance of the AUASI, the absence of an accepted standard definition for BPH suggests that comparisons across datasets should be approached with caution.

PREVALENCE AND INCIDENCE

Recent data from NHANES-III suggest that BPH and LUTS are common in men 30 years of age and older and increase with age; nocturia was the most prevalent of the obstructive symptoms measured (6) (Table 2). Among men aged 60 to 69, nearly three out of four men complained of nocturia; the proportion was nearly 83% among men 70 years and older, illustrating the increasing burden of LUTS that occurs with aging. However, NHANES-III captured only nocturia, urinary hesitancy, incomplete emptying, weak stream, and surgery. Other population-based studies, such as the Massachusetts Male Aging Study (MMAS), may provide more accurate assessments

Table 2. Prevalence of specific lower urinary tract symptoms and noncancer prostate surgery in US men over 30 years of age, NHANES III[a]

Age at Interview (yr)	Actual (weighted) Sample Size	Nocturia (times per night) 0	1	2	3+	Incomplete Emptying	Hesitancy	Weak Stream[b]	Noncancer Prostate Surgery[c]
30–39	1,601 (20,737,223)	64.8 ± 1.8	27.3 ± 1.6	5.3 ± 0.9	2.6 ± 0.6	6.1 ± 0.9	2.4 ± 0.6	...	...
40–49	1,307 (16,103,901)	54.4 ± 2.1	36.2 ± 2.3	6.1 ± 1.0	3.3 ± 0.7	8.0 ± 1.1	4.4 ± 0.8	...	...
50–59	935 (10,486,737)	40.7 ± 2.1	39.1 ± 2.3	13.2 ± 1.4	7.0 ± 1.0	10.2 ± 1.6	4.8 ± 1.0	...	...
60–69	1,250 (8,888,814)	28.0 ± 2.0	41.7 ± 2.1	20.3 ± 2.0	10.0 ± 1.1	17.4 ± 1.7	10.7 ± 1.2	44.8 ± 2.6	8.0 ± 1.2
70+	1,631 (7,310,268)	16.9 ± 1.7	36.4 ± 1.7	26.1 ± 1.7	20.6 ± 1.8	22.7 ± 1.5	14.1 ± 1.3	55.8 ± 1.8	22.4 ± 1.1
P-value[c]		< 0.0001	0.57	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0003	< 0.0001
Among men who never had prostate surgery									
60–69	1,163 (8,181,653)	28.1 ± 2.2	42.4 ± 2.2	20.0 ± 1.9	9.5 ± 1.0	16.2 ± 1.5	10.0 ± 1.4	44.8 ± 2.8	...
70+	1,245 (5,671,346)	17.3 ± 2.0	37.0 ± 2.2	25.5 ± 2.0	20.2 ± 2.0	22.0 ± 1.5	14.0 ± 1.6	56.8 ± 1.9	...
P-value[c]		< 0.0001	0.04	0.02	< 0.0001	0.003	0.03	0.0002	...

...data not available.

Key: NHANES III, Third National Health and Nutrition Examination Survey.

Data presented as the percentage ± standard error, unless otherwise noted.

[a]Estimates are based on civilian non-institutionalized participants who were not observed in bed or in a wheelchair/stretcher or with leg paralysis/paresis and who gave a response to at least one lower urinary tract symptom or surgery question. Proxy respondents were excluded.

[b]Question not asked of men 30 to 59 years old.

[c]Where symptom prevalences are presented for more than two age groups, reported one-sided P values are for a test of increasing prevalence with age. Where symptoms are presented for only two age groups, reported one-sided P values are for a test of higher prevalence in the older men compared with the younger men and were calculated from a two-sample normal test with unequal variances.

SOURCE: Reprinted from Urology, 59, Platz EA, Smit E, Curhan GC, Nyberg LM, Giovannucci E, Prevalence of and racial/ethnic variation in lower urinary tract symptoms and noncancer prostate surgery in US men, 877–883, Copyright 2002, with permission from Elsevier.

Table 3. Prevalence of clinical benign prostatic hyperplasia at follow-up, by age category (Massachusetts Male Aging Study)

	Total	Age at Baseline (yrs) 40–49		50–59		60–70		P-value for Trend Across Age[a]
Total	1019	394		353		272		...
Clinical diagnosis of BPH[b]	185	33	8.4%	71	20.1%	81	29.8%	0.001
Underwent TURP for BPH	42	3	0.8%	16	4.5%	23	8.5%	0.001
Clinical diagnosis or TURP for BPH[c]	198	33	8.4%	74	21.0%	91	33.5%	0.001
On medication for enlarged or swollen prostate	48	4	1.0%	23	6.5%	21	7.7%	0.001
On medication or history of TURP for BPH[d]	86	7	1.8%	36	10.2%	43	15.8%	0.001

...data not available.

[a]Mantel-Haenszel extension test.

[b]Either frequent or difficult urination and told by a health professional that they had an enlarged or swollen prostate.

[c]Clinical diagnosis or history of TURP, “clinical BPH.”

[d]On medication or history of TURP for BPH, “severe clinical BPH.”

SOURCE: Reprinted from Journal of Clinical Epidemiology, 54, Meigs JB, Mohr B, Barry MJ, Collins MM, McKinlay JB, Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men, 935–944, Copyright 2001, with permission from Elsevier Science.

Table 4. Frequency of benign prostatic hyperplasia[a] listed as a diagnosis in male VA patients seeking outpatient care, rate[b]

	1999		2000		2001	
	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis
Total	6,098	10,654	5,705	11,650	4,811	11,406
Age						
40–44	955	1,339	965	1,426	808	1,280
45–54	2,420	3,707	2,318	3,938	1,966	3,703
55–64	5,748	9,419	5,247	9,652	4,275	8,821
65–74	8,427	15,075	7,650	16,102	6,210	15,231
75–84	9,293	17,068	8,328	18,300	6,799	17,556
85+	9,109	16,223	8,563	17,663	7,136	17,199
Race/ethnicity						
White	7,663	13,055	6,993	13,688	5,889	12,809
Black	6,677	10,061	6,143	10,101	5,126	9,140
Hispanic	7,683	10,978	7,779	11,940	6,131	11,123
Other	5,900	9,459	5,128	9,201	4,302	8,681
Unknown	3,846	7,846	3,858	9,629	3,481	10,466
Region						
Midwest	6,348	11,220	5,766	12,225	4,890	11,996
Northeast	6,406	11,078	6,046	12,154	5,158	12,114
South	6,047	10,497	5,720	11,604	4,695	11,078
West	5,499	9,724	5,171	10,390	4,484	10,379
Insurance status						
No insurance/self-pay	4,837	8,034	4,525	8,451	3,747	8,008
Medicare/Medicare supplemental	9,040	16,754	7,938	17,533	6,557	16,682
Medicaid	4,830	7,942	5,034	8,466	4,359	7,936
Private insurance/HMO/PPO	5,977	10,420	5,354	11,046	4,319	10,544
Other insurance	4,844	8,286	4,451	8,217	3,778	7,808
Unknown	5,834	8,370	4,534	6,946	1,675	4,691

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for BPH alone (no bladder stones).

[b]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

of prevalence because they also include irritative symptoms such as urinary frequency and urgency (7). In the MMAS cohort, BPH was identified by clinical diagnosis or history of surgery for BPH. The prevalence ranged from 8.4% in men 40 to 49 years of age to 33.5% in men aged 60 to 70 (Table 3).

These trends are further supported by 2001 data from the Veterans Health Administration (VA), in which the prevalence of BPH listed as the primary diagnosis during outpatient visits ranged from 808 per 100,000 in men aged 40 to 44 to 7,136 per 100,000 in men older than 85 (Table 4). The rate for all men 45 and older more than doubled when BPH was listed as any diagnosis. Between 1999 and 2001, the number of male veterans with outpatient visits for BPH as a primary diagnosis decreased, while the number of visits with BPH listed as any diagnosis increased. That these rates are lower than those reported in the MMAS suggests that older male veterans may also access care for their BPH outside the VA system. Nonetheless, the VA data support the association with age that has been observed in other populations.

The Olmsted County Study (OCS) and the Flint Men's Health Study have been used to produce a variety of estimates regarding the prevalence, incidence, and natural history of BPH. The initial OCS cohort was randomly selected from a sample stratified on age and residence (City of Rochester vs balance of Olmsted County); the sampling frame was constructed from the Rochester Epidemiology Project. This sampling frame identified approximately 95% of the residents (according to the 1990 census) and included only Caucasian males. The Flint cohort was closely modeled after the OCS and included a probability sample of African American men selected from households or group dwelling units located in Flint, Michigan, and from selected census tracts in neighboring Genessee County. Prior history of prostate cancer or prior operations on the prostate gland were exclusion criteria for both the Flint Men's Health Study and the OCS. Eligible men were stratified into ten-year age groups: 40 to 49, 50 to 59, 60 to 69, and 70 to 79. Comprehensive interviews were performed to obtain information on potential personal and environmental risk factors for prostate cancer; the AUASI; family history of cancer; health behaviors such as smoking, drinking, and physical activity; occupational or other exposures to selected

Table 5. Urinary symptom frequency (percentage of men with urinary symptoms occurring more than rarely)

	Age Group (yrs)			
	40–49	50–59	60–69	70+
Total number of patients	800	612	436	271
% with symptoms showing strong age relation				
Nocturia	16	29	42	55
Weak stream	25	34	39	49
Stopping or starting	18	25	29	32
Feeling cannot wait	28	32	42	46
Feeling bladder not empty	16	17	23	23
% with symptoms not showing age relation				
Frequent urination (within 2 hrs)	34	34	36	35
Pain or burning	5	6	4	7
Strain or push	12	15	13	15
Repeat within 10 mins	12	11	18	11
Dribbling	37	43	44	36
Difficulty starting	14	18	20	19
Wet clothing	23	25	24	22
Obstructive score[a]				
% with score greater than 7	16	24	27	30
Corrected[b]	15	21	24	29
Median score	3	4	4	4
Corrected[c]	2	3	4	4
AUA score:				
% with score greater than 7	26	33	41	46
Corrected[d]	24	31	36	44
Median score	4	5	6	7

[a]Obstructive score is the sum of weak stream, stopping and starting, dribbling, hesitancy, and incomplete emptying.

[b]Corrected proportion is the age-stratified, weighted mean of dichtomous (0 and 1) variables with weights n/N (responders) and (N-n)/N (initial nonresponders), where N corresponds to the total number of randomly selected eligible and invited men, and n is the number of participants in the main study cohort, within the age decade.

[c]Corrected median scores were calculated by replicating nonresponder questionnaire data to simulate all nonresponders and calculating the median of the combined data for respondents and initial nonresponders. This approach assumes that initial nonresponders for whom data were obtained are representative of all refusals.

[d]AUA composite symptom frequency score not available from the nonresponder study. Corrected proportions were obtained by decreasing the study cohort proportions by the percentage reduction observed for AUA bother score, assuming a similar relationship would apply to the frequency score. Calculation of corrected AUA score median is not practical.

SOURCE: Reprinted from Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, Lieber MM, The prevalence of prostatism: a population-based survey of urinary symptoms, Journal of Urology, 150, 85–89, Copyright 1993, with permission from Lippincott Williams & Wilkins.

Table 6. Clinical correlates of benign prostatic hyperplasia (Flint Men's Health Study)

		Age Group (yrs)				P-value	
	Overall	**40–49**	**50–59**	**60–69**	**70–79**	ANOVA	Trend
Mean prostate vol ± SE (cc)	26.6 ± 0.5	23.3 ± 0.7	26.7 ± 0.8	32.9 ± 1.6	32.8 ± 2.0	0.0001	0.0001
Mean peak flow ± SE (cc/sec)	22.3 ± 0.9	25.6 ± 1.7	20.5 ± 1.2	18.2 ± 1.3	15.4 ± 1.5	0.0002	0.0001
Mean symptom score ± SE	7.3 ± 0.4	6.4 ± 0.6	7.5 ± 0.6	9.0 ± 0.7	7.7 ± 1.1	0.08	0.03
Mean bothersomeness score ± SE	4.0 ± 0.3	2.9 ± 0.5	4.4 ± 0.6	5.4 ± 0.6	5.4 ± 1.0	0.01	0.0001
% symptom score greater than 7	39.6	31.7	43.2	51.7	38.6	0.04	0.07
% bothersomeness score greater than 3	35.0	25.0	36.0	52.9	50.0	0.0004	0.0001

SOURCE: Reprinted from Wei JT, Schottenfeld D, Cooper K, Taylor JM, Faerber GJ, Velarde MA, Bree R, Montie JE, Cooney KA, The natural history of lower urinary tract symptoms in black American men: relationships with aging, prostate size, flow rate and bothersomeness, Journal of Urology, 165, 1,521–1,525, Copyright 2001, with permission from Lippincott Williams & Wilkins.

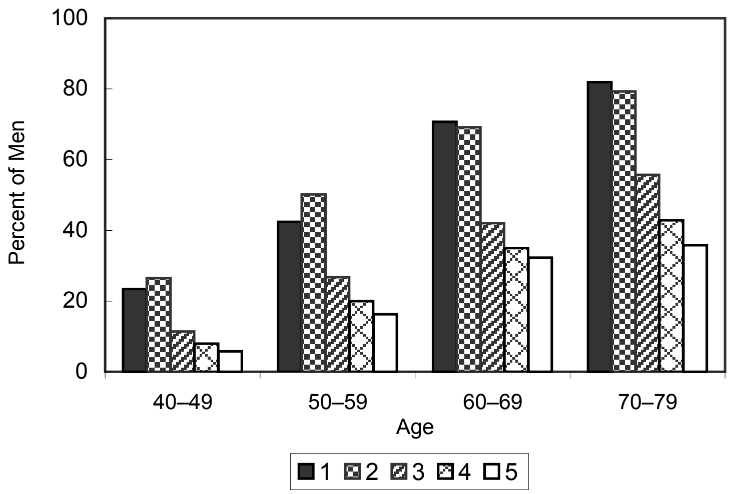

Figure 2. Age-specific prevalence of benign prostatic hyperplasia.
Note: Bar 1, prevalence of pathologically defined benign prostatic hyperplasia from a compilation of five autopsy studies (*n* = 1,075); bars 2 and 3, clinical prevalence in the Baltimore Longitudinal Study of Aging (*n* = 1,075); bar 2 is based on history and physical examination and bar 3 is based on the presence of an enlarged prostate on manual rectal examination; bar 4, prevalence is based on an enlarged prostate on manual rectal examination from a compilation of life insurance examinations (*n* = 6,975); bar 5, community prevalence in Rochester, Minnesota, based on case definition using symptoms, prostate size, and urinary flow rates (*n* = 457).

SOURCE: Adapted from Guess HA, Benign Prostatic hyperplasia: antecedents and natural history, Epidemiologic Reviews, 1992, 14, 131–153, with permission of Oxford University Press.

Table 7. Incidence of acute urinary retention, by baseline age and lower urinary tract symptom severity

	None-to-Mild Symptoms (AUASI ≤ 7)		Moderate-to-Severe Symptoms (AUASI > 7)	
Age	Incidence/1,000 Person-Years	(95% CI)	Incidence/1,000 Person-Years	(95% CI)
40–49	2.6	(0.8–6.0)	3.0	(0.4–10.8)
50–59	1.7	(0.3–4.8)	7.4	(2.7–16.1)
60–69	5.4	(2.0–11.6)	12.9	(6.2–23.8)
70–79	9.3	(3.4–20.3)	34.7	(20.2–55.5)

Total person-years 8344.4, median years of follow-up (25th, 75th percentile) 4.2 (3.6, 4.7).

SOURCE: Reprinted from Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM, Natural history of prostatism: risk factors for acute urinary retention, Journal of Urology, 158, 481–487, Copyright 1997, with permission from Lippincott Williams & Wilkins.

chemicals; general health condition; history of chronic illnesses; sexual activity; health services utilization; and demographic characteristics. Subjects were invited to complete a clinical examination that included serum prostate specific antigen (PSA), as well as transrectal ultrasonography and uroflowmetry. These studies captured a broader range of LUTS than was possible in NHANES-III (6). In the OCS, moderate-to-severe LUTS, defined as AUASI greater than 7, ranged from 26% in men 40 to 49 years of age to 46% in men 70 and older (Table 5) (8, 9).

Using the OCS definition to identify cases, the Flint Men's Health Study found moderate to severe LUTS in 39.6% of African American men, also with a strong age association (Table 6) (10). In autopsy series, the prevalence of histological BPH is even more common (Figure 2) (11). Clinical samples based on men presenting for care allow for more detailed data but may be biased by type and severity of symptoms.

Collectively, all these studies illustrate the great prevalence of LUTS and document the burden of it that occurs with increasing age. As noted above, moderate-to-severe LUTS, defined as AUASI greater than 7, ranged from 26% in the fifth decade of life to 46% in the eighth decade. NHANES-III found no racial/ethnic variation in the prevalence of obstructive symptoms; however, overall LUTS (including irritative symptoms) appear to occur with greater severity in African American men.

NATURAL HISTORY

The natural history of BPH/LUTS is more accurately estimated in community-based cohorts than in self-selected patients seeking medical attention. The former are more likely to represent the full spectrum of illness and less likely to be biased by socioeconomic factors such as access to healthcare. Longitudinal data from the OCS suggest an annual prostate growth rate of 1.6% diagnosed by transrectal ultrasonography (12) and an average annual increase of 0.2 AUASI point (13). Over a median follow-up period of 42 months in the OCS, the proportion of men reporting moderate-to-severe LUTS increased from 33% to 49% (13).

Urinary retention, considered to represent the final symptomatic stage of progressive BPH, occurred in the OCS at an overall incidence of 6.8 episodes per 1,000 person-years of follow-up; subset analyses revealed 34.7 episodes per 1,000 person-years of follow-up in men in their seventies who had moderate-to-severe symptoms (Table 7) (14). These rates are comparable to data subsequently reported in the Health Professionals Followup Study, in which men 45 to 83 years of age were followed from 1992 to 1997. A total of 82 men developed acute urinary retention during 15,851 person-years of follow-up (15). Both studies showed that age, more severe symptoms, and larger prostate size were associated with an increase in the risk of urinary retention.

Table 8. Association between baseline measures of lower urinary tract dysfunction and risk of any treatment during follow-up

	Unadjusted[a]		Unadjusted (clinic cohort)[b]		Adjusted[c]		Adjusted[d]	
Baseline Characteristic	**Relative Risk**	**95% CI**	**Relative Risk**	**95% CI**	**Relative Risk**	**95% CI**	**Relative Risk**	**95% CI**
Age								
40–49[e]	1.0	...	1.0	...	1.0	...	1.0	...
50–59	4.4	2.5–7.7	5.1	1.5–17.9	3.3	0.9–12.0	4.2	1.2–14.8
60–69	7.7	4.4–13.3	10.8	3.2–37.0	3.7	1.0–14.0	4.0	1.1–14.8
70–79	8.7	4.8–15.6	10.1	2.8–36.9	3.2	0.8–12.7	3.1	0.8–12.3
Symptom severity (score)								
None-to-mild (7 or less)[e]	1.0	...	1.0		1.0	...	1.0	...
Moderate-to-severe (greater than 7)	5.0	3.6–7.0	8.4	4.0–17.5	5.3	2.5–11.1	5.6	2.6–11.9
Peak urinary flow rate (ml/sec)								
Greater than 12[e]	1.0	...	1.0	...	1.0	...	1.0	...
12 or Less	3.7	2.7–5.0	5.2	2.9–9.6	2.7	1.4–5.3	2.8	1.4–5.5
Prostate volume (ml)								
30 or Less[e]	...	...	1.0	...	1.0		...	...
Greater than 30	...	...	4.2	2.2–8.2	2.3	1.1–4.7	...	...
Serum PSA (ng/ml)								
1.4 or less[e]	...	...	1.0	...	...	...	1.0	...
Greater than 1.4	...	...	4.0	2.2–7.3	...	...	2.1	1.1–4.2

...data not available.

Association qualified as relative risk with associated 95% CI.

[a]Bivariate (crude) models based on entire cohort.

[b]Bivariate (crude) models based on subset randomly selected with clinical examination.

[c]Multivariate models adjusting for all factors simultaneously, including prostate volume, based on subset with clinical examination.

[d]Multivariate models adjusting for all factors simultaneously, including serum PSA, based on subset with clinical examination.

[e]Reference category.

SOURCE: Reprinted from Jacobsen SJ, Jacobsen DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM, Treatment for benign prostatic hyperplasia among community dwelling men: The Olmstead County study of urinary symptoms and health status, Journal of Urology, 162, 1,301–1,306, Copyright 1999, with permission from Lippincott Williams & Wilkins.

Table 9. Use of imaging tests in evaluation of benign prostatic hyperplasia and/or lower urinary tract symptoms in the male Medicare population, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	217,760	14,977	133,580	8,107	76,380	5,101
Intravenous pyelogram	56,280	3,871	25,400	1,542	14,760	986
Ambulatory surgery center	6,600	454	3,460	210	1,560	104
Inpatient	8,120	558	2,760	168	2,080	139
Hospital outpatient	920	63	520	32	260	17
Physician office	40,640	2,795	18,660	1,132	10,860	725
Transrectal ultrasound	150,960	10,382	99,560	6,042	52,360	3,497
Ambulatory surgery center	5,760	396	4,940	300	4,060	271
Inpatient	3,880	267	1,660	101	1,440	96
Hospital outpatient	900	62	620	38	440	29
Physician office	140,420	9,657	92,340	5,604	46,420	3,100
CT scan abdomen/pelvis with contrast	5,700	392	5,200	316	5,220	349
Ambulatory surgery center	320	22	160	9.7	140	9.3
Inpatient	2,660	183	2,460	149	3,040	203
Hospital outpatient	80	5.5	100	6.1	60	4.0
Physician office	2,640	182	2,480	151	1,980	132
CT scan abdomen/pelvis without contrast	2,420	166	1,680	102	2,460	164
Ambulatory surgery center	140	9.6	60	3.6	100	6.7
Inpatient	1,160	80	920	56	1,440	96
Hospital outpatient	20	1.4	0	0	20	1.3
Physician office	1,100	76	700	42	900	60
CT scan abdomen/pelvis with and without contrast	1,900	131	1,520	92	1,460	97
Ambulatory surgery center	180	12	140	8.5	80	5.3
Inpatient	560	39	660	40	620	41
Hospital outpatient	20	1.4	60	3.6	0	0
Physician office	1,140	78	660	40	760	51
CT scan abdomen, contrast use unspecified						
Inpatient	500	35	220	13	120	8.0

[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 men with benign prostatic hyperplasia.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 10. Diagnostic studies for lower urinary tract symptoms in elderly male Medicare beneficiaries (5% sample, 1991 to 1995)					
	1991	**1992**	**1993**	**1994**	**1995**
Uroflowmetry					
Complex	6,717	7,575	8,528	8,687	8,607
Simple	1,059	936	802	608	535
Cystometrogram					
Complex	2,146	2,081	1,905	1,978	1,917
Simple	622	535	463	450	414
Pressure flow study					
Bladder	274	324	354	492	514
Intra-abdominal	183	226	238	329	343

SOURCE: Reprinted from Baine WB, Yu W, Summe JP, Weis KA, Epidemiologic trends in the evaluation and treatment of lower urinary tract symptoms in elderly male Medicare patients from 1991 to 1995, Journal of Urology, 160, 816–820, Copyright 1998, with permission from Lippincott Williams & Wilkins.

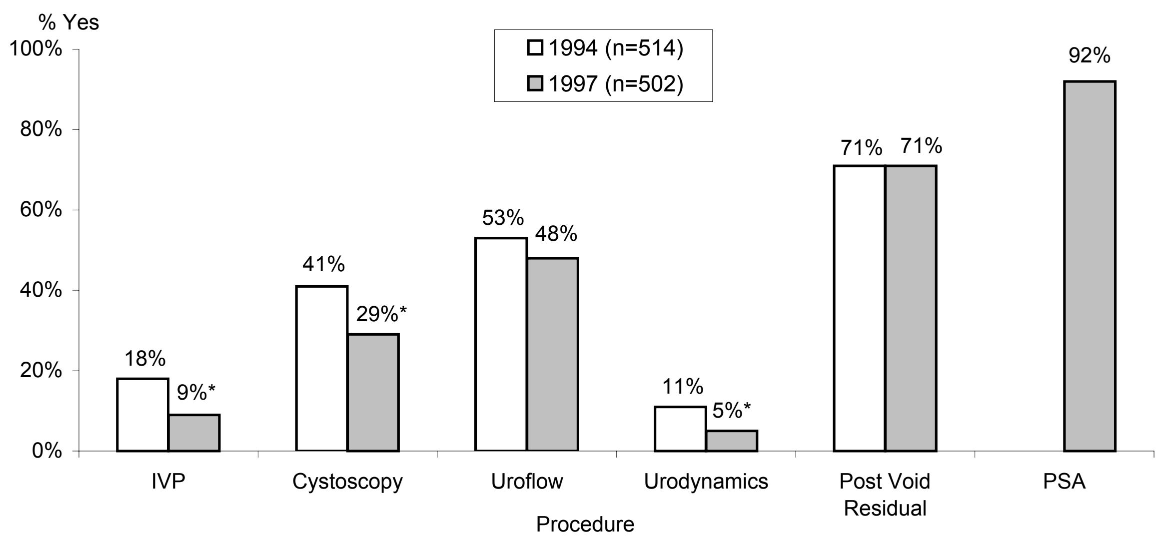

Figure 3. Tests routinely ordered in diagnostic evaluation of patients with BPH.

***Significantly less than in 1994 (p < 0.05).**

SOURCE: Adapted from Journal of Urology, 160, Gee WF, Holtgrewe HL, Blute ML, Miles BJ, Naslund MJ, Nellans RE, O'Leary MP, Thomas R, Painter MR, Meyer JJ, Rohner TJ, Cooper TP, Blizzard R, Fenninger RB, Emmons L, 1997 American Urological Assocation Gallup Survey: changes in diagnosis and management of prostate cancer and benign prostatic hyperplasia, and other practice trends from 1994 to 1997, 1,804–1,807, copyright 1998, with permission from Lippincott Williams & Wilkins.

RISK FACTORS

OCS data revealed that age, prostate volume, and peak urinary flow rate were each significantly associated with AUASI scores but accounted for only 13% of symptom variability. The odds of moderate to severe symptoms increased with age after the fifth decade of life, from 1.9, to 2.9, to 3.4 for men in the sixth, seventh and eighth decades, respectively. Even after adjusting for age, the odds of moderate-to-severe symptoms were 3.5 times greater for men with prostates larger than 50 cc (as determined by transrectal ultrasonography) than for men with smaller prostates. In addition, a peak urinary flow of less than 10 ml/sec was associated with a 2.4-fold risk of moderate-to-severe symptoms (14).

OCS data also showed age to be associated with an increased risk of acute urinary retention. After adjusting for baseline symptom severity and peak urinary flow rate, the relative risk of urinary retention increased after the fifth decade of life, from 0.9, to 2.1, to 4.8 for men in the sixth, seventh, and eighth decades, respectively. Men with baseline AUASI greater than 7 and peak flow rates of 12 ml/sec or less were 2.3 and 2.1 times more likely to develop urinary retention, respectively (14). After multivariate adjustment, increasing age, presence of moderate-to-severe LUTS, decreased peak flow rate, and prostate size (or PSA) were associated with an increased likelihood of receiving treatment for BPH (Table 8).

CLINICAL EVALUATION

Traditionally, intravenous pyelogram (IVP) and transrectal ultrasound have been the most commonly employed imaging examinations for BPH, even though the AHCPR BPH guidelines do not recommend their routine use (16). As expected, following the dissemination of the BPH guidelines in 1994, the use of IVP and TRUS in the Medicare population decreased consistently (Table 9). By 1998, the utilization rates for IVP and TRUS were only 986 per 100,000 and 3,497 per 100,000, representing 75% and 66% decreases from 1992, respectively. CT scans were uncommon in the evaluation of men with BPH.

Other commonly used methods for assessing lower urinary tract function include uroflowmetry, cystometrogram, and pressure flow studies. Medicare claims data indicate that between 1991 and 1995, use of complex uroflowmetry and pressure flow studies increased, while the use of cystometrograms decreased modestly (Table 10). Independent validation of these observations appeared in the 1997 American Urological Association (AUA) Gallup Poll survey of practicing urologists in the United States (5). This survey noted a decrease in the utilization of IVP, uroflowmetry, and urodynamic studies but also noted very high utilization rates for measurement of post-void bladder residual and serum PSA in men with BPH—71% and 92%, respectively (Figure 3).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient and Outpatient Care

Historically, transurethral resection of the prostate (TURP) was the second most commonly performed operation in the United States (cataract surgery was the most common). However, since the introduction of effective alternative approaches in the 1990s, urologists have increasingly recommended pharmacological therapy and minimally invasive procedures (5). Coincident with the increased popularity of these approaches was an increase in the rate of outpatient visits for BPH: from 10,116 per 100,000 in 1994 to 14,473 per 100,000 in 2000 (Table 11). BPH-related visits to emergency rooms declined from 330 per 100,000 in 1994 to 218 per 100,000 in 2000 (Table 12), although the overlapping confidence intervals around these rates should lead to caution in interpretation.

Pharmaceutical Management

Alpha blockers and 5-alpha reductase inhibitors have become first-line therapy for men with symptomatic BPH. The AUA Gallup Poll surveys from 1994 to 1997 found that 88% of urologists recommended alpha blockers for men with moderate urinary symptoms and evidence of prostate enlargement of less than 40 cc. The use of alpha blockers for men with prostates larger than 40 cc was still highly prevalent at 69% (5).

Table 11. Physician office visits and hospital outpatient visits for benign prostatic hyperplasia and/or lower urinary tract symptoms, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Primary reason	2,899,300	6,371 (5,495–7,248)	3,658,367	7,484 (6,294–8,675)	3,990,359	7,754 (6,281–9,226)	4,418,425	8,201 (6,765–9,637)
Any reason	4,603,426	10,116 (8,826–11,406)	6,112,287	12,505 (10,856–14,153)	6,443,185	12,520 (10,531–14,508)	7,797,781	14,473 (12,406–16,540)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population, 40 years and older.

SOURCES: National Hospital Ambulatory Medical Care Survey—Outpatient File, 1994, 1996, 1998, 2000; National Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

Table 12. Emergency room visits by adult males with benign prostatic hyperplasia and/or lower urinary tract symptoms listed as primary diagnosis, count, rate[a] (95% CI)

	Count	Rate
1994	150,377	330 (201–460)
1996	117,716	241 (130–352)
1998	155,923	303 (194–412)
2000	117,413	218 (117–319)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population, 40 years and older.

SOURCE: National Hospital Ambulatory Medical Care Survey— ER File, 1994, 1996, 1998, 2000.

The Medical Therapy of Prostatic Symptoms (MTOPS) Study, a multicenter, randomized controlled trial sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases, evaluated whether treatment with doxazosin (an alpha blocker) and finasteride (a 5-alpha reductase inhibitor) in combination was more effective than either drug alone in preventing the clinical progression of BPH. Clinical progression was defined as either a worsening in the AUASI score of 4 points or more, acute urinary retention, incontinence, renal insufficiency, or recurrent urinary tract infection. Results from MTOPS suggest that combination therapy was twice as effective as monotherapy in reducing the risk of progression (66% risk reduction for combination, 39% for doxazosin, and 34% for finasteride) (17).

Additional details on the medications prescribed to treat men with LUTS are available from the National Ambulatory Medical Care Survey (NAMCS) (Table 13). In 1994 and 1996, terazosin was the primary pharmacological agent used for BPH, being prescribed in 14% to 15% of BPH visits. However, with the introduction of more specific selective agents, terazosin was replaced by doxazosin and tamsulosin, which in 2000 constituted 23% of the prescriptions written at BPH-related outpatient visits. The prescription of finasteride in 6.5% and 7.3% of BPH visits in 1994 and 2000, respectively, suggests that it is used in a specific subset of men with BPH.

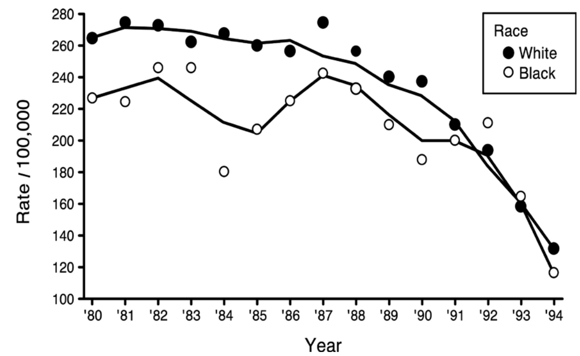

Figure 4. **Annual age-adjusted discharge rate for prostatectomy, 1980 to 1994, by race. Data from: National Hospital Discharge Survey.**

SOURCE: Reprinted with permission from Urology, 53, Xia Z, Roberts RO, Schottenfeld D, Lieber MM, Jacobsen SJ, Trends in prostatectomy for benign prostatic hyperplasia among black and white men in the United States: 1980 to 1994, 1,154–1,159, 1999, with permission from Elsevier Science.

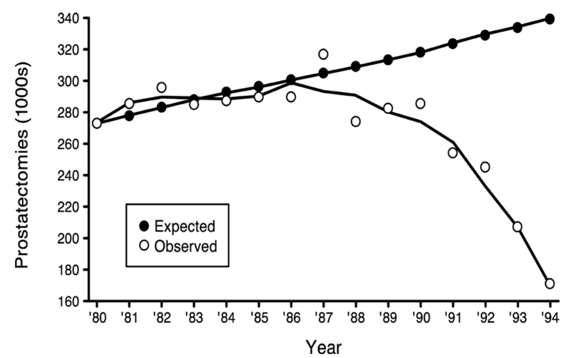

Figure 5. **Observed and expected number of discharges for prostatectomy, 1980 to 1994; expected number based on 1980 discharge rates. Data from: National Hospital Discharge Survey.**

SOURCE: Reprinted with permission from Urology, 53, Xia Z, Roberts RO, Schottenfeld D, Lieber MM, Jacobsen SJ, Trends in prostatectomy for benign prostatic hyperplasia among black and white men in the United States: 1980 to 1994, 1,154–1,159, 1999, with permission from Elsevier Science.

Table 13. Count of prescriptions written at physicians' offices during visits for benign prostatic hyperplasia and/or lower urinary tract symptoms

	1992		1994		1996		1998		2000	
Medicine	# of Rx	% of Visits for BPH at Which This Rx Was Given	# of Rx	% of Visits for BPH at Which This Rx Was Given	# of Rx	% of Visits for BPH at Which This Rx Was Given	# of Rx	% of Visits for BPH at Which This Rx Was Given	# of Rx	% of Visits for BPH at Which This Rx Was Given
Terazosin/Hytrin™	*	*	688,717	15	830,314	14	*	*	*	*
Doxazosin/Cardura™	*	*	*	*	*	*	*	*	819,043	11
Tamsulosin/Flomax™	*	*	*	*	*	*	*	*	870,889	12
Oxybutynin/Ditropan™	*	*	*	*	*	*	*	*	*	*
Detrol™	*	*	*	*	*	*	*	*	*	*
Detrol SA™	*	*	*	*	*	*	*	*	*	*
Finasteride/Proscar™	*	*	289,070	6.5	*	*	*	*	552,483	7.3
Ditropan XL™	*	*	*	*	*	*	*	*	*	*

Rx, prescription.
*Figure does not meet standard for reliability or precision.
SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 14. Use of inpatient surgical procedures to treat symptoms of benign prostatic hyperplasia

Surgical Procedure	1994	1996	1998	2000
Open prostatectomy	5,648	4,617	4,341	4,354
TURP	136,377	103,644	88,907	87,407
Balloon dilatation	279	161	148	161
Laser prostatectomy	0	10,616	3,019	2,045
TUNA	0	0	0	35
TUMT	0	0	0	14

TURP, transurethral resection of the prostate; TUNA, transurethral needle ablation; TUMT, transurethral microwave therapy.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 15. Inpatient stays by male Medicare beneficiaries with benign prostatic hyperplasia and/or lower urinary tract symptoms listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	154,320	1,048 (1,043–1,053)	82,060	539 (535–543)	59,760	413 (409–416)
Total < 65	5,420	175 (171–180)	3,240	94 (91–97)	2,600	76 (73–79)
Total 65+	148,900	1,280 (1,273–1,286)	78,820	669 (665–674)	57,160	518 (513–522)
Age						
65–74	78,240	1,081 (1,073–1,089)	37,600	523 (518–528)	25,380	395 (390–400)
75–84	57,800	1,637 (1,623–1,650)	33,580	918 (908–928)	25,340	692 (684–701)
85–94	12,560	1,589 (1,562–1,617)	7,420	875 (855–894)	6,320	730 (712–748)
95+	300	386 (343–430)	220	268 (233–304)	120	137 (113–161)
Race/ethnicity						
White	135,820	1,095 (1,089–1,101)	72,260	556 (552–560)	52,600	430 (426–434)
Black	10,380	815 (799–830)	6,820	493 (481–504)	4,180	313 (304–323)
Asian	…	…	180	247 (211–283)	560	408 (375–442)
Hispanic	…	…	1,080	544 (512–576)	1,240	369 (349–390)
N. American Native	…	…	60	298 (224–373)	120	429 (354–504)
Region						
Midwest	39,400	1,062 (1,052–1,073)	21,440	556 (549–564)	16,920	458 (451–464)
Northeast	35,780	1,128 (1,117–1,140)	17,540	551 (543–560)	10,960	394 (387–402)
South	55,840	1,066 (1,057–1,075)	28,020	511 (505–517)	21,600	402 (397–408)
West	20,740	923 (911–936)	13,080	564 (554–574)	9,180	410 (402–419)

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier Files, 1992, 1995, 1998.

Table 16. Visits to ambulatory surgery centers by male Medicare beneficiaries for benign prostatic hyperplasia and/or lower urinary tract symptoms listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	72,260	491 (487–494)	62,520	411 (408–14)	53,900	372 (369–375)
Total < 65	3,340	108 (104–112)	3,720	108 (105–111)	3,480	101 (98–105)
Total 65+	68,920	592 (588–597)	58,800	499 (495–503)	50,420	457 (453–461)
Age						
65–74	41,080	568 (562–573)	33,380	464 (460–469)	26,660	415 (410–420)
75–84	23,940	678 (669–686)	21,680	593 (585–601)	19,540	534 (526–541)
85–94	3,780	478 (463–493)	3,580	422 (408–436)	4,120	476 (461–490)
95+	120	155 (128–182)	160	195 (165–226)	100	114 (92–137)
Race/ethnicity						
White	62,580	505 (501–509)	54,820	422 (418–425)	47,220	386 (383–390)
Black	5,700	447 (436–459)	5,620	406 (395–416)	4,220	316 (307–326)
Asian	…	…	280	384 (339–429)	400	292 (263–320)
Hispanic	…	…	480	242 (220–263)	1,020	304 (285–323)
N. American Native	…	…	…	…	…	…
Region						
Midwest	24,840	670 (661–678)	19,480	505 (498–512)	17,420	471 (464–478)
Northeast	18,640	588 (579–596)	12,900	406 (399–413)	11,480	413 (406–421)
South	24,660	471 (465–477)	24,960	455 (449–461)	20,040	373 (368–379)
West	4,100	182 (177–188)	5,040	217 (211–223)	4,880	218 (212–224)

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Surgical Management

The advent of pharmacotherapy was associated with a dramatic decline in hospitalizations for TURP throughout the 1990s (Figures 4 and 5 and Table 14) (18), most notably between 1992 and 1995 (Table 15). This decline is consistent with published literature that demonstrates that the use of TURP peaked during the 1980s but declined between 1991 and 1997 by 50% among Caucasian men and 40% among African American men suffering from BPH (19). Table 16 presents Medicare data illustrating that surgery for BPH declined across almost all age, racial/ethnic, and geographic strata of patients. Overall, surgical visits by Medicare beneficiaries declined from 491 per 100,000 in 1992 to 372 per 100,000 in 2000. There was a slight increase in the rate of BPH surgeries in the West between 1992 and 1995, but the rate remained stable in 1998. Among those who were hospitalized for BPH surgery, lengths of stay (LOS) were shorter, consistent with trends following widespread adoption of prospective payment and managed care systems (Table 17). By 2000, the mean LOS was less than 3 days in all but the most elderly patients.

In the 1990s, several minimally invasive surgical therapies (MIST) were introduced. These include laser ablation, transurethral needle ablation (TUNA), transurethral microwave therapy (TUMT), high-energy focused ultrasound (HIFU), and hot-water thermotherapy. The 1997 AUA Gallup Poll of practicing urologists indicated that while 95% had performed TURP in the prior year, only 26% had performed a laser prostatectomy. Only 3% had performed TUNA or TUMT (5). Use of minimally invasive therapies is highly dependent on the availability and cost of

Table 17. Trends in mean inpatient length of stay (days) for adult males hospitalized with benign prostatic hyperplasia and/or lower urinary tract symptoms listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	3.8	3.1	3.1	2.8
Age				
40–44	3.3	2.2	2.8	3.3
45–54	3.1	2.6	2.6	2.1
55–64	3.2	2.6	2.8	2.4
65–74	3.5	2.9	2.9	2.7
75–84	4.2	3.4	3.3	3.0
85+	5.3	4.4	4.3	4.0
Race/ethnicity				
White	3.7	3.1	3.1	2.8
Black	4.5	3.5	3.6	3.6
Asian/Pacific Islander	2.9	2.9	3.1	3.1
Hispanic	3.9	3.4	3.7	2.9
Other	4.5	2.9	3.2	3.1
Region				
Midwest	3.8	3.3	3.2	2.9
Northeast	4.8	3.7	3.7	3.2
South	3.6	3.0	2.9	2.8
West	2.7	2.4	2.7	2.4
MSA				
Rural	3.7	3.1	3.0	2.8
Urban	3.8	3.1	3.1	2.8

MSA, metropolitan statistical area.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

special instrumentation. As a result, not all MIST procedures have survived. According to data from the Healthcare Cost and Utilization Project (HCUP), of the MIST procedures performed in the inpatient setting, only TUNA and TUMT increased by the end of the decade (Table 14). Data from Medicare indicate that the majority of TUNA and TUMT procedures were performed in the ambulatory surgery center setting or physician office, as opposed to the inpatient setting, as expected given their minimally invasive nature (Table 18). BPH procedures in ambulatory surgery centers on commercially insured men 65 to 74 years of age increased substantially toward the end of the decade, from 264 per 100,000 in 1998 to 352 per 100,000 in 2000 (Table 19).

Age-adjusted data from NHANES-III revealed no difference in the odds of BPH surgery by racial/ethnic group, education, geographic region, or urban/rural area; however, never-married men were 70% less likely to have undergone BPH surgery (6).

Nursing Home Care

The aging of the US population has increased the number of men with BPH. Curiously, this phenomenon is not reflected in data from the National Nursing Home Survey, which indicates the presence of BPH in only 5,760 to 6,034 per 100,000 male nursing home residents (Table 20). The lower than expected number of cases identified may reflect administrative undercoding of BPH as a comorbid condition.

ECONOMIC IMPACT

The economic burden of BPH can be stratified into three areas: (1) direct medical costs associated with treatment; (2) indirect costs associated with absenteeism, work limitations, and premature mortality; and (3) intangible costs associated with pain, suffering, and grief.

Direct Costs

We estimate the direct cost of medical services provided at hospital inpatient and outpatient settings, emergency departments, and physicians' offices to treat BPH in the United States in 2000 to have been approximately $1.1 billion (Table 21). This estimate does not include the costs of outpatient prescriptions and nonprescription medications or alternative medicine visits reported by a small percentage of men with BPH. After adjusting for inflation (data not shown), total medical spending for BPH has declined over time, particularly among the Medicare population (Tables 21 and 22). This reduction in spending is largely attributable to a dramatic decline in inpatient expenditures. Total hospitalization spending for BPH fell by more than half among Medicare beneficiaries age 65 and over, from $743 million in 1992 to $315 million in 1998 (in nominal $).

Spending on outpatient prescription drugs for the treatment of BPH in 1996–1998 was $194 million annually, according to estimates from the Medical Expenditure Panel Survey (MEPS). The majority of the prescriptions and pharmacy spending were

Table 18. Surgical procedures used to treat symptoms of benign prostatic hyperplasia among male adult Medicare beneficiaries, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	174,260	11,986	122,860	7,456	95,340	6,366
Open prostatectomy	6,420	442	3,760	228	2,880	192
Ambulatory surgery center	0	0	0	0	0	0
Inpatient	6,380	439	3,740	227	2,860	191
Hospital outpatient	0	0	0	0	0	0
Physician office	40	2.8	20	1.2	20	1.3
Balloon dilation	1,080	74	200	12	320	21
Ambulatory surgery center	440	30	40	2.4	180	12
Inpatient	600	41	140	8.5	140	9.3
Hospital outpatient	20	1.4	0	0	0	0
Physician office	20	1.4	20	1.2	0	0
TUNA	0	0	0	0	420	28
Ambulatory surgery center	0	0	0	0	360	24
Inpatient	0	0	0	0	0	0
Hospital outpatient	0	0	0	0	0	0
Physician office	0	0	0	0	60	4.0
TURP	165,880	11,409	105,560	6,406	79,800	5,329
Ambulatory surgery center	1,720	118	8,620	523	7,660	512
Inpatient	162,560	11,180	96,000	5,826	71,360	4,765
Hospital outpatient	0	0	140	8.5	140	9.3
Physician office	1,600	110	800	49	640	43
Laser prostatectomy	0	0	12,600	765	7,720	516
Ambulatory surgery center	0	0	7,560	459	4,720	315
Inpatient	0	0	4,860	295	2,820	188
Hospital outpatient	0	0	160	10	100	6.7
Physician office	0	0	20	1.2	80	5.3
TUIP	880	61	740	45	860	57
Ambulatory surgery center	260	18	220	13	380	25
Inpatient	620	43	460	28	480	32
Hospital outpatient	0	0	20	1.2	0	0
Physician office	0	0	40	2	0	0
TUMT	0	0	0	0	3,340	223
Ambulatory surgery center	0	0	0	0	2,760	184
Inpatient	0	0	0	0	40	2.7
Hospital outpatient	0	0	0	0	20	1.3
Physician office	0	0	0	0	520	35

TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate; TUIP, transurethral incision of the prostate; TUMT, transurethral microwave therapy.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 male adult Medicare beneficiaries with a diagnosis of benign prostatic hyperplasia and/or lower urinary tract symptoms rate is per 100,000 Medicare beneficiaries with a diagnosis of BPH/LUTS.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 19. Visits to ambulatory surgery centers for benign prostatic hyperplasia and/or lower urinary tract symptoms procedures listed as primary procedure by males having commercial health insurance, count[a], rate[b]

	1998		2000	
	Count	Rate	Count	Rate
Total	254	58	434	83
Age				
40–44	12	*	13	*
45–54	48	24	81	35
55–64	130	128	233	190
65–74	46	264	78	352
75–84	15	*	26	*
85+	3	*	3	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1998, 2000.

Table 20. Male nursing home residents with an admitting or current diagnosis of benign prostatic hyperplasia and/or lower urinary tract symptoms, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Total[b]	23,576	5,760 (4,762–6,759)	28,492	6,626 (5,526–7,727)	26,929	6,034 (4,986–7,082)
Age						
40–84	13,966	5,056 (3,912–6,199)	16,877	5,649 (4,420–6,878)	13,747	4,551 (3,439–5,663)
85+	9,611	7,222 (5,273–9,172)	11,615	8,852 (6,581–11,122)	13,182	9,141 (6,897–11,384)
Race						
White	19,142	5,756 (4,645–6,867)	25,535	7,364 (6,080–8,649)	24,195	6,759 (5,521–7,998)
Other	4,268	5,707 (3,402–8,012)	2,930	3,659 (1,686–5,632)	2,734	3,174 (1,473–4,875)

[a]Rate per 100,000 nursing home residents in the same demographic stratum.
[b]Persons of unspecified race are included in the totals.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

for Hytrin™, followed by Cardura™ and Proscar™ (Table 23).

To examine the incremental medical costs associated with a diagnosis of BPH, we used data from 280,000 primary beneficiaries aged 18 to 64 with employer-provided insurance coverage in 1999. We estimated medical expenditures for persons with and without a primary diagnosis of BPH in 1999, controlling for differences in insurance coverage (medical and drug benefits), patient demographics, and health status (medical comorbidities). These data estimate the incremental direct annual medical costs for BPH to be $2,577 (Table 24). The average annual cost for men without a BPH claim was $3,138, while the claim for those with BPH was $5,715.

Indirect Costs

Work lost by men with BPH was measured by MarketScan in 1999 and is shown in Tables 25 and 26. One-tenth of the men with BPH missed work, losing an average of 7.3 hours annually. Each visit for outpatient care was associated with an average work loss of 4.7 hours. Because this dataset does not provide the proportion of working men who have BPH, it is impossible to gauge the aggregate extent of indirect costs as missed work from MarketScan

Table 21. Expenditures for benign prostatic hyperplasia and share of costs, by site of service (% of total)

	Year			
Service Type	1994	1996	1998	2000
Total[a]	$1,067,100,000	$1,045,800,00	$1,036,200,000	$1,099,500,000
Inpatient	$740,600,000 (69.4%)	$633,800,000 (60.6%)	$566,800, 000 (54.7%)	$579,400,000 (52.7%)
Physician Office	$278,500,000 (26.1%)	$365,000,000 (34.9%)	$409,300,00 (39.5%)	$472,800,000 (43.0%)
Hospital Outpatient	$23,500,000 (2.2%)	$26,100,000 (2.5%)	$29,000,000 (2.8%)	$22,000,000 (2.0%)
Emergency Room	$24,500,000 (2.3%)	$20,900,000 (2.0%)	$31,000,000 (3.0%)	$25,300,000 (2.3%)

[a]Total unadjusted expenditures exclude spending on outpatient prescription drugs for the treatment of BPH. Average drug spending for BPH-related conditions is estimated at $194 million annually for the period 1996 to 1998.

NOTE: Percentages may not add to 100% because of rounding.

SOURCES: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 22. Expenditures for Medicare beneficiaries age 65 and over for treatment of benign prostatic hyperplasia, by site of service (% of total)

	Year		
Service Type	1992	1995	1998
Total	$1,132,000,000	$861,300,000	$776,000,000
Inpatient	$743.100,000 (54.7%)	$408,400,000 (47.4%)	$315,000,000 (40.6%)
Outpatient			
Physician Office	$291,200,000 (54.7%)	$322,500,000 (37.4%)	$327,500,000 (42.2%)
Hospital Outpatient	$8,700,000 (54.7%)	$11,900,000 (1.4%)	$13,400,000 (1.7%)
Ambulatory Surgery	$73,400,000 (54.7%)	$100,000,000 (11.6%)	$100,300,000 (12.9%)
Emergency Room	$15,500,000 (54.7%)	$18,500,000 (2.1%)	$19,800,000 (2.6%)

NOTE: Percentages may not add to 100% because of rounding.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

analyses. Inclusion of indirect costs greatly increases estimates of the overall economic burden of BPH.

CONCLUSIONS

The substantial amount of data documenting the prevalence of BPH and its therapies attests to the tremendous impact of this condition on the health and quality of life of American men. One of the most basic and yet most difficult tasks facing the medical community will be to standardize the definition of clinical BPH, recognizing that the diagnosis is rarely histologically confirmed. Standardization of the clinical definition would allow for consistency among studies and would facilitate research on the prevention, diagnosis, and treatment of this condition.

Increasingly, BPH therapy trends indicate a move away from the gold-standard operative options toward less-invasive pharmacologic or MIST options. The use of medication for BPH has had the most obvious impact, with the proliferation of newer agents that specifically act on the prostate and bladder. Analogous to TURP, the use of most MIST procedures for BPH has declined, with the exception of TUNA and TUMT, which increased during the final years of the 1990s. Ongoing reevaluation of these trends will be necessary as newer therapies are made available and to determine the proportion of men initially started on pharmacologic agents who eventually go on to have more invasive therapy.

Although this chapter summarizes a number of important trends, others, including evolving

Table 23. Average annual spending and use of selected outpatient prescription drugs for treatment of benign prostatic hyperplasia, 1996–1998[a]

Drug Name	Number of Rx Claims	Mean Price	Total Expenditures
Hytrin™	1,923,054	$67.39	$129,594,632
Cardura™	605,744	$49.26	$29,838,949
Proscar™	518,038	$66.77	$34,589,375
Total			$194,022,956

Rx, prescription.

[a]Estimates include prescription drug claims with a corresponding diagnosis of BPH and exclude drugs for which number of claims could not be reliably estimated due to data limitations. Including expenditures for excluded prescription drugs for which the number of claims could not be reliably estimated would increase total drug spending by approximately 2%, to $198.6 million.

SOURCE: Medical Expenditure Panel Survey, 1996–1998.

Table 24. Estimated annual expenditures of privately insured male employees with and without a medical claim for benign prostatic hyperplasia in 1999[a]

	Annual Expenditures (per person)			
	Persons without BPH (N=270,431)	Persons with BPH (N=8,483)		
	Total	Total	Medical	Rx Drugs
Total	$3,138	$5,715	$4,544	$1,170
Age				
45–54	$3,227	$5,550	$4,440	$1,109
55–64	$3,293	$5,765	$4,573	$1,170
Region				
Midwest	$3,018	$6,339	$5,221	$1,117
Northeast	$3,035	$5,080	$3,977	$1,102
South	$3,327	$6,405	$5,153	$1,252
West	$3,169	$7,023	$5,624	$1,399

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.

SOURCE: Ingenix, 1999.

Table 25. Average annual work loss of persons treated for benign prostatic hyperplasia (BPH) and/or lower urinary tract symptoms (LUTS) (95% CI)

			Average Work Absence (hrs)		
	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
BPH/LUTS	2,013	10%	0.2 (0.1–0.3)	7.1 (4.6–9.6)	7.3 (4.8–9.8)

[a]Individuals with an inpatient or outpatient claim for BPH/LUTS and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: MarketScan, 1999.

Table 26. Average work loss associated with a hospitalization or an ambulatory care visit for benign prostatic hyperplasia (BPH) and/or lower urinary tract symptoms (LUTS) (95% CI)

	Inpatient Care		Outpatient Care	
	Number of Hospitalizations[a]	Average Work Absence (hrs)	Number of Outpatient Visits	Average Work Absence (hrs)
BPH/LUTS	*	*	3,036	4.7 (3.3–6.1)

*Figure does not meet standard for reliability or precision.

[a]Unit of observation is an episode of treatment. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

SOURCE: MarketScan, 1999.

technologies and the use of complementary and alternative therapies for BPH, remain poorly characterized. These options have garnered a great deal of public interest, but their efficacy, particularly in relation to established therapies, remains largely undetermined. Moreover, these trends will undoubtedly have a major impact on healthcare costs. Similarly, measures of the indirect costs of BPH care are poorly quantified, and the cost-effectiveness of pharmacologic and surgical interventions for BPH remains uncertain. Efforts to examine the cost implications of new therapies should be undertaken as a prerequisite for widespread adoption.

Future efforts must also address the underlying etiology of BPH. Clinical epidemiological studies that focus on the effects of sociodemographic factors such as race/ethnicity and access to healthcare on BPH prevalence and the relationship between LUTS and other conditions such as diabetes and sexual dysfunction have the potential to improve care. Given the dramatic trends of the past 10 years and the persistent variation in the management of BPH, quality of care delivered for BPH should be evaluated. The delivery of high-quality care should be the goal of all clinicians, and that goal goes hand in hand with the dissemination of evidence-based guidelines (2).

REFERENCES

1. McConnell JD, Barry MJ, Bruskewitz RC. Benign Prostatic Hyperplasia: Diagnosis and Treatment. Clinical Practice Guideline. Agency for Health Care Policy and Research. Clinical Practice Guidelines Quick Reference Guide for Clinicians 1994;8:1-17.
2. Jacobsen SJ, Girman CJ, Guess HA, Oesterling JE, Lieber MM. New diagnostic and treatment guidelines for benign prostatic hyperplasia. Potential impact in the United States. Arch Intern Med 1995;155:477-81.
3. Jacobsen SJ, Guess HA, Panser L, Girman CJ, Chute CG, Oesterling JE, Lieber MM. A population-based study of healthcare-seeking behavior for treatment of urinary symptoms. The Olmsted County Study of Urinary Symptoms and Health Status Among Men. Arch Fam Med 1993;2:729-35.
4. Barry MJ, Fowler FJ, Jr., O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148:1549-57; discussion 1564.
5. Gee WF, Holtgrewe HL, Blute ML, Miles BJ, Naslund MJ, Nellans RE, O'Leary MP, Thomas R, Painter MR, Meyer JJ, Rohner TJ, Cooper TP, Blizzard R, Fenninger RB, Emmons L. 1997 American Urological Association Gallup survey: Changes in diagnosis and management of prostate cancer and benign prostatic hyperplasia, and other practice trends from 1994 to 1997. J Urol 1998;160:1804-7.
6. Platz EA, Smit E, Curhan GC, Nyberg LM, Giovannucci E. Prevalence of and racial/ethnic variation in lower urinary tract symptoms and noncancer prostate surgery in U.S. men. Urology 2002;59:877-83.
7. Meigs JB, Mohr B, Barry MJ, Collins MM, McKinlay JB. Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men. J Clin Epidemiol 2001;54:935-44.
8. Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, Lieber MM. The prevalence of prostatism: a population-based survey of urinary symptoms. J Urol 1993;150:85-9.
9. Girman CJ, Jacobsen SJ, Guess HA, Oesterling JE, Chute CG, Panser LA, Lieber MM. Natural history of prostatism: relationship among symptoms, prostate volume and peak urinary flow rate. J Urol 1995;153:1510-5.
10. Wei JT, Schottenfeld D, Cooper K, Taylor JM, Faerber GJ, Velarde MA, Bree R, Montie JE, Cooney KA. The natural history of lower urinary tract symptoms in black American men: relationships with aging, prostate size, flow rate and bothersomeness. J Urol 2001;165:1521-5.
11. Guess HA. Benign prostatic hyperplasia: antecedents and natural history. Epidemiol Rev 1992;14:131-53.
12. Rhodes T, Girman CJ, Jacobsen SJ, Roberts RO, Guess HA, Lieber MM. Longitudinal prostate growth rates during 5 years in randomly selected community men 40 to 79 years old. J Urol 1999;161:1174-9.
13. Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM. Treatment for benign prostatic hyperplasia among community dwelling men: the Olmsted County study of urinary symptoms and health status. J Urol 1999;162:1301-6.
14. Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, Lieber MM. Natural history of prostatism: risk factors for acute urinary retention. J Urol 1997;158:481-7.
15. Meigs JB, Barry MJ, Giovannucci E, Rimm EB, Stampfer MJ, Kawachi I. Incidence rates and risk factors for acute urinary retention: the health professionals followup study. J Urol 1999;162:376-82.
16. Andersen JT, Jacobsen O, Standgaard L. The diagnostic value of intravenous pyelography in infravesical obstruction in males. Scand J Urol Nephrol 1977;11:225-30.
17. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL Jr, Dixon CM, Kusek JW, Lepor H, McVary KT, Nyberg LM, Jr, Clarke HS, Crawford ED, Diokno A, Foley JP, Foster HE, Jacobs SC, Kaplan SA, Kreder KJ, Lieber MM, Lucia MS, Miller GJ, Menon M, Milam DF, Ramsdell JW, Schenkman NS, Slawin KM, Smith JA; Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2449-51.
18. Xia Z, Roberts RO, Schottenfeld D, Lieber MM, Jacobsen SJ. Trends in prostatectomy for benign prostatic hyperplasia among black and white men in the United States: 1980 to 1994. Urology 1999;53:1154-9.
19. Wasson JH, Bubolz TA, Lu-Yao GL, Walker-Corkery E, Hammond CS, Barry MJ. Transurethral resection of the prostate among Medicare beneficiaries: 1984 to 1997. For the Patient Outcomes Research Team for Prostatic Diseases. J Urol 2000;164:1212-5.

CHAPTER 3

Prostate Cancer

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Prostate Cancer

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INTRODUCTION

Prostate cancer is the most common solid tumor found in American men. One in approximately every 6 American men over the age of 50 will be diagnosed with prostate cancer in his lifetime (1). This astonishing statistic underscores the significance of this cancer not only as a urologic disease, but also as a general public health burden. It should be noted that the lifetime risk of prostate cancer has increased considerably in the past 15 years, following the introduction of prostate-specific antigen (PSA) testing. Although the risk of being diagnosed with prostate cancer is high, the risk of dying of the disease is much lower: Roughly one in every 33 American men over the age of 50 actually dies of prostate cancer. In this respect, there is truth in the clinical adage, "More men die with prostate cancer than of it." While the mortality burden associated with prostate cancer is less than might be expected, the physical, psychological, and economic burdens are considerable.

DEFINITION AND DIAGNOSIS

Unlike malignant neoplasms arising in other organs, of which there are numerous pathologic subtypes, the overwhelming majority of malignant prostate tumors are primary adenocarcinomas arising from the glandular tissue within the prostate. Roughly 85% of these tumors occur in the periphery of the gland and are multifocal in nature. In addition to adenocarcinoma, rare pathologic variants also arise in the prostate, including mucinous adenocarcinoma, small cell (neuroendocrine) carcinoma, squamous cell carcinoma, rhabdomyosarcoma, and leiomyosarcoma. Finally, the prostate can be invaded by malignant neoplasms from other organs, including transitional cell carcinoma of the bladder and lymphoma (2). While these rare pathologic variants are of academic importance, we refer exclusively to primary adenocarcinoma in this discussion. Table 1 presents the diagnosis and procedure codes associated with prostate cancer.

Prior to the 1980s, men with prostate cancer usually presented in one of three ways: (1) they had lower urinary tract symptoms, which the doctor believed were due to benign prostatic hyperplasia (BPH), and then underwent transuretheral resection of the prostate (TURP) and were incidentally found to have prostate cancer on pathologic analysis of the TURP specimen; (2) they presented with advanced prostate cancer causing bony pain and/or severe local symptoms, a biopsy then confirmed the suspected diagnosis, and treatment was initiated; and (3) a digital rectal exam revealed an abnormality that led to a prostate biopsy.

Patterns of care in prostate cancer have changed tremendously in the past 20 years, altering the way patients with this tumor present and how they are evaluated before and after diagnosis. To understand current trends in prostate cancer, it is necessary to be familiar with three important scientific/clinical advances that have impacted the care of older men with prostate disease in North America and Western Europe. The first of these three "turning points" was the introduction of nerve-sparing radical retropubic

Table 1. Codes used in the diagnosis and management of prostate cancer

Males 40 years or older with one or more of the following:	
ICD-9 diagnosis codes	
185	Malignant neoplasm of prostate
233.4	Carcinoma in situ of prostate
236.5	Neoplasm of uncertain behavior of prostate
ICD-9 procedure codes	
60.13	Closed [percutaneous] biopsy of seminal vesicles
60.5	Radical prostatectomy
60.62	Perineal prostatectomy
CPT procedure codes	
55810	Prostatectomy, perineal radical
55812	Prostatectomy, perineal radical; with lymph node biopsy(s) (limited pelvic lymphadenectomy)
55815	Prostatectomy, perineal radical; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric and obturator nodes
55840	Prostatectomy, retropubic radical, with or without nerve sparing
55842	Prostatectomy, retropubic radical, with or without nerve sparing; with lymph node biopsy(s) (limited pelvic lymphadenectomy)
55845	Prostatectomy, retropubic radical, with or without nerve sparing; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes
55859	Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy
55860	Exposure of prostate, any approach, for insertion of radioactive substance
55862	Exposure of prostate, any approach, for insertion of radioactive substance; with lymph node biopsy(s) (limited pelvic lymphadenectomy)
55865	Exposure of prostate, any approach, for insertion of radioactive substance; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric and obturator nodes
55866	Laparoscopy, surgical prostatectomy, retropubic radical, including nerve sparing
55873	Cryosurgical ablation of the prostate (includes ultrasonic guidance for interstitial cryosurgical probe placement)
J9217[a]	Leuprolide acetate (for depot suspension), 7.5 mg
J9218[a]	Leuprolide acetate, per 1 mg
J9219[a]	Leuprolide acetate implant, 65 mg
J9202[a]	Goserelin acetate implant, per 3.6 mg

[a]Included in definition of outpatient and physician office visits only.

prostatectomy in 1982 (3). This surgical technique allowed the urologic surgeon to preserve during prostatectomy the neurovascular bundles that course lateral to the prostate. This preserved erectile function after surgery, making the operation more palatable to patients. This surgical innovation was a driving force behind the increasing utilization of surgery to treat prostate cancer in the late 1980s and early 1990s (discussed later in this chapter). It also removed some of the stigma of a prostate cancer diagnosis and increased public awareness of the disease. The second turning point was the development of effective oral therapies for lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH). Although BPH is discussed elsewhere in greater detail in this compendium, it deserves mention here as well, since most men with prostate cancer have pathologic evidence of BPH. Prior to the introduction and widespread use of alpha-blocker therapy for the treatment of LUTS/BPH in the early 1990s, the

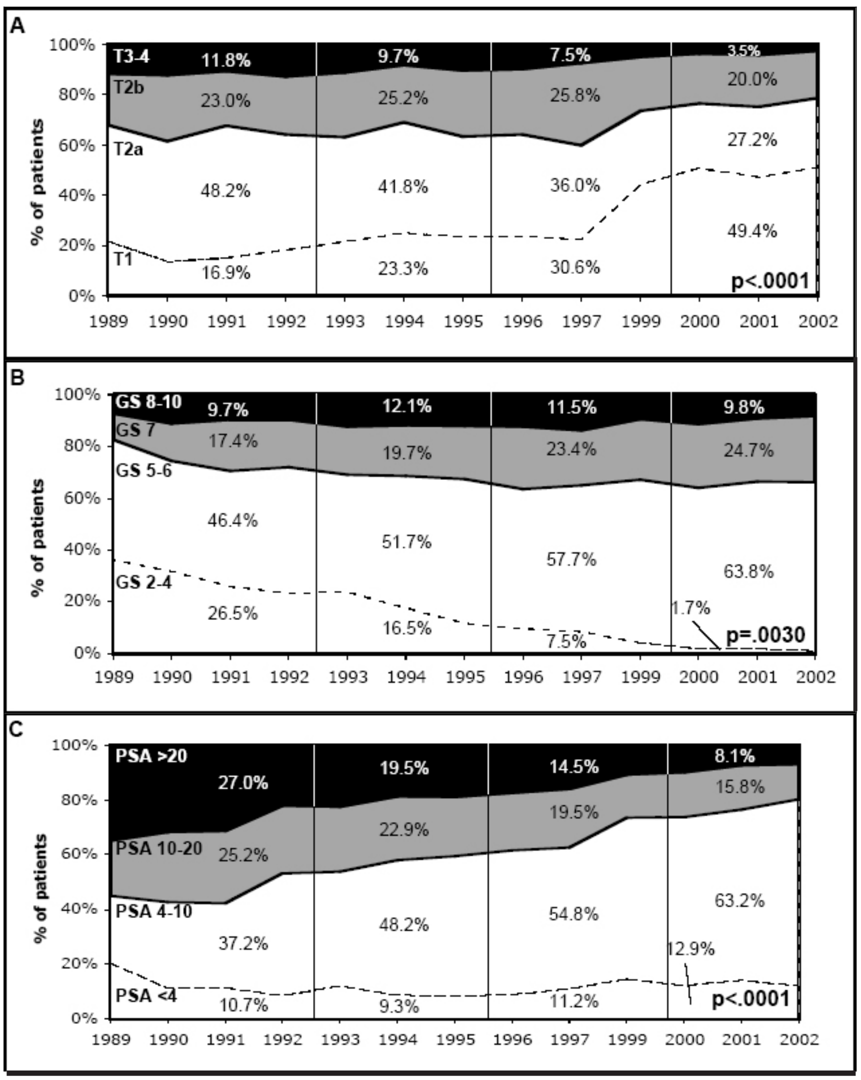

Figure 1. **Time trends in individual risk characteristics for prostate cancer.**

A: clinical T stage; B: Gleason score; C: serum PSA levels. Characteristic levels defining low, intermediate, and high risk are shaded white, gray, and black, respectively.

SOURCE: Reprinted from Journal of Urology, 170, Cooperberg MR, Lubeck DP, Mehta SS, Carroll PR. Time trends in clinical risk stratification for prostate cancer: implications for outcomes (data from CaPSURE), S21–S27, Copyright 2003, with permission from American Urological Association.

Table 2. Use of prostate needle biopsy with and without transrectal ultrasound (TRUS) among Medicare beneficiaries, count[a], rate[b], age-adjusted rate[c]

	1992					1995				
	Count	Rate		Age-Adjusted Rate	% with ultrasound guidance	Count	Rate		Age-Adjusted Rate	% with ultrasound guidance
Total[d]	450,200	2,935	(2,897–2,973)		49	330,460	2,035	(2,005–2,066)		67
A ge										
40–49	380	68	(38–99)		37	180	25	(8.7–41.5)		33
50–59	2,920	418	(350–485)		43	3,420	405	(345–466)		77
60–69	119,720	2,088	(2,036–2,141)		51	99,700	1,739	(1,691–1,787)		69
70–79	248,000	4,135	(4,064–4,207)		50	177,240	2,789	(2,732–2,846)		68
80+	79,180	3,362	(3,260–3,465)		44	49,920	1,929	(1,854–2,004)		59
Race/ethnicity										
White	391,820	3,005	(2,963–3,046	2,991	50	285,480	2,039	(2,006–2,073)	2,039	67
Black	33,500	2,737	(2,607–2,866)	2,715	41	30,460	2,231	(2,120–2,342)	2,189	64
Hispanic	…	...		…	…	3,540	1,795	(1,533–2,057)	1,896	66
Asian	...	...		...	...	1,440	1,804	(1,391–2,216)	1,703	53
Region										
Midwest	112,440	3,037	(2,959–3,115)	3,061	48	79,780	2,074	(2,010–2,137)	2,084	66
Northeast	99,620	3,116	(3,031–3,201)	3,092	31	75,500	2,275	(2,203–2,346)	2,245	53
South	169,840	3,252	(3,184–3,320)	3,256	58	125,940	2,249	(2,194–2,303)	2,256	74
West	65,020	2,268	(2,191–2,345)	2,262	56	45,360	1,463	(1,404–1,523)	1,469	74

	1998					2001				
	Count	Rate		Age-Adjusted Rate	% with ultrasound guidance	Count	Rate		Age-Adjusted Rate	% with ultrasound guidance
Total[d]	275,060	1,630	(1,603–1,657)		70	282,640	1,601	(1,575–1,627)		78
Age										
40–49	380	47	(26–68)		68	420	48	(27–68)		67
50–59	3,960	401	(345–456)		64	4,660	406	(354–458)		71
60–69	78,780	1,401	(1,358–1,445)		73	84,600	1,467	(1,423–1,511)		80
70–79	150,080	2,258	(2,208–2,309)		71	150,100	2,206	(2,157–2,256)		78
80+	41,860	1,494	(1,430–1,557)		63	42,860	1,403	(1,344–1,462)		73
Race/ethnicity										
White	238,960	1,662	(1,632–1,691)	1,646	71	240,040	1,594	(1,566–1,622)	1,580	79
Black	23,740	1,644	(1,551–1,737)	1,751	66	27,480	1,752	(1,660–1,844)	1,851	72
Hispanic	5,180	1,342	(1,180–1,504)	1,342	69	5,400	1,268	(1,118–1,419)	1,226	69
Asian	2,700	1,507	(1,255–1,760)	1,373	70	2,740	1,090	(908–1,272)	955	65
Region										
Midwest	72,080	1,840	(1,780–1,899)	1,841	67	71,560	1,777	(1,719–1,835)	1,774	78
Northeast	58,400	1,725	(1,663–1,787)	1,680	62	53,820	1,546	(1,488–1,604)	1,502	72
South	103,200	1,748	(1,701–1,796)	1,765	75	111,700	1,789	(1,742–1,835)	1,821	81
West	38,060	1,161	(1,109–1,213)	1,172	76	41,620	1,193	(1,142–1,243)	1,180	80

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries age 40 and above in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

primary therapy for this condition was TURP (4). As mentioned above, patients undergoing TURP for LUTS were sometimes found to have prostate cancer upon pathologic analysis of the surgical specimen. Therefore, as TURP rates dropped in the late 1980s and early 1990s (4), the number of men who had prostate cancer diagnosed in this way dropped as well. The third and perhaps most important of the three landmark events was the introduction of PSA testing. First described in the general medical literature in 1987, PSA, a serine protease, was purported to be a reliable screening test for the presence of occult prostate cancer and an accurate tumor marker after the diagnosis was established and treatment rendered (5). The use of prostate cancer screening, in the form of a PSA test and a digital rectal examination (DRE), increased exponentially in the early 1990s, changing the primary method by which prostate cancer was detected and the way in which men presented with the disease.

The majority of patients with prostate cancer now present with asymptomatic localized disease detected either by an elevated PSA test or an abnormal DRE. Data from Cooperberg and colleagues (6) document that nearly half of patients with newly diagnosed prostate cancer presented with clinical stage T1 disease in 2000, as shown in Figure 1. Patients who present with symptoms tend to have LUTS, such as nocturia, hesitancy, and intermittency. Patients presenting with a large, bulky tumor causing bilateral ureteral obstruction or painful bony metastases, fairly common prior to the introduction of PSA testing, are now quite rare.

The primary method of determining whether prostate cancer is present is the transrectal prostate needle biopsy. Historically, prostate biopsies were

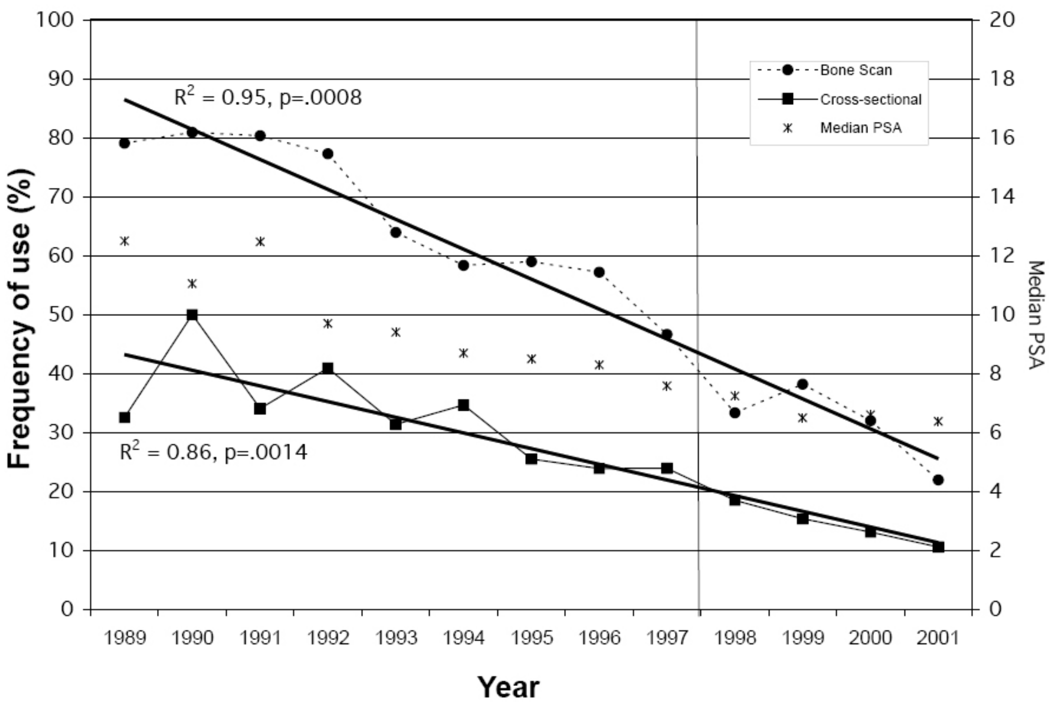

Figure 2. Time trends in imaging test utilization rates in patients at low and intermediate risk for prostate cancer showing percent that underwent bone scan or cross-sectional imaging per year of diagnosis.

SOURCE: Reprinted from Journal of Urology, 168, Cooperberg MR, Lubeck DP, Grossfeld GD, Mehta SS, Carroll PR, Contemporary trends in imaging test utilization for prostate cancer staging: data from the cancer of the prostate strategic urologic research endeavor, 491–495, Copyright 2002, with permission from American Urological Association.

performed transperineally, often with fine-needle aspiration techniques. Advances in ultrasound technology and improvements in spring-loaded needle designs led to the widespread adoption of the transrectal ultrasound-guided prostate needle biopsy as the primary diagnostic approach. As illustrated in Table 2, data from a 5% Medicare sample indicate that biopsy rates were highest in 1992 (2,935 biopsies per 100,000 male Medicare beneficiaries), then declined and stabilized by 2001 (1,601 per 100,000). This decline and stabilization represent the exhaustion of the "prevalent pool" of prostate cancer patients who were diagnosed soon after the introduction of PSA testing. The relatively stable but high rate between 1998 (1,630 per 100,000) and 2001 documents the considerable burden that prostate cancer screening places on healthcare resources. The positive biopsy rate within the 5% Medicare sample for 2001 was 40.3%, indicating that more than half of the men undergoing biopsy were not immediately found to have prostate cancer. The positive biopsy rate was approximated by identifying new ICD-9 coding of prostate cancer in the 6-month period that followed the biopsy. The Medicare biopsy data also revealed interesting regional and ethnic variation. The age-adjusted biopsy rate was highest in the South and lowest in the West. The exact reasons for the disparities are unclear, but it is difficult to ascribe them to clinical differences among older men in the different regions. In addition, the percentage of biopsies performed using ultrasound guidance increased from 49% in 1992 to 78% in 2001. While this is consistent with clinical guidelines and the diffusion of advanced ultrasound technologies into the community, it should be noted that the Northeast region consistently had lower rates of ultrasound utilization than other geographic areas. In addition, African American men were less likely to undergo an ultrasound-guided biopsy than were

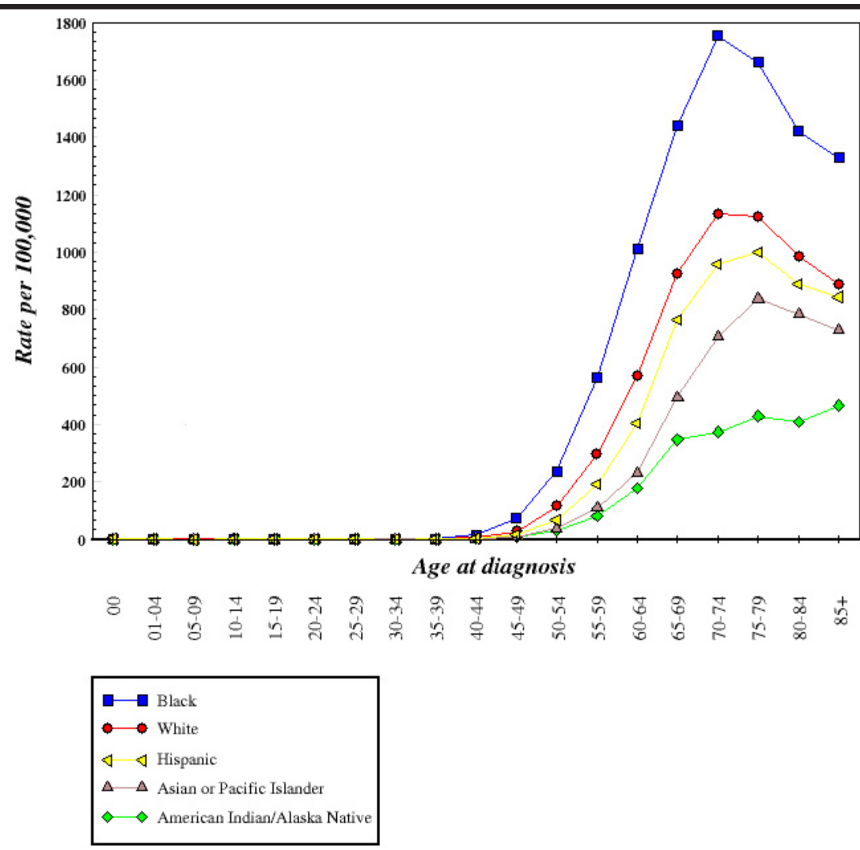

Figure 3. Crude incidence rates for prostate cancer, by race/ethnicity.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov).

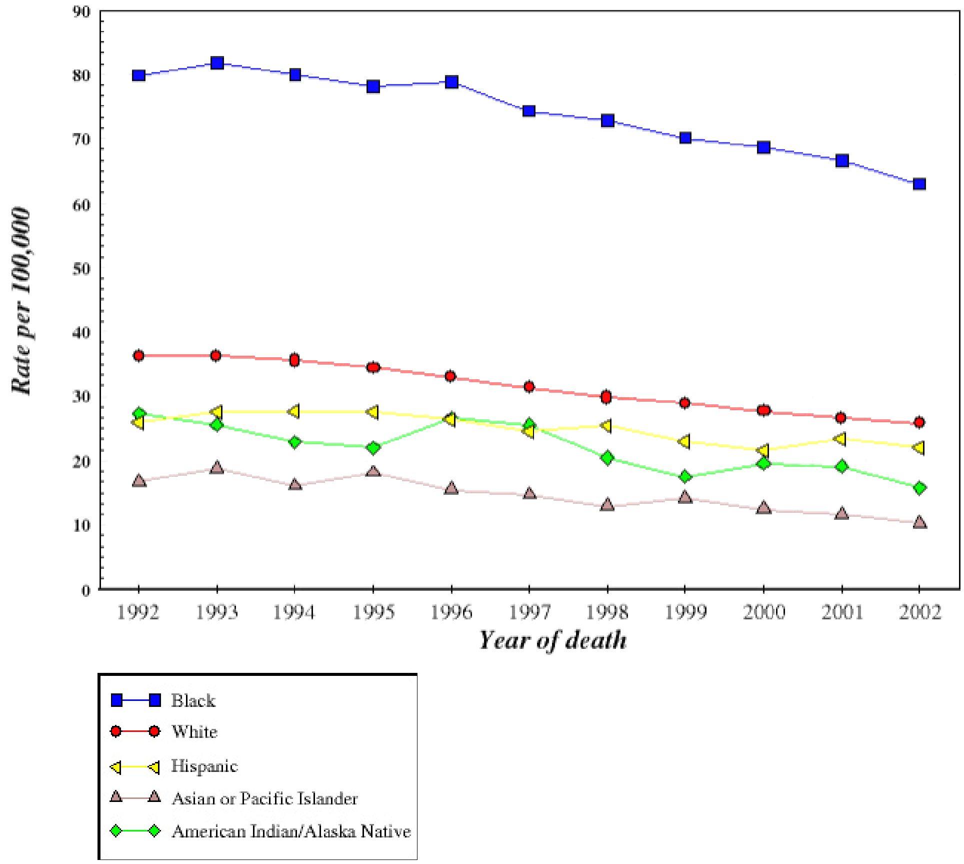

Figure 4. **Mortality rates for prostate cancer, 1992–2002, age-adjusted, all ages, by race/ethnicity.**

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov).

Caucasian men at all time points. These regional and ethnic differences in patterns of care merit further study, as they may represent correctable differences in access to care.

Once the diagnosis of prostate cancer is established, the workup depends upon the suspected stage at presentation. Patients with higher PSA levels, more pathologically undifferentiated tumors, and/or suspected metastatic disease routinely undergo nuclear medicine scans to determine if the cancer is present in the bone. The use of routine bone scans in newly diagnosed prostate cancer has steadily declined in recent years as patients have presented with earlier-stage disease (7). Routine computed tomography (CT) and/or magnetic resonance imaging (MRI) add little to the staging of prostate cancer. Neither CT nor routine MRI is particularly helpful in accurately identifying nodal involvement (8-10). Some researchers have suggested that MRI imaging with an endorectal coil can identify extracapsular extension of prostate cancer and aid in decision-making (11). However, the ability to perform these procedures is generally limited to selected academic centers; hence, MRI has a minimal role in the staging of prostate cancer in the community. It is important to note that although their use has declined, these imaging studies are still probably employed more often than needed. The CaPSURE™ database, a large observational disease registry of prostate cancer survivors, documents that despite guidelines recommending limited imaging for patients presenting with lower-stage disease, in 2001 roughly 25% of low- and intermediate-risk patients underwent bone scan, and 10% underwent CT or MRI (Figure 2) (7).

RISK FACTORS

Age, Race, and Family History

Age, race, and family history are well-established and often-quoted risk factors for prostate cancer incidence. The incidence of prostate cancer rises dramatically with age, as shown in Figure 3, peaking at age 70–74 at 1,134 per 100,000 for Caucasians and 1,753 per 100,000 for African Americans (12). Figure 3 also illustrates the trend in prostate cancer incidence by racial/ethnic group in the United States. African American men have an incidence rate persistently higher than that of any other racial-ethnic group—for each age group, their rate of developing prostate cancer is roughly 1.5 to 2 times higher than the rate for Caucasians. The rate of prostate cancer mortality among African American men is also approximately twice that of Caucasians (Figure 4). In contrast, American Indian/Alaskan Natives have the lowest incidence of prostate cancer in the United States, and Asians/Pacific Islanders have the lowest mortality rate from it (12). Although the data are equivocal, it appears that Hispanic men may have a somewhat lower risk of developing prostate cancer than Caucasian men. Further research regarding this important topic is necessary, as the number of Hispanic men in the US population is increasing.

As shown in Figure 5, the incidence of prostate cancer worldwide varies dramatically, with men in China and parts of Southeast Asia having incidence rates of less than 5 to 10 per 100,000, (13) compared with African American men in the United States, who have a rate of 265 per 100,000 (age-standardized 2002 rates) (13). These dramatic differences by racial/ethnic group have led researchers to examine risk factors for prostate cancer that may vary by race or culture. Another explanation for worldwide regional variations may be differing use of PSA screening in different countries.

Family history is also an important risk factor. A man with a history of prostate cancer in a first-degree relative has approximately two to three times the risk of a man without such a family history. This association appears to be consistent across African Americans, Caucasians, and Asians (14). At least one study reported a higher prevalence of familial

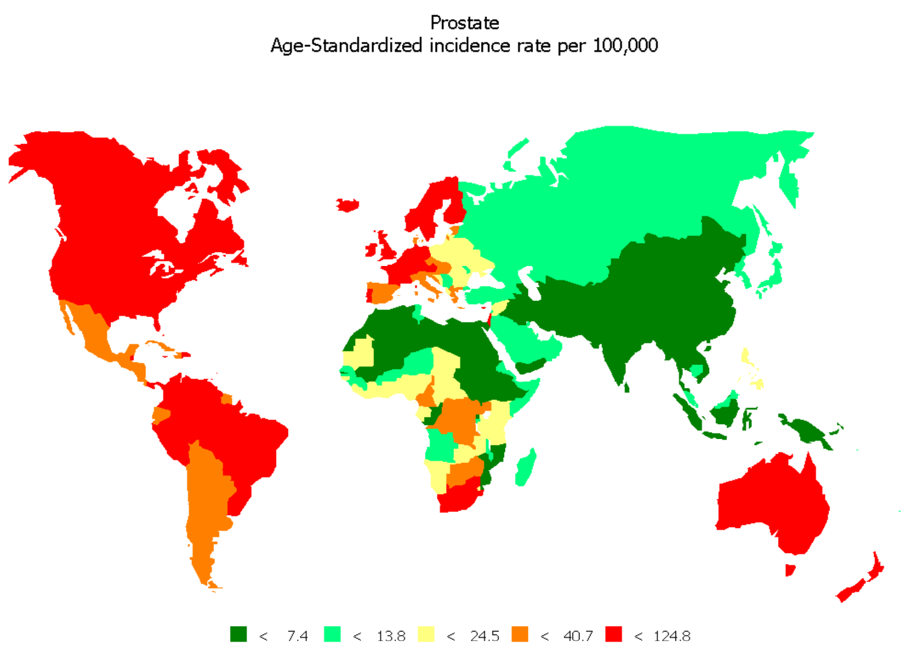

Figure 5. Worldwide incidence of prostate cancer.

SOURCE: Globocan 2002, International Agency for Research on Cancer.

prostate cancer among African Americans than in Caucasians (31% vs 22%) (15). These associations suggest that there may be an important hereditary genetic component to prostate cancer etiology. Based on a large study of twins from several Scandinavian countries, it has been estimated that 42% (95% CI, 29–50%) of the variation in prostate cancer occurrence may be due to hereditary factors (16). However, this estimate does not take into account the potential effects of gene/environment interactions on the risk of developing prostate cancer.

Diet

The dramatic differences in prostate cancer incidence worldwide have led researchers to examine several environmental risk factors that vary by culture, especially diet. The majority of the evidence for diet and prostate cancer focuses on relationships with incidence of the disease, not with progression or mortality. The epidemiology of diet and prostate cancer was recently reviewed in detail (17) and is summarized below and in Table 3.

Vegetables, Fruits, and Related Micronutrients

Although the data are mixed, it is likely that vegetables and soy/legumes impart some protective benefit against risk of developing prostate cancer (18-25). Tomatoes, tomato products, and lycopene (the primary carotenoid in tomatoes) have been consistently linked to a reduced risk of incident prostate

Table 3. Nutritional risk factors for prostate cancer incidence, recurrence, and mortality

Food or nutrient	Direction of Association with Risk of Prostate Cancer Incidence	Direction of Association with Prostate Cancer Recurrence or Mortality	Overall Quality of Evidence
Selenium	Inverse		Strong
Tomatoes and lycopene	Inverse	Inverse[a] (possible postdiagnostic effect on recurrence)	Good
Other carotenoids (e.g., Beta-carotene)	Inverse, esp. among those low in other carotenoids	Inverse[a] (prediagnostic supplemental beta-carotene effect on mortality, by MnSOD status)	Good[a]
Vitamin E	Inverse (effect seen mainly among smokers)	Inverse[a] (possible prediagnostic effect for mortality)	Good
Vitamin D	Inverse		Good
Calcium and dairy	Null to positive (inverse for calcium supplements and early-stage disease[a])		Good
Red meat	Positive		Good
Fish/marine omega-3 fatty acids	Inverse	Inverse[a] (possible prediagnostic effect for mortality; possible pre- and postdiagnostic effects for recurrence)	Fair to good
Soy/isoflavones	Null to inverse	Null for PSA recurrence after treatmenta	Fair[a]
Tea/polyphenols	Null to inverse		Fair[a]
Zinc	Positive		Fair[a]
Heterocyclic amines	Positive		Fair[a]

[a]Limited data available

SOURCE: Chan JM, Gann PH, Giovannucci EL, Role of diet in prostate cancer development and progression, J Clin Oncol, 2005, 23(32):8,152-8,160. Reprinted with permission from the American Society of Clinical Oncology.

cancer. While fewer data exist on other carotenoids, some studies have observed inverse associations with intake or levels of plasma lutein, beta-cryptoxanthin, and zeaxanthin (24, 26-36)

Soy consumption is fairly low in most Western populations, where many of the largest epidemiologic studies with the most follow-up have been conducted, making its effects difficult to study. In a few epidemiologic studies that have examined soy or its primary phytochemicals (genistein, daidzein, and equol), inverse associations have been observed, (32, 37-40) although they have not always been statistically significant (41, 42).

Vitamin E has been associated with a reduction of up to 40% in the risk of prostate cancer incidence and mortality (43-47) and is the focus of an ongoing primary prevention study, the Selenium and Vitamin E Cancer Prevention Trial (SELECT). The Alpha-Tocopherol Beta-Carotene (ATBC) Cancer Prevention Trial found a statistically significant 30–40% reduction in prostate cancer incidence and mortality among men randomized to daily 50 IU supplements of alpha-tocopherol (a common supplement form of vitamin E) vs placebo (48). Interestingly, all participants in this trial, which was originally focused on lung cancer as an outcome, had a substantial smoking history; and in the Health Professionals Follow-Up Study (HPFS), greater supplemental vitamin E intake was associated with decreased risk of advanced prostate cancer only among smokers (46). Some studies (46, 49-53) have observed no association between prostate cancer and vitamin E.

Selenium may have pro-apoptotic, antiangiogenic, antiproliferative, or antioxidant properties to protect against prostate cancer (54-69). The Nutrition Prevention of Cancer Trial (59) reported a halving of risk of prostate cancer incidence among men randomized to selenium supplements vs placebo; several prospective studies have observed 50–65% reductions in prostate cancer associated with greater physiologic measures of selenium (54, 60, 64).

Milk, Dairy, and Calcium

Several studies (70-72) have found milk, calcium, and dairy products to be associated with a greater risk of prostate cancer. In the HPFS, for example, men who consumed > 2000 mg vs < 500 mg of calcium daily had almost five times the risk of developing advanced prostate cancer (73). However, secondary results from a randomized clinical trial on calcium supplements and colorectal adenomas reported a null to inverse association between prostate cancer and calcium supplements. The majority of cases observed in that trial were early-stage PSA-detected cancers, whereas many observational studies have reported elevated risks from milk, dairy, or calcium for advanced or metastatic prostate cancer. It has been hypothesized that this apparent discrepancy between trial and observational studies' results may be due to calcium having different actions on prostate cancer development depending on tumor stage, phenotype, or timing within the disease course. The leading hypothesized mechanism by which dairy or milk intake may affect prostate cancer risk involves the effects of calcium intake on circulating levels of 1,25(OH)2,D3, the most biologically active form of vitamin D, which has been shown to inhibit growth of prostate cancer cells (18, 74).

Meat and Fat

Several studies suggest that total and specific fats and meat intake may be associated with prostate cancer. While results are mixed, saturated and alpha-linolenic fatty acids have been positively associated with prostate cancer risk, while long-chain marine omega-3 fatty acids may impart some protection. Saturated fatty acids or meat may affect prostate cancer through the insulin-like growth factor-I (IGF-I) and androgen pathways (75-82).

There is suggestive epidemiologic evidence that fish or the marine omega-3 fatty acids may afford some protection against prostate cancer (83-87). It is hypothesized that they or their ratio to omega-6 fatty acids may influence inflammatory pathways by inhibiting production of prostaglandins (i.e., PGE2) or modulating COX-2 expression and may thereby potentially affect prostate cancer development (88-96). Further evidence of a role for inflammation in prostate cancer comes from data suggesting that non-steroidal anti-inflammatory drugs may be inversely associated with prostate cancer risk (97-99).

Gene-Diet Interactions

Recent studies have identified potential gene-diet interactions associated with prostate cancer risk, adding support to the evidence of involvement of vegetables and related micronutrients in prostate cancer. Manganese-superoxide dismutase (MnSOD) is an antioxidant enzyme that has been identified as a potential tumor-suppressor gene in prostate cancer (100, 101). A few studies have found that a specific MnSOD variant is related to a greater risk of prostate cancer (28, 102). In the Physicians' Health Study (PHS), men with the MnSOD Ala/Ala genotype had a 50% *lower* risk of prostate cancer if they had high serum levels of antioxidants (i.e., selenium, vitamin E, and lycopene combined) but a twofold *increased* risk if they were low in antioxidants, compared with men who did not have the Ala/Ala genotype and who had low antioxidant levels (p-value for interaction = 0.02) (28, 103). A similar interaction effect was observed for beta-carotene randomization vs placebo (the PHS was also a randomized clinical trial for heart disease and cancer): men with the Ala/Ala variant who were assigned beta-carotene had a 63% lower risk of fatal prostate cancer than those assigned to placebo (p-value for interaction = 0.03).

All of the studies discussed above address the relationship between various dietary risk factors and prostate cancer incidence. There are also limited data on the effect of diet after diagnosis, specifically the effect of diet on recurrence and/or survival. Several studies of diet and prostate cancer incidence observed stronger associations with risk of advanced, metastatic, or fatal prostate cancer (e.g., for lycopene/tomatoes, vitamin E, selenium, milk/calcium, zinc, meat/saturated and alpha-linolenic fatty acid, fish) (17). In the HPFS, higher tomato sauce and fish intake *after* diagnosis were associated with reduced risks of prostate cancer recurrence and progression in a cohort of prostate cancer survivors (104). A few studies of men with prostate cancer reported that lycopene or tomato sauce may decrease PSA or tumor volume; these results must be interpreted cautiously, however, as the studies were small, some did not have a control group, (105) and some had unbalanced randomization (106). One study reported a greater risk of prostate cancer death associated with higher saturated fat intake after diagnosis (107)

Hormonal Risk Factors

Insulin-like growth factor-I (IGF-I), sex hormones, and their associated binding proteins have also been examined for their potential biological roles in prostate cancer development and progression. IGF-I has been consistently positively associated with the development of prostate cancer (80, 81). The recently completed Prostate Cancer Prevention Trial (PCPT) (108) specifically studied the 5-alpha reductase inhibitor, finasteride, as a preventive agent. While the study found that finasteride substantially reduced prostate cancer risk, the results were controversial and further study is needed.

Body Size and Physical Activity

The evidence for an association between body size and risk of prostate cancer remains equivocal, with some studies reporting small to moderate positive associations, (109-114) the majority of studies observing no association, (14, 115-122), and a few reporting inverse associations (115, 123-125). Overall, studies have not reported any strong relationships between adult body size and the risk of prostate cancer. A few prospective studies suggest that body mass index (BMI) is slightly positively associated with risk of prostate cancer mortality (126, 127). This is consistent with additional findings that obesity at the time at diagnosis and plasma leptin correlate positively with worse tumor features (128-131).

Studies on physical activity have had conflicting results, (14, 111, 113, 120, 132-151) but some suggest an inverse association (74, 120, 132, 136, 137, 140-143, 145-147, 150, 152-154). A review by Torti et al. (154) in 2004 reported that among 27 studies published between 1976 and 2002 examining physical activity and prostate cancer, 16 observed a reduced risk associated with greater activity levels, and nine of these had statistically significant results.

PREVALENCE AND INCIDENCE

In the United States, prostate cancer has an estimated annual incidence of 176 cases per 100,000 men (Table 4). According to the American Cancer Society, in 2006, 234,460 men in the United States will develop prostate cancer and 27,350 men will die of it (Table 4) (155). While prostate cancer is the third leading cause of cancer in men, after lung/bronchus and colorectal, and is estimated to cause 118,200 deaths in 2006, (155) it is also clear that many more men are diagnosed with prostate cancer than will die from the disease each year. The prevalence of prostate cancer,

Table 4. Incidence[a], mortality[a], estimated new cases, and deaths for the most common cancer sites among men in the United States, 2006

	Cancer Site			
	Incidence	Mortality	Estimated new cases	Estimated new deaths
Lung/bronchus	77.8	73.5	92,700 (13%)	90,330 (31%)
Colon & Rectum	42.1	19.9	72,800 (10%)	27,870 (10%)
Prostate	176.3	28.1	234,460 (33%)	27,351 (9%)
Urinary Bladder	35.9	7.5	44,690 (6%)	8,990 (3%)

[a]Rate per 100,000, age-adjusted to the US standard population.

SOURCE: Cancer Statistics, 2006. American Cancer Society Surveillance Research.

by age category, is 3% for men aged 60–64; 6% for men 65–69; 10% for men 70–74; 13% for men 75–79; 15% for men 80–84; and 14% for men over 85. More than 1.8 million men are estimated to live with the disease in the United States (156).

Recent trends in prostate cancer incidence in the United States reflect the increasing use of serum-based PSA testing to screen for the disease (Figure 6) (157). During the past two decades, incidence rates peaked in 1992 at 237 per 100,000 (age-adjusted, all races and ages) (12), declined steeply until 1995, and then rose at approximately 1.7% per year through 2000. In 2000, 2001, and 2002, the annual age-adjusted incidence rates were 180, 181, and 176 per 100,000, respectively (Table 5). In contrast, mortality rates have been steadily declining at approximately 4% per year since 1994 (157). It is speculated that this decline reflects the beneficial effects of early diagnosis with

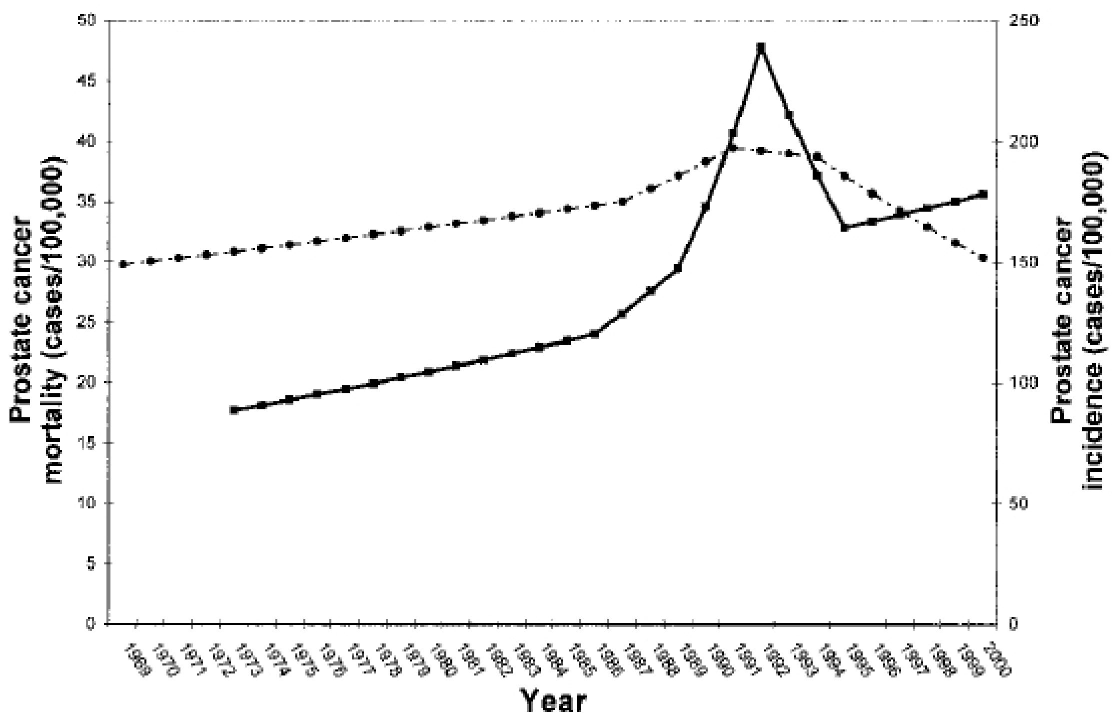

Figure 6. Prostate cancer incidence (solid line) and mortality (broken line).

SOURCE: Reprinted from Journal of Urology, 172, Chan JM, Jou RM, Carroll PR, The relative impact and future burden of prostate cancer in the United States, S13–S17, Copyright 2004, with permission from American Urological Association..

Table 5. Incidence rates for prostate cancer, by race/ethnicity and age, age-adjusted[a]

	All Males			White Males			Black Males		
	All	< 65	≥ 65	All	< 65	≥ 65	All	< 65	≥ 65
Year of Diagnosis									
1975	94	14	650	92	13	640	141	27	929
1976	98	15	674	97	14	674	141	29	911
1977	100	15	691	99	14	681	159	29	1,057
1978	99	15	681	98	15	671	148	27	985
1979	103	15	715	102	15	708	162	26	1,100
1980	106	15	731	105	15	728	161	34	1,040
1981	109	17	745	108	16	743	162	34	1,042
1982	108	16	743	107	16	740	168	32	1,110
1983	112	17	764	111	17	762	171	34	1,117
1984	112	17	764	110	16	758	179	37	1,158
1985	115	18	790	115	18	785	170	32	1,126
1986	119	19	813	119	18	815	168	34	1,093
1987	134	22	908	134	21	917	189	36	1,244
1988	137	22	934	139	22	942	191	35	1,267
1989	145	24	983	146	24	989	192	37	1,261
1990	171	29	1,152	172	29	1,165	222	44	1,449
1991	215	39	1,429	216	39	1,439	288	57	1,883
1992	237	49	1,535	238	49	1,540	327	77	2,051
1993	209	51	1,306	204	49	1,275	342	94	2,063
1994	180	49	1,088	174	47	1,052	311	94	1,806
1995	169	50	989	163	48	961	279	97	1,531
1996	168	53	965	164	52	938	280	99	1,526
1997	173	55	985	169	54	962	278	96	1,537
1998	169	55	964	165	53	946	280	101	1,519
1999	181	61	1,017	176	58	989	286	110	1,499
2000	180	61	1,001	176	59	982	284	112	1,478
2001	181	63	993	178	61	987	261	112	1,291
2002	176	64	954	172	62	935	276	114	1,396

[a]Rates are per 100,000 and are age-adjusted to the 2000 United States standard population.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) Public-Use Data (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

PSA screening or improved treatments. However, it has also been noted that declines in mortality may be attributable to other causes, such as earlier and widespread use of androgen deprivation therapy. Specifically, Lu-Yao and colleagues (158) compared prostate-cancer-specific mortality between two population-based cohorts of men with prostate cancer from King County, Washington, and the state of Connecticut. Although PSA utilization rates and treatment patterns differed widely between the two populations, prostate cancer mortality was comparable, implying that more-intensive screening was not associated with the drop in mortality. Formal, randomized, clinical-trial data on PSA screening in the general population are anticipated from the European Randomized Screening for Prostate Cancer Trial and the Prostate, Lung, Colorectal, and Ovary cancer trial within the next several years. These data should provide a better understanding of the value of prostate cancer screening in reducing mortality. When considering epidemiologic data, it is important to recognize the difference between mortality, the deaths in the general population due to the specific disease, and survival, which is limited to the patient cohort with the disease.

Survival rates, median age at diagnosis, and stage at diagnosis have also changed drastically over the past 20 years due to the effects of PSA screening (Table 6). During the intervals 1975–1979 and 1985–1989, 73% of prostate cancer diagnoses were localized or regional. In contrast, during 1995–2001, 91% of diagnoses were localized or regional (Table 7). Across the same three

Table 6. Survival rates for prostate cancer, by race/ethnicity, diagnosis year, stage, and age

	All Males			White Males			Black Males		
	All	< 50	≥ 50	All	< 50	≥ 50	All	< 50	≥ 50
5-Year Survival Rates									
Year of Diagnosis									
1960–1963[a]	…	…	…	50.0	…	…	35.0	…	…
1970–1973[a]	…	…	…	63.0	…	…	55.0	…	…
1974–1976[b]	67.1	71.5	65.5	68.1	73.0	66.4	58.4	60.7	57.0
1977–1979[b]	71.1	75.8	69.4	72.2	77.5	70.3	62.6	64.4	61.7
1980–1982[b]	73.4	76.4	72.3	74.5	78.0	73.3	64.8	66.7	63.8
1983–1985[b]	74.8	75.7	74.5	76.2	77.5	75.8	63.9	64.6	63.5
1986–1988[b]	81.2	81.3	81.2	82.7	83.1	82.6	69.3	69.8	69.1
1989–1991[b]	90.7	90.2	90.8	92.0	91.3	92.2	80.8	82.3	80.2
1992–1994[b]	97.3	96.3	97.7	98.1	97.0	98.6	92.4	93.4	91.9
1995–2000[b]	99.3[c]	99.1	99.7	100[c]	99.5	100	96.0[c]	98.1	95.1c
1995–2000[b]									
All Stages	99.3	99.1	99.7	100	99.5	100	96.0	98.1	95.1
Localized/Regional	100	100	100	100	100	100	100	100	100
Distant	33.5	30.5	34.6	32.7	30.3	33.6	29.0	31.1	28.0
Unstaged	81.4	89.3	79.4	82.8	91.3	80.9	75.5	82.6	72.4
5-Year Survival Rates, 1995–2000[b]									
Age at Diagnosis									
< 45	91.7	…	…	91.3	…	…	95.4	…	…
45–54	97.2	…	…	97.5	…	…	96.8	…	…
55–64	99.7	…	…	100	…	…	98.4	…	…
65–74	100	…	…	100	…	…	98.1	…	…
75+	94.8	…	…	96.5	…	…	87.5	…	…
< 65	99.1	…	…	99.5	…	…	98.1	…	…
65+	99.7	…	…	100	…	…	95.1	…	…

…data unavailable

[a]Rates are based on End Results data from a series of hospital registries and one population-based registry.

[b]Rates are from SEER 9 areas. They are based on data from population-based registries in Connecticut, Puerto Rico, Utah, Iowa, Hawaii, Atlanta, Detroit,Seattle-Puget Sound, and San Francisco-Oakland. Rates are based on follow up of patients into 2001.

[c]The difference in rates between 1974–1976 and 1995–2000 is statistically significant ($p < 0.05$).

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 7. Stage distribution by race/ethncity for prostate cancer patients, all ages, 1975–79, 1985–89, and 1995–2001

	1975–1979			1985–1989			1995–2001		
	All	White	Black	All	White	Black	All	White	Black
Localized	73%	73%	66%	73%	74%	65%	91%	91%	89%
Regional	0%	0%	0%	0%	0%	0%	0%	0%	0%
Distant	20%	19%	28%	16%	15%	25%	5%	5%	7%
Unstaged	7%	8%	5%	11%	11%	11%	4%	4%	5%

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

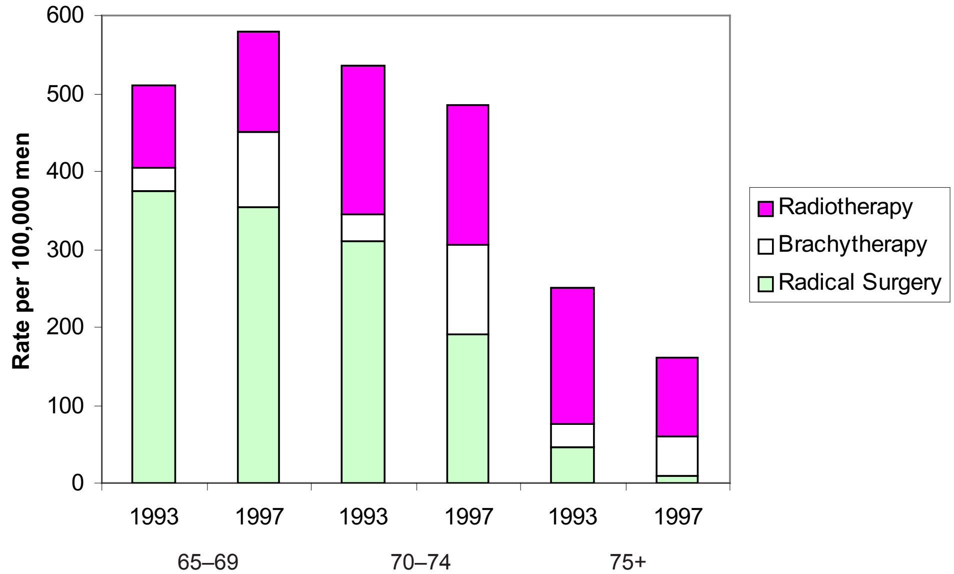

Figure 7. Patterns of treatment use for prostate cancer, 1993–1997.

SOURCE: Adapted from Urology, 58, Bubolz T, Wasson JH, Lu-Yao G, Barry MJ, Treatments for prostate cancer in older men: 1984–1997,Urol, 58: 977–982, Copyright 2001, with permission from Elsevier.

time intervals, the percentage with distant disease at diagnosis decreased from 20% to 16% to 5% (Table 7). This shift in disease stage at diagnosis has been accompanied by an increase in five-year survival rates. Of the men diagnosed with local or regional prostate cancer in 1973, 61% survived 5 years. For men diagnosed in 1981, the survival rate increased to 74%; for those diagnosed in 1989, it rose to 87%; and of those diagnosed in 1995–2000, 100% survived 5 years (155, 159). With PSA screening, men are also being diagnosed at earlier ages. In 1980, the median ages at diagnosis for Caucasian men and African American men were 72 and 70 years, respectively (159). During 1998–2002, the median ages at diagnosis were 68 and 65 years for Caucasian and African American men, respectively (160). These shifts are expected with the introduction of a new screening technology that effectively increases lead-time bias and increases the number of overdetected cases. The key question is whether discovering prostate cancer cases earlier in the disease course will make it possible to alter the natural history of the illness. Further research and additional follow-up will shed more light on this important issue.

TREATMENT

Localized Disease

There are numerous therapeutic options for men with newly diagnosed localized prostate cancer. Unfortunately, there is little level I evidence (i.e., from randomized clinical trials) that one particular therapy is superior to another in terms of survival. In fact, the only adequately sized randomized clinical trial completed to date compared radical surgery to conservative management (watchful waiting) and found that surgery did afford an overall survival advantage, although it required nearly 10 years of follow-up for the difference to become statistically significant (161). The lack of conclusive evidence leads to wide variation in the use of the various therapies and may ultimately impact quality of care. The four most common treatment modalities in localized prostate cancer are radical prostatectomy, external beam radiotherapy, interstitial brachytherapy, and watchful waiting. There is also limited utilization of cryosurgery, proton-beam radiotherapy, and other technologies.

Radical Prostatectomy

Surgery is the most common treatment modality for localized prostate cancer, particularly in younger men. Bubolz et al. (162) reviewed rates of surgery, radiotherapy, and brachytherapy from 1984 to 1997 in a 20% sample of the Medicare part A dataset. As shown in Figure 7, utilization rates for surgery were much higher than the rates for the two other treatment modalities in men aged 65–69. In all three age groups shown in Figure 7, the utilization of interstitial brachytherapy increased from 1993 to 1997; for men aged 70–74, utilization rates for surgery and external beam radiotherapy were similar by 1997. In the oldest age group, surgery rates were much lower, which is to be expected, as available guidelines (163) for prostate cancer state that surgery is not appropriate in men with a life expectancy of less than 10 years.

Utilization rates for radical prostatectomy are notably higher in men younger than 65. Ellison et al. (164), using data from the SEER program to assess utilization rates for radical prostatectomy from 1989 to 1995, found that the rate more than doubled between 1989 and 1992 (from 78 men per 100,000 men to 206 per 100,000), likely due to the introduction of PSA testing and the rapid increase in the number of men newly diagnosed with prostate cancer. The rate then decreased by one-third between 1992 and 1995 (to 146 per 100,000 men). During this time period, as shown in Figure 8, radical prostatectomy rates dropped off significantly in older patients (decreasing 51% in men aged 70–74 and 71% in men 75 or older). However, rates in younger men continued to increase between 1992 and 1995, rising 42% in men 45–49 years of age and 18% in men aged 50–54. These temporal trends mirror changes in detection rates and widespread realization by clinicians that aggressive surgical treatment of localized prostate cancer in elderly men (who have relatively short life expectancies) is not clinically indicated in most cases.

Data from the Healthcare Cost and Utilization Project (HCUP) confirm these findings and provide us with a more recent assessment of trends in

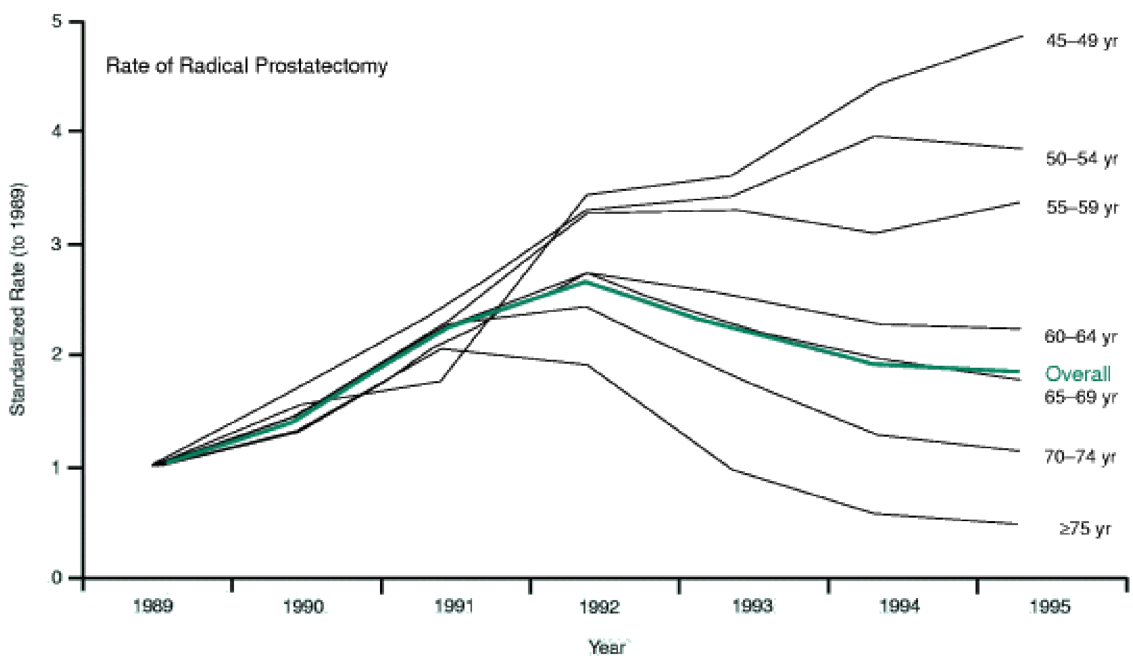

Figure 8. Rate of radical prostatectomy, age-stratified annual rates, standardized to 1989.

SOURCE: Reprinted from Effective Clinical Practice, 2, Ellison LM., Heaney JA, Birkmeyer JD, Trends in the use of radical prostatectomy for treatment of prostate cancer, 228–233, Copyright 1999, with permission from American College of Physicians.

Table 8. Radical prostatectomy in men hospitalized for a primary diagnosis of prostate cancer, count, rate[a] (95% CI), rate per 100,000 prostate cancer hosptializations[b] (95% CI)

	1994					1996				
	Count	Rate		Rate per 100,000 hospitalizations for primary diagnosis of Prostate Cancer		Count	Rate		Rate per 100,000 hospitalizations for primary diagnosis of Prostate Cancer	
Total[c]	58,254	128	(128–128)	50,553	(50,440–50,666)	61,952	127	(126–127)	57,851	(57,710–57,992)
Age										
40–54	5,467	23	(23–24)	4,744	(4,721–4,768)	7,573	29	(29–30)	7,072	(7,039–7,104)
55–64	22,683	236	(235–237)	19,684	(19,621–19,749)	25,288	254	(254–255)	23,614	(23,552–23,676)
65–74	28,444	361	(360–362)	24,684	(24,612–24,756)	27,861	341	(340–342)	26,017	(25,938–26,095)
75–84	1,649	43	(42–45)	1,431	(1,395–1,467)	1,220	29	(28–30)	1,139	(1,086–1,193)
85+	*	*		*		*	*		*	
Race/ethnicity										
White	39,405	107	(106–107)	34,196	(34,103–34,288)	42,773	108	(108–109)	39,942	(39,828–40,056)
Black	4,218	105	(102–103)	3,660	(3,640–3,680))	5,188	116	(116–116)	4,845	(4,832–4,857)
Hispanic	1,529	50	(50–51)	1,327	(1,313–1,342	1,626	20	(49–50)	1,518	(1,503–1,533)
Region										
Midwest	14,167	133	(132–134)	12,294	(12,233–12,357)	16,212	139	(138–139)	15,139	(15,092–15,187)
Northeast	9,287	96	(95–96)	8,059	(8,014–8,104)	12,237	124	(124–125)	11,427	(11,384–11,470)
South	23,509	153	(152–153)	20,401	(20,317–20,485)	23,450	137	(136–137)	21,898	(21,793–22,002)
West	11,291	116	(115–116)	9,798	(9,766–9,831)	10,052	98	(98–99)	9,387	(9,317–9,458)
MSA										
Rural	6,255	50	50 (50–51)	5,428	(5,401–5,456)	5,898	50	(49–50)	5,508	(5,455–5,559)
Urban	51,768	157	(156–157)	44,924	(44,814–45,034)	55,883	151	(151–151)	52,184	(52,054–52,314)

	1998					2000				
	Count	Rate		Rate per 100,000 hospitalizations for primary diagnosis of Prostate Cancer		Count	Rate		Rate per 100,000 hospitalizations for primary diagnosis of Prostate Cancer	
Total[c]	50,943	99	(99–99)	57,861	(57,744–57,978)	58,191	108	(108–108)	61,949	(61,825–62,073)
Age										
40–54	7,439	27	(27–27)	8,449	(8,416–8,483)	10,198	35	(35–35)	10,856	(10,821–10,892)
55–64	21,267	201	(200–201)	24,155	(24,090–24,218)	26,135	234	(234–235)	27,822	(27,755–27,888)
65–74	21,161	263	(262–264)	24,034	(23,959–24,109)	20,815	259	(258–260)	22,159	(22,076–22,242)
75–84	1,076	24	(23–25)	1,222	(1,176–1,270)	1,026	21	(20–22)	1,092	(1,045–1,139)
85+	*	*		*		*	*		*	
Race/ethnicity										
White	32,845	80	(80–81)	37,305	(37,211–37,399)	35,009	82	(82–82)	37,269	(37,177–37,362)
Black	4,307	90	(89–90)	4,892	(4,859–4,925)	4,784	94	(93–94)	5,093	(5,065–5,121)
Hispanic	2,117	55	(55–56)	2,404	(2,383–2,426)	2,210	55	(54–55)	2,353	(2,329–2,377)
Region										
Midwest	11,749	99	(98–99)	13,344	(13,285–13,403)	13,853	110	(110–111)	14,747	(14,698–14,796)
Northeast	10,994	108	(107–108)	12,487	(12,427–12,548)	12,924	123	(123–124)	13,758	(13,696–13,821)
South	17,307	95	(95–95)	19,657	(19,582–19,731)	20,758	108	(108–108)	22,098	(22,016–22,180)
West	10,893	98	(97–98)	12,372	(12,337–12,408)	10,657	92	(92–92)	11,345	(11,298–11,392)
MSA										
Rural	5,183	42	(42–42)	5,887	(5,855–5,919)	5,888	45	(45–46)	6,268	(6,237–6,298)
Urban	45,599	117	(116–117)	51,791	(51,678–51,904)	52,245	128	(127–128)	55,615	(55,498–55,737)

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male 40+ civilian non-institutionalized population.

[b]Rate per 100,000 male 40+ visits with radical prostatectomy performed is based on estimated number of visits for prostate cancer in HCUP_NIS 1994–2000.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE:Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

radical prostatectomy. As shown in Table 8, radical prostatectomy rates were relatively stable in 1994 and 1996 (128 and 127, respectively, per 100,000 men over the age of 40), but they decreased in 1998 to 99 per 100,000 and then increased again in 2000 to 108 per 100,000. One could hypothesize that the decline in 1998 was due to the increasing use of brachytherapy (which was "reintroduced" in the mid-1990s), and the moderate increase in 2000 was related to increased awareness that brachytherapy monotherapy was best reserved for men with low-risk disease (i.e., Gleason 6 or less and PSA <10 ng/ml) (165). Similar declines were seen in the Veterans Affairs (VA) population (Table 9) between 1998 and 2003, although the rates seemed to stabilize slightly later in this population. This may be related to the fact that brachytherapy was not as readily available at VA facilities. Importantly, when prostatectomy rates were stratified by age, rates dropped consistently in older patients (over age 65), while there were consistent increases in the rates for younger patients (40–54 years of age). In summary, there have been significant changes in the utilization of radical prostatectomy in the last 15 years, with the overall rate of use decreasing in older men but increasing in younger men. There is also considerable ethnic and geographic variation, which is to be expected in the absence of conclusive level I evidence to guide therapy.

Table 9. VA users with radical prostatectomy for prostate cancer patients,1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	1,508	1,539	1,625	1,491	1,815	1,467	1,880	1,254	2,005	1,154	2,168	1,132
Age	1,705	1,378	1,742	1,408			1,633	1,320	1,547	1,251	1,498	1,211
40–44	7	2,525	12	4,808	8	3,089	9	3,524	24	9,137	14	5,236
45–54	244	5,431	279	6,224	322	7,173	313	6,977	332	7,397	330	7,349
55–64	656	4,435	743	5,025	800	5,409	719	4,864	686	4,639	684	4,626
65–74	764	1,480	681	1,319	671	1,301	577	1,118	491	952	459	889
75–84	32	66	25	53	14	29	14	29	14	29	12	24
85+	3	68	1	29	0	0	1	18	0	0	0	0
Gender												
Male	1,508	1,539	1,625	1,491	1,815	1,467	1,880	1,254	2,005	1,154	2,168	1,132
Female	0	0	0	0	0	0	0	0	0	0	0	0
Race/ethnicity												
White	1,037	1,463	1,079	1,330	1,184	1,260	1,248	1,070	1,303	958	1,089	742
Black	392	1,827	460	2,016	498	2,084	490	1,912	422	1,551	390	1,384
Hispanic	44	2,013	32	1,413	42	1,730	37	1,376	70	2,392	48	1,546
Other	17	1,595	23	1,973	23	1,801	21	1,472	25	1,529	16	920
Unknown	18	755	31	1,935	68	3,128	84	2,368	185	3,111	625	5,377
Insurance Status												
No insurance/ self-pay	1,123	1,980	1,269	2,045	1,338	2,153	1,315	1,983	1,368	1,934	1,482	2,120
Medicare	94	621	119	510	198	504	264	432	307	390	355	368
Medicaid	1	1,724	0	0	3	5,357	3	2,290	3	1,493	3	1,282
Private Insurance/HMO	284	1,102	229	984	265	1,219	272	1,257	312	1,330	313	1,301
Other Insurance	6	2,390	8	2,540	11	2,296	26	4,586	14	2,226	15	1,935
Unknown	0	0	0	0	0	0	0	0	1	0	0	0
Region												
Eastern	174	1,159	194	1,107	196	941	183	655	236	695	267	718
Central	265	1,671	304	1,670	352	1,736	337	1,332	423	1,227	478	1,174
Southern	614	1,579	660	1,543	705	1,451	821	1,377	821	1,193	897	1,162
Western	455	1,613	467	1,532	562	1,652	539	1,457	525	1,439	526	1,444

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.
SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 10. Distribution (%) of treatments for prostate cancer, by year of diagnosis

	1992 (N=103,979)	1995 (N=72,337)
Radical prostatectomy	31.6	34.1
External beam radiation	30.1	26.3
Radiation implant	1.4	2.2
Hormone	12.0	11.7
Other treatment	4.9	4.1
No treatment	20.0	21.6

SOURCE: Reprinted from Cancer, 83, Mettlin CJ, Murphy GP, Rosenthal DS, Menck HR, The National Cancer Data Base report on prostate carcinoma after the peak in incidence rates in the U.S., 1,679–1,684, Copyright 1998, with permission from Wiley.

External Beam Radiation Therapy

Radiation therapy can be delivered to the prostate for cancer control and cure through a number of different modalities, including external beam radiation (in the form of three-dimensional conformal beam therapy or intensity-modulated radiotherapy), permanent implantation of radioactive seeds (interstitial brachytherapy), and temporary transperineal implantation of radiation sources to deliver higher treatment doses (so-called high dose rate, HDR). These modalities can be used alone or in combination. There is little epidemiologic data on HDR treatment or other forms of radiation, such as proton-beam therapy, however, so we will not address these relatively uncommon modalities.

External beam radiotherapy (EBRT) is the most commonly used form of radiotherapy for prostate cancer. A review of the Medicare part A dataset by Bubolz et al. (145, 162), shown in Figure 7, documented that EBRT rates were relatively stable for all prostate cancer patients, except those over age 75, from 1993 to 1997. In the older patients, EBRT utilization dropped, reflecting the general realization by providers that many of these patients did not require any treatment, given their relatively short life expectancy.

While the data from the Medicare population are informative, most Medicare recipients are over the age of 65 and may not be representative of the entire population of men with prostate cancer, since the average age at diagnosis has dropped in the past decade. Therefore, it is helpful to review information from other data sources that include younger men. Mettlin and colleagues (166) reviewed data from

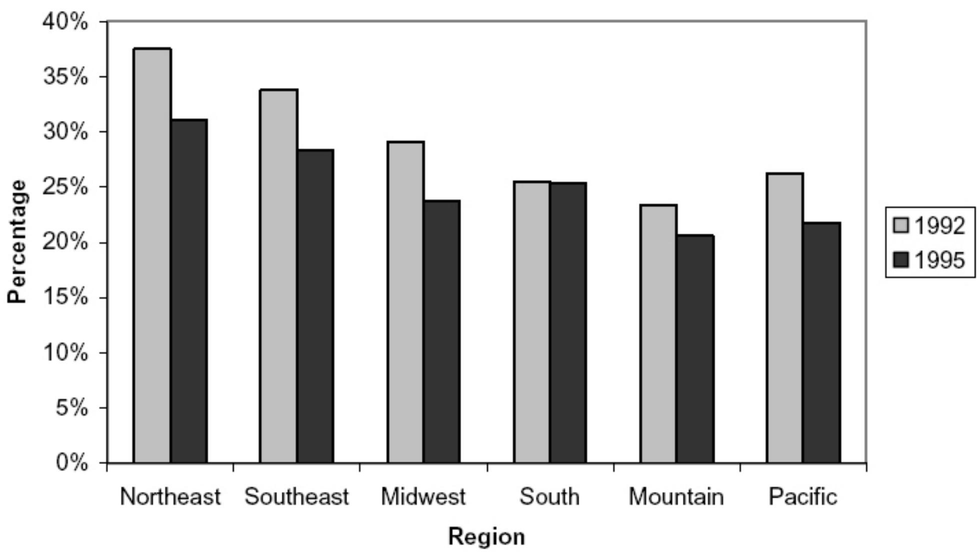

Figure 9. Proportions of patients treated for prostate cancer by external beam radiation therapy, 1992–1995, by region.

SOURCE: Adapted from Cancer, 83, Mettlin CJ, Murphy GP, Rosenthal DS, Menck HR, The National Cancer Data Base report on prostate carcinoma after the peak in incidence rates in the U.S., 1,679–1,684, Copyright 1998, with permission from Wiley.

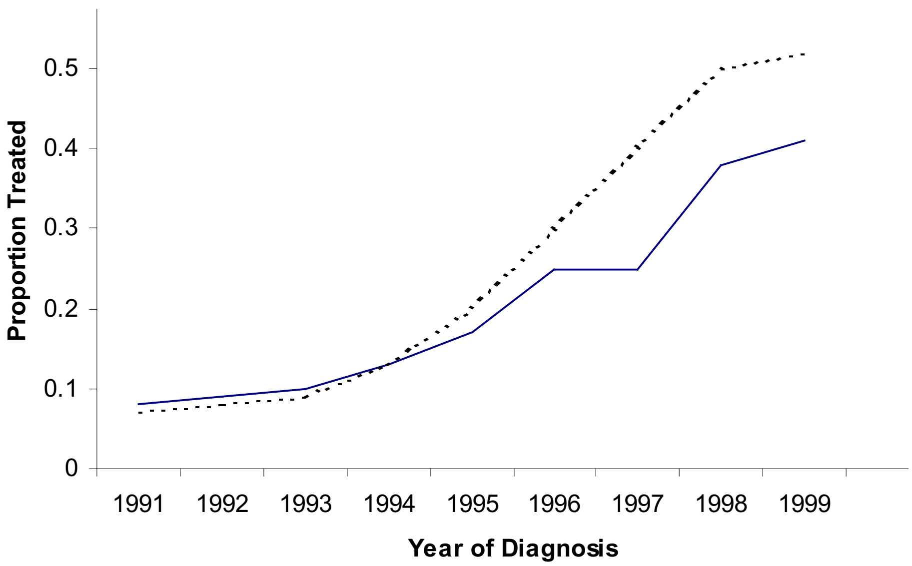

Figure 10. Trends in androgen deprivation therapy (ADT) with external beam radiation therapy (EBRT) at diagnosis for prostate cancer patients, age-standardized, in African American (solid line) and Caucasian (dashed line) men.

SOURCE: Adapted from Urology, 64, Zeliadt SB, Potosky AL, Etzioni R, Ramsey SD, Penson DF. Racial disparity in primary and adjuvant treatment for nonmetastatic prostate cancer: SEER-Medicare trends 1991 to 1999, 1,171–1,176, Copyright 2004, with permission from Elsevier.

the American College of Surgeons National Cancer Database (NCDB), which includes information from 1,114 hospitals in the United States. As shown in Table 10, 30% of patients diagnosed in 1992 and 26% of those in 1995 received EBRT as treatment for prostate cancer. This decrease in the use of EBRT was accompanied by an increase in the use of radical prostatectomy. As shown in Figure 9, there was considerable geographic variation in the use of EBRT. It was used more commonly in the Northeast, where 31% of patients received EBRT in 1995; it was used least commonly in the Pacific region (for only 22% of patients).

In patients of all ages, EBRT was often accompanied by the use of androgen ablation therapy, Zeliadt and colleagues (167) studied the use of adjuvant hormone ablation therapy with EBRT in the SEER-Medicare dataset and found that the use of this combined therapy increased steadily in the past decade. As shown in Figure 10, approximately 40% of African American and 50% of Caucasian men in the SEER-Medicare dataset who received EBRT had adjuvant hormone ablation therapy. Although this practice is supported by level I evidence in intermediate- and high-risk patients (168, 169), there are no data to support its use in low-risk patients. Given the increasing number of patients presenting with low-risk disease (6), it is likely that increasing numbers of them are receiving adjuvant hormone ablation, although there are currently no data to support this practice.

Interstitial Brachytherapy

Permanent radioactive seed implantation was originally described in the 1970s. The technique was performed using an open surgical approach, but it was associated with a high complication rate and fell out of favor. With advances in ultrasonography and computed tomography, interstitial brachytherapy (IB) performed using a transperineal approach gained popularity in the mid 1990s. Data from the NCDB document that while the overall proportion of prostate cancer patients treated with IB was small, it increased steadily throughout the 1990s (170). As shown in Figure 11, the proportion of stage I patients treated with IB increased from 2.0% in 1992

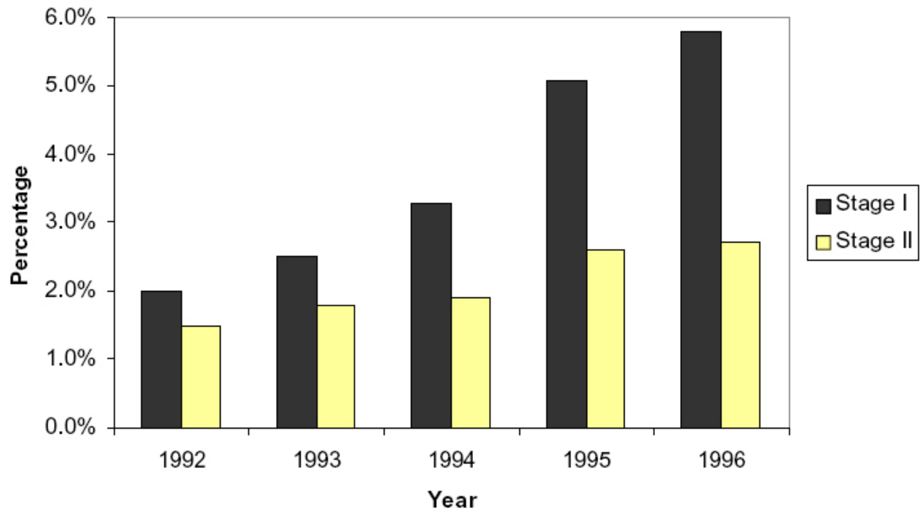

Figure 11. Proportions of 89,060 American Joint Committee on Cancer Stage I and 185,407 Stage II prostate cancer patients treated by radiation implant, by year.

Source: Adapted from Cancer, 86, Mettlin CJ, Murphy GP, McDonald CJ, Menck HR, The National Cancer Data base Report on increased use of brachytherapy for the treatment of patients with prostate carcinoma in the U.S., 1,877–1,882, Copyright 1999, with permission from Wiley.

to 5.8% in 1996, and the proportion of stage II patients increased from 1.5% in 1992 to 2.7% in 1996. It is likely that a number of generally recognized high-volume centers were driving this trend, as is reflected in the geographic variation in utilization shown in Figure 12. Enthusiasm for IB may be declining, however, as the treatment often must be accompanied by a boost of external beam radiotherapy or adjuvant hormone therapy. Many patients electing IB cite the lack of sexual side effects and the short time away from work as reasons for choosing this treatment (171), but if IB must be combined with other treatment modalities, these advantages may be lost. This underscores the need for more data on outcomes following IB and treatment decision making in prostate cancer.

Watchful Waiting/Conservative Management

It is clear that PSA screening has led to an increase in the number of "overdetected" prostate cancers (172). Some patients likely do not require any treatment, as the disease will not progress quickly enough to be clinically meaningful. The challenge for providers is to determine which patients have indolent disease and which require therapy. A population-based study of men in Connecticut who initially elected conservative management for prostate cancer in the 1970s indicated that those with lower Gleason scores (6 or less) and older men are much less likely to die of prostate cancer than of other unrelated causes (152). Clearly, these data and others (173) document that watchful waiting is a reasonable treatment option for some men with prostate cancer.

From an epidemiologic perspective, it is difficult to estimate accurately the number of men with prostate cancer who are treated with conservative management. In men with suspected prostate cancer and other comorbid conditions, doctors often do not aggressively pursue the diagnosis of prostate cancer, because they would not actively treat the malignancy if the diagnosis were made. Therefore, any estimates of the use of watchful waiting are likely to underestimate true utilization. In addition, many patients who initially elect watchful waiting have difficulty with the psychological burden of a cancer diagnosis and later opt for aggressive therapy, although it may not be clinically indicated. This can lead to differing definitions of conservative management in different publications.

Zeliadt and colleagues (167) examined the use of conservative management in men with localized

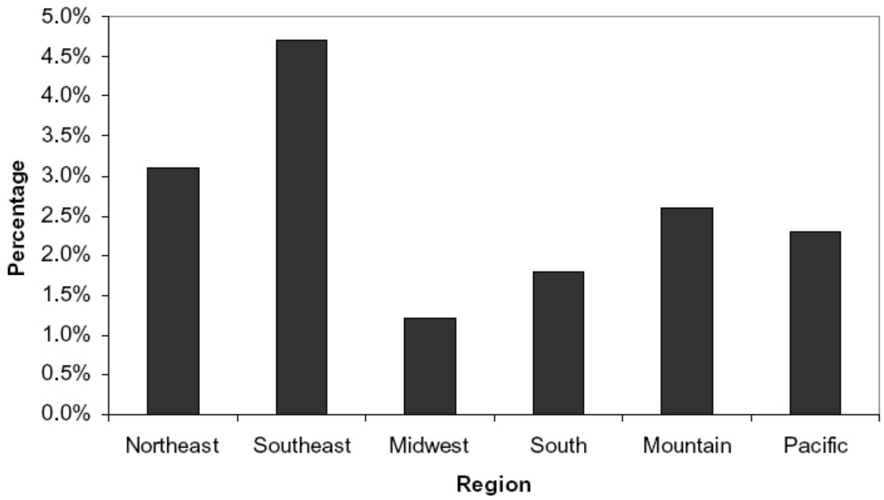

Figure 12. Proportion of 274,188 American Joint Committee on Cancer Stage I and II prostate cancer patients treated with brachytherapy, by region, 1992–1996.

SOURCE: Adapted from Cancer, 86, Mettlin CJ, Murphy GP, McDonald CJ, Menck HR, The National Cancer Data base Report on increased use of brachytherapy for the treatment of patients with prostate carcinoma in the U.S., 1,877–1,882, Copyright 1999, with permission from Wiley.

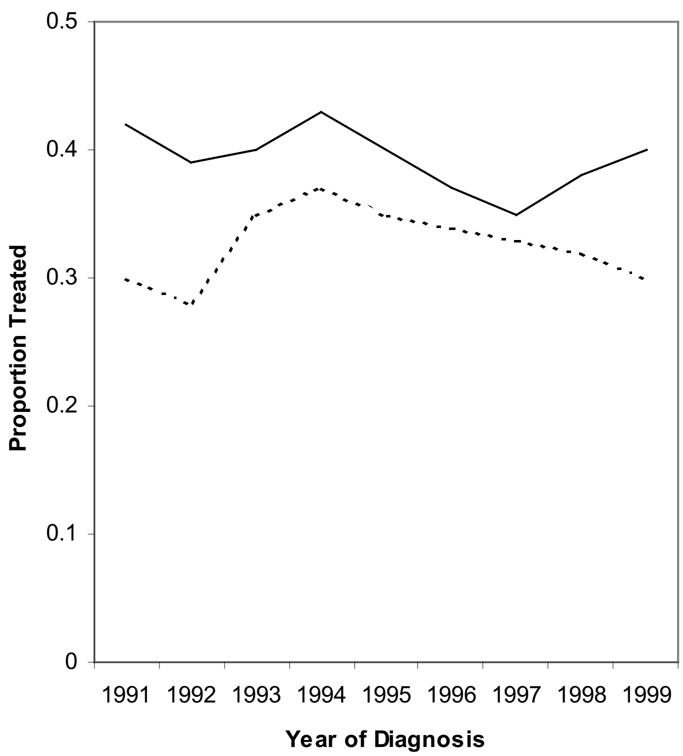

Figure 13. Proportion of men with prostate cancer selecting conservative management, age-standardized, in African American (solid line) and Caucasian (dashed line) men.

SOURCE: Adapted from Urology, 64, Zeliadt SB, Potosky AL, Etzioni R, Ramsey SD, Penson DF. Racial disparity in primary and adjuvant treatment for nonmetastatic prostate cancer: SEER-Medicare trends 1991 to 1999, 1,171–1,176, Copyright 2004, with permission from Elsevier.

prostate cancer in the SEER-Medicare dataset. They defined conservative management as either no treatment or treatment with primary hormone ablation therapy. As shown in Figure 13, 35–44% of African American men with localized prostate cancer and 27–36% of Caucasian men received conservative management. Within this group, roughly 30–40% received some form of hormone ablation therapy, while the remaining 60–70% received no other therapy. It is worth noting that there was considerable racial/ethnic variation in utilization rates, although there is no clinical evidence to support these differences. In addition, numerous studies have noted racial/ethnic differences in PSA surveillance among men electing watchful waiting or aggressive therapies (167, 174). However, as noted earlier, the SEER-Medicare dataset comprises primarily patients over the age of 65 and may not be representative of the general population of men with localized prostate cancer. Nevertheless, the data underscore the need for additional research in the epidemiology of conservative management of prostate cancer, with particular focus on racial disparities in access to and quality of care.

Metastatic Prostate Cancer

The cornerstone of treatment for advanced prostate cancer is hormone ablation therapy. Hormone ablation can be achieved with a number of medications that inhibit the production of or block the effect of testosterone. Alternatively, testosterone production can be halted by the surgical removal of the testicles (orchiectomy). In 1994, the total Medicare expenditure for medical androgen suppression therapy in the treatment of prostate cancer was $477,851,000, which was 34% of the total Medicare expenditure for the disease that year (175). As shown in Figure 14, the use of such medications increased greatly in the 1990s, contributing to higher Medicare expenditures for treatment of the disease. To some degree, the increasing use of hormone ablation therapy may be associated with the fact that in the past it was a fairly lucrative practice for healthcare providers.

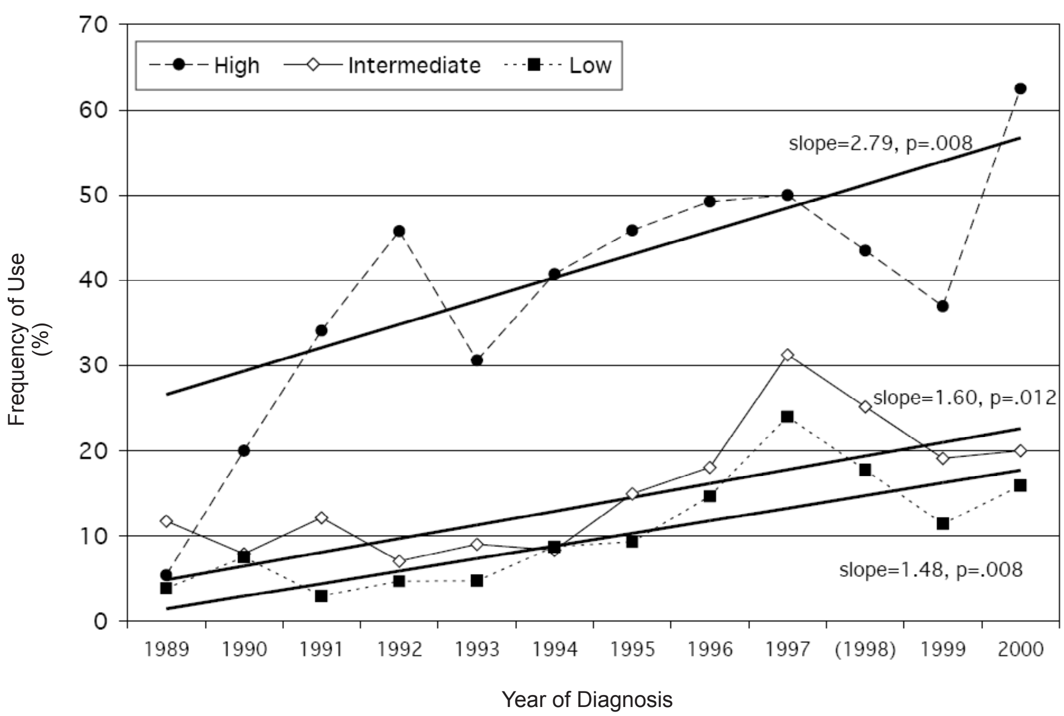

Figure 14. Time trends in the use of primary hormonal ablation therapy, by risk group.

SOURCE: Reprinted from Cooperberg MR, Grossfeld GD, Lubeck DP, Carroll PR. National practice patterns and time trends in androgen ablation for localized prostate cancer. Journal of the National Cancer Institute, 2003, 95(13):981–989, by permission of Oxford University Press.

Table 11. Hormonal therapy for men with prostate cancer, age-adjusted rate[a]

	1999			2000			2001		
	Count	Rate		Count	Rate		Count	Rate	
Total	15,243	13,985	(13,763–14,207)	16,918	13,674	(13,468–13,880)	19,099	12,744	(12,563–12,924)
Age	17,433	14,090	(13,881-14,300)				15,644	12,645	(12,447–12,843)
40–44	2	641	(0–1,529)	11	4,247	(1,737–6,757)	11	4,405	(1,675–7,136)
45–54	320	7,140	(6,337–7,942)	317	7,062	(6,284–7,839)	317	7,055	(6,328–7,782)
55–64	1,575	10,651	(10,109–11,192)	1,501	10,149	(9,636–10,663)	1,420	9,599	(9,133–10,065)
65–74	7,241	14,037	(13,699–14,376)	6,930	13,434	(13,118–13,750)	6,232	12,080	(11,801–12,359)
75–84	7,634	15,798	(15,408–16,188)	7,468	15,454	(15,104–15,805)	6,959	14,400	(14,102–14,699)
85+	660	15,446	(14,141–16,752)	691	16,160	(14,955–17,365)	706	16,516	(15,454–17,577)
Race/ethnicity									
White	10,487	12,944	(12,696–13,191)	11,880	12,682	(12,454–12,910)	13,609	11,724	(11,527–11,921)
Black	4,209	18,490	(17,931–19,048)	4,364	18,327	(17,783–18,871)	4,649	18,244	(17,719–18,768)
Hispanic	218	9,499	(8,238–10,760)	281	11,317	(9,994–12,640)	319	11,520	(10,256–12,785)
Other	173	15,017	(12,780–17,255)	191	15,317	(13,145–17,489)	200	14,378	(12,385–16,371)
Unknown	156	8,844	(7,456–10,231)	202	8,074	(6,960–9,187)	322	7,761	(6,913–8,609)
Region									
Eastern	1,946	11,105	(10,611–11,598)	2,136	10,256	(9,821–10,691)	2,575	9,213	(8,857–9,569)
Central	2,869	15,758	(15,181–16,334)	3,137	15,469	(14,928–16,011)	3,653	14,443	(13,974–14,911)
Southern	6,251	14,614	(14,251–14,976)	7,036	14,479	(14,141–14,817)	8,034	13,474	(13,180–13,769)
Western	4,177	13,700	(13,284–14,115)	4,609	13,546	(13,155–13,937)	4,837	13,072	(12,703–13,440)

	2002			2003		
	Count	Rate		Count	Rate	
Total	21,106	12,147	(11,983–12,311)	21,472	11,212	(11,062-11,362)
Age	14,803	11,965	(11,722–12,157)	13,563	10,963	(10,778-11,147)
40–44	14	5,584	(2,284–8,884)	9	3,665	(950-6,380)
45–54	323	7,201	(6,500–7,903)	279	6,208	(5,555-6,860)
55–64	1,327	8,971	(8,555–9,387)	1,180	7,980	(7,623-8,337)
65–74	5,732	11,111	(10,856–11,366)	5,100	9,887	(9,653-10,122)
75–84	6,725	13,916	(13,649–14,183)	6,313	13,065	(12,819-13,310)
85+	682	15,950	(15,039–16,860)	681	15,928	(15,119-16,736)
Race/ethnicity						
White	14,713	11,283	(11,101-11,466)	13,554	10,504	(10,327–10,681)
Black	4,840	18,110	(17,600-186,20)	4,675	17,382	(16,884–17,881)
Hispanic	369	12,142	(10,903-13,381)	365	11,471	(10,294–12,648)
Other	235	15,280	(13,326-17,233)	237	15,430	(13,465–17,394)
Unknown	949	7,874	(7,373-8,375)	2,641	8,557	(8,231–8,884)
Region						
Eastern	2,970	8,749	(8,435-9,064)	2,991	8,046	(7,757–8,334)
Central	4,526	13,126	(12,743-13,508)	5,061	12,434	(12,091–12,776)
Southern	8,932	12,977	(12,708-13,246)	9,112	11,802	(11,559–12,044)
Western	4,678	12,819	(12,452-13,186)	4,308	11,827	(11,474–12,181)

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Pharmacy Benefits Management Version 3.0 (PBM), Department of Veterans Affairs.

Table 12. Inpatient hospital stays by male Medicare beneficiaries with prostate cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	87,540	588 (570–605)		50,620	333 (320–346)		38,840	268 (256–280)		37,840	245 (234–256)	
Total < 65	1,720	55 (43–67)		1,740	51 (40–61)		1,460	42 (33–52)		1,860	49 (39–59)	
Total 65+	85,820	729 (707–751)	729	48,880	415 (399–432)	410	37,380	339 (323–354)	337	35,980	310 (295–324)	309
Age												
65–69	27,620	679 (643–714)		17,260	448 (418–478)		12,680	376 (346–405)		12,340	349 (321–376)	
70–74	27,720	853 (808–897)		15,240	457 (425–489)		11,500	377 (346–408)		10,520	342 (313–371)	
75–79	16,580	732 (683–782)		7,360	324 (291–358)		5,700	250 (221–279)		5,820	237 (210–264)	
80–84	8,720	666 (603–728)		5,300	381 (336–427)		3,800	276 (237–315)		3,540	237 (202–271)	
85–89	3,780	634 (544–724)		2,340	367 (301–434)		2,580	397 (328–465)		2,500	346 (285–406)	
90–94	1,200	592 (443–742)		1,060	501 (367–636)		920	428 (304–551)		1,040	449 (327–571)	
95–97	160	396 (121–671)		200	531 (202–859)		180	455 (159–750)		140	364 (94–635)	
98+	40	105 (0–250)		120	271 (54–488)		20	42 (0–123)		80	147 (3.7–291)	
Race/ethnicity												
White	74,280	591 (572–610)	592	42,800	329 (315–343)	330	32,200	263 (250–276)	263	31,400	240 (228–252)	240
Black	8,600	674 (611–737)	646	5,860	423 (375–472)	412	4,880	366 (320–411)	355	4,680	319 (278–360)	315
Asian	…	…	…	100	137 (16–258)	137	160	117 (36–198)	131	140	68 (18–119)	68
Hispanic	…	…	…	560	282 (178–386)	282	740	220 (150–291)	215	640	170 (111–229)	160
N. American Native	…	…	…	40	199 (0–472)	298	60	215 (0–458)	143	100	300 (36–565)	240
Region												
Midwest	20,840	562 (528–596)	566	11,700	304 (279–328)	300	10,220	276 (252–300)	279	9,620	253 (231–276)	259
Northeast	18,620	587 (550–625)	573	11,760	370 (340–400)	360	7,420	267 (240–294)	270	6,720	230 (205–255)	221
South	32,260	616 (586–646)	616	19,360	353 (331–375)	357	14,960	279 (259–299)	277	15,180	261 (243–280)	262
West	14,720	609 (566–653)	622	7,200	310 (278–343)	322	5,700	255 (225–284)	251	5,660	229 (202–255)	231

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 13. Most common procedures during inpatient hospital stays for prostate cancer listed as primary diagnosis, count, rate[a] (95% CI), rate per visits[b] (95% CI)

	1994			1996		
	Count	Rate per 100,000 population	Rate per 100,000 hospitalizations for Prostate Cancer	Count	Rate per 100,000 population	Rate per 100,000 hospitalizations for Prostate Cancer
Radical Prostatectomy	58,254	128 (128–128)	50,553 (50,440–50,666)	61,952	127 (126–127)	57,851 (57,710–57,992)
Regional Lymph Node Excision	29,677	65 (63–67)	25,753 (24,880–26,627)	33,667	69 (65–73)	31,439 (29,549–33,329)
Transurethral Prostatectomy[c]	30,822	68 (65–70)	26,747 (25,810–27,684)	...	...	...
Other Transurethral Prostatectomy	...	...	...	23,045	47 (45–49)	21,520 (20,664–22,376)

	1998			2000		
	Count	Rate per 100,000 population	Rate per 100,000 hospitalizations for Prostate Cancer	Count	Rate per 100,000 population	Rate per 100,000 hospitalizations for Prostate Cancer
Radical Prostatectomy	50,943	99 (99–99)	57,861 (57,744–57,978)	58,191	108 (108–109)	61,949 (61,825–62,073)
Regional Lymph Node Excision	26,458	51 (45–58)	30,050 (26,074–34,027)	28,487	53 (50–55)	30,326 (28,946–31,705)
Transurethral Prostatectomy[c]	...	...	...	...	...	...
Other Transurethral Prostatectomy	18,605	36 (35–38)	21,131 (20,222–22,040)	16,738	31 (30–32)	17,819 (17,035–18,603)

[a]Rate per 100,000 is based on 1994–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of U.S. adult male 40+ civilian noninstitutional population.

[b]Rate per 100,000 male 40+ visits is based on estimated number of visits for prostate cancer in HCUP_NIS 1994–2000.

[c]Transurethral prostatectomy only made the top three procedure list in 1994.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994–2000.

Data from the VA pharmacy-benefits-management dataset indicate that in a closed healthcare system in which there is no financial incentive to use these medications, medical hormone ablation use actually decreased from a peak rate of 13,985 per 100,000 male veterans over the age of 40 with a diagnosis of prostate cancer in 1999 to 11,212 per 100,000 in 2003 (Table 11). It should be noted that there are numerous other possible explanations for the increase in the use of hormone ablation therapy in the 1990s, including patient preference over orchiectomy, increased use as primary therapy for localized disease, and increased use in the adjuvant setting following radiotherapy, although it would be hard for any one of these factors alone to explain the marked increase. It is possible that recent changes in Medicare reimbursement for outpatient administration of chemotherapeutic agents may affect hormone ablation utilization rates, particularly in men with asymptomatic recurrent or metastatic disease.

There are limited options for patients who fail to respond to hormone ablation therapy. Few effective chemotherapeutic agents exist for men with hormone-resistant prostate cancer, and the survival advantage afforded by these drugs is minimal. There is little epidemiologic data on the use of chemotherapeutic agents in the treatment of prostate cancer. Nevertheless, recent data from the Southwest Oncology Group document a clear survival advantage for men with metastatic diseases treated with docetaxel-based therapy (176, 177).

TRENDS IN HEALTHCARE RESOURCE UTILZATION

Inpatient Care

Table 12 shows the total number of inpatient stays by male Medicare beneficiaries with a primary diagnosis of prostate cancer during 1992 and 2001. Almost 86,000 were hospitalized with a primary diagnosis of prostate cancer in 1992. In contrast, fewer than 36,000 had hospital stays in 2001. The age-adjusted rate of inpatient stays declined from 729 per 100,000 to 309 per 100,000 between 1992 and 2001. It is likely that inpatient care utilization rates are related to changes in treatment patterns—specifically, radical prostatectomy rates, since this is the most common inpatient procedure among prostate cancer patients in the HCUP dataset (Table 13). Therefore, the decrease in inpatient hospitalization likely reflects the decline in prostatectomy utilization rates discussed earlier (Figure 8). The decrease in inpatient hospitalization rates also likely reflects the marked lowering of age at diagnosis that resulted from the introduction of PSA screening in the 1990s. As men started being diagnosed at younger ages, treatments that required hospitalization (i.e., surgery) also occurred earlier in life. Hence, fewer men 65 or older (the population eligible for Medicare) were experiencing their initial diagnosis of and treatment for prostate cancer.

Table 14. Inpatient hospital stays for prostate cancer listed as primary diagnosis for 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b]

	1994–2000		
	Count	4-year Rate	Rate
Total[c]	407,042	815 (780–851)	204
Age			
40–44	1,651	16 (13–19)	4.0
45–54	33,749	211 (189–234)	53
55–64	118,051	1,143 (1,064–1,223)	286
65–74	161,183	2,006 (1,929–2,084)	502
75–84	69,400	1,598 (1,544–1,652)	400
85+	23,009	2,441 (2,338–2,544)	610
Race/ethnicity			
White	260,321	651 (614–687)	163
Black	37,954	821 (769–872)	205
Hispanic	14,584	412 (368–456)	103
Region			
Midwest	96,752	827 (766–887)	207
Northeast	89,190	887 (817–956)	222
South	148,779	851 (772–929)	213
West	72,322	677 (626–728)	169
MSA			
Urban	352,310	939 (893–985)	235
Rural	53,269	429 (397–461)	107

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male 40+ civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 15. Length of stay (LOS) for primary diagnosis for prostate cancer

	1994				1996			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total[a]	116,018	5.4	5	216	107,776	4.5	4	1,426
Age								
40–44	265	5.3	4	30	463	4.1	4	8
45–54	6,407	5.1	5	48	8,273	4.1	4	57
55–64	29,746	5.4	5	88	31,054	4.1	4	79
65–74	50,380	5.3	5	191	43,878	4.3	4	231
75–84	22,663	5.3	3	216	18,333	4.8	3	1,233
85+	6,558	6.2	4	70	5,775	7.5	4	1,426
Race/ethnicity								
White	76,077	5.3	5	122	72,557	4.5	4	1,426
Black	10,246	6.5	5	216	10,485	4.8	4	79
Hispanic	3,608	5.6	5	85	3,336	4.9	4	67
Region								
Midwest	27,488	5.4	5	100	26,674	4.3	4	61
Northeast	22,822	6.6	5	216	23,982	4.7	4	112
South	45,639	5.2	5	99	39,419	4.2	4	115
West	20,069	4.4	4	191	17,702	4.9	3	1,426
MSA								
Rural	16,755	5.6	5	191	13,704	4.7	4	57
Urban	98,610	5.4	5	216	93,723	4.4	4	1,426

	1998				2000			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total[a]	88,628	4	3	162	94,620	3.7	3	133
Age								
40–44	373	3.9	3	19	550	3.1	3	8
45–54	8,060	3.7	3	84	11,009	3.4	3	79
55–64	25,814	3.7	3	111	31,437	3.4	3	72
65–74	34,142	3.8	3	81	32,783	3.6	3	118
75–84	14,958	4.2	3	65	13,446	4.4	3	133
85+	5,281	5.7	3	162	5,394	5.2	3	111
Race/ethnicity								
White	55,679	3.8	3	162	56,009	3.6	3	118
Black	8,540	4.6	3	84	8,683	4.8	3	133
Hispanic	3,825	4.8	4	65	3,814	4.5	3	104
Region								
Midwest	20,405	4.0	3	73	22,184	3.7	3	111
Northeast	19,941	4.3	3	81	22,445	4.2	3	133
South	31,024	3.8	3	111	32,697	3.7	3	113
West	17,258	3.7	3	162	17,293	3.3	3	79
MSA								
Rural	11,408	4.1	3	162	11,402	3.9	3	111
Urban	76,833	3.9	3	111	83,144	3.7	3	133

MSA, metropolitan statistical area.
US adult male 40+ civilian non-institutionalized population.
[a]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 12 also indicates that the inpatient hospitalization rate was greater for African Americans than for Caucasians at all time points, likely reflecting the increasing incidence of the disease in this racial group. Trends in geographical variation in inpatient utilization are also interesting. Although there was a marked decrease in inpatient hospitalization in all geographic regions, the decrease between 1992 and 2001 was most striking in the West and the Northeast. The reasons for this are unclear but may reflect geographical trends in screening and treatment practices during this time period.

Data from the HCUP nationwide inpatient sample indicate similar rates (Table 14). Not surprisingly, hospitalization rates for prostate cancer in rural regions were less than half the rates in urban areas during 1994–2000. There was also geographic variation, with the West having the lowest hospitalization rates in the country.

As inpatient hospitalization rates dropped, length of stay associated with hospitalization dropped as well (Table 15). Across age and racial groups and geographic regions, the median length of stay declined between 1994 and 2000. Patients were hospitalized for the least amount of time (mean of 3.3–4.4 days) in the West in all the time periods examined and hospitalized longest in the Northeast (mean of 4.2–6.6 days). While hospitalization rates tended to be lower in rural than in urban areas, the average length of stay in rural hospitals was slightly longer than that in urban hospitals. African Americans and Hispanics tended to have slightly longer hospital stays than Caucasians during each of the years examined. This trend may underlie or be driven by geographic differences as well.

Outpatient Care

Most radiation therapy is delivered in the outpatient hospital setting. In fact, with the exception of the immediate period surrounding surgery, most prostate cancer survivors access the healthcare system as outpatients. We focus here on three aspects of outpatient care: physician office visits, hospital outpatient visits, and ambulatory surgery visits.

Physician Office Visits

Data from the National Ambulatory Medical Care Survey (NAMCS) document that the average annual age-adjusted rate of physician office visits for prostate cancer in 1992–2000 was 5,001 per 100,000 American males over the age of 40 (Table 16). The rate was 5,449 per 100,000 in 1992, and it declined to a low of 3,870 per 100,000 in 1998. It then jumped to 5,828 per 100,000 in 2000. The exact reasons for these shifts are unclear. In this time period, men aged 75–84 had the highest rate of office visits, 112,069 per 100,000, as compared with 54,445 per 100,000 for men 65–74 and 5,930 per 100,000 for men 40–64. This may be explained by the fact that older patients are least likely to undergo aggressive therapy for localized disease and most likely to elect conservative management. Therefore, they may be seen more often by their providers and may require more outpatient care.

Data from the Medicare sample do not show the same decline between 1992 and 1998. Rather, as shown in Table 17, they indicate that the rate of physician office visits increased from 1992 to 1995 and remained relatively stable after that, reflecting changes in the age-adjusted incidence rate of prostate cancer. Differences between the NAMCS and Medicare data may be explained by the fact that the Medicare patients are older and likely have somewhat different patterns of care than the younger patients in the NAMCS sample. Also, the NAMCS is primarily a research database, while the Medicare dataset is an administrative database, which may explain some of the difference. There is considerable geographic variation in physician office visit rates in both the NAMCS and Medicare samples, although the differences are not consistent between the two datasets. It is likely that physician office visits are related to patterns of care in primary treatment choice. The relation of primary treatment to geographic region and patient age would explain the differing patterns of geographic variation between the two samples.

It is often assumed that most outpatient office visits for prostate cancer are to urologists, and NAMCS data confirm this. In 1992–2000, 12,236,564 office visits for prostate cancer were reported in NAMCS (Table 16). Of these, 8,662,617 were to urologists, and 3,573,947 were to non-urologists (Table 18). The overall annualized rate was 5,001 visits per 100,000 men, while the annualized office visit rate to urologists was 3,540 per 100,000 and to all other specialists was 1,461 per 100,000. Effectively, 71% of all annual office visits

Table 16. Physician office visits for prostate cancer listed as primary diagnosis, count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000				
	Count	Rate		Annualized Rate	Age-Adjusted Rate
Total[d]	12,236,564	25,004	(22,810–27,198)	5,001	25,034
Age					
40–64	2,118,240	5,930	(4,647–7,212)	1,186	
65–74	4,399,702	54,445	(46,664–62,226)	10,889	
75–84	4,739,092	112,069	(95,718–128,421)	22,414	
85+	979,530	108,031	(79,820–136,242)	21,606	
Race/ethnicity					
White	10,498,163	26,644	(24,119–29,170)	5,329	25,313
Other	1,738,401	18,227	(14,001–22,452)	3,645	23,366
Region					
Midwest	2,906,931	25,262	(20,840–29,683)	5,052	25,086
Northeast	3,718,177	37,425	(31,362–43,488)	7,485	36,556
South	3,187,693	18,669	(15,599–21,740)	3,734	18,435
West	2,423,763	23,256	(18,398–28,114)	4,651	24,738
MSA					
MSA	10,498,173	28,760	(25,998–31,522)	5,752	28,935
Non-MSA	1,738,391	13,979	(11,014–16,943)	2,796	13,835

	1992				1994			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	2,450,034	5,449	(4,410–6,487)	5,449	2,234,586	4,910	(4,112–5,709)	4,910
Age								
40–64	*	*			301,211	914	(515–1,314)	
65–74	832,868	10,070	(6,717–13,423)		783,398	9,946	(7,212–12,681)	
75–84	1,007,893	26,753	(18,874–34,632)		993,754	26,205	(19,613–32,796)	
85+	*	*			*	*		
Race/ethnicity								
White	2,217,258	5,998	(4,799–7,197)	5,730	1,893,654	5,120	(4,222–6,018)	4,881
Other	*	*		*	340,932	4,000	(2,270–5,730)	5,109
Region								
Midwest	*	*		*	595,052	5,590	(3,971–7,209)	5,649
Northeast	817,237	8,649	(6,016–11,282)	8,360	695,338	7,164	(4,685–9,643)	7,018
South	647,909	4,207	(2,690–5,723)	4,139	595,211	3,868	(2,760–4,976)	3,868
West	614,662	6,544	(3,718–9,369)	6,885	348,985	3,573	(2,303–4,843)	3,687
MSA								
MSA	2,156,249	6,651	(5,305–7,997)	6,922	1,838,675	5,559	(4,557–6,561)	5,781
Non-MSA	*	*		*	395,911	3,184	(1,985–4,384)	2,843

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Table 16 (continued). Physician office visits for prostate cancer listed as primary diagnosis, count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	2,420,055	4,951 (3,924–5,978)	4,951	1,991,798	3,870 (2,971–4,770)	3,870	3,140,091	5,828 (4,751–6,906)	5,828
Age									
40–64	*	*		*	*		616,205	1,541 (863–2,219)	
65–74	964,667	1,798 (8,159–15,436)		765,200	9,508 (6,360–12,656)		1,053,569	13,115 (8,809–17,421)	
75–84	826,418	19,600 (11,962–27,239)		655,783	14,461 (7,774–21,148)		1,255,244	25,974 (18,418–33,531)	
85+	*	*		*	*		*	*	
Race/ethnicity									
White	2,159,471	5,475 (4,239–6,712)	5,232	1,667,407	4,077 (3,028–5,125)	3,891	2,560,373	5,994 (4,797–7,192)	5,712
Other	*	*	*	*	*	*	579,718	5,193 (2,731–7,656)	6,402
Region									
Midwest	520,291	4,457 (2,604–6,310)	4,485	*	*	*	1,100,234	8,747 (5,931–11,563)	8,976
Northeast	665,572	6,753 (4,106–9,400)	6,523	784,053	7,689 (4,760–10,618)	7,622	755,977	7,223 (4,418–10,028)	6,982
South	670,950	3,915 (2,479–5,351)	3,878	*	*	*	806,504	4,193 (2,588–5,797)	4,162
West	563,242	5,516 (2,804–8,228)	5,787	*	*	*	477,376	4,116 (2,625–5,608)	4,341
MSA									
MSA	1,965,145	5,307 (4,114–6,500)	5,406	1,683,174	4,310 (3,172–5,447)	4,417	2,854,930	6,975 (5,585–8,365)	7,099
Non-MSA	*		*	*	*	*	285,161	2,203 (1,326–3,079)	2,068

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population, 40 years and older.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 17. Physician office visits by male Medicare beneficiaries with prostate cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	1,600,000	10,738 (10,668–10,808)		2,370,000	15,543 (15,462–15,625)	
Total < 65	19,220	615 (577–654)		36,040	1,046 (998–1,094)	
Total 65+	1,580,000	13,424 (13,337–13,511)	14,389	2,330,000	19,785 (19,684–19,887)	20,978
Age						
65–69	295,800	7,267 (7,155–7,380)		398,440	10,344 (10,208–10,480)	
70–74	422,160	12,984 (12,820–13,147)		614,140	18,417 (18,231–18,603)	
75–79	419,420	18,529 (18,303–18,755)		606,600	26,741 (26,484–26,999)	
80–84	284,660	21,728 (21,413–22,044)		444,260	31,975 (31,629–32,322)	
85–89	124,620	20,902 (20,440–21,363)		205,980	32,339 (31,825–32,853)	
90–94	29,480	14,555 (13,868–15,242)		52,520	24,846 (24,023–25,670)	
95–97	3,280	8,119 (6,928–9,309)		6,280	16,658 (14,976–18,340)	
98+	880	2,318 (1,641–2,995)		1,420	3,205 (2,472–3,939)	
Race/ethnicity						
White	1,390,000	11,047 (10,969–11,124)	10,991	2,070,000	15,961 (15,872–16,050)	15,882
Black	127,840	10,019 (9,786–10,252)	10,039	219,620	15,860 (15,588–16,133)	16,593
Asian	…	…	…	8,980	12,322 (11,254–13,389)	11,690
Hispanic	…	…	…	16,380	8,250 (7,709–8,792)	8,814
N. American Native	…	…	…	640	3,181 (2,097–4,264)	2,883
Region						
Midwest	362,260	9,766 (9,631–9,902)	9,826	531,420	13,786 (13,632–13,940)	13,942
Northeast	344,580	10,866 (10,713–11,019)	10,909	573,600	18,035 (17,846–18,224)	17,937
South	603,420	11,520 (11,398–11,642)	11,465	875,680	15,962 (15,825–16,099)	16,014
West	272,220	11,270 (11,091–11,448)	11,213	356,680	15,381 (15,173–15,589)	15,111

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Table 17 (continued). Physician office visits by male Medicare beneficiaries with prostate cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	2,240,000	15,472 (15,388–15,555)		2,280,000	14,785 (14,705–14,864)	
Total < 65	42,720	1,243 (1,191–1,296)		46,820	1,230 (1,180–1,280)	
Total 65+	2,200,000	19,900 (19,795–20,005)	20,561	2,230,000	19,227 (19,126–19,328)	19,759
Age						
65–69	363,940	10,778 (10,630–10,926)		368,740	10,421 (10,278–10,563)	
70–74	573,240	18,792 (18,596–18,988)		545,520	17,721 (17,531–17,912)	
75–79	594,320	26,025 (25,771–26,280)		598,920	24,414 (24,174–24,655)	
80–84	414,980	30,115 (29,773–30,458)		433,660	28,977 (28,652–29,302)	
85–89	193,160	29,687 (29,190–30,183)		220,620	30,494 (30,020–30,969)	
90–94	50,180	23,327 (22,527–24,126)		57,380	24,765 (23,979–25,551)	
95–97	5,500	13,896 (12,372–15,419)		6,060	15,773 (14,144–17,402)	
98+	2,000	4,181 (3,378–4,983)		2,200	4,055 (3,312–4,797)	
Race/ethnicity						
White	1,950,000	15,951 (15,859–16,042)	15,865	1,960,000	15,008 (14,922–15,095)	14,919
Black	206,760	15,491 (15,216–15,765)	16,107	217,460	14,819 (14,561–15,076)	15,414
Asian	14,940	10,894 (10,157–11,631)	10,704	15,020	7,330 (6,825–7,834)	6,871
Hispanic	39,920	11,893 (11,403–12,383)	12,167	41,960	11,167 (10,717–11,618)	11,024
N. American Native	1,200	4,292 (3,230–5,354)	4,220	1,360	4,084 (3,132–5,036)	2,823
Region						
Midwest	505,180	13,661 (13,504–13,817)	13,708	495,440	13,044 (12,893–13,196)	13,056
Northeast	507,460	18,259 (18,056–18,462)	18,050	504,160	17,253 (17,060–17,447)	17,033
South	861,120	16,044 (15,905–16,183)	16,292	894,900	15,410 (15,279–15,541)	15,620
West	330,420	14,775 (14,567–14,983)	14,389	344,760	13,930 (13,737–14,123)	13,674

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 18. Physician office visits by physician specialty for prostate cancer listed as primary diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], rate per 100,000 visits[c] (95% CI)

Physician Specialty	Count	Rate		Annualized Rate	Rate Per 100,000 visitsfor Prostate Cancer	
Total	12,236,564	25,004	(22,810–27,198)	5,001	100,000	(91,225–108,775)
Urology	8,662,617	17,701	(16,400–19,002)	3,540	70,793	(65,589–75,997)
All Other	3,573,947	7,303	(5,640–8,966)	1,461	29,207	(22,555–35,859)

[a]Rate per 100,000 is based on 1992–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male 40+ civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Rate per 100,000 male 40+ visits is based on estimated number of visits for prostate cancer in NAMCS 1992–2000.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

for prostate cancer were to urologists, while 29% were to other physicians.

Hospital Outpatient Visits

Hospital outpatient visits by prostate cancer patients are driven by a number of factors, the most important being that radiation therapy, whether EBRT or IB, is usually given in the hospital outpatient setting. We would expect to see significant variation in outpatient visit rates by geographic region and by age, as these two factors are correlated with receipt of radiotherapy as primary treatment. This is, in fact, what the data show. Table 19 presents data from the Medicare sample which indicate that hospital outpatient visits remained relatively stable from 1992 to 2001, but they were higher for men 75–79 years of age and those who live in the Northeast. These men were also more likely to receive radiotherapy, as documented in Table 10 and Figure 7.

Ambulatory Surgery Visits

As with outpatient hospital visits, ambulatory surgery center (ASC) visits for prostate cancer are driven by a number of unique factors and procedures. In particular, interstitial brachytherapy can be performed in ASCs, as can bilateral simple orchiectomy and various palliative/diagnostic procedures such as cystoscopy with stent placement or other minor interventions. Thus, one would expect ASC visits to vary regionally and with age, as these factors predict the use of IB and surgical hormone ablation therapy. As shown in Table 20, data from the Medicare dataset confirm these trends, and data from the National Survey of Ambulatory Surgery (Table 21) are similar.

ECONOMIC IMPACT

Medical expenditures for the treatment of prostate cancer in the United States totaled $1.3 billion in 2000, nearly 30% more than in 1994 (Table 22). The growth in spending occurred despite a reduction in hospitalization costs as treatment shifted from inpatient to outpatient settings. Spending on treatment provided in physician offices more than tripled between 1994 and 2000, while expenditures for ambulatory surgery more than doubled over this period. By 2000, inpatient expenditures accounted for 48% of total spending on prostate cancer, down from 69% in 1994.

Because prostate cancer primarily affects older males, more than two-thirds of all spending on the condition was borne by the Medicare program. Medicare reimbursements for prostate cancer totaled $846 million in 1992 and $927 million in 2001 (Table 23). Medicare spending among beneficiaries under 65 rose from $16 million in 1992 to more than $38 million in 2001, largely due to increased screening.

Individual-level expenditures were estimated using risk-adjusted regression models controlling for age, work status, geographic location, and health plan characteristics. Among males 40 to 64 years of age with employer-provided insurance, average annual expenditures for prostate cancer totaled $11,445, compared with $4,426 for similar men without the condition (Table 24).

Table 19. Hospital outpatient visits by male Medicare beneficiaries with prostate cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	258,420	1,735	(1,705–1,765)		235,760	1,549	(1,521–1,577)	
Total < 65	4,760	152	(133–172)		7,640	222	(200–244)	
Total 65+	253,660	2,155	(2,118–2,192)	2,235	228,120	1,937	(1,902–1,973)	1,973
Age								
65–69	50,920	1,251	(1,203–1,299)		57,640	1,496	(1,442–1,551)	
70–74	85,720	2,636	(2,559–2,714)		70,360	2,110	(2,041–2,179)	
75–79	72,300	3,194	(3,092–3,296)		54,480	2,402	(2,313–2,491)	
80–84	33,000	2,519	(2,399–2,639)		30,140	2,169	(2,061–2,278)	
85–89	10,060	1,687	(1,541–1,834)		11,020	1,730	(1,587–1,873)	
90–94	1,480	731	(565–897)		3,660	1,731	(1,483–1,980)	
95–97	140	347	(89–604)		580	1,538	(9,84–2,093)	
98+	40	105	(0–250)		240	542	(237–847)	
Race/ethnicity								
White	213,500	1,700	(1,668–1,732)	1,683	188,260	1,448	(1,419–1,477)	1,435
Black	32,540	2,550	(2,428–2,673)	2,596	38,380	2,772	(2,649–2,894)	2,858
Asian	…	...		…	1,320	1,811	(1,378–2,245)	1,894
Hispanic	…	...		…	3,220	1,622	(1,374–1,870)	1,672
N. American Native	…	...		…	140	696	(184–1,208)	895
Region								
Midwest	71,060	1,916	(1,853–1,978)	1,894	71,500	1,855	(1,795–1,915)	1,826
Northeast	84,300	2,658	(2,579–2,738)	2,673	66,960	2,105	(2,035–2,176)	2,126
South	65,060	1,242	(1,200–1,285)	1,258	65,400	1,192	(1,152–1,233)	1,209
West	35,960	1,489	(1,420–1,557)	1,480	29,100	1,255	(1,191–1,319)	1,241

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	239,780	1,656	(1,627–1,686)		271,280	1,759	(1,730–1,789)	
Total < 65	8,080	235	(212–258)		10,500	276	(252–299)	
Total 65+	231,700	2,098	(2,061–2,136)	2,128	260,780	2,245	(2,207–2,283)	2,271
Age								
65–69	49,680	1,471	(1,414–1,529)		57,660	1,629	(1,570–1,689)	
70–74	72,260	2,369	(2,293–2,445)		77,660	2,523	(2,444–2,601)	
75–79	64,620	2,830	(2,734–2,926)		72,960	2,974	(2,879–3,069)	
80–84	29,680	2,154	(2,045–2,262)		35,800	2,392	(2,283–2,502)	
85–89	11,480	1,764	(1,621–1,907)		13,160	1,819	(1,681–1,957)	
90–94	3,660	1,701	(1,457–1,946)		3,060	1,321	(1,113–1,529)	
95–97	220	556	(227–884)		420	1,093	(627–1,559)	
98+	100	209	(25–393)		60	111	(0–236)	
Race/ethnicity								
White	193,820	1,585	(1,554–1,616)	1,576	219,800	1,681	(1,650–1,712)	1,674
Black	32,240	2,415	(2,299–2,532)	2,475	36,620	2,495	(2,383–2,608)	2,559
Asian	3,160	2,304	(1,949–2,659)	2,450	2,120	1,035	(839–1,230)	1,064
Hispanic	5,220	1,555	(1,368–1,742)	1,609	5,140	1,368	(1,202–1,534)	1,309
N. American Native	680	2,432	(1,624–3,240)	2,647	1,040	3,123	(2,288–3,958)	3,003
Region								
Midwest	69,220	1,872	(1,810–1,934)	1,838	77,920	2,051	(1,988–2,115)	2,051
Northeast	66,160	2,380	(2,300–2,461)	2,370	72,960	2,497	(2,417–2,577)	2,498
South	63,200	1,178	(1,137–1,218)	1,191	71,800	1,236	(1,196–1,277)	1,249
West	36,840	1,647	(1,573–1,722)	1,688	44,040	1,779	(1,706–1,853)	1,753

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 20. Ambulatory surgery visits by male Medicare beneficiaries with prostate cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	45,900	308 (296–321)		34,220	225 (214–235)		39,920	276 (264–288)		41,660	270 (259–282)	
Total < 65	600	19 (12–26)		500	15 (8.8–20)		1,280	37 (28–46)		1,820	48 (38–58)	
Total 65+	45,300	385 (369–401)	411	33,720	286 (273–300)	297	38,640	350 (334–366)	353	39,840	343 (328–358)	343
Age												
65–69	8,840	217 (197–237)		7,820	203 (183–223)		8,780	260 (236–284)		11,260	318 (292–344)	
70–74	12,320	379 (349–409)		9,040	271 (246–296)		13,000	426 (393–459)		13,100	426 (393–458)	
75–79	11,940	527 (485–570)		8,560	377 (342–413)		9,500	416 (379–453)		9,540	389 (354–424)	
80–84	7,880	601 (542–661)		5,380	387 (341–433)		4,700	341 (298–385)		4,020	269 (232–306)	
85–89	3,300	553 (469–638)		2,400	377 (309–444)		2,160	332 (269–395)		1,500	207 (160–254)	
90–94	920	454 (323–585)		460	218 (129–307)		460	214 (126–301)		380	164 (90–238)	
95–97	100	248 (30–465)		60	159 (0–340)		40	101 (0–240)		40	104 (0–247)	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	39,120	311 (298–325)	308	29,100	224 (212–235)	224	35,000	286 (273–300)	285	35,960	275 (262–288)	274
Black	4,480	351 (305–397)	376	4,120	298 (257–338)	299	3,740	280 (240–320)	294	4,060	277 (239–315)	285
Asian	…	…	…	80	110 (2.7–217)	110	120	88 (18–158)	73	300	146 (72–221)	146
Hispanic	…	…	…	180	91 (31–150)	111	460	137 (81–193)	125	640	170 (111–229)	160
N. American Native	…	…	…	40	199 (0–472)	199	20	72 (0–211)	72	40	120 (0–285)	60
Region												
Midwest	14,580	393 (365–422)	386	10,940	284 (260–308)	292	11,240	304 (279–329)	300	11,420	301 (276–325)	299
Northeast	9,560	301 (274–328)	317	7,020	221 (198–244)	221	8,960	322 (293–352)	330	8,280	283 (256–311)	289
South	16,220	310 (288–331)	311	12,440	227 (209–245)	225	14,600	272 (252–292)	272	16,260	280 (261–299)	279
West	5,440	225 (198–252)	211	3,580	154 (132–177)	146	4,840	216 (189–244)	215	5,400	218 (192–244)	216

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 21. Ambulatory surgery visits for prostate cancer listed as primary diagnosis, 1994–1996 (merged and by year), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996			
	Count	Rate	Annualized Rate	Age-Adjusted Rate
Total	136,925	289 (257–321)	96	287
Age				
40–64	23,490	68 (48–89)	23	
65–74	48,819	606 (499–712)	202	
75–84	49,808	1,232 (1,005–1,459)	411	
85+	14,808	1,719 (1,152–2,286)	573	
Region				
Midwest	50,169	451 (376–526)	150	449
Northeast	24,667	252 (168–337)	84	246
South	42,872	261 (215–307)	87	265
West	19,217	192 (131–253)	64	192

	1994			1995			1996		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total	50,328	111 (89–132)	111	39,964	84 (68–100)	84	46,633	95 (78–113)	95
Age									
40–64	*	*	*	5,820	17 (9.71–24)		9,671	27 (16–38)	
65–74	18,085	230 (158–301)		14,441	178 (121–234)		16,293	199 (144–255)	
75–84	19,743	521 (372–669)		13,976	340 (231–448)		16,089	382 (247–517)	
85+	*	*	*	*	*		*	*	
Region									
Midwest	17,995	169 (121–217)	170	18,046	169 (117–210)	161	14,128	121 (85–157)	121
Northeast	10,161	*	104	*	*	*	9,835	100 (51–148)	98
South	14,210	92 (68–117)	93	13,475	81 (53–108)	83	15,187	89 (61–116)	88
West	7,962	82 (37–126)	85	*	*	*	7,483	73 (39–108)	76

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population, 40 years and older.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Table 22. Expenditures for prostate cancer, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$129,108,028	12.9%	$62,988,055	6.5%	$112,133,820	11.8%	$174,484,751	13.5%
Physician Office	$97,839,385	9.8%	$115,394,094	12.0%	$143,409,456	15.1%	$305,584,466	23.6%
Ambulatory Surgery	$76,645,818	7.6%	$77,341,725	8.0%	$141,018,192	14.9%	$179,080,421	13.8%
Emergency Room	$9,590,867	1.0%	$10,444,787	1.1%	$13,811,416	1.5%	$15,553,104	1.2%
Inpatient	$689,630,760	68.8%	$697,677,985	72.4%	$537,794,704	56.7%	$621,098,169	47.9%
TOTAL	$1,002,814,857		$963,846,646		$948,167,588		$1,295,800,912	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

This suggests that the annual incremental costs associated with prostate cancer exceed $7,000 per person. Average spending was higher among younger men (aged 40–54) and in the West, although regional variation was modest.

In addition to direct costs of medical care, prostate cancer can result in productivity losses through work absences. Overall, 26% of privately insured men in treatment for prostate cancer missed some work because of the condition. The average work loss was 20.9 hours per year (Table 25). Employees hospitalized for prostate cancer missed an average of 10.5 additional days of work (Table 26). Work loss for outpatient visits was less (2 hours per visit, on average) but was cumulatively similar due to the higher volume of outpatient treatment.

Max and colleagues (178) estimated the indirect costs of prostate cancer in California by estimating patients' lost (lifetime) earnings, discounted at a 3% annual rate. They estimated that the indirect costs due to premature mortality totaled $180 million, equal to the direct medical costs of treating the condition.

Medicare expenditures for medical androgen suppression therapy amounted to $478 million in 1994, 34% of the total Medicare expenditure for prostate cancer (155). These figures are likely to have increased over the past decade as the use of drug therapy has increased rapidly. Medicare has recently decreased the reimbursement rates for outpatient hormonal ablation therapy, which will likely decrease the overall economic burden of this treatment in the future. Nevertheless, these treatments still contribute greatly to the overall cost of prostate cancer in the United States.

Table 23. Expenditures for Medicare beneficiaries for treatment of prostate cancer, by site of service (% of total)

	Age 65 and over							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$199,884,080	24.1%	$185,917,800	28.4%	$215,481,000	30.0%	$250,870,360	28.2%
Physician Office	$74,274,100	9.0%	$107,163,440	16.4%	$158,207,040	22.0%	$227,776,200	25.6%
Ambulatory Surgery	$53,091,600	6.4%	$53,952,000	8.2%	$116,847,360	16.2%	$160,356,000	18.0%
Emergency Room	$2,455,000	0.3%	$2,665,680	0.4%	$1,869,840	0.3%	$2,218,220	0.2%
Inpatient	$500,158,960	60.3%	$305,255,600	46.6%	$226,821,840	31.5%	$247,542,400	27.9%
TOTAL	$829,863,740		$654,954,520		$719,227,080		$888,763,180	
	Under 65							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$2,522,800	15.6%	$5,149,360	27.7%	$6,003,440	26.6%	$8,998,500	23.3%
Physician Office	$922,560	5.7%	$1,910,120	10.3%	$3,118,560	13.8%	$4,447,900	11.5%
Ambulatory Surgery	$805,200	5.0%	$0	0.0%	$3,526,400	15.6%	$8,342,880	21.6%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$11,936,800	73.7%	$11,558,820	62.1%	$9,952,820	44.0%	$16,872,060	43.6%
TOTAL	$16,187,360		$18,618,300		$22,601,220		$38,661,340	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 24. Estimated annual expenditures for privately insured employees with and without a medical claim for prostate cancer in 2002[a]

	Annual Expenditures (per person)					
	Males Age 50–64 without Prostate Cancer (N=203,181)			Males Age 50–64 with Prostate Cancer (N=3,135)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$3,182	$1,244	$4,426	$9,551	$1,894	$11,445
Age						
50–54	$3,302	$1,306	$4,608	$8,108	$1,797	$9,905
55–59	$3,460	$1,291	$4,751	$6,997	$1,768	$8,765
60–64	$3,302	$1,159	$4,461	$6,181	$1,859	$8,040
Region						
Midwest	$2,996	$1,232	$4,228	$8,989	$1,888	$10,877
Northeast	$3,110	$1,332	$4,442	$9,331	$2,033	$11,364
South	$3,322	$1,175	$4,497	$9,965	$1,782	$11,747
West	$3,439	$1,238	$4,677	$10,317	$1,908	$12,225

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 40 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions. Predicted expenditures for males age 40 to 49 are omitted due to small sample size.

SOURCE: Ingenix, 2002.

Table 25. Average annual work loss of males treated for prostate cancer, 1999 (95%CI)

			Average Work Absence (hrs)		
	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
Total	315	26%	11.6 (5.2–18)	9.2 (4.9–13.6)	20.9 (13–28.8)
Age					
30–39	1	0%	0	0	0
40–49	24	21%	4.3 (0–10.4)	21.2 (0–57.7)	25.5 (0–68)
50–64	290	27%	12.3 (5.3–19.2)	8.3 (4.5–12.1)	20.6 (12.6–28.5)
Region					
Midwest	81	23%	4 (0–9.9)	4 (0.4–7.5)	8 (1.3–14.7)
Northeast	52	29%	19.2 (0–44.1)	6.8 (0.7–13)	26.1 (0.5–51.6)
South	110	25%	8.9 (2.5–15.2)	10.3 (1.9–18.7)	19.1 (7.4–30.8)
West	29	31%	29.9 (0–72.5)	7.8 (0–16)	37.7 (0–80.6)
Unknown	43	28%	11.5 (0–26.2)	20.3 (-1.3–41.9)	31.9 (6.2–57.5)

…data not available.

[a]Individuals with an inpatient or outpatient claim for prostate cancer and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

Table 26. Average work loss[a] associated with a hospital stay or an ambulatory care visit for prostate cancer (95% CI)

	Number of Inpatient Stays	Average Hours Missed for Inpatient Stays	Number of Outpatient Visits	Average Hours Missed for Outpatient Visits
Total	43	85.2 (44–127)	1324	2.2 (1–3)
Age				
30–39	…	…	1	0
40–49	4	25.5 (0–73)	116	4.4 (2–7)
50–64	39	91.4 (46–137)	1207	2.0 (1–3)
Region				
Midwest	5	65.6 (0–182)	339	0.9 (0–2)
Northeast	11	90.9 (0–214)	198	1.8 (0–3)
South	15	64.9 (26–103)	476	2.4 (1–3.)
West	5	173.5 (0–469)	118	1.9 (0–4)
Unknown	7	70.9 (0–162)	193	4.5 (2–4)

…data not available

[a]Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of outpatient visit.

Source: Marketscan Health and Productivity Management, 1999.

CONCLUSIONS

Prostate cancer is the most common urologic malignancy and the most common solid cancer found in American men. Disease incidence and patterns of care for this condition have changed dramatically in the past 20 years, following the introduction of prostate-specific antigen testing, which has resulted in widespread screening for this cancer throughout the United States and Western Europe. Although a number of randomized clinical trials assessing the effectiveness of prostate cancer screening are currently underway, the value of this clinical practice remains unproven. Despite this, prostate cancer screening has been embraced by the clinical community and the general population and likely will continue to be widely used.

There are numerous risk factors for prostate cancer. Although some of these are immutable (e.g., age, race, and family history), others are modifiable and could be the target of interventions that would allow primary prevention of the condition. Changes in diet, obesity, and physical activity, if these factors are proven to be associated with the development and aggressiveness of prostate cancer, could impact incidence and outcomes. This is a fertile area for further research.

Patterns of care have also changed tremendously in the past 20 years. Some of these changes are directly related to the introduction of PSA testing, while other reflect improved understanding of prostate cancer by both clinicians and researchers. In particular, older men with short life expectancies are, on average, receiving less-aggressive therapy than in the past, reflecting clinicians' realization that older men are at decreased risk of prostate cancer mortality, due to competing comorbid diseases. In contrast, more men are being diagnosed at younger ages and with earlier-stage disease and are therefore undergoing more-aggressive therapies for their condition. Surgical rates have consistently increased in these younger patients. There is considerable racial and geographic variation in treatment utilization; however, this is probably the result of clinical uncertainty as to which treatment is best for men with localized prostate cancer. Additional clinical trial data are desperately needed to identify which patients are best served by which therapies. Level I evidence regarding clinical outcomes following various therapies for localized prostate cancer is needed to reduce the clinical uncertainty surrounding this condition and to ensure high-quality care for all men diagnosed with prostate cancer in the United States.

Finally, there is a tremendous economic burden associated with the diagnosis and treatment of prostate cancer in the United States. While some of the costs are unavoidable, it may be possible to reduce this economic burden by generating better clinical data and removing certain financial incentives associated with various treatments. Specifically, hormone ablation therapy is probably overused in men with localized prostate cancer. Recent changes in Medicare reimbursement for these agents will likely affect their utilization and reduce the economic burden of the disease.

RECOMMENDATIONS

There is an abundance of administrative data sources and observational cohorts for prostate cancer research. While many of these resources have proven valuable in addressing research questions, a great deal of important work remains to be done, much of which cannot be completed with the existing datasets. New resources must be developed in order to answer pressing research questions. In general, recommendations for future work can be divided into three categories: primary prevention, screening issues, and identification of optimal treatment strategies.

Primary Prevention

Further research should be undertaken to examine the association of certain modifiable risk factors and the development of prostate cancer. If independent relationships are identified, appropriate interventions should be designed and studied as primary prevention strategies. Primary prevention of prostate cancer may represent the most cost-effective way to reduce the burden of the disease. The following specific issues in primary prevention require further study:

- Better understanding of gene-diet interactions. These interactions are modifiable and may be useful not only for prevention, but also for clinical trial stratification, as some of them may also predict more-aggressive cancers.
- Identification of specific therapeutic agents for primary prevention (i.e., anti-inflammatory agents or compounds that modify the hormonal milieu).

Prostate Cancer Screening

Randomized clinical trials to evaluate the effectiveness of prostate cancer screening are currently under way. Once these studies are completed, appropriate steps should quickly be taken to incorporate the findings into clinical practice. Specifically, if prostate cancer screening is found to reduce mortality in a cost-effective manner and ultimately result in greater benefit than harm, programs should be enacted to ensure population-wide access to screening and treatment. If the randomized studies indicate that prostate cancer screening is ineffective, is not cost-effective, or does more harm than good, appropriate policy steps should be taken to discourage screening in the general population.

Identification of Optimal Treatment Strategies

There is a pressing need to generate high-quality evidence regarding the effectiveness of the various therapies for localized prostate cancer. While randomized clinical trials are desperately needed, they may not be feasible in the current healthcare environment, and observational cohorts that extensively control for potentially confounding factors may be needed. Much of the racial/ethnic and geographic variation in prostate cancer care is likely related to clinical uncertainty surrounding the condition. New, high-quality data on the effectiveness of various therapies could be used to generate clinical treatment guidelines that would improve the quality of care. Specifically, the following important research areas should be addressed:

- Development of independent clinical biomarkers for indolent vs aggressive prostate cancers.
- Identification of the treatments that result in the best outcomes in different patient groups. Outcomes that should be addressed include mortality, health-related quality of life, and economic costs of treatment.
- Determination of which patients require adjuvant therapies for localized prostate cancer.
- Longer-term follow-up of prostate cancer cohorts to improve understanding of the survivorship experience and to optimize the treatment of this effectively chronic disease.
- Adoption of indicators of high-quality care.

REFERENCES

1. Merrill RM, Weed DL, Feuer EJ. The lifetime risk of developing prostate cancer in white and black men. Cancer Epidemiol Biomarkers Prev 1997;6:763-8.
2. Epstein JI. Pathology of Prostatic Neoplasia. In: Walsh PC, ed. Campbell's Urology. Philadelphia: Saunders, 2002:3025-37.
3. Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. Journal of Urology 1982;128:492-7.
4. Wasson JH, Bubolz TA, Lu-Yao GL, Walker-Corkery E, Hammond CS, Barry MJ. Transurethral resection of the prostate among medicare beneficiaries: 1984 to 1997. For the Patient Outcomes Research Team for Prostatic Diseases. J Urol 2000;164:1212-5.
5. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med 1987;317:909-16.
6. Cooperberg MR, Lubeck DP, Mehta SS, Carroll PR. Time trends in clinical risk stratification for prostate cancer: implications for outcomes (data from CaPSURE). J Urol 2003;170:S21-5; discussion S26-7.
7. Cooperberg MR, Lubeck DP, Grossfeld GD, Mehta SS, Carroll PR. Contemporary trends in imaging test utilization for prostate cancer staging: data from the cancer of the prostate strategic urologic research endeavor. J Urol 2002;168:491-5.
8. Purohit RS, Shinohara K, Meng MV, Carroll PR. Imaging clinically localized prostate cancer. Urol Clin North Am 2003;30:279-93.
9. Bernstein MR, Cangiano T, D'Amico A, Chittams J, Hardy C, Whittington RD, Tomaszewski JE, Schnall MD, Wein AJ, Malkowicz SB. Endorectal coil magnetic resonance imaging and clinicopathologic findings in T1c adenocarcinoma of the prostate. Urol Oncol 2000;5:104-107.
10. Tiguert R, Gheiler EL, Tefilli MV, Oskanian P, Banerjee M, Grignon DJ, Sakr W, Pontes JE, Wood DP, Jr. Lymph node size does not correlate with the presence of prostate cancer metastasis. Urology 1999;53:367-71.
11. Yu KK, Scheidler J, Hricak H, Vigneron DB, Zaloudek CJ, Males RG, Nelson SJ, Carroll PR, Kurhanewicz J. Prostate cancer: prediction of extracapsular extension with endorectal MR imaging and three-dimensional proton MR spectroscopic imaging. Radiology 1999;213:481-8.
12. National Cancer Institute. SEER Cancer Statistics Review 1975-2002 Available at http://www.seer.cancer.gov.
13. Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. Int J Cancer 2000;85:60-7.
14. Whittemore AS, Kolonel LN, Wu AH, John EM, Gallagher RP, Howe GR, Burch JD, Hankin J, Dreon DM, West DW, et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. J Natl Cancer Inst 1995;87:652-61.
15. Cotter MP, Gern RW, Ho GY, Chang RY, Burk RD. Role of family history and ethnicity on the mode and age of prostate cancer presentation. Prostate 2002;50:216-21.
16. Lichtenstein P, Holm NV, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M, Pukkala E, Skytthe A, Hemminki K. Environmental and heritable factors in the causation of cancer--analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med 2000;343:78-85.
17. Chan JM, Gann PH, Giovannucci EL. Role of diet in prostate cancer development and progression. J Clin Oncol 2005;23:8152-60.
18. Chan JM, Giovannucci EL. Vegetables, fruits, associated micronutrients, and risk of prostate cancer. Epidemiol Rev 2001;23:82-6.
19. Etminan M, Takkouche B, Caamano-Isorna F. The role of tomato products and lycopene in the prevention of prostate cancer: a meta-analysis of observational studies. Cancer Epidemiol Biomarkers Prev 2004;13:340-5.
20. Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of tomato products, lycopene, and prostate cancer risk. J Natl Cancer Inst 2002;94:391-8.
21. Giovannucci E, Ascherio A, Rimm EB, Stampfer MJ, Colditz GA, Willett WC. Intake of carotenoids and retinol in relation to risk of prostate cancer. J Natl Cancer Inst 1995;87:1767-1776.
22. Wu K, Erdman JW, Jr., Schwartz SJ, Platz EA, Leitzmann M, Clinton SK, DeGroff V, Willett WC, Giovannucci E. Plasma and Dietary Carotenoids, and the Risk of Prostate Cancer: A Nested Case-Control Study. Cancer Epidemiol Biomarkers Prev 2004;13:260-269.
23. Vogt TM, Mayne ST, Graubard BI, Swanson CA, Sowell AL, Schoenberg JB, Swanson GM, Greenberg RS, Hoover RN, Hayes RB, Ziegler RG. Serum lycopene, other serum carotenoids, and risk of prostate cancer in US Blacks and Whites. Am J Epidemiol 2002;155:1023-32.
24. Lu QY, Hung JC, Heber D, Go VL, Reuter VE, Cordon-Cardo C, Scher HI, Marshall JR, Zhang ZF. Inverse associations between plasma lycopene and other carotenoids and prostate cancer. Cancer Epidemiol Biomarkers Prev 2001;10:749-56.
25. Gann PH, Ma J, Giovannucci E, Willett W, Sacks FM, Hennekens CH, Stampfer MJ. Lower prostate cancer risk in men with elevated plasma lycopene levels: Results of a prospective analysis. Cancer Research 1999;59:1225-1230.
26. Schuurman AG, Goldbohm RA, Brants HA, van den Brandt PA. A prospective cohort study on intake of retinol, vitamins C and E, and carotenoids and prostate cancer risk (Netherlands). Cancer Causes Control 2002;13:573-82.
27. Cook NR, Stampfer MJ, Ma J, Manson JE, Sacks FM, Buring JE, Hennekens CH. Beta-carotene supplementation for patients with low baseline levels and decreased risks of total and prostate carcinoma. Cancer 1999;86:1783-1792.

28. Li H, Kantoff PW, Giovannucci E, Leitzmann MF, Gaziano JM, Stampfer MJ, Ma J. Manganese superoxide dismutase polymorphism, prediagnostic antioxidant status, and risk of clinical significant prostate cancer. Cancer Res 2005;65:2498-504.
29. Singh SV, Srivastava SK, Choi S, Lew KL, Antosiewicz J, Xiao D, Zeng Y, Watkins SC, Johnson CS, Trump DL, Lee YJ, Xiao H, Herman-Antosiewicz A. Sulforaphane-induced cell death in human prostate cancer cells is initiated by reactive oxygen species. J Biol Chem 2005;280:19911-24.
30. Garikapaty VP, Ashok BT, Chen YG, Mittelman A, Iatropoulos M, Tiwari RK. Anti-carcinogenic and anti-metastatic properties of indole-3-carbinol in prostate cancer. Oncol Rep 2005;13:89-93.
31. Joseph MA, Moysich KB, Freudenheim JL, Shields PG, Bowman ED, Zhang Y, Marshall JR, Ambrosone CB. Cruciferous vegetables, genetic polymorphisms in glutathione s-transferases m1 and t1, and prostate cancer risk. Nutr Cancer 2004;50:206-13.
32. Kolonel LN, Hankin JH, Whittemore AS, Wu AH, Gallagher RP, Wilkens LR, John EM, Howe GR, Dreon DM, West DW, Paffenbarger RS. Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. Cancer Epidemiol Biomarkers Prev 2000;9:795-804.
33. Cohen JH, Kristal AR, Stanford JL. Fruit and vegetable intake and prostate cancer risk. Journal of the National Cancer Institute 2000;92:61-68.
34. Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: Findings from case-control studies in Canada. Nutrition and Cancer 1999;34:173-184.
35. Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of cruciferous vegetables and prostate cancer. Cancer Epidemiol Biomarkers Prev 2003;12:1403-9.
36. Key TJ, Schatzkin A, Willett WC, Allen NE, Spencer EA, Travis RC. Diet, nutrition and the prevention of cancer. Public Health Nutr 2004;7:187-200.
37. Lee MM, Gomez SL, Chang JS, Wey M, Wang RT, Hsing AW. Soy and isoflavone consumption in relation to prostate cancer risk in China. Cancer Epidemiol Biomarkers Prev 2003;12:665-8.
38. Sonoda T, Nagata Y, Mori M, Miyanaga N, Takashima N, Okumura K, Goto K, Naito S, Fujimoto K, Hirao Y, Takahashi A, Tsukamoto T, Fujioka T, Akaza H. A case-control study of diet and prostate cancer in Japan: possible protective effect of traditional Japanese diet. Cancer Sci 2004;95:238-42.
39. Jacobsen B, Knutsen S, Fraser G. Does high soy milk intake reduce prostate cancer incidence? The Adventist Health Study (United States). Cancer Causes and Control 1998;9:553-557.
40. Hebert JR, Hurley TG, Olendzki BC, Teas J, Ma Y, Hampl JS. Nutritional and socioeconomic factors in relation to prostate cancer mortality: a cross-national study. J Natl Cancer Inst 1998;90:1637-47.
41. Strom SS, Yamamura Y, Duphorne CM, Spitz MR, Babaian RJ, Pillow PC, Hursting SD. Phytoestrogen intake and prostate cancer: a case-control study using a new database. Nutr Cancer 1999;33:20-5.
42. Nomura AM, Hankin JH, Lee J, Stemmermann GN. Cohort study of tofu intake and prostate cancer: no apparent association. Cancer Epidemiol Biomarkers Prev 2004;13:2277-9.
43. Vlajinac HD, Marinkovic JM, Ilic MD, Kocev NI. Diet and prostate cancer: a case-control study. Eur J of Cancer 1997; 33:101-7.
44. Tzonou A, Signorello LB, Lagiou P, Wuu J, Trichopoulos D, Trichopoulou A. Diet and cancer of the prostate: a case-control study in Greece. Int J Cancer 1999;80:704-708.
45. Deneo-Pellegrini H, De Stefani E, Ronco A, Mendilaharsu M. Foods, nutrients and prostate cancer: a case-control study in Uraguay. British Journal of Cancer 1999;80:591-597.
46. Chan JM, Stampfer MJ, Ma J, Rimm EB, Willett WC, Giovannucci EL. Supplemental vitamin E intake and prostate cancer risk in a large cohort of men in the United States. Cancer Epidemiol Biomarkers Prev 1999;8:893-899.
47. Goodman GE, Schaffer S, Omenn GS, Chen C, King I. The association between lung and prostate cancer risk, and serum micronutrients: results and lessons learned from beta-carotene and retinol efficacy trial. Cancer Epidemiol Biomarkers Prev 2003;12:518-26.
48. Heinonen OP, Albanes D, Virtamo J, Taylor PR, Huttunen JK, Harman AM, Haapakoski J, Malila N, Rautalahti M, Ripatti S, Maenpaa H, Teerenhovi L, Koss L, Virolainen M, Edwards BK. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: Incidence and mortality in a controlled trial. J Natl Cancer Inst 1998;90:440-446.
49. Hartman T, Albanes D, Pietinen P, Hartman AM, Rautalahti M, Tangrea JA, Taylor PR. The association between baseline vitamin E, selenium, and prostate cancer in the Alpha-Tocoperol, Beta-Carotene Cancer Prevention Study. Cancer Epidemiology, Biomarkers & Prevention 1998;7:335-340.
50. Rodriguez C, Jacobs EJ, Mondul AM, Calle EE, McCullough ML, Thun MJ. Vitamin E supplements and risk of prostate cancer in U.S. men. Cancer Epidemiol Biomarkers Prev 2004;13:378-82.
51. Hsing AW, Comstock GW, Abbey H, Polk BF. Serologic precursors of cancer. Retinol, carotenoids, and tocopherol and risk of prostate cancer. J Natl Cancer Inst 1990;82:941-946.

52. Hayes RB, Bogdanovicz JFAT, Schroeder FH, De Bruijn A, Raatgever JW, Van der Maas J, Oishi K, Yoshida O. Serum retinol and prostate cancer. Cancer 1988;62:2021-2026.
53. Nomura AMY, Stemmermann GN, Lee J, Craft NE. Serum micronutrients and prostate cancer in Japanese Americans in Hawaii. Cancer Epidemiol Biomarkers Prev 1997;6:487-491.
54. Helzlsouer KJ, Huang HY, Alberg AJ, Hoffman S, Burke A, Norkus EP, Morris JS, Comstock GW. Association Between alpha-Tocopherol, gamma-Tocopherol, Selenium, and Subsequent Prostate Cancer. J Natl Cancer Inst 2000;92:2018-2023.
55. Combs GF, Jr. Status of selenium in prostate cancer prevention. Br J Cancer 2004;91:195-9.
56. Nelson MA, Porterfield BW, Jacobs ET, Clark LC. Selenium and prostate cancer prevention. Semin Urol Oncol 1999;17:91-6.
57. Brooks JD, Metter EJ, Chan DW, Sokoll LJ, Landis P, Nelson WG, Muller D, Andres R, Carter HB. Plasma selenium level before diagnosis and the risk of prostate cancer development. J Urol 2001;166:2034-8.
58. van den Brandt PA, Zeegers MP, Bode P, Goldbohm RA. Toenail selenium levels and the subsequent risk of prostate cancer: a prospective cohort study. Cancer Epidemiol Biomarkers Prev 2003;12:866-71.
59. Duffield-Lillico AJ, Dalkin BL, Reid ME, Turnbull BW, Slate EH, Jacobs ET, Marshall JR, Clark LC. Selenium supplementation, baseline plasma selenium status and incidence of prostate cancer: an analysis of the complete treatment period of the Nutritional Prevention of Cancer Trial. BJU Int 2003;91:608-12.
60. Li H, Stampfer MJ, Giovannucci EL, Morris JS, Willett WC, Gaziano JM, Ma J. A prospective study of plasma selenium levels and prostate cancer risk. J Natl Cancer Inst 2004;96:696-703.
61. Combs GF, Clark LC, Turnbull BW. Reduction of cancer risk with an oral supplement of selenium. Biomed Environ Sci 1997;10:227-34.
62. Combs GF, Jr., Clark LC, Turnbull BW. Reduction of cancer mortality and incidence by selenium supplementation. Med Klin (Munich) 1997;92 Suppl 3:42-5.
63. Nomura AM, Lee J, Stemmermann GN, Combs GF. Serum selenium and subsequent risk of prostate cancer. Cancer Epidemiol Biomarkers Prev 2000;9:883-7.
64. Yoshizawa K, Willett WC, Morris SJ, Stampfer MJ, Spiegelman D, Rimm EB, Giovannucci E. Study of prediagnostic selenium level in toenails and the risk of advanced prostate cancer. J Natl Cancer Inst 1998;90:1219-24.
65. Corcoran NM, Najdovska M, Costello AJ. Inorganic selenium retards progression of experimental hormone refractory prostate cancer. J Urol 2004;171:907-10.
66. Waters DJ, Shen S, Cooley DM, Bostwick DG, Qian J, Combs GF, Jr., Glickman LT, Oteham C, Schlittler D, Morris JS. Effects of dietary selenium supplementation on DNA damage and apoptosis in canine prostate. J Natl Cancer Inst 2003;95:237-41.
67. Webber MM, Perez-Ripoll EA, James GT. Inhibitory effects of selenium on the growth of DU-145 human prostate carcinoma cells in vitro. Biochemical & Biophyscial Research Communications 1985;130:603-609.
68. Venkateswaran V, Fleshner NE, Sugar LM, Klotz LH. Antioxidants block prostate cancer in lady transgenic mice. Cancer Res 2004;64:5891-6.
69. Karunasinghe N, Ryan J, Tuckey J, Masters J, Jamieson M, Clarke LC, Marshall JR, Ferguson LR. DNA stability and serum selenium levels in a high-risk group for prostate cancer. Cancer Epidemiol Biomarkers Prev 2004;13:391-7.
70. Chan JM, Giovannucci EL. Dairy products, calcium, and vitamin D and risk of prostate cancer. Epidemiol Rev 2001;23:87-92.
71. Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Fakhrabadi-Shokoohi D, Giovannucci EL, Thun MJ, Calle EE. Calcium, dairy products, and risk of prostate cancer in a prospective cohort of United States men. Cancer Epidemiol Biomarkers Prev 2003;12:597-603.
72. Qin LQ, Xu JY, Wang PY, Kaneko T, Hoshi K, Sato A. Milk consumption is a risk factor for prostate cancer: meta-analysis of case-control studies. Nutr Cancer 2004;48:22-7.
73. Giovannucci E, Rimm EB, Wolk A, Ascherio A, Stampfer MJ, Colditz GA, Willett WC. Calcium and fructose intake in relation to risk of prostate cancer. Cancer Res 1998;58:442-447.
74. Giovannucci EL, Liu Y, Leitzmann MF, Stampfer MJ, Willett WC. A prospective study of physical activity and incident and fatal prostate cancer. Arch Intern Med 2005;165:1005-10.
75. Allen NE, Appleby PN, Davey GK, Key TJ. Hormones and diet: low insulin-like growth factor-I but normal bioavailable androgens in vegan men. Br J Cancer 2000;83:95-7.
76. Habito RC, Montalto J, Leslie E, Ball MJ. Effects of replacing meat with soyabean in the diet on sex hormone concentrations in healthy adult males. Br J Nutr 2000;84:557-63.
77. Norrish AE, Ferguson LR, Knize MG, Felton JS, Sharpe SJ, Jackson RT. Heterocyclic amine content of cooked meat and risk of prostate cancer. J Natl Cancer Inst 1999;91:2038-44.
78. Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer MJ. Prospective study of plasma fatty acids and risk of prostate cancer. J Natl Cancer Inst 1994;86:281-6.

79. Ngo TH, Barnard RJ, Cohen P, Freedland S, Tran C, deGregorio F, Elshimali YI, Heber D, Aronson WJ. Effect of isocaloric low-fat diet on human LAPC-4 prostate cancer xenografts in severe combined immunodeficient mice and the insulin-like growth factor axis. Clin Cancer Res 2003;9:2734-43.
80. Pollak MN, Schernhammer ES, Hankinson SE. Insulin-like growth factors and neoplasia. Nat Rev Cancer 2004;4:505-18.
81. Chan JM, Stampfer MJ, Ma J, Gann P, Gaziano JM, Pollak M, Giovannucci E. Insulin-like growth factor-I (IGF-I) and IGF binding protein-3 as predictors of advanced-stage prostate cancer. J Natl Cancer Inst 2002;94:1099-106.
82. 11th Report on Carcinogens, available at http://ntp.niehs.nih.gov/ntp/roc/toc11.html.
83. Terry P, Lichtenstein P, Feychting M, Ahlbom A, Wolk A. Fatty fish consumption and risk of prostate cancer. Lancet 2001;357:1764-6.
84. Augustsson K, Michaud DS, Rimm EB, Leitzmann MF, Stampfer MJ, Willett WC, Giovannucci E. A prospective study of intake of fish and marine fatty acids and prostate cancer. Cancer Epidemiol Biomarkers Prev 2003;12:64-7.
85. Norrish AE, Skeaff CM, Arribas GL, Sharpe SJ, Jackson RT. Prostate cancer risk and consumption of fish oils: a dietary biomarker-based case-control study. Br J Cancer 1999;81:1238-42.
86. Terry PD, Rohan TE, Wolk A. Intakes of fish and marine fatty acids and the risks of cancers of the breast and prostate and of other hormone-related cancers: a review of the epidemiologic evidence. Am J Clin Nutr 2003;77:532-43.
87. Leitzmann MF, Stampfer MJ, Michaud DS, Augustsson K, Colditz GC, Willett WC, Giovannucci EL. Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer. Am J Clin Nutr 2004;80:204-16.
88. Rose DP, Connolly JM. Effects of fatty acids and eicosanoid synthesis inhibitors on the growth of two human prostate cancer cell lines. Prostate 1991;18:243-254.
89. Karmali RA. Fatty acids: inhibition. Am J Clin Nutr 1987;45(s):225-229.
90. Chung BH, Mitchell SH, Zhang JS, Young CY. Effects of docosahexaenoic acid and eicosapentaenoic acid on androgen-mediated cell growth and gene expression in LNCaP prostate cancer cells. Carcinogenesis 2001;22:1201-6.
91. Kobayashi N, Leung P, Hong J, Barnard J, Freedland SJ, Elashoff D, Heber D, Henning S, Varr B, Said J, Giri D, Reddy S, Bagga D, Glaspy JA, Cohen P, Aronson WJ. Inhibitory effect of dietary fish oil (omega-3 fatty acids) on human prostate cancer progression in severe-combined immunodeficienct mice. abstract, AACR Frontiers in Cancer Prevention Third Annual Meeting 2004:133.
92. Chaudry AA, Wahle KW, McClinton S, Moffat LE. Arachidonic acid metabolism in benign and malignant prostatic tissue in vitro: effects of fatty acids and cyclooxygenase inhibitors. Int J Cancer 1994;57:176-80.
93. Tjandrawinata RR, Hughes-Fulford M. Up-regulation of cyclooxygenase-2 by product-prostaglandin E2. In: Honn KV, et al., eds. Eicosanoids and Other Bioactive Lipids in Cancer Inflammation and Radiation Injury 3. New York: Plenum Press, 1997:163-170.
94. Chen Y, Hughes-Fulford M. Human prostate cancer cells lack feedback regulation of low-density lipoprotein receptor and its regulator, SREBP2. Int J Cancer 2001;91:41-5.
95. Hughes-Fulford M, Chen Y, Tjandrawinata RR. Fatty acid regulates gene expression and growth of human prostate cancer PC-3 cells. Carcinogenesis 2001;22:701-7.
96. Aronson WJ, Glaspy JA, Reddy ST, Reese D, Heber D, Bagga D. Modulation of omega-3/omega-6 polyunsaturated ratios with dietary fish oils in men with prostate cancer. Urology 2001;58:283-8.
97. Platz EA, Rohrmann S, Pearson JD, Corrada MM, Watson DJ, De Marzo AM, Landis PK, Metter EJ, Carter HB. Nonsteroidal anti-inflammatory drugs and risk of prostate cancer in the Baltimore Longitudinal Study of Aging. Cancer Epidemiol Biomarkers Prev 2005;14:390-6.
98. Mahmud S, Franco E, Aprikian A. Prostate cancer and use of nonsteroidal anti-inflammatory drugs: systematic review and meta-analysis. Br J Cancer 2004;90:93-9.
99. Jacobs EJ, Rodriguez C, Mondul AM, Connell CJ, Henley SJ, Calle EE, Thun MJ. A large cohort study of aspirin and other nonsteroidal anti-inflammatory drugs and prostate cancer incidence. J Natl Cancer Inst 2005;97:975-80.
100. Venkataraman S, Jiang X, Weydert C, Zhang Y, Zhang HJ, Goswami PC, Ritchie JM, Oberley LW, Buettner GR. Manganese superoxide dismutase overexpression inhibits the growth of androgen-independent prostate cancer cells. Oncogene 2005;24:77-89.
101. Venkataraman S, Wagner BA, Jiang X, Wang HP, Schafer FQ, Ritchie JM, Patrick BC, Oberley LW, Buettner GR. Overexpression of manganese superoxide dismutase promotes the survival of prostate cancer cells exposed to hyperthermia. Free Radic Res 2004;38:1119-32.
102. Woodson K, Tangrea JA, Lehman TA, Modali R, Taylor KM, Snyder K, Taylor PR, Virtamo J, Albanes D. Manganese superoxide dismutase (MnSOD) polymorphism, alpha-tocopherol supplementation and prostate cancer risk in the alpha-tocopherol, beta-carotene cancer prevention study (Finland). Cancer Causes Control 2003;14:513-8.
103. van Gils CH, Bostick RM, Stern MC, Taylor JA. Differences in base excision repair capacity may modulate the effect of dietary antioxidant intake on prostate cancer risk: an example of polymorphisms in the XRCC1 gene. Cancer Epidemiol Biomarkers Prev 2002;11:1279-84.
104. Chan JM, Holick CN, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Giovannucci EL. Diet after diagnosis and the risk of prostate cancer progression, recurrence, and death (United States). Cancer Causes Control 2006;17:199-208.

105. Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, Breemen RR, Ashton D, Bowen P. Oxidative DNA damage in prostate cancer patients consuming tomato sauce-based entrees as a whole-food intervention. J Natl Cancer Inst 2001;93:1872-1879.
106. Kucuk O, Sarkar FH, Djuric Z, Sakr W, Pollak MN, Khachik F, Banerjee M, Bertram JS, Wood DP, Jr. Effects of lycopene supplementation in patients with localized prostate cancer. Exp Biol Med (Maywood) 2002;227:881-5.
107. Meyer F, Bairati I, Shadmani R, Fradet Y, Moore L. Dietary fat and prostate cancer survival. Cancer Causes Control 1999;10:245-51.
108. Thompson IM, Goodman PJ, Tangen CM, Lucia MS, Miller GJ, Ford LG, Lieber MM, Cespedes RD, Atkins JN, Lippman SM, Carlin SM, Ryan A, Szczepanek CM, Crowley JJ, Coltman CA, Jr. The influence of finasteride on the development of prostate cancer. N Engl J Med 2003;349:215-24.
109. Andersson SO, Wolk A, Bergstrom R, Adami HO, Engholm G, Englund A, Nyren O. Body size and prostate cancer: a 20-year follow-up study among 135006 Swedish construction workers. J Natl Cancer Inst 1997;89:385-9.
110. Engeland A, Tretli S, Bjorge T. Height, body mass index, and prostate cancer: a follow-up of 950000 Norwegian men. Br J Cancer 2003;89:1237-42.
111. Putnam SD, Cerhan JR, Parker AS, Bianchi GD, Wallace RB, Cantor KP, Lynch CF. Lifestyle and anthropometric risk factors for prostate cancer in a cohort of Iowa men. Ann Epidemiol 2000;10:361-9.
112. Sung JF, Lin RS, Pu YS, Chen YC, Chang HC, Lai MK. Risk factors for prostate carcinoma in Taiwan: a case-control study in a Chinese population. Cancer 1999;86:484-91.
113. Cerhan JR, Torner JC, Lynch CF, Rubenstein LM, Lemke JH, Cohen MB, Lubaroff DM, Wallace RB. Association of smoking, body mass, and physical activity with risk of prostate cancer in the Iowa 65+ Rural Health Study (United States). Cancer Causes & Control 1997;8:229-238.
114. Gronberg H, Damber L, Damber JE. Total food consumption and body mass index in relation to prostate cancer risk: a case-control study in Sweden with prospectively collected exposure data. J Urol 1996;155:969-74.
115. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Willett WC. Height, body weight, and risk of prostate cancer. Cancer Epidemiol Biomarkers Prev 1997;6:557-63.
116. Nilsen TI, Vatten LJ. Anthropometry and prostate cancer risk: a prospective study of 22,248 Norwegian men. Cancer Causes Control 1999;10:269-75.
117. Hsing AW, Deng J, Sesterhenn IA, Mostofi FK, Stanczyk FZ, Benichou J, Xie T, Gao YT. Body size and prostate cancer: a population-based case-control study in China. Cancer Epidemiol Biomarkers Prev 2000;9:1335-41.
118. Hsieh CC, Thanos A, Mitropoulos D, Deliveliotis C, Mantzoros CS, Trichopoulos D. Risk factors for prostate cancer: a case-control study in Greece. Int J Cancer 1999;80:699-703.
119. Schuurman AG, Goldbohm RA, Dorant E, van den Brandt PA. Anthropometry in relation to prostate cancer risk in the Netherlands Cohort Study. Am J Epidemiol 2000;151:541-9.
120. Clarke G, Whittemore AS. Prostate cancer risk in relation to anthropometry and physical activity: the National Health and Nutrition Examination Survey I Epidemiological Follow-Up Study. Cancer Epidemiol Biomarkers Prev 2000;9:875-81.
121. Lee IM, Sesso HD, Paffenbarger RS, Jr. A prospective cohort study of physical activity and body size in relation to prostate cancer risk (United States). Cancer Causes Control 2001;12:187-93.
122. Jonsson F, Wolk A, Pedersen NL, Lichtenstein P, Terry P, Ahlbom A, Feychting M. Obesity and hormone-dependent tumors: cohort and co-twin control studies based on the Swedish Twin Registry. Int J Cancer 2003;106:594-9.
123. Giovannucci E, Rimm EB, Liu Y, Leitzmann M, Wu K, Stampfer MJ, Willett WC. Body mass index and risk of prostate cancer in U.S. health professionals. J Natl Cancer Inst 2003;95:1240-4.
124. Porter MP, Stanford JL. Obesity and the risk of prostate cancer. Prostate 2005;62:316-21.
125. Daniell HW. A better prognosis for obese men with prostate cancer. J Urol 1996;155:220-5.
126. Rodriguez C, Patel AV, Calle EE, Jacobs EJ, Chao A, Thun MJ. Body mass index, height, and prostate cancer mortality in two large cohorts of adult men in the United States. Cancer Epidemiol Biomarkers Prev 2001;10:345-53.
127. Okasha M, McCarron P, McEwen J, Smith GD. Body mass index in young adulthood and cancer mortality: a retrospective cohort study. J Epidemiol Community Health 2002;56:780-4.
128. Freedland SJ, Terris MK, Presti JC, Jr., Amling CL, Kane CJ, Trock B, Aronson WJ. Obesity and biochemical outcome following radical prostatectomy for organ confined disease with negative surgical margins. J Urol 2004;172:520-4.
129. Kane CJ, Bassett WW, Sadetsky N, Silva S, Wallace K, Pasta DJ, Cooperberg MR, Chan JM, Carroll PR. Obesity and prostate cancer clinical risk factors at presentation: data from CaPSURE. J Urol 2005;173:732-6.
130. Amling CL, Riffenburgh RH, Sun L, Moul JW, Lance RS, Kusuda L, Sexton WJ, Soderdahl DW, Donahue TF, Foley JP, Chung AK, McLeod DG. Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. J Clin Oncol 2004;22:439-45.

131. Chang S, Hursting SD, Contois JH, Strom SS, Yamamura Y, Babaian RJ, Troncoso P, Scardino PS, Wheeler TM, Amos CI, Spitz MR. Leptin and prostate cancer. Prostate 2001;46:62-7.
132. Lund Nilsen TI, Johnsen R, Vatten LJ. Socio-economic and lifestyle factors associated with the risk of prostate cancer. Br J Cancer 2000;82:1358-63.
133. Pu YS. Prostate cancer in Taiwan: epidemiology and risk factors. Int J Androl 2000;23 Suppl 2:34-6.
134. Liu S, Lee IM, Linson P, Ajani U, Buring JE, Hennekens CH. A prospective study of physical activity and risk of prostate cancer in US physicians. Int J Epidemiol 2000;29:29-35.
135. Villeneuve PJ, Johnson KC, Kreiger N, Mao Y. Risk factors for prostate cancer: results from the Canadian National Enhanced Cancer Surveillance System. The Canadian Cancer Registries Epidemiology Research Group. Cancer Causes Control 1999;10:355-67.
136. Giovannucci E, Leitzmann M, Spiegelman D, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. A prospective study of physical activity and prostate cancer in male health professionals. Cancer Res 1998;58:5117-22.
137. Hartman TJ, Albanes D, Rautalahti M, Tangrea JA, Virtamo J, Stolzenberg R, Taylor PR. Physical activity and prostate cancer in the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study (Finland). Cancer Causes & Control 1998;9:11-18.
138. Ilic M, Vlajinac H, Marinkovic J. Case-control study of risk factors for prostate cancer. Br J Cancer 1996;74:1682-6.
139. Andersson SO, Baron J, Wolk A, Lindgren C, Bergstrom R, Adami HO. Early life risk factors for prostate cancer: a population-based case-control study in Sweden. Cancer Epidemiol Biomarkers Prev 1995;4:187-92.
140. Thune I, Lund E. Physical activity and the risk of prostate and testicular cancer: a cohort study of 53,000 Norwegian men. Cancer Causes Control 1994;5:549-56.
141. Hsing AW, McLaughlin JK, Zheng W, Gao YT, Blot WJ. Occupation, physical activity, and risk of prostate cancer in Shanghai, People's Republic of China. Cancer Causes Control 1994;5:136-40.
142. Dosemeci M, Hayes RB, Vetter R, Hoover RN, Tucker M, Engin K, Unsal M, Blair A. Occupational physical activity, socioeconomic status, and risks of 15 cancer sites in Turkey. Cancer Causes Control 1993;4:313-21.
143. Lee IM, Paffenbarger RS, Hsieh CC. Physical activity and risk of prostatic cancer among college alumni. Am J Epidemiol 1992;135:169-79.
144. Le Marchand L, Kolonel LN, Yoshizawa CN. Lifetime occupational physical activity and prostate cancer risk. Am J Epidemiol 1991;133:103-11.
145. Brownson RC, Chang JC, Davis JR, Smith CA. Physical activity on the job and cancer in Missouri. Am J Public Health 1991;81:639-42.
146. Albanes D, Blair A, Taylor PR. Physical activity and risk of cancer in the NHANES I population. Am J Public Health 1989;79:744-750.
147. Vena JE, Graham S, Zielezny M, Brasure J, Swanson MK. Occupational exercise and risk of cancer. Am J Clin Nutr 1987;45 (suppl):318-327.
148. Yu H, Harris RE, Wynder EL. Case-control study of prostate cancer and socioeconomic factors. Prostate 1988;13:317-325.
149. Severson RK, Nomura AMY, Grove JS, Stemmermann GN. A prospective analysis of physical activity and cancer. Am J Epidemiol 1989;130:522-529.
150. Patel AV, Rodriguez C, Jacobs EJ, Solomon L, Thun MJ, Calle EE. Recreational physical activity and risk of prostate cancer in a large cohort of U.S. men. Cancer Epidemiol Biomarkers Prev 2005;14:275-9.
151. Friedenreich CM, McGregor SE, Courneya KS, Angyalfi SJ, Elliott FG. Case-control study of lifetime total physical activity and prostate cancer risk. Am J Epidemiol 2004;159:740-9.
152. Albertsen PC, Fryback DG, Storer BE, Kolon TF, Fine J. Long-term survival among men with conservatively treated localized prostate cancer [see comments]. Jama 1995;274:626-31.
153. Jian L, Shen ZJ, Lee AH, Binns CW. Moderate physical activity and prostate cancer risk: a case-control study in China. Eur J Epidemiol 2005;20:155-60.
154. Torti DC, Matheson GO. Exercise and prostate cancer. Sports Med 2004;34:363-9.
155. American Cancer Society. Cancer facts and figures, 2006.
156. January 2002 complete prevalence count. available at http://srab.cancer.gov/prevalence/canques.html.
157. Chan JM, Jou RM, Carroll PR. The relative impact and future burden of prostate cancer in the United States. J Urol 2004;172:S13-6; discussion S17.
158. Lu-Yao G, Albertsen PC, Stanford JL, Stukel TA, Walker-Corkery ES, Barry MJ. Natural experiment examining impact of aggressive screening and treatment on prostate cancer mortality in two fixed cohorts from Seattle area and Connecticut. Bmj 2002;325:740.
159. Brawley OW. Prostate carcinoma incidence and patient mortality: the effects of screening and early detection. Cancer 1997;80:1857-63.
160. National Cancer Institute. SEER Cancer Statistics Review 1975-2002.
161. Bill-Axelson A, Holmberg L, Ruutu M, Haggman M, Andersson SO, Bratell S, Spangberg A, Busch C, Nordling S, Garmo H, Palmgren J, Adami HO, Norlen BJ, Johansson JE. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med 2005;352:1977-84.
162. Bubolz T, Wasson JH, Lu-Yao G, Barry MJ. Treatments for prostate cancer in older men: 1984-1997. Urology 2001;58:977-82.
163. The American Urological Association. Prostate Cancer Clinical Guidelines Panel. Report on the management of clinically localized prostate cancer. 1995.;Available at:http://www.auanet.org/timssnet/products/guidelines/main_reports/pca.pdf.

164. Ellison LM, Heaney JA, Birkmeyer JD. Trends in the use of radical prostatectomy for treatment of prostate cancer. Eff Clin Pract 1999;2:228-33.
165. Blasko JC, Mate T, Sylvester JE, Grimm PD, Cavanagh W. Brachytherapy for carcinoma of the prostate: techniques, patient selection, and clinical outcomes. Semin Radiat Oncol 2002;12:81-94.
166. Mettlin CJ, Murphy GP, Rosenthal DS, Menck HR. The National Cancer Data Base Report on Prostate Carcinoma after the Peak in Incidence Rates in the U. S. Cancer 1998;83:1679-84.
167. Zeliadt SB, Potosky AL, Etzioni R, Ramsey SD, Penson DF. Racial disparity in primary and adjuvant treatment for nonmetastatic prostate cancer: SEER-Medicare trends 1991 to 1999. Urology 2004;64:1171-6.
168. Bolla M, Gonzalez D, Warde P, Dubois JB, Mirimanoff RO, Storme G, Bernier J, Kuten A, Sternberg C, Gil T, Collette L, Pierart M. Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin. N Engl J Med 1997;337:295-300.
169. Bolla M, Collette L, Blank L, Warde P, Dubois JB, Mirimanoff RO, Storme G, Bernier J, Kuten A, Sternberg C, Mattelaer J, Lopez Torecilla J, Pfeffer JR, Lino Cutajar C, Zurlo A, Pierart M. Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): a phase III randomised trial. Lancet 2002;360:103-6.
170. Mettlin CJ, Murphy GP, Rosenthal DS, Menck HR. The National Cancer Data Base Report on Increased Use of Brachytherapy for the Treatment of Patients with Prostate Carcinoma in the U.S. Cancer 1999;86:1877-82.
171. Holmboe ES, Concato J. Treatment decisions for localized prostate cancer: asking men what's important. Journal of General Internal Medicine 2000;15:694-701.
172. Etzioni R, Penson DF, Legler JM, di Tommaso D, Boer R, Gann PH, Feuer EJ. Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. J Natl Cancer Inst 2002;94:981-90.
173. Johansson JE, Holmberg L, Johansson S, Bergstrom R, Adami HO. Fifteen-year survival in prostate cancer. A prospective, population-based study in Sweden. Jama 1997;277:467-71.
174. Shavers VL, Brown M, Klabunde CN, Potosky AL, Davis W, Moul JW, Fahey A. Race/Ethnicity and the Intensity of Medical Monitoring Under 'Watchful Waiting' for Prostate Cancer. Medical Care 2004;42:239-250.
175. AHCPR. Relative Effectiveness and Cost-Effectiveness of Methods of Androgen Suppression in the Treatment of Advanced Prostate Cancer. Evidence Report/Technology Assessment 1999;4:Available at:
176. Petrylak DP, Tangen CM, Hussain MH, Lara PN, Jr., Jones JA, Taplin ME, Burch PA, Berry D, Moinpour C, Kohli M, Benson MC, Small EJ, Raghavan D, Crawford ED. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. N Engl J Med 2004;351:1513-20.
177. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, Oudard S, Theodore C, James ND, Turesson I, Rosenthal MA, Eisenberger MA. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med 2004;351:1502-12.
178. Max W, Rice DP, Sung HY, Michel M, Breuer W, Zhang X. The economic burden of prostate cancer, California, 1998. Cancer 2002;94:2906-13.

CHAPTER 4

Interstitial Cystitis and Painful Bladder Syndrome

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Interstitial Cystitis and Painful Bladder Syndrome

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INTRODUCTION

Interstitial cystitis (IC) and painful bladder syndrome (PBS) are enigmatic chronic conditions characterized by frequent urination and bladder pain. Onset frequently occurs in the patient's fourth decade or after (Figure 1), and the disease typically fluctuates in severity but rarely resolves completely. Patients suffer considerable morbidity over the course of their lives, especially during the most productive years for work and family life. Although the data presented in this chapter focus on the direct medical costs of IC, patients are equally, if not more, affected by loss of work opportunities, effects on relationships, and overall diminished quality of life. Progress in addressing this disease has been painstakingly slow due to a lack of understanding of the underlying pathophysiology, significant disagreements about its diagnosis, lack of a marker for the disease or its activity, and lack of effective treatments. The National Institutes of Health has funded a number of initiatives in both the clinical and the basic science of IC over the past 15 years.

DEFINITION AND DIAGNOSIS

For most of the 20th century, IC was a relatively clearly defined disease characterized by severe objective bladder inflammation, fibrosis, and ulcer formation. The ulcers consisted of discrete, red, bleeding areas on the bladder wall termed *Hunner's ulcers* (1). IC was considered a rare condition, almost a clinical oddity. Modern thinking about IC dates to the work of Messing and Stamey (2), who in 1978 described the "early diagnosis" of IC based on cystoscopic identification of glomerulations (pinpoint bleeding areas) that occur after bladder distention under anesthesia. Since that time, there has been a steadily increasing appreciation of IC in clinical medicine. This "rare" disease was recently estimated to be present in 700,000 to 1,000,000 adult women in the United States, and some researchers have reported even higher figures. In 1987, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) sponsored a conference to review the accumulated knowledge of IC; a statement from this meeting (3) included a research definition of IC. The definition encompasses inclusion and exclusion criteria that describe the syndrome and identify a relatively homogeneous patient population. The exclusion criteria can be divided into two groups—first, other diseases that cause bladder symptoms and that, if present, could engender doubt about IC as the source of symptoms (e.g., radiation cystitis); and second, symptom and test-result parameters that eliminate individuals with atypical characteristics.

This was an important beginning for clinical IC research. The goals of the NIDDK statement's authors were modest: "The purpose of these criteria is not to define the disease but to ensure that in any group studies that adhere to these inclusion and exclusion criteria the populations will be relatively comparable." Despite the original intent, these criteria have been widely adopted as a *de facto* definition of IC in clinical medicine and continue to be used today, especially outside the United States (4). One study

Table 1. Codes used in the diagnosis of interstitial cystitis[a] and painful bladder syndrome[b]

Individuals 18 years or older with one or more of the following:	
ICD-9 diagnosis codes	
595.1	Chronic interstitial cystitis
625.8[c]	Other specified symptoms associated with female genital organs
625.9[c]	Unspecified symptom associated with female genital organs
CPT procedure codes	
51700	Bladder irrigation, simple, lavage, and/or instillation
52000	Cystourethroscopy, separate procedure
52260	Cystourethroscopy, with dilation of bladder for IC; general or conduction (spinal) anesthesia
52265	Cystourethroscopy, with dilation of bladder for IC; local anesthesia
52281	Cystourethroscopy, with calibration and/or dilation of urethral stricture or stenosis, with or without meatotomy, with or without injection procedure for cystography, male or female

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.

[c]Must occur with 788.41.

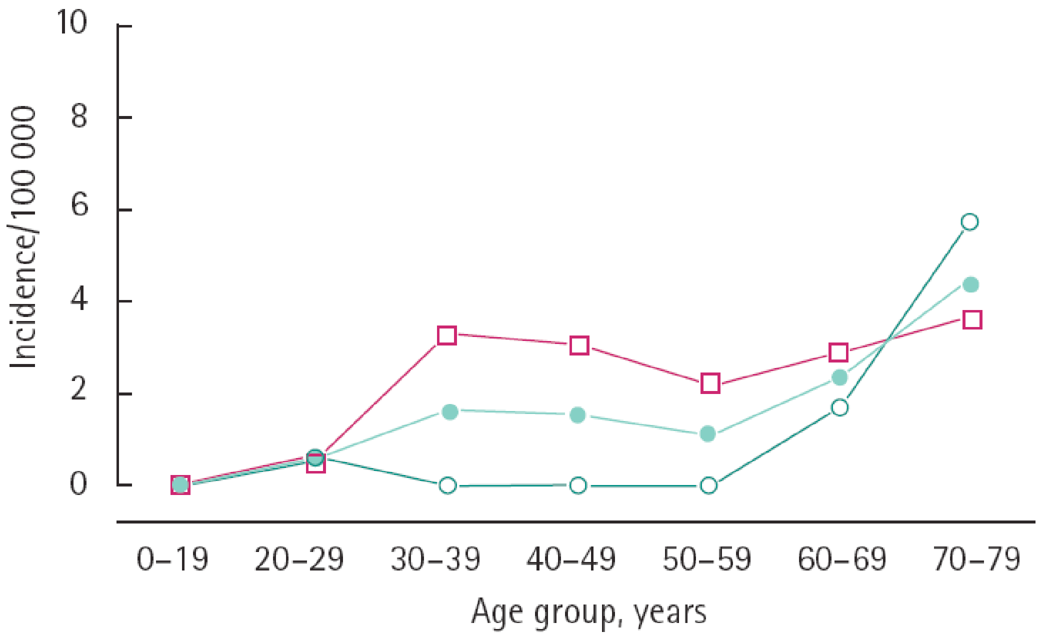

Figure 1. **Age specific incidence rates for males (open circles), females (squares), and all patients (closed circles) with interstitial cystitis[a] in Olmsted County, MN 1976–1996.**
[a]Interstitial cystitis, ICD-9 code 595.1.

SOURCE: Reprinted from BJU International, 91, Roberts RO, Bergstralh EJ, Bass SE, Lightner DJ, Lieber MM, Jacobsen SJ. Incidence of physician-diagnosed interstitial cystitis in Olmsted County: a community-based study, 181–185, Copyright 2003,with permission from Blackwell Publishing.

that examined the usefulness of the NIDDK criteria found that 90% of subjects meeting the criteria were believed by the experts to have IC, but more than 60% of patients diagnosed with IC by the same experts did not meet the strict criteria. There is general agreement that use of strict criteria for diagnosis of IC leaves out the majority of patients and may capture only a small minority of the overall population. This is of great importance and must be kept in mind when interpreting the data presented in this chapter.

Indeed, at this time, the diagnosis of IC is highly controversial. The International Continence Society proposed new definitions in 2002 to clarify terminology. The term *Painful Bladder Syndrome* (PBS) was defined as "the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and night-time frequency, in the absence of proven urinary tract infection or other obvious pathology." Under the new definitions, the term *IC* is reserved for those patients "with typical cystoscopic and histological features." This definition presumes that inflammation (classically with mononuclear inflammatory cells, including mast cell infiltration) is an inherent part of the disease. However, a large study of bladder biopsies in the NIDDK's tissue databank did not reveal predominant inflammation in the majority of cases (5). The term *PBS* accounts for patients with typical IC symptoms but without the cystoscopic finding of IC. The reasoning was that these changes in the bladder may evolve, and the patient should be reinvestigated periodically. However, there is little evidence to indicate that the presence or absence of cystoscopic findings is useful in directing treatment, and PBS can also be used to describe patients who are diagnosed and treated without a detailed investigation. In fact, US clinicians are increasingly treating patients for IC/PBS based on the history, physical examination, and urinalysis,

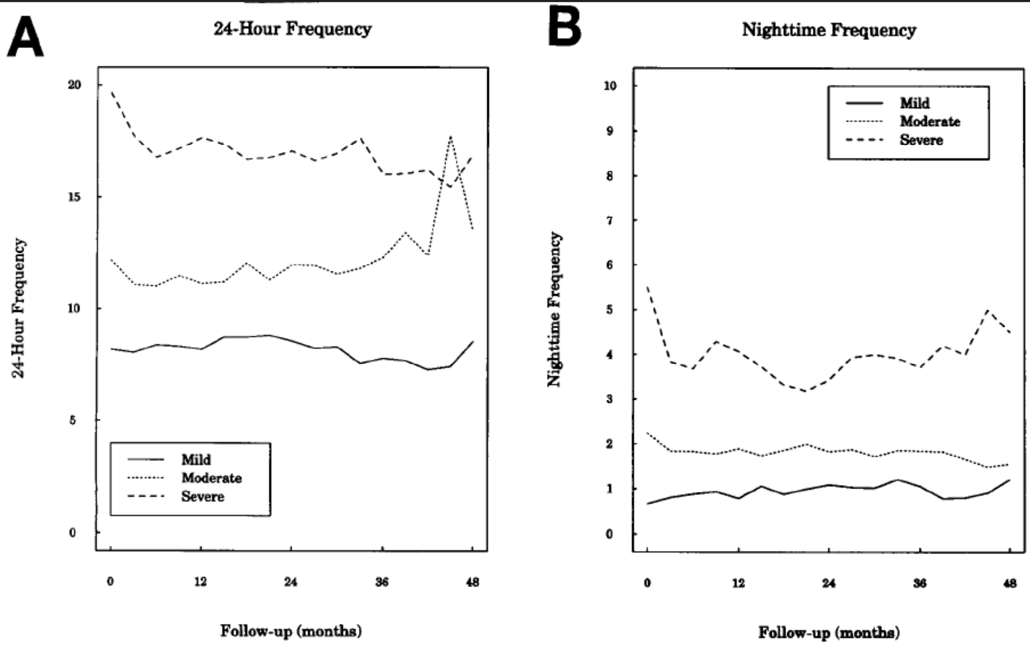

Figure 2. Mean urinary frequency measured from voiding log, by baseline severity of symptoms.

SOURCE: Reprinted from Journal of Urology, 163, Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JM, and the Interstitial Cystitis Data Base Study Group. A prospective study of interstitial cystitis: Results of longitudinal followup of the interstitial cystitis data base cohort, 1,434–1,439, Copyright 2000, with permission from American Urological Association.

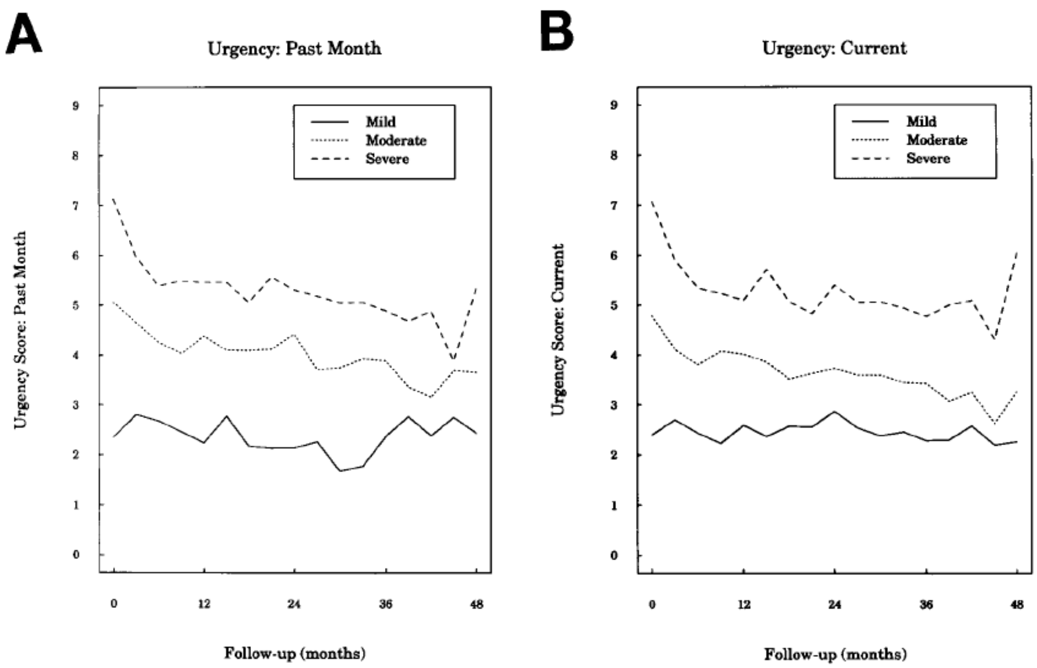

Figure 3. Mean urgency scores on 0 to 9 Likert scale with time by severity of urgency.

SOURCE: Reprinted from Journal of Urology, 163, Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JM, and the Interstitial Cystitis Data Base Study Group. A prospective study of interstitial cystitis: Results of longitudinal followup of the interstitial cystitis data base cohort, 1,434–1,439, Copyright 2000, with permission from American Urological Association.

Table 2. Differences in quality of life between women with interstitial cystitis[a] and those in the overall Nurses' Health Study I and II, adjusted for age and comorbidity

	Adjusted for Age Only			Adjusted for Age and Other Comorbidity		
SF-36 Scale	Difference	SE	P-value	Difference	SE	P-value
Physical function	-1.65	1.68	0.32	-0.73	1.59	0.65
Role-physical	-13.09	3.38	< 0.001	-11.58	3.29	< 0.001
Bodily pain	-9.82	2.00	< 0.001	-8.89	1.89	< 0.001
Vitality	-7.69	1.91	< 0.001	-7.10	1.88	< 0.001
Social funcion	-7.20	2.01	< 0.001	-6.59	1.98	< 0.001
Role-emotional	-0.06	3.07	0.98	0.23	3.06	0.94
Mental health	-3.52	1.50	0.02	-3.26	1.45	0.03

[a]Interstitial cystitis, ICD-9 code 595.1.

SOURCE: Reprinted from Journal of Urology, 164, Michael YL, Kawachi I, Stampfer MJ, Colditz GA, Curhan GC. Quality of life among women with interstitial cystitis, 423–427, Copyright 2000, with permission from American Urological Association.

whereas European physicians generally advocate universal use of urodynamic testing, cystoscopy under anesthesia, bladder distention, and biopsy.

Given the ongoing definitional evolution, we created code-based criteria for PBS for the analyses presented here. This approach should be considered exploratory, because PBS was not in use prior to 2002. Each table in this chapter indicates which code-based definition was employed.

In the United States, a simple bladder instillation procedure, the potassium sensitivity test, performed in the physician's office, has been put forward as a practical method of diagnosing IC/PBS (6). However, extensive data on this procedure published over the past few years indicate that the test may be overly sensitive, as estimates of the patient population derived from its use are 10 to 25 times higher than estimates derived from other methodologies. There is great hope for a urine or serum diagnostic test, perhaps based on the newly discovered protein, antiproliferative factor, which appears to have a high sensitivity and specificity (7, 8). At present, no assay is available outside of the research setting. A simple laboratory assay would enormously facilitate research in IC/PBS and is probably the single most important priority in this area for the future. Table 1 presents diagnosis and procedure codes associated with IC/PBS.

MANIFESTATIONS OF DISEASE

As in most diseases, IC/PBS patients have a wide range of symptom severity. Increased frequency of urination—10 to 15 times per day—is the norm, and severely affected patients must urinate more than once per hour. However, incontinence is relatively uncommon. The *sine qua non* of IC/PBS is bladder pain that increases with filling and diminishes with voiding. Thus, IC patients need to have nearly constant access to a bathroom to avert severe bladder pain. This disrupts sleep and severely affects quality of life. Some patients may have pain that is constant and severe, whereas others may have minimal pain as long as they can urinate at the first sense of filling. Although IC/PBS is said to be characterized by flares and remissions, there is little data about its time course, and the data that exist suggest that the overall course is relatively stable, at least after the symptoms have been present for a year or so. One population followed in a four-year study had little overall change in frequency, nocturia, or pain after the first observation period (Figures 2 and 3). Nevertheless, the impact of IC/PBS on patients is substantial. When compared with a population matched for age and health problems, IC/PBS patients had significantly worse quality of life in the SF-36 domains of role-physical, bodily pain, vitality, social function, and mental health (Table 2).

RISK FACTORS

The only clear risk factor for IC/PBS is female gender: The female:male ratio is approximately 9:1. Symptoms typically start in women's twenties and thirties (Table 3), a time when bacterial cystitis is a common problem. Although many patients do report that their symptoms began after an episode of acute bacterial cystitis, the best current research does not implicate bacteria in the pathophysiology,

Table 3. Characteristics of confirmed cases of interstitial cystitis[a] in the Nurses' Health Study (NHS)

Variable	Mean	Range
NHS I		
Age at first symptoms (yrs.)	46.8	5–66
Age at diagnosis (yrs.)	54.4	28–67
Delay to diagnosis (yrs.)	7.1	0–32
Year Symptoms began	1980	1946–1993
Year Diagnosed	1987	1969–1994
NHS II		
Age at first symptoms (yrs.)	30.5	5–47
Age at diagnosis (yrs.)	35.8	19–48
Delay to diagnosis (yrs.)	5.3	0–22
Year Symptoms began	1985	1965–1995
Year Diagnosed	1990	1975–1996

[a]By self-report.

SOURCE: Reprinted from Journal of Urology, 161, Curhan GC, Speizer FE, Hunter DJ, Curhan SG, Stampfer MJ.Epidemiology of interstitial cystitis:A population based study, 549–552, Copyright 1999, with permission from American Urological Association.

beyond a possible role in initiation. There are many associations with other diseases, including irritable bowel syndrome, fibromyalgia, lupus, and allergies (9). Recent work suggests that there may be a genetic component, as first-degree female relatives of IC/PBS patients have a 17-fold greater risk of the disease (10).

TREATMENT

A wide variety of treatments exist for IC/PBS, including behavioral therapies, oral and intravesical medications, and surgery. First-line therapy usually includes behavioral techniques such as dietary restrictions to avoid acidic food and other possible irritants, bladder training to improve bladder capacity, and relaxation techniques. Most of the oral medications used are older drugs that are used “off-label” without ever having been formally studied in patients with IC/PBS. Urinary analgesics such as phenazopyridine (Pyridium™), nonsteroidal anti-inflammatory drugs (NSAIDs), and mild narcotics such as codeine are commonly employed. Although anticholinergic agents have no clear role in the treatment of bladder pain, these bladder relaxants are commonly used, and some patients receive benefit. Tricyclic antidepressants are a mainstay of therapy, and randomized, controlled clinical trial data have demonstrated efficacy for amitriptyline over placebo (11, 12). Antihistamines, particularly hydroxyzine, are frequently used and can be especially helpful for patients with systemic allergies. The only FDA-approved oral medication for IC/PBS is pentosanpolysulfate (Elmiron™). This drug is designed to augment the protective glycosaminoglycan (GAG) layer of the bladder and thus hypothesized to prevent toxic and inflammatory agents in the urine from penetrating the subepithelial layer. General pain management principles, including use of long-acting narcotics (for those with severe daily pain) and combination therapy, are appropriate for IC/PBS patients, as they are for all patients with chronic pain. Unfortunately, none of these agents is highly effective, and patients are often subject to polypharmacy with the attendant side effects.

Intravesical therapy, particularly with dimethylsulfoxide (DMSO), has long been a mainstay of therapy. It is the only other FDA-approved drug for treatment of IC/PBS. DMSO is typically instilled weekly for six weeks, often mixed as a “cocktail” with local anesthetic agents, steroids, and heparin (another GAG layer analog). The technique is attractive, as the drug can be delivered directly to the bladder without systemic side effects. However, the procedure is invasive and painful for some patients. It is also inconvenient and expensive, as each treatment requires a physician visit. Although there is an initial high response rate, relapse is common. Therefore, many clinicians suggest monthly maintenance therapy for those patients who respond. Recent trials with novel intravesical agents such as Bacillus Calmette-Guerin, hyaluronic acid, and resiniferatoxin have been disappointing. A current trend is the use of local anesthetics in combination with a GAG analog, without DMSO.

Surgical therapy includes endoscopic treatment, implantable nerve stimulators, and radical surgery. Endoscopic bladder distention offers temporary relief of symptoms for about 40% of patients in most series. The effect rarely lasts longer than three to six months, except in the subset of patients with bladder ulcers. Cauterization of ulcers can produce dramatic pain relief, which in some cases can last a year or more. The sacral nerve stimulator, InterStim, is FDA-approved for urinary frequency and urgency, and a number of investigators have reported good initial success rates in IC/PBS patients (13). Patients with less-severe pain

Table 4a. Demographic characteristics of survey respondents who did or did not report having had interstitial cystitis, by age, gender, race/ethnicity, and region

	Self-reported IC	No IC
Age		
18–24	7.3%	14.2%
25–34	27.0%	23.0%
35–44	22.7%	21.6%
45–54	18.4%	13.7%
55–64	6.4%	11.4%
65–74	8.1%	9.8%
75–84	8.0%	5.1%
85+	2.0%	1.3%
Gender		
Male	6.0%	47.8%
Female	94.0%	52.2%
Race/ethnicity		
White	74.8%	76.2%
Black	11.9%	11.1%
Hispanic	13.3%	9.1%
Other	0.0%	3.6%
Region		
Northeast	24.5%	20.7%
Midwest	35.9%	24.0%
South	27.6%	34.2%
West	12.0%	21.1%

SOURCE: Adapted from Journal of Urology, Clemens JQ, Payne CK, Pace J. Prevalence of self-reported interstitial cystitis in a nationally representative United States survey, 307A, Copyright 2005, with permission from American Urological Association.

Table 4b. Prevalence of self-reported interstitial cystitis in NHANES, by age, gender, race/ethnicity, and region

	Proportion in NHANES with IC
Age	
18–24	0.2%
25–34	0.6%
35–44	0.5%
45–54	0.6%
55–64	0.3%
65–74	0.4%
75–84	0.8%
85+	0.7%
Gender	
Male	0.1%
Female	0.8%
Race/ethnicity	
White	0.5%
Black	0.5%
Hispanic	0.7%
Other	0.0%
Region	
Northeast	0.6%
Midwest	0.7%
South	0.4%
West	0.3%

NHANES, National Health and Nutrition Examination Survey,

SOURCE: Adapted from Journal of Urology, Clemens JQ, Payne CK, Pace J. Prevalence of self-reported interstitial cystitis in a nationally representative United States survey, 307A, Copyright 2005, with permission from American Urological Association.

seem to respond best. Finally, patients who are totally refractory to conservative measures may be treated with urinary diversion with or without cystectomy. In some cases, pelvic pain may persist even after removal of the bladder. There is great need for innovative approaches to treating patients with IC/PBS.

PREVALENCE AND INCIDENCE

Prevalence

The diagnosis of IC/PBS is controversial and is based primarily on symptoms; there is no objective marker to establish the presence of the disease, so studies to define its prevalence and incidence are difficult to conduct. In general, such studies utilize one of three methods: patient self-reported history, physician diagnosis, or identification of symptoms that suggest IC/PBS. The use of different methodologies has resulted in widely disparate prevalence estimates.

Patient Self-Reports

Two studies have assessed the prevalence of self-reported histories of IC/PBS. The first was conducted as part of the 1989 National Health Interview Survey (NHIS), and the second was part of the third National Health and Nutrition Examination Surveys (NHANES III), which was conducted between 1988 and 1994. Both studies provide a representative snapshot of the non-institutionalized US population, but neither includes longitudinal observations.

The same definition of disease was used in both studies. Participants were asked, “Have you ever had symptoms of a bladder infection (such as pain in your bladder and frequent urination) that lasted more than 3 months?” Those who answered “Yes” were then

Table 5. Prevalence of interstitial cystitis[a] in the Nurses' Health Study (NHS)

	Number of Cases	Total	Prevalence per 100,000 women
NHS I			
45–49	4	5,965	67
50–54	9	17,488	52
55–59	7	19,131	37
60–64	9	18,906	48
65–69	13	18,931	69
70–74	5	10,774	46
Total	63	91,555	52
NHS II			
30–34	9	13,669	66
35–39	15	27,372	55
40–44	23	31,800	72
45–49	16	20,587	79
Total	63	93,428	67

[a]By self-report.

SOURCE: Reprinted from Journal of Urology, 161, Curhan GC, Speizer FE, Hunter DJ, Curhan SG, Stampfer MJ.Epidemiology of interstitial cystitis:A population based study, 549–552, Copyright 1999, with permission from American Urological Association.

asked, “When you had this condition, were you told that you had interstitial cystitis or painful bladder syndrome?” An affirmative answer to both questions was considered to define the presence of IC/PBS.

The prevalence estimates obtained from these two studies were virtually identical. In the NHIS, the overall prevalence was 500 per 100,000 population, and the prevalence in women was 865 per 100,000 (14). In NHANES III, the prevalence was 470 per 100,000 population (60 per 100,000 men and 850 per 100,000 women) (15, 16), for a total of 82,832 men and

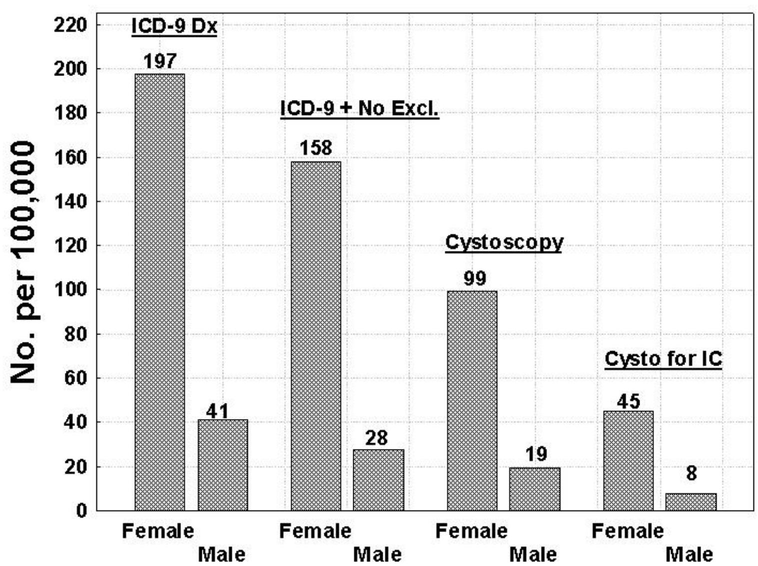

Figure 4. Gender specific prevalence of interstitial cystitis[a] in a managed care population.
[a]Interstitial cystitis, ICD-9 code 595.1.

Dx, diagnosis; No Excl., no exclusions; Cysto, cystoscopy.

SOURCE: Reprinted from Journal of Urology, 173, Clemens JQ, Meenan RT, Rosetti MC, Gao SY, Calhoun EA. Prevalence and incidence of interstitial cystitis in a managed care population, 98–102, Copyright 2005, with permission from American Urological Association.

1,218,631 women. Demographics from NHANES are presented in Tables 4a and 4b.

These results should be interpreted with caution, since a degree of misclassification is certainly present due to inaccurate patient recall and confusion between IC/PBS and other forms of cystitis. Therefore, the true prevalence of IC/PBS could be lower than that reported. On the other hand, many patients never seek treatment, and patient surveys consistently indicate that symptoms are typically present for years before a diagnosis is made; thus the prevalence of the disease could also be underestimated, since affirmative answers require the patient to have been diagnosed by a physician. In any case, these results suggest that chronic painful bladder symptoms are a common occurrence in the US population.

Physician Diagnosis

Physician diagnoses of IC/PBS have been used to determine the prevalence rate in multiple studies. Many of these studies utilized surveys of practicing urologists to assess the estimated number of IC/PBS patients seen in the office, with subsequent extrapolation. Such studies are subject to significant recall bias and do not generate reliable population-based prevalence estimates. To date, two population-based studies have been conducted to assess the prevalence of a physician diagnosis of IC/PBS. Data from participants in the Nurses' Health Study (NHS) cohorts I and II yielded prevalence estimates ranging from 52 to 67 per 100,000 women (Table 5). These estimates were based on self-reports, with accuracy evaluated using standardized criteria extrapolated from medical records. A subsequent study calculated the prevalence of physician-diagnosed IC/PBS in men and women in a managed-care population in the Pacific Northwest (15). The prevalence of this diagnosis was 197 per 100,000 women and 41 per 100,000 men (Figure 4). These rates decreased to 99 per 100,000 women and 19 per 100,000 men if the definition was limited to individuals who had undergone cystoscopy. This latter definition is close to that used in the NHS, and the resulting prevalence estimate for women is similar.

Studies that utilize physician diagnoses to define the presence of IC/PBS may underestimate the true prevalence, because they do not identify patients with undiagnosed disease. Furthermore, physicians who are not familiar with the condition may not assign the diagnosis when it is present. Others may be reluctant to label a patient with the diagnosis, since doing so could cause anxiety or stigmatization. Patients lacking medical insurance and those culturally disinclined to seek Western medical care are also excluded from the diagnosis.

Symptoms Suggestive of IC/PBS

Studies that assess the prevalence of physician-diagnosed IC/PBS may underestimate the true prevalence of the condition if some cases are not accurately diagnosed. Therefore, assessment of the presence of symptoms that suggest IC/PBS may provide a more sensitive method for estimating the true burden of the condition. One such study has been performed in a population of managed-care enrollees in the Pacific Northwest (16). Three definitions of IC/PBS symptoms were used in this study. Definition 1 consisted of self-reported pelvic pain for at least three months, along with urinary urgency or frequency for at least three months. Definition 2 included the Definition 1 criteria plus the presence of pain increasing as the bladder fills or pain relieved by urination. Definition 3 used results from a validated condition-specific questionnaire (the IC Symptom Index and IC Problem Index). Presence of IC/PBS for this definition was defined as a score of 12 or more on both the IC Symptom Index and IC Problem Index, including ≥ 2 episodes of nocturia and a pain score of 2 or greater. The resulting prevalence estimates were 11,200 per 100,000 women and 6,200 per 100,000 men (Definition 1); 3,300 per 100,000 women and 1,400 per 100,000 men (Definition 2); and 6,200 per 100,000 women and 2,300 per 100,000 men (Definition 3). Using Definition 3, a previous study in Finnish women demonstrated a prevalence of 450 per 100,000 (17).

From these studies, it is clear that the prevalence of IC/PBS symptoms is much greater than the prevalence of a physician diagnosis of the disease. However, other conditions may result in similar symptoms, and the predictive value of these symptoms in identifying true cases of IC/PBS is unknown. The validated questionnaires that exist are useful for evaluating patients diagnosed with IC/PBS, but they have not been shown to be useful in diagnosis. Furthermore, there is no standardized method of inquiring about the presence of the symptoms. It is apparent that

Table 6. Inpatient hospital stays for interstitial cystitis[a] listed as primary diagnosis, count, rate[b] (95% CI), age-adjusted rate[c]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	1,301	0.7 (0.5–0.9)	0.7	1,088	0.6 (0.4–0.7)	0.6	1,615	0.8 (0.6–1.1)	0.8	1,466	0.7 (0.5–0.9)	0.7
Age												
18–34	267	0.4 (0.2–0.6)		208	0.3 (0.2–0.5)		324	0.5 (0.2–0.8)		245	0.4 (0.2–0.6)	
35–44	181	0.5 (0.2–0.7)		*	*		297	0.7 (0.3–1.0)		358	0.8 (0.4–1.2)	
45–54	193	0.7 (0.3–1.0)		*	*		*			284	0.8 (0.5–1.1)	
55–64	202	1.0 (0.6–1.4)		161	0.8 (0.4–1.1)		191	0.9 (0.6–1.1)		*	*	
65–74	265	1.5 (0.8–2.2)		197	1.1 (0.7–1.5)		238	1.3 (0.9–1.7)		261	1.5 (1.0–1.9)	
75+	193	1.6 (1.0–2.1)		245	1.8 (1.3–2.4)		294	2.1 (1.1–3.1)		195	1.3 (0.9–1.8)	
Gender												
Male	175	0.2 (0.1–0.3)	0.2	176	0.2 (0.1–0.3)	0.2	228	0.2 (0.2–0.3)	0.3	158	0.2 (0.1–0.2)	0.2
Female	1,126	1.2. (0.8–1.5)	1.2	912	0.9 (0.7–1.1)	0.9	1,388	1.4 (0.9–1.8)	1.3	1,308	1.3 (1.0–1.6)	1.2
Race/ethnicity												
White	945	0.7 (0.4–0.9)	0.6	802	0.6 (0.5–0.7)	0.5	1,210	0.8 (0.5–1.2)	0.8	970	0.7 (0.4–0.9)	0.6
Other	*	*	*	*	*	*	*	*	*	170	0.3 (0.2–0.5)	0.4
Region												
Midwest	535	1.2 (0.5–1.9)	1.2	308	0.7 (0.4–0.9)	0.7	328	0.7 (0.4–1.1)	0.7	421	1.0 (0.6–1.3)	1.0
Northeast	310	0.8 (0.5–1.1)	0.8	211	0.6 (0.4–0.7)	0.5	*	*	*	*	*	*
South	293	0.5 (0.3–0.7)	0.5	388	0.6 (0.3–0.8)	0.6	*	*	*	516	0.7 (0.5–1.0)	0.7
West	162	0.4 (0.2–0.6)	0.4	181	0.4 (0.2–0.6)	0.5	331	0.8 (0.5–1.1)	0.8	248	0.6 (0.3–0.8)	0.6
MSA												
Rural	*	*	*	*	*	*	*	*	*	338	0.8 (0.4–1.2)	0.7
Urban	1,115	0.8 (0.6–1.0)	0.8	949	0.6 (0.5–0.8)	0.6	1,304	0.9 (0.6–1.1)	0.9	1,123	0.7 (0.5–0.9)	0.7

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Interstitial cystitis, ICD-9 code 595.1

[b]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 7. Hospital outpatient visits by Medicare beneficiaries with interstitial cystitis[a] listed as primary diagnosis, count[b], rate[c] (95% CI), age-adjusted rate[d]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[e]	1,300	3.7 (2.8–4.6)	3.7	1,240	3.5 (2.6–4.4)	3.5	1,760	5.2 (4.2–6.3)	5.2	2,800	7.9 (6.6–9.3)	7.9
Total < 65	440	7.9 (4.6–11)		280	4.6 (2.2–7.0)		500	8.0 (4.9–11)		1,180	17 (12–21)	
Total 65+	860	2.9 (2.1–3.8)		960	3.3 (2.4–4.2)		1,260	4.6 (3.5–5.8)		1,620	5.7 (4.5–7.0)	
Age												
65–69	100	1.1 (0.1–2.1)		140	1.7 (0.4–2.9)		340	4.6 (2.4–6.9)		500	6.6 (4.0–9.2)	
70–74	420	5.5 (3.2–7.9)		280	3.6 (1.7–5.5)		400	5.7 (3.2–8.2)		400	5.8 (3.2–8.3)	
75–79	160	2.8 (0.9–4.7)		380	6.7 (3.7–9.7)		360	6.4 (3.4–9.3)		300	5.0 (2.5–7.6)	
80–84	120	3.2 (0.6–5.7)		100	2.5 (0.3–4.8)		100	2.6 (0.3–4.9)		220	5.4 (2.2–8.6)	
85+	60	2.9 (0–6.2)		60	2.8 (0–5.9)		60	2.7 (0–5.9)		180	7.7 (2.7–13)	
Gender												
Male	80	0.5 (0–1.1)	0.4	80	0.5 (0–1.0)	0.5	220	1.5 (0.6–2.4)	1.5	520	3.4 (2.1–4.7)	2.9
Female	1,220	6.1 (4.6–7.6)	6.2	1,160	5.7 (4.3–7.2)	5.7	1,540	8.1 (6.3–9.9)	8.0	2,280	11 (9.4–14)	12
Race/ethnicity												
White	1,240	4.2 (3.2–5.2)	4.2	1,180	3.9 (2.9–4.9)	3.9	1,620	5.7 (4.5–6.9)	5.6	2,160	7.2 (5.9–8.6)	7.1
Black	40	1.3 (0–3.2)	1.3	60	1.9 (0–4.0)	1.9	100	3.2 (0.4–6.1)	3.2	560	16 (10–22)	17
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	0	0	0	40	5.7 (0–14)	5.7	40	5.0 (0–12)	5.0
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	400	4.6 (2.6–6.6)	3.7	580	6.4 (4.1–8.8)	6.4	360	4.2 (2.2–6.1)	4.2	600	6.8 (4.4–9.3)	6.6
Northeast	200	2.6 (1.0–4.2)	2.9	180	2.3 (0.8–3.9)	2.3	560	8.4 (5.3–12)	8.7	1,100	16 (12–20)	16
South	300	2.5 (1.2–3.7)	2.5	280	2.2 (1.0–3.4)	2.0	480	3.9 (2.3–5.4)	4.2	720	5.4 (3.7–7.2)	5.3
West	400	7.3 (4.1–10)	8.4	200	3.9 (1.5–6.3)	3.9	360	7.3 (3.9–11)	5.7	380	7.0 (3.9–10)	7.4

…data not available.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Unweighted counts multiplied by 20 to arrive at values in the table.

[c]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[d]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

estimates of symptom prevalence may vary widely due to factors such as response bias, use of different methods to define IC/PBS symptoms, and potential real differences among the populations studied.

Incidence

Few attempts have been made to estimate the incidence (new diagnoses) of IC/PBS. In a community-based study in Olmsted County, MN, physician-assigned diagnoses of IC/PBS were identified using medical records from the Rochester Epidemiology Project (18). The overall age- and sex-adjusted incidence rate was 1.1 per 100,000 per year for the interval from 1976 to 1996. The age-adjusted incidence rates were 1.6 per 100,000 women and 0.6 per 100,000 men (Figure 1). The median number of episodes of care-seeking for symptoms before diagnosis was 1 for women and 4.5 for men. In this study, the cumulative incidence rate (an estimate of prevalence) was 114 per 100,000 by age 80. A subsequent review of physician diagnoses of IC/PBS in Kaiser Permanente Northwest enrollees identified a much higher yearly incidence: 21 per 100,000 women and 4 per 100,000 men (15).

Table 8. Physician office visits for interstitial cystitis[a] listed as any diagnosis, 1992–2000 (merged), count, rate[b] (95% CI), annualized rate[c]

	1992–2000		
	Count	5-Year Rate	Annualized Rate
Total[d]	974,129	508 (337–679)	102
Age			
< 55	593,574	428 (235–621)	86
55+	380,555	718 (359–1,077)	144
Race/ethnicity			
White	956,335	662 (435–889)	132
Gender			
Female	922,936	922 (597–1,247)	184
Male	*	*	*
MSA	*	*	*
MSA	837,017	571 (375–766)	114
Non-MSA	*	*	*

*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area.
[a]Interstitial cystitis, ICD-9 code 595.1.
[b]Rate per 100,000 is based on 1992 - 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population.
[c]Average annualized rate per year.
[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.
NOTE:Counts may not sum to total due to rounding.
SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

INTERSTITIAL CYSTITIS

The datasets used in this compendium have several limitations that are evident when one attempts to study healthcare resource utilization for IC. First, most of the detailed information is limited to elderly individuals (e.g., in the Medicare and Veterans Affairs databases). Since IC occurs in people of all ages, only a minority of individuals with the disorder is represented. Second, because the datasets that provide information about individuals of all ages typically include smaller patient populations, the estimates obtained are often imprecise. Third, the identification of individuals with IC is based on a physician-coded diagnosis of the condition (ICD-9 code 595.1). As a result, individuals with undiagnosed IC, those who are not accurately coded, and those who are misdiagnosed or without access to medical care are not included in the estimates. These limitations should be kept in mind when reviewing the resource utilization data presented here.

Inpatient Care

The vast majority of the care provided for patients with IC occurs in the outpatient setting. However, inpatient admissions may occasionally be required for pain control or in conjunction with certain treatments (e.g., cystectomy, pain control following bladder hydrodistention). According to data from the Healthcare Cost and Utilization Project (HCUP), the rate of inpatient hospital stays for IC in 2000 was 0.7 per 100,000 population (Table 6), for a total of 1,446 admissions. The rate in women was 1.3 per 100,000; in men, it was 0.2 per 100,000. Virtually all those admitted were Caucasian. These numbers appear stable across the years analyzed (1994, 1996, 1998, and 2000). The hospitalization rate increases with age, which may reflect the presence of medical comorbidities. Alternatively, older patients with more-chronic

Table 9. Physician outpatient visits for individuals with interstitial cystitis[a] having commercial health insurance, count, rate[b]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis	64	9	92	8	250	14	336	17	386	22
Age										
18–24	3	*	4	*	13	*	23	*	29	*
25–34	16	*	15	*	55	13	76	17	76	21
35–44	26	*	39	12	81	16	93	17	100	21
45–54	10	*	22	*	59	15	98	21	109	26
55–64	8	*	11	*	36	18	35	14	61	26
65+	1	*	1	*	6	*	11	*	11	*
Gender										
Female	59	15	84	15	232	26	308	30	359	41
Male	5	*	8	*	18	*	30	3.0	27	*
As Any Diagnosis	83	11	122	11	322	18	480	24	546	31
Age										
18–24	4	*	7	*	14	*	29	*	37	17
25–34	18	*	22	*	69	17	105	24	103	28
35–44	35	16	50	16	106	21	130	23	145	31
45–54	15	*	29	*	8	21	144	30	155	37
55–64	9	*	13	*	41	21	56	23	85	36
65+	2	*	1	*	9	*	16	*	21	*
Gender										
Female	74	19	114	20	293	33	440	43	506	58
Male	9	*	8	*	27	*	41	4.1	41	4.7

*Figure does not meet standard for reliability or precision.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Rate per 100,000 based on member months of enrollment in calendar years for individuals in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

symptoms may undergo more-aggressive treatments that require hospitalization. The preponderance of admissions occurs in urban settings, perhaps indicating that more-invasive treatment is rendered at urban referral centers.

Outpatient Care

Hospital Outpatient Visits: Medicare Data

The rates of hospital outpatient visits for Medicare beneficiaries with a diagnosis of IC for 1992, 1995, 1998, and 2001 are presented in Table 7. During this period, the rate increased by 110%, from 3.7 per 100,000 in 1992 to 7.9 per 100,000 in 2001. This increase was evident in both men and women, although the rise was more dramatic in men.

Physician Office Visits

Physician office visit rates for patients with IC were determined from the National Ambulatory Medical Care Survey (NAMCS), data from which are reported from the even years from 1992 to 2000 (Table 8). Based on data from these five years combined, the annualized rate was 102 office visits per 100,000 population. Small cell sizes preclude analysis of trends over time. Virtually all visits were by Caucasian women in metropolitan areas, and the rate was higher in patients over age 55. Additional analysis showed that 92% of the visits were to urologists.

Data on physician office visits for IC as a primary or secondary diagnosis in individuals who had commercial insurance through United Healthcare in 1994, 1996, 1998, 2000, and 2002 are presented in Table 9. During this interval, the rate of visits with IC as any diagnosis increased from 11 to 31 per 100,000. The rate in women increased from 19 to 58 per 100,000. In

Table 10. Physician office visits by Medicare beneficiaries with interstitial cystitis[a] listed as primary diagnosis, count[b], rate[c] (95% CI), age-adjusted rate[d]

	1992				1995				1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[e]	27,520	79	(75–83)	79	32,860	93	(88–97)	93	38,600	115	(110–120)	115	39,500	112	(107–117)	112
Total < 65	2,240	40	(33–48)		3,640	59	(51–68)		5,280	85	(75–95)		7,540	107	(96–118)	
Total 65+	25,280	86	(81–91)		29,220	100	(95–105)		33,320	122	(116–128)		31,960	113	(108–119)	
Age																
65–69	7,460	83	(74–91)		8,260	98	(88–107)		7,260	99	(89–109)		7,940	105	(95–116)	
70–74	7,940	105	(94–115)		8,800	114	(103–125)		10,500	150	(137–163)		8,900	128	(116–140)	
75–79	5,480	95	(84–107)		6,360	112	(99–124)		7,980	141	(127–155)		7,160	120	(107–132)	
80–84	2,680	71	(59–83)		4,040	102	(88–116)		5,300	138	(121–154)		5,800	143	(126–159)	
85–89	1,440	70	(54–86)		1,300	60	(45–74)		1,700	78	(61–94)		1,600	69	(54–84)	
90–94	220	26	(11–42)		440	49	(28–69)		540	60	(37–82)		540	57	(35–78)	
95–97	20	11	(0–31)		20	11	(0–31)		40	20	(0–47)		20	10	(0–30)	
98+	40	27	(0–63)		0	0			0	0			0	0		
Race/ethnicity																
White	25,940	88	(83–93)	88	30,380	100	(95–105)	99	35,220	124	(118–130)	123	35,520	119	(113–124)	118
Black	800	27	(19–35)	24	1,600	50	(39–61)	53	1,640	53	(41–64)	55	2,180	64	(52–76)	65
Asian	…	...		…	40	24	(0–57)	12	40	13	(0–30)	13	180	38	(13–63)	42
Hispanic	…	...		…	200	50	(19–81)	50	560	80	(50–109)	91	460	58	(34–82)	53
N. American Native	…	...		…	0	0		0	20	37	(0–109)	37	40	60	(0–142)	60
Gender																
Male	3,360	23	(19–26)	22	3,320	22	(18–25)	23	4,500	31	(27–35)	31	5,460	35	(31–40)	35
Female	24,160	121	(114–127)	121	29,540	146	(139–154)	146	34,100	179	(170–187)	179	34,040	171	(163–180)	172
Region																
Midwest	6,760	77	(69–86)	74	6,980	77	(69–86)	73	7,380	86	(77–94)	85	8,700	99	(90–108)	97
Northeast	3,840	50	(43–57)	50	4,760	62	(54–70)	64	6,300	94	(84–104)	94	6,260	91	(81–101)	91
South	12,280	100	(93–108)	106	15,600	123	(114–131)	125	17,920	145	(135–154)	148	17,360	131	(122–140)	132
West	4,440	81	(70–92)	76	5,360	103	(91–116)	101	6,740	136	(122–151)	128	6,680	124	(110–137)	124

…data not available.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Unweighted counts multiplied by 20 to arrive at values in the table.

[c]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[d]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 11. Physician office visits by Medicare beneficiaries with interstitial cystitis[a], count[b], number of visits per person

	1992		1995		1998		2001	
	Count	No. Visits/ person	Count	No. Visits/ person	Count	No. Visits/ person	Count	No. Visits/ person
Total	27,520	2.0	32,860	2.0	38,580	2.1	39,500	1.9
Age								
< 65	2,240	2.3	3,620	2.1	5,140	2.2	7,500	2.1
65–69	7,480	2.0	7,720	1.9	7,200	1.8	7,620	2.0
70–74	7,840	2.1	9,260	2.2	10,440	2.1	9,080	2.1
75–79	5,420	1.9	6,420	2.0	7,960	2.1	7,220	1.7
80–84	2,780	1.8	4,020	2.1	5,460	2.2	5,880	2.0
85–89	1,480	1.7	1,360	2.0	1,800	1.9	1,640	1.6
90–94	220	1.6	440	2.1	540	1.9	540	1.6
95–97	20	1.0	20	1.0	40	2.0	20	1.0
98+	40	2.0	20	1.0	40	2.0	20	1.0
Gender								
Male	3,300	1.9	3,320	1.9	4,500	1.9	5,460	2.1
Female	24,220	2.0	29,540	2.0	34,080	2.1	34,040	1.9

[a]Interstitial cystitis, ICD-9 code 595.1.
[b]Unweighted counts multiplied by 20 to arrive at values in the table.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

three-fourths of the visits, IC was listed as the primary diagnosis.

The rates of physician office visits for Medicare beneficiaries with a diagnosis of IC in 1992, 1995, 1998, and 2001 are presented in Table 10. During this period, the rate increased from 79 per 100,000 in 1992 to 112 per 100,000 in 2001. These findings are consistent with the increase in Medicare hospital outpatient visits for IC discussed above. The yearly number of office visits per person diagnosed with IC was stable at 2.0 visits per person throughout the time periods examined (Table 11). Table 12 compares the number of visits for

Table 12. Physician office visits by Medicare beneficiaries with interstitial cystitis[a] or painful bladder syndrome[b], by specialty of care, count[c], rate[d] (95% CI)

	1992		1995		1998		2001	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total								
Urologists	24,500	65 (62–69)	28,380	86 (76–84)	34,080	84 (80–88)	34,680	83 (79–86)
Gynecologists	380	1.0 *	760	1.9 (1.3–2.5)	940	2.3 (1.6–3.0)	1,240	2.9 (2.2–3.7)
Primary care	3,040	8.1 (6.8–9.4)	2,980	7.6 (6.3–8.8)	5,460	13 (12–15)	5,420	13 (11–14)
Other	2,140	6.4 (4.6–6.8)	1,200	2.2 (2.3–3.8)	2,100	5.2 (4.2–6.1)	2,600	6.2 (5.1–7.2)

…data not available.
*Figure does not meet standard for reliability or precision.
[a]Interstitial cystitis, ICD-9 code 595.1.
[b]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.
[c]Unweighted counts multiplied by 20 to arrive at values in the table.
[d]Rate per 100,000 people 65 years and older eligible for Medicare.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 13. Ambulatory surgery visits with interstitial cystitis[a] listed as any diagnosis, 1994–1996 (merged), count, rate[b] (95%CI), annualized rate[c]

	1994–1996		
	Count	3-Year Rate	Annualized Rate
Total	70,224	37 (31–44)	12
Age			
18–24	*	*	*
25–34	12,090	30 (17–42)	10
35–44	19,905	48 (28–67)	16
45–54	10,426	34 (18–51)	11
55–64	*	*	*
65–74	11,505	64 (43–84)	21
75–84	*	*	*
85+	*	*	*
Gender			
Male	*	*	*
Female	64,231	65 (53–77)	22

*Figure does not meet standard for reliability or precision.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population.

[c]Average annualized rate per year.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

IC/PBS by specialty and indicates that in 2001, 80% of the visits were to urologists.

Ambulatory Surgery Visits

Data from the National Survey of Ambulatory Surgery (NSAS) from 1994 to 1996 show an annualized visit rate of 12 per 100,000 per year. In women, the rate was 22 per 100,000 (Table 13). Table 14 shows the corresponding rates for individuals who had commercial health insurance for the even years from 1994 to 2000. During this period, there was a slight increase in the rate for IC as any diagnosis, from 12 per 100,000 to 19 per 100,000, and an increase in women from 23 per 100,000 to 34 per 100,000. The majority of these visits (89%) listed IC as the primary diagnosis. For Medicare beneficiaries, the rate of ambulatory visits remained stable at 12 to 13 per 100,000 between 1992 and 2001 (17 to 20 per 100,000 women) (Table 15). These rates do not reflect additional outpatient procedures performed in the office or hospital setting.

Physician Office Procedures

Table 16 examines trends in office procedures for IC in Medicare beneficiaries in 1992, 1995, 1998, and 2001. Data are presented for bladder irrigation/instillation (CPT code 51700) and cystoscopy (CPT code 52000). Additional procedures examined included cystoscopy with hydrodistention for IC (CPT codes 52260 and 52265) and cystoscopy with urethral dilation (CPT code 52281), but there were too few counts for these conditions to generate reliable data. The rates presented in Table 16 reflect the number of procedures per 100,000 individuals with a diagnosis of IC. The bladder instillation rate was relatively stable, from 50,000 to 70,000 per 100,000, and it was lower in the Northeast than in other regions. There was a slight but consistent decline in the cystoscopy rate with time, from 9,091 per 100,000 in 1992 to 7,515 per 100,000 in 2001. Small cell sizes preclude an analysis of cystoscopy use by region. Table 17 presents the cumulative procedure rates by summing the data from 1992, 1995, 1998, and 2001. The annualized rate for bladder irrigation was 63,319 per 100,000. The annualized rate for cystoscopy was 8,574 per 100,000; for cystoscopy with hydrodistention, 1,043 per 100,000; and for cystoscopy with urethral dilation, 1,021 per 100,000. The relatively low rate observed for cystoscopy with hydrodistention may reflect the greater age of this population. It is possible that many of these individuals underwent hydrodistention at a younger age at the time of diagnosis.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

PAINFUL BLADDER SYNDROME

The data utilized previously in this chapter to assess healthcare resource utilization for IC are limited to patients with a coded physician diagnosis (ICD-9 code 595.1). To assess the healthcare resource utilization for PBS, we used the following definition for the condition: individuals with ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 (other specified symptoms associated with

Table 14. Ambulatory surgery visits by individuals with interstitial cystitis[a] having commercial health insurance, count, rate[b]

	Year									
	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	86	12	139	12	238	13	319	16	281	16
Age										
18–24	6	*	11	*	21	*	28	*	27	*
25–34	20	*	27	*	41	10	74	17	50	14
35–44	35	16	45	14	74	15	89	16	78	17
45–54	20	*	38	16	62	16	72	15	81	19
55–64	5	*	16	*	34	17	45	18	37	16
65+	0	*	2	*	7	*	11	*	8	*
Gender										
Female	83	21	190	23	221	25	296	29	261	30
Male	3	*	9	*	17	*	23	*	20	*
As Any Diagnosis										
Total	92	12	158	14	285	16	400	20	326	19
Age										
18–24	6	*	13	*	24	*	33	13	29	*
25–34	20	*	32	12	52	13	92	21	62	17
35–44	38	18	52	16	90	18	107	19	92	20
45–54	23	*	42	17	72	18	92	19	92	22
55–64	5	*	17	*	40	20	59	24	41	17
65+	0	*	2	*	7	*	17	*	10	*
Gender										
Female	88	23	148	26	267	30	368	36	301	34
Male	4	*	10	*	18	*	32	3	25	*

* Figure does not meet standard for reliability or precision.
[a]Interstitial cystitis, ICD-9 code 595.1.
[b]Rate per 100,000 based on member months of enrollment in calendar years for individuals in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 15. Ambulatory surgery visits by Medicare beneficiaries with interstitial cystitis[a] listed as primary diagnosis, count[b], rate[c] (95% CI), age-adjusted rate[d]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[e]	4,420	13 (11–14)	13	4,160	12 (10–13)	12	3,920	12 (10–13)	12	4,160	12 (10–13)	12
Total < 65	320	5.8 (2.9–8.6)		520	8.5 (5.2–12)		560	9.0 (5.7–12)		1,020	14 (10–18)	
Total 65+	4,100	14 (12–16)		3,640	12 (11–14)		3,360	12 (10–14)		3,140	11 (9.4–13)	
Age												
65–69	1,100	12 (9.0–15)		1,060	13 (9.2–16)		680	9.3 (6.2–12)		940	12 (8.9–16)	
70–74	1,360	18 (14–22)		1,300	17 (13–21)		1,440	21 (16–25)		900	13 (9.2–17)	
75–79	1,040	18 (13–23)		480	8.4 (5.1–12)		740	13 (8.9–17)		680	11 (7.5–15)	
80–84	460	12 (7.2–17)		580	15 (9.3–20)		360	9.4 (5.0–14)		480	12 (7.1–16)	
85–89	100	4.9 (0.6–9.1)		180	8.3 (2.9–14)		100	4.6 (0.5–8.6)		100	4.3 (0.5–8.1)	
90+	40	4.8 (0–11)		40	4.4 (0–11)		40	4.4 (0–10)		20	2.1 (0–6.2)	
Gender												
Male	480	3.2 (1.9–4.5)	3.2	340	2.2 (1.2–3.3)	2.5	560	3.9 (2.4–5.3)	4.4	620	4.0 (2.6–5.4)	3.9
Female	3,940	20 (17–22)	20	3,820	19 (16–22)	19	3,360	18 (15–20)	17	3,540	18 (15–20)	18
Race/ethnicity												
White	4,240	14 (12–16)	14	3,780	12 (11–14)	12	3,640	13 11–15)	13	3,640	12 (10–14)	12
Black	140	4.7 (1.2–8.2)	5.4	280	8.7 (4.1–13)	9.3	180	5.8 (2.0–9.6)	5.8	440	13 (7.5–18)	13
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	40	10 (0–24)	10	60	8.5 (0–18)	8.5	40	5.0 (0–12)	5.0
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	1,540	18 (14–22)	17	1,440	16 (12–20)	16	1,160	13 (10.0–17)	13	740	8.4 (5.7–11)	8.4
Northeast	1,360	18 (13–22)	17	620	8.1 (5.2–11)	7.6	900	13 (9.5–17)	13	1,280	19 (14–23)	17
South	1,140	9.3 (6.9–12)	10	1,780	14 (11–17)	14	1,380	11 (8.5–14)	11	1,740	13 (10–16)	14
West	380	6.9 (3.8–10)	6.9	300	5.8 (2.9–8.7)	6.2	460	9.3 (5.5–13)	9.3	360	6.7 (3.6–9.7)	7.0

…data not available.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Unweighted counts multiplied by 20 to arrive at values in the table.

[c]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[d]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 16. Use of bladder irrigation (CPT 51700) and cystourethroscopy (CPT 52000) in the physician office setting for Medicare beneficiaries with interstitial cystitis[a], count[b], rate[c] (95% CI), age-adjusted rate[d]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Bladder Irrigation (CPT code 51700)						
Total[e]	12,620	56,239 (44,404–68,074)		15,940	68,830 (54,040–81,620)	
Gender						
Male	1,360	39,766 (5,363–74,169)	45,029	2,280	63,687 (8,972–118,402)	67,598
Female	11,260	59,201, (46,663–71,739)	58,254	13,660	68,574 (55,551–81,597)	67,871
Region						
Midwest	2,960	53,430 (31,894–74,965)	50,903	3,380	58,478 (38,469–78,486)	51,211
Northeast	760	17,593 (4,487–30,698)	18,981	1,520	41,989 (19,370–64,608)	40,884
South	6,960	81,119 (56,521–105,717)	84,382	8,640	86,922 (59,618–114,225)	90,946
West	1,940	51,053 (27,373–74,732)	45,789	2,400	60,000 (33,330–86,670)	61,500
Cystourethroscopy (CPT code 52000)						
Total	2,040	9,091 (7,233–10,948)		1,980	8,426 (6,717–10,134)	
Gender						
Male	140	* *	*	180	* *	*
Female	1,900	9,989 (7,889–12,090)	9,989	1,800	9,036 (7,106–10,966)	9,036

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Bladder Irrigation (CPT code 51700)						
Total[e]	12,840	48,489 (39,494–57,484)		18,140	69,479 (55,575–83,382)	
Gender						
Male	1,500	37,313 (14,438–60,189)	36,816	840	20,000 (7,250–32,750)	19,048
Female	11,340	50,490 (40,697–60,283)	50,579	17,300	78,976 (62,639–95,313)	79,250
Region						
Midwest	2,820	50,357 (32,680–68,035)	49,286	4,280	69,256 (46,617–91,894)	67,961
Northeast	620	14,027 (4,711–23,344)	15,837	700	17,588 (0–38,588)	21,106
South	7,340	69,937 (47,270–80,604)	63,240	9,520	85,125 (60,390–109,860)	84,409
West	2,040	42,678 (23,618–61,738)	43,933	3,620	81,532 (43,559–119,504)	82,432
Cystourethroscopy (CPT code 52000)						
Total	2,080	7,855 (6,302–9,408)		2,000	7,515 (6,051–8,979)	
Gender						
Male	200	* *	*	280	* *	*
Female	1,880	8,370 (6,621–10,120)	8,281	1,720	7,678 (6,078–9,279)	8,044

*Figure does not meet standard for reliability or precision.
[a]Interstitial cystitis, ICD-9 code 595.1.
[b]Unweighted counts multiplied by 20 to arrive at values in the table.
[c]Rate per 100,000 Medicare beneficiaries 65 years and older with interstitial cystitis (as defined by ICD-9 code 595.1 only).
[d]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[e]Persons of other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 17. Procedure use in the physician office setting for Medicare beneficiaries with interstitial cystitis[a], 1992–2001, count[b], annualized rate[c], age-adjusted annualized rate[d]

	CPT code 51700			CPT code 52000			CPT codes 52260 and 52265			CPT code 52281		
Group	Count	Annualized Rate	Age-Adjusted Annualized Rate	Count	Annualized Rate	Age-Adjusted Annualized Rate	Count	Annualized Rate	Age-Adjusted Annualized Rate	Count	Annualized Rate	Age-Adjusted Annualized Rate
Total[e]	14,880	63,319		2,015	8,574		245	1,043		240	1,021	
Age												
65–69	4,115	62,160		540	8,157		115	1,737		40	604	
70–74	4,295	64,684		660	9,940		55	828		70	1,054	
75–79	3,645	69,561		445	8,492		50	954		85	1,622	
80–84	1,985	59,789		265	7,982		25	753		40	1,205	
85–89	770	63,115		65	5,328		0	0		0	0	
90–94	70	18,421		40	10,526		0	0		5	1,316	
Gender												
Male	1,495	41,760	43,575	200	5,587	5,307	10	279	279	30	838	838
Female	13,385	67,194	66,867	1,815	9,111	9,137	235	1,180	1,180	210	1,054	1,029
Race/ethnicity												
White	14,085	64,729	64,522	1,895	8,709	8,709	235	1,080	1,020	235	1,080	1,057
Black	395	39,500	41,500	40	4,000	4,500	10	1,000	1,000	5	500	500
Asian	20	50,000	50,000	5	12,500	12,500	0	0	0	0	0	0
Hispanic	30	21,429	25,000	25	17,857	14,286	0	0	0	0	0	0
N. American Native	0	0	0	0	0	0	0	0	0	0	0	0
Region												
Midwest	3,360	58,131	55,104	325	5,623	5,536	85	1,471	1,471	15	260	260
Northeast	900	24,862	26,519	280	7,735	7,459	55	1,519	1,381	50	1,381	1,243
South	8,110	81,590	82,847	955	9,608	9,809	65	654	704	140	1,408	1,358
West	2,500	62,500	62,250	420	10,500	10,125	40	1,000	1,000	35	875	875

Based on CPT code 51700 (bladder irrigation, simple, lavage, and/or instillation), CPT code 52000 (cystourethroscopy, separate procedure), CPT code 52260 (cystourethroscopy, with dilation of bladder for IC; general or conduction (spinal) anethesia), 52265 (cystourethroscopy, with dilation of bladder for IC, local anethesia), CPT code 52281 (cystourethroscopy, with calibration and/or dilation of urethral stricture or stenosis, with or without meatotomy, with or without injection procedure for cystography, male or female).

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Unweighted counts multiplied by 20 to arrive at values in the table.

[c]Rate per 100,000 Medicare beneficiaries with interstitial cystitis age 65+ in 1995.

[d]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

female genital organs) or 625.9 (unspecified symptoms associated with female genital organs). This definition is based on the presence of coded symptoms rather than a label of interstitial cystitis and may give a more accurate assessment of the burden of PBS or undiagnosed IC. We recognize that this definition may include individuals with etiologies other than PBS to explain the symptoms. Furthermore, men with PBS are excluded by definition. In general, counts were very low for these codes. These limitations should be taken into account when interpreting the following data.

Outpatient Care

Physician outpatient visits related to PBS in the United Healthcare–insured population for 1994 to 2002 are presented in Table 18. The visit rate was 8.2 per 100,000 in 2002, and it appeared to increase during the analyzed time periods. PBS was listed as the primary diagnosis in approximately two-thirds of these visits. Age-specific analyses could not be performed due to

Table 18. Physician outpatient visits for females with painful bladder syndrome[a] having commercial health insurance, count, rate[b]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Procedure										
Total	4	*	19	*	44	5	51	5	52	6
Age										
18–24	1	*	1	*	7	*	6	*	4	*
25–34	0	0	9	*	11	*	12	*	8	*
35–44	0	0	3	*	14	*	18	*	19	*
45–54	2	*	5	*	7	*	11	*	13	*
55–64	1	*	0	0	4	*	2	*	4	*
65–74	0	0	1	*	1	*	2	*	3	*
75–84	0	0	0	0	0	0	0	0	1	*
85+	0	0	0	0	0	0	0	0	0	0
Region										
Midwest	4	*	15	*	33	8	31	6	33	7
Northeast	0	0	0	0	1	*	1	*	3	*
Southeast	0	0	4	*	7	*	18	*	14	*
West	0	0	0	0	3	*	1	*	2	*
As Any Procedure										
Total	5	*	27	*	65	7	79	8	72	8
Age										
18–24	1	*	1	*	10	*	11	*	6	*
25–34	0	0	14	*	21	*	17	*	13	*
35–44	1	*	5	*	19	*	28	*	24	*
45–54	2	*	5	*	8	*	17	*	18	*
55–64	1	*	1	*	6	*	4	*	6	*
65–74	0	0	1	*	1	*	2	*	4	*
75–84	0	0	0	0	0	0	0	0	1	*
85+	0	0	0	0	0	0	0	0	0	0
Region										
Midwest	5	*	22	*	51	12	47	10	47	10
Northeast	0	0	0	0	1	*	4	*	3	*
Southeast	0	0	5	*	10	*	24	*	20	*
West	0	0	0	0	3	*	4	*	2	*

*Figure does not meet standard for reliability or precision.
[a]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.
[b]Rate per 100,000 based on member months of enrollment in calendar years.for individuals in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 19. Estimated annual expenditures for privately insured employees with and without a medical claim for interstitial cystitis[a] in 2002[b]

	Annual Expenditures (per person)					
	Persons without Interstitial Cystitis (N=477,339)			Persons with Interstitial Cystitis (N=244)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$2,993	$1,176	$4,169	$5,772	$2,648	$8,420
Age						
35–44	$2,597	$1,011	$3,608	$8,405	$1,915	$10,320
45–64	$3,352	$1,341	$4,693	$5,801	$2,987	$8,788
Gender						
Male	$2,912	$1,105	$4,017	$3,560	$2,785	$6,345
Female	$3,109	$1,278	$4,387	$5,996	$2,457	$8,453
Region						
Midwest	$2,980	$1,121	$4,101	$5,749	$2,550	$8,299
Northeast	$2,806	$1,254	$4,060	$5,414	$2,826	$8,240
South	$3,156	$1,153	$4,309	$6,088	$2,570	$8,658
West	$2,949	$1,157	$4,106	$5,688	$2,634	$8,322

Rx, Prescription.

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions. Predicted expenditures for persons age 18 to 34 are omitted due to small sample size.

SOURCE: Ingenix, 2002.

low cell sizes. The rate of hospital outpatient visits for PBS during this time interval was negligible.

ECONOMIC IMPACT

The economic impact of disease includes direct costs paid to the medical system and indirect costs borne by the individual and society. Direct costs include payments to physicians for inpatient and outpatient care, payments to hospitals for inpatient care, payments for outpatient procedures and tests, and the costs of prescription drugs, among others. Indirect costs include potentially measurable items such as the consequences of time away from work (borne by the individual, employers, and colleagues) and lost productivity when at work. Disease also has substantial impact through indirect costs that are more difficult to measure—work, education, and social opportunities not pursued; general decrements in quality of life; loss of family and social support; and even depression, divorce, and, for some IC/PBS patients, suicide. The databases used in this compendium contain information primarily on direct costs of disease; this section presents the available data while also pointing out deficiencies in the dataset and areas where indirect costs are particularly important. The definitions used for these analyses are the same as those used in other chapters in the assessment of healthcare resource utilization.

Cost of Disease per Individual

Medical and pharmacy claims from 25 large employers for 1.8 million covered lives yielded data that included both primary and secondary beneficiaries from 1999 and 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 17 disease conditions, including diabetes, asthma, and hypertension.

Although <0.1% of claims were related to IC, the cost of the disease is significant. In 2002, the mean annual cost associated with IC was $8,420 vs $4,169 for those without IC (Table 19). When the same

Table 20. Estimated annual expenditures of privately insured employees with and without a medical claim for painful bladder syndrome[a] in 2002[b]

	Annual Expenditures (per person)					
	Females without Painful Bladder Syndrome (N=192,045)			Females with Painful Bladder Syndrome (N=207)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$3,314	$1,336	$4,650	$6,931	$2,115	$9,046
Age						
18–34	$2,738	$755	$3,493	$6,390	$1,809	$8,199
35–44	$3,198	$1,171	$4,369	$6,959	$1,991	$8,950
45–54	$3,503	$1,523	$5,026	$5,182	$2,188	$7,370
55–64	$3,463	$1,518	$4,981	$8,904	$2,269	$11,173
Region						
Midwest	$3,325	$1,236	$4,561	$6,954	$1,981	$8,935
Northeast	$3,057	$1,411	$4,468	$6,392	$2,239	$8,631
South	$3,565	$1,369	$4,934	$7,454	$1,913	$9,367
West	$3,065	$1,208	$4,273	$6,409	$2,144	$8,553

Rx, Prescription.

[a]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.

[b]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions.

SOURCE: Ingenix, 2002.

analysis was performed to identify patients with PBS, the results were similar: $9,046 for those with PBS vs $4,650 for those without (Table 20). Analysis of specific subgroups reveals the following:

- The cost is disproportionately associated with women. The diagnosis of IC/PBS results in costs of almost $1,750 more per patient for females than for males.
- Unlike the costs for other urologic conditions such as BPH and urolithiasis, the costs for IC/PBS are nearly identical throughout all geographic regions. This may reflect the limited treatment options, which provide little room for variation in patterns of care.
- In IC patients, costs appear to be disproportionately borne by those in the most productive years of life (the extra costs per individual for those 35–44 are $6,712, while extra costs for those 45–64 are $4,095); there is no clear cost/age trend in PBS patients.
- Prescription drugs make up approximately 31% of costs for IC patients but only 23% of those for PBS patients. This may reflect a greater focus on diagnostic evaluation in PBS patients, or it may represent less use of specific IC therapy (DMSO and pentosanpolysulfate (Elmiron™)). Costs of prescription drugs appear to increase with age in both populations.

Table 21. Expenditures for interstitial cystitis[a], by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Physician Office	$20,954,831	40.7%	$22,820,538	40.7%	$23,184,294	39.3%	$36,804,504	55.8%
Ambulatory Surgery	$23,305,305	45.3%	$25,380,286	45.3%	$27,387,360	46.5%	$20,122,316	30.5%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$7,221,197	14.0%	$7,864,134	14.0%	$8,351,413	14.2%	$9,001,117	13.7%
TOTAL	$51,481,333		$56,064,958		$58,923,067		$65,927,937	

[a]Interstitial cystitis, ICD-9 code 595.1.

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 22. Expenditures for Medicare beneficiaries for treatment of interstitial cystitis[a], by site of service (% of total)

	Age 65 and over							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$90,300	1.6%	$140,160	1.9%	$105,840	1.3%	$268,920	2.9%
Physician Office	$2,351,040	42.9%	$3,301,860	45.5%	$3,965,080	49.6%	$6,328,080	67.1%
Ambulatory Surgery	$3,042,200	55.5%	$3,807,440	52.5%	$3,931,200	49.1%	$2,829,140	30.0%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$5,483,540		$7,249,460		$8,002,120		$9,426,140	

	Under 65							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	---	0.0%	---	0.0%	---	0.0%	$153,400	5.8%
Physician Office	$288,960	100.0%	$425,880	100.0%	$834,240	100.0%	$1,817,140	68.4%
Ambulatory Surgery	---	0.0%	---	0.0%	---	0.0%	$686,460	25.8%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$288,960		$425,880		$834,240		$2,657,000	

[a]Interstitial cystitis, ICD-9 code 595.1.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

This investigation of the costs of IC/PBS includes only direct medical costs; it does not include non-medical economic and non-economic costs such as missed work, lost productivity, and poor quality of life. Nevertheless, the medical costs alone appear to present a major burden to the healthcare system, with $2 spent on IC/PBS patients for every dollar spent on those without the disease. Further investigation is warranted to evaluate the nature and effectiveness of the expenditures and to improve disease management.

National Expenditures on IC/PBS

In addition to individual costs, we examined trends in national expenditures through a compilation of utilization data from national surveys and corresponding reimbursement information (see Methods Chapter). Data were insufficient to estimate expenditures for PBS; hence the following discussion is limited to expenditures for IC.

As shown in Table 21, national expenditures for IC increased by 29% between 1994 and 2000, to $66 million. These estimates do not include the costs of ancillary services such as lab tests or radiographic procedures. During this period, spending shifted significantly from the ambulatory surgery setting to the physician office setting. Between 1994 and 2000, the proportion of IC expenditures in physician offices setting grew by 76%, while inpatient spending increased 25% ambulatory surgery spending fell slightly. These changes may reflect decreased physician enthusiasm for potentially therapeutic interventions such as hydrodistention, which are performed under anesthesia. Medicare data (Table 22) display similar trends in sites of service.

Absence from Work

We examined the Marketscan Health and Productivity Management database for 1999, which includes enrollees with at least one inpatient or outpatient claim for IC/PBS, to determine the relationship between a diagnosis of IC/PBS and missed work. The dates for missed work were analyzed in relation to the dates of claims to create an association between the underlying condition and the time away from work.

Seventy-eight patients were identified with some type of visit (inpatient or outpatient) with a diagnosis of IC; 22% of these missed some work during the year (Table 23). As would be expected, there was minimal loss of work for inpatient care. An average total of 13 hours of work were missed (95% CI, 1.6–24.4). Men missed twice as much work as women, but only 19 observations are included. More work was missed in Midwest and South than in the Northeast and West. The same analysis using the PBS definition produced a total of 1,646 observations (20 times more than for

Table 23. Average annual work loss of persons treated for interstitial cystitis[a], 1999 (95% CI)

	Number of Workers[b]	% Missing Work	Average Work Absence (hrs) Inpatient[c]	Outpatient[c]	Total
Total	78	22%	0.2 (0–0.6)	12.8 (1.4-24.2)	13 (1.6–24.4)
Age					
18–29	8	13%	0	3 (0–10.1)	3 (0–10.1)
30–39	11	18%	0	1.3 (0–3.9)	1.3 (0–3.9)
40–49	26	31%	0.6 (0–1.9)	9.7 (1.7-17.8)	10.3 (2.4–18.3)
50–64	33	18%	0	21.5 (0–48.2)	21.5 (0–48.2)
Gender					
Male	19	21%	0.8 (0–2.6)	22.1 (0–65.3)	22.9 (0–66.1)
Female	59	22%	0	9.8 (2.1–17.5)	9.8 (2.1–17.5)
Region					
Midwest	20	40%	0	19.8 (0–41.4)	19.8 (0–41.4)
Northeast	9	11%	1.8 (0–5.9)	0	1.8 (0–5.9)
South	24	17%	0	19.5 (0–53.2)	19.5 (0–53.2)
West	7	29%	0	3.5 (0–10.6)	3.5 (0–10.6)
Unknown	18	11%	0	6.2 (0–15.3)	6.2 (0–15.3)

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Individuals with an inpatient or outpatient claim for interstitial cystitis and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[c]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: Marketscan Health and Productivity Management, 1999.

Table 24. Average annual work loss of persons treated for painful bladder syndrome[a], 1999 (95% CI)

	Number of Workers[b]	% Missing Work	Average Work Absence (hrs) Inpatient[c]	Outpatient[c]	Total
Total	1,646	15%	0.6 (0–1.2)	5.1 (4.2–5.9)	5.7 (4.6–6.8)
Age					
18–29	239	19%	0.3 (0–0.6)	5.7 (3.4–8.1)	6 (3.6–8.4)
30–39	416	16%	1.2 (0–2.9)	6.1 (4.1–8.1)	7.3 (4.6–10)
40–49	492	16%	0.7 (0–2.1)	5.3 (3.7–6.9)	6 (3.9–8.2)
50–64	499	11%	0.1 (0–0.3)	3.7 (2.4–5.0)	3.8 (2.6–5.1)
Gender					
Male	374	12%	0.1 (0–0.4)	3.6 (2.1–5.1)	3.7 (2.2–5.2)
Female	1,272	16%	0.7 (0–1.5)	5.5 (4.5–6.5)	6.3 (4.9–7.6)
Region					
Midwest	441	20%	0.5 (0–1.3)	5.7 (4.1–7.4)	6.2 (4.1–8.2)
Northeast	129	8%	0.1 (0–0.4)	3 (0.8–5.2)	3.1 (0.9–5.3)
South	564	16%	1.3 (0–2.8)	5.4 (3.8–6.9)	6.6 (4.4–8.8)
West	196	13%	0 0	4.2 (1.6–6.7)	4.2 (1.6–6.7)
Unknown	316	13%	0.2 (0–0.5)	5.1 (3.1–7.2)	5.3 (3.3-7.4)

[a]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.

[b]Individuals with an inpatient or outpatient claim for painful bladder syndrome and for whom absence data were collected. Work loss based on reported absenses contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[c]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: Marketscan Health and Productivity Management, 1999.

IC) and found that 15% of the patients missed some work (Table 24). An average total of 5.7 hours of work were missed, including contiguous absences (95% CI, 4.6–6.8). The regional trends were the same, but the gender trend was reversed, with females missing twice as much work as males.

It is likely that this methodology substantially underestimates work loss for IC patients. The disease is characterized by flares that may cause missed or reduced work, but since patients experience the flares regularly and there is little effective treatment, they may not visit the doctor. When there is no medical claim to associate with the time off work the event is not captured in the database.

Pain medication may be prescribed by phone, and in such cases there is no medical claim to associate with the time off work.

Costs for Treatment of IC/PBS

The Ingenix database was used to examine the specific expenditures for common medications and procedures for the subset of the working, insured population and their families (Tables 25 and 26). The database gives the first glimpse into how patients with IC/PBS are evaluated and treated. Unfortunately, it does not provide information about radiographic procedures and other tests that might be performed.

Limited data are available about prescription drug use. The Ingenix database includes categories for pentosanpolysulfate (Elmiron™), tricyclic antidepressants (imipramine and amitriptyline), antibiotics, and narcotic pain medications (Table 25). While there is no direct information about prescriptions for intravesical medications, data on the use of intravesical instillations as procedures are included.

Antibiotics remain the most common treatment for IC/PBS, with >60% of both groups filling at least one prescription during the year. The mean number of prescriptions is about two. Narcotic pain medications were used by 45% of IC patients and 51% of PBS patients. However, the average patient received less than one 30-day supply, so it appears that narcotics are used intermittently, rather than for continuous pain control. The biggest difference between IC and PBS patients is in the use of Elmiron™, which was prescribed for 30.8% of IC patients and only 3.1% of PBS patients. This may not be surprising, since Elmiron™ is approved for use for IC and therefore requires acknowledgement of the condition by the treating physician. Patients with IC/PBS symptoms who are not diagnosed with IC by the treating physician tend not to be prescribed the medication. It is notable that the average IC patient received only 1.8 30-day prescriptions for Elmiron™, despite the fact that standard therapy consists of an initial three- to six-month trial.

Cystoscopy is used commonly, for 15% of the IC population, compared with <1% of those without IC (Table 26). There is little difference in utilization between IC/PBS patients. It appears that cystoscopy was most commonly performed in the office setting for PBS patients (only one-third had additional procedures), but nearly all IC patients underwent bladder dilation or urethral calibration/dilation at the time of cystoscopy, procedures that are more commonly performed under anesthesia. Office cystoscopy is primarily a diagnostic procedure to rule out other conditions, whereas cystoscopy under anesthesia with bladder distention can reveal the characteristic changes of IC and can provide some symptomatic relief. It is not clear how this clinical decision is being made.

Bladder instillation therapy has been a mainstay of IC management for many years. DMSO has been the traditional agent, often mixed into a "cocktail" with steroids, anesthetic agents, and heparin. Recently, some clinicians have advocated using pentosanpolysulfate (Elmiron™) to replace heparin or as a separate treatment, often combined with anesthetic agents. Bladder instillations were performed in 17.4% of IC patients in the database (Table 26) and in 1.5% of PBS patients. No information is provided about which drug combinations were used. This is surprising, as several groups have advocated for the use of potassium sensitivity testing as the first step in the diagnosis of IC/PBS. The database does not distinguish between diagnostic and therapeutic bladder instillations, so the infrequent use of instillations in PBS patients suggests that this test is infrequently employed.

CONCLUSIONS

Because no objective marker exists for IC/PBS, the exact prevalence of the disorder is not currently known. The prevalence of a formal physician diagnosis of IC

Table 25. Pharmaceutical use in commercially insured individuals with interstitial cystitis[a] or painful bladder syndrome[b], in 2001

		IC/PBS		Interstitial Cystitis		Painful Bladder Syndrome	
	All People 18+	No	Yes	All	Conditional on Use of Drug	All	Conditional on Use of Drug
Count	1,042,066	1,040,924	1,142	688		478	
Mean Age	52	52	51	54		46	
Interstitial Cystitis	0.07%	0%	60%	100%		5%	
Painful Bladder Syndrome	0.05%	0%	42%	3%		100%	
Interstitial Cystitis/Painful Bladder Syndrome	0.11%	0%	100%	100%		100%	
Percent of people who took each drug in 2001							
Antibiotic	40%	40%	64%	61%		69%	
Narcotic	20.25%	20.22%	46.76%	44.91%		51.05%	
Elmiron	0.04%	0.02%	18.83%	30.81%		3.14%	
Tofranil (brand)	0.02%	0.02%	0.09%	0%		0.21%	
Imipramine (generic)	0.21%	0.21%	2.45%	2.33%		2.72%	
Mean number of prescriptions per person in 2001							
Antibiotic	0.87	0.87	1.93	1.78	2.95	2.17	3.23
Narcotic	0.61	0.61	2.00	2.10	4.71	2.30	4.57
Elmiron	0	0	0.77	1.27	4.11	0.09	2.93
Tofranil (brand)	0	0	0	0	0	0.01	5.00
Imipramine (generic)	0.01	0.01	0.07	0.07	3.00	0.07	2.54
Mean number of 30-day equivalent prescriptions per person in 2001							
Antibiotic	0.32	0.32	0.61	0.60	1.00	0.64	0.96
Narcotic	0.25	0.25	0.67	0.75	1.69	0.61	1.20
Elmiron	0	0	1.09	1.80	5.85	0.11	3.36
Tofranil (brand)	0	0	0	0	0	0.01	5.50
Imipramine (generic)	0.01	0.01	0.08	0.08	3.51	0.08	3.00
Mean expendituresc per person for prescriptions in 2001							
Antibiotic	$35.14	$35.10	$68.49	$61.81		$79.12	
Narcotic	$19.65	$19.62	$53.08	$63.90		$41.73	
Elmiron	$0.35	$0.14	$188.53	$311.00		$16.73	
Tofranil (brand)	$0.11	$0.11	$0.55	$0.00		$1.30	
Imipramine (generic)	$0.22	$0.21	$0.98	$0.97		$0.95	

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.

[c]Expenditure is defined as what the patient paid + what the insurance plan paid + any coordination-of-benefits amount.

SOURCE: Ingenix, 2001.

Table 26. Procedure use in commercially insured individuals with interstitial cystitis[a] or painful bladder syndrome[b], in 2001

	All People 18+	IC/PBS		Interstitial Cystitis		Painful Bladder Syndrome	
		No	Yes	All	Conditional on Use of Procedure	All	Conditional on Use of Procedure
Percent of people who had at least one claim for procedure in 2001							
Cystourethroscopy, separate procedure (CPT code 52000)	0.89%	0.87%	15.24%	16.28%		14.85%	
Bladder irrigation, simple, lavage and/or instillation (CPT code 51700)	0.04%	0.03%	10.77%	17.44%		1.46%	
Cystourethroscopy, with calibration and/or dilation of urethra (CPT code 52281)	0.11%	0.11%	4.20%	5.52%		2.51%	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; general or conduction (spinal) anesthesia (CPT code 52260)	0.02%	0%	11.03%	17.59%		2.93%	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; local anesthesia (CPT code 52265)	0%	0%	0.53%	0.87%		0%	
Mean number of procedures per person in 2001							
Cystourethroscopy, separate procedure (CPT code 52000)	0.01	0.01	0.18	0.20	1.21	0.17	1.11
Bladder irrigation, simple, lavage and/or instillation (CPT code 51700)	0	0	0.35	0.57	3.28	0.06	3.86
Cystourethroscopy, with calibration and/or dilation of urethra (CPT code 52281)	0	0	0.05	0.06	1.05	0.03	1.17
Cystourethroscopy, with dilation of bladder for interstitial cystitis; general or conduction (spinal) anesthesia (CPT code 52260)	0	0	0.14	0.23	1.32	0.03	1.14
Cystourethroscopy, with dilation of bladder for interstitial cystitis; local anesthesia (CPT code 52265)	0	0	0.01	0.01	1.00	0	0
Mean expendituresc per person for listed procedure in 2001							
Cystourethroscopy, separate procedure (CPT code 52000)	$3.05	$3.00	$44.56	$51.81		$39.18	
Bladder irrigation, simple, lavage and/or instillation (CPT code 51700)	$0.11	$0.06	$41.98	$69.18		$12.54	
Cystourethroscopy, with calibration and/or dilation of urethra (CPT code 52281)	$0.50	$0.49	$13.48	$17.19		$7.95	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; general or conduction (spinal) anesthesia (CPT code 52260)	$0.08	$0.02	$57.04	$90.05		$16.66	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; local anesthesia (CPT code 52265)	$0.01	$0	$1.90	$3.15		$0	
Aggregate expenditures for listed procedure in 2001							
Cystourethroscopy, separate procedure (CPT code 52000)	$3,176,667	$3,125,782	$50,885	$35,647		$18,728	
Bladder irrigation, simple, lavage and/or instillation (CPT code 51700)	$111,186	$63,248	$47,938	$47,599		$5,995	
Cystourethroscopy, with calibration and/or dilation of urethra (CPT code 52281)	$523,213	$507,824	$15,389	$11,829		$3,799	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; general or conduction (spinal) anesthesia (CPT code 52260)	$81,445	$16,302	$65,143	$61,956		$7,965	
Cystourethroscopy, with dilation of bladder for interstitial cystitis; local anesthesia (CPT code 52265)	$5,946	$3,778	$2,168	$2,168		$0	

[a]Interstitial cystitis, ICD-9 code 595.1.

[b]Painful bladder syndrome, ICD-9 code 788.41 (urinary frequency), along with either ICD-9 code 625.8 or 625.9.

[c]Expenditure is defined as what the patient paid + what the insurance plan paid + any coordination-of-benefits amount.

SOURCE: Ingenix, 2001.

is relatively low (approximately 200 per 100,000), but the prevalence of IC-like symptoms is much higher (approximately 5,000 per 100,000). The prevalence of symptomatic but undiagnosed IC/PBS is not known and will be difficult to determine given the lack of an objective marker. Data on the prevalence of IC/PBS in ethnic minorities are practically nonexistent.

Outpatient visits related to IC/PBS are increasing. This may be due to an increased awareness of the disorder or to a national increase in the number of patients. The rate of ambulatory surgery visits for IC/PBS has declined, which may indicate a trend toward a clinical diagnostic approach and away from procedure-based diagnosis/therapy. More than 90% of office visits associated with a coded diagnosis of IC were to urologists. It is probable that many more patients with IC/PBS are seen by other physicians and are not accurately diagnosed. Therefore, the true burden of IC/PBS to the US healthcare system is probably underestimated in administrative data that rely solely on physician coding to identify the disorder.

The economic impact of IC/PBS has been incompletely studied. Data presented in this chapter indicate that a diagnosis of IC/PBS is associated with a twofold increase in direct medical costs, compared with the costs for individuals without the disorder. There are no available data about indirect costs, which are likely to be substantial.

RECOMMENDATIONS

The etiology of IC/PBS is unknown, and none of the currently available treatments has demonstrated consistent or dramatic success in alleviating patient symptoms. Much work is needed to understand better the etiology of IC/PBS so that effective treatments can be developed. To some extent, this huge deficiency supersedes the recommendations below. Nevertheless, investigation of the following topics would improve our understanding of IC/PBS:

- Efforts to develop an objective marker for IC/PBS should continue. Such a marker would greatly aid in determining the true prevalence of the disorder and would provide valuable information about the etiology of IC/PBS. This could potentially lead to more-effective treatments.
- An ICD-9 code for PBS should be established. This would encourage clinicians to use current terminology for IC and PBS in coding and would greatly facilitate understanding of the impact of the disease.
- A standard definition of IC/PBS should be developed for epidemiologic purposes. This would allow meaningful comparisons to be made among different populations.
- Comprehensive epidemiologic studies of IC/PBS should be performed, including:
    - All adult age ranges
    - Ethnic minorities
    - Efforts to establish the prevalence of undiagnosed IC/PBS
    - Longitudinal data collection to provide information about the natural history of the condition and its cumulative impact over time.
- Studies should evaluate the burden of IC/PBS on the uninsured/underinsured population. Anecdotal experience suggests that these patients may use different resources (e.g., emergency room visits), but this must be confirmed with studies.
- The direct and indirect costs of IC/PBS should be assessed. Surprisingly little has been done in this area. To assess the true societal burden of IC/PBS, the costs of the disorder must be better quantified. Current treatment patterns for individuals with IC/PBS should be assessed, and more studies of the direct costs of the disease are needed to confirm the information presented in this chapter. In addition, no information is currently available about the indirect costs of IC/PBS despite the fact that those costs may be the primary burden of this condition.

REFERENCES

1. Hunner G. A rare type of bladder ulcer in women: report of cases. Boston Med Surg J 1915;172:660-64.
2. Messing EM, Stamey TA. Interstitial cystitis: early diagnosis, pathology, and treatment. Urology 1978;12:381-92.
3. Gillenwater JY, Wein AJ. Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Workshop on Interstitial Cystitis, National Institutes of Health, Bethesda, Maryland, August 28-29, 1987. J Urol 1988;140:203-6.
4. Payne CK, Terai A, Komatsu K. Research criteria versus clinical criteria for interstitial cystitis. Int J Urol 2003;10 Suppl:S7-S10.
5. Tomaszewski JE, Landis JR, Russack V, Williams TM, Wang LP, Hardy C, Brensinger C, Matthews YL, Abele ST, Kusek JW, Nyberg LM. Biopsy features are associated with primary symptoms in interstitial cystitis: results from the interstitial cystitis database study. Urology 2001;57:67-81.
6. Parsons CL, Stein PC, Bidair M, Lebow D. Abnormal sensitivity to intravesical potassium in interstitial cystitis and radiation cystitis. Neurourol Urodyn 1994;13:515-20.
7. Keay SK, Zhang CO, Shoenfelt J, Erickson DR, Whitmore K, Warren JW, Marvel R, Chai T. Sensitivity and specificity of antiproliferative factor, heparin-binding epidermal growth factor-like growth factor, and epidermal growth factor as urine markers for interstitial cystitis. Urology 2001;57:9-14.
8. Keay SK, Szekely Z, Conrads TP, Veenstra TD, Barchi JJ, Jr., Zhang CO, Koch KR, Michejda CJ. An antiproliferative factor from interstitial cystitis patients is a frizzled 8 protein-related sialoglycopeptide. Proc Natl Acad Sci U S A 2004;101:11803-8.
9. Alagiri M, Chottiner S, Ratner V, Slade D, Hanno PM. Interstitial cystitis: unexplained associations with other chronic disease and pain syndromes. Urology 1997;49:52-7.
10. Warren JW, Jackson TL, Langenberg P, Meyers DJ, Xu J. Prevalence of interstitial cystitis in first-degree relatives of patients with interstitial cystitis. Urology 2004;63:17-21.
11. van Ophoven A, Pokupic S, Heinecke A, Hertle L. A prospective, randomized, placebo controlled, double-blind study of amitriptyline for the treatment of interstitial cystitis. J Urol 2004;172:533-6.
12. van Ophoven A, Hertle L. Long-term results of amitriptyline treatment for interstitial cystitis. J Urol 2005;174:1837-40.
13. Peters KM, Konstandt D. Sacral neuromodulation decreases narcotic requirements in refractory interstitial cystitis. BJU Int 2004;93:777-9.
14. Jones CA, Nyberg L. Epidemiology of interstitial cystitis. Urology 1997;49:2-9.
15. Clemens JQ, Meenan RT, Rosetti MC, Gao SY, Calhoun EA. Prevalence and incidence of interstitial cystitis in a managed care population. J Urol 2005;173:98-102; discussion 102.
16. Clemens JQ, Meenan RT, O'Keeffe Rosetti MC, Brown SO, Gao SY, Calhoun EA. Prevalence of interstitial cystitis symptoms in a managed care population. J Urol 2005;174:576-80.
17. Leppilahti M, Tammela TL, Huhtala H, Auvinen A. Prevalence of symptoms related to interstitial cystitis in women: a population based study in Finland. J Urol 2002;168:139-43.
18. Roberts RO, Bergstralh EJ, Bass SE, Lightner DJ, Lieber MM, Jacobsen SJ. Incidence of physician-diagnosed interstitial cystitis in Olmsted County: a community-based study. BJU Int 2003;91:181-5.

CHAPTER 5

Urinary Incontinence in Women

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Urinary Incontinence in Women

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INTRODUCTION

Urinary incontinence affects from 15% to 50% of community-dwelling women of all ages. It is one of the most prevalent chronic diseases, although it is often not recognized by the US healthcare system. The direct cost of urinary incontinence for women in the United States was $12.4 billion in 1995 dollars (1). Approximately one in ten women in the United States undergoes surgery for urinary incontinence or pelvic organ prolapse, and a sizable minority of women bear the cost of pads, medications, and nonsurgical therapies.

Population-based studies estimate that a large proportion of adult women report the symptom of urinary incontinence. As many as three-fourths of US women report at least some urinary leakage and studies consistently find that 20 to 50% report more-frequent leakage. While some authors have interpreted this to mean that nearly half of American women "suffer" from incontinence, others point out that many women with occasional incontinence are not sufficiently bothered by it to seek care. Of greater clinical relevance is an improved understanding of the number of women with severe or more-frequent leakage, estimated fairly uniformly at 7% to 10% by various researchers. Currently, there is little understanding of the number of women whose lives are truly impacted by urinary incontinence or of its true burden on American women. Indeed, the demarcation between incontinence as a symptom and incontinence as a disease is far from clear. For example, 25% of female college varsity athletes lose urine when doing provocative exercise, and most do not consider it a problem; indeed, most experts would agree that these young women do not have a major health problem. Conversely, most experts would agree that middle-aged women who lose urine throughout the day, wear pads, curtail desired activities because of leakage, and truly suffer have a disease and would benefit from treatment.

Studies that inquire about the presence of "any" or "occasional" incontinence may overestimate the actual burden of incontinence on the healthcare system, but available data on incontinence treatment underestimate the actual burden, given that many women with bothersome leakage do not seek care. While readily available information about incontinence treatment in adult women in the United States indicates only the lowest possible burden urinary incontinence presents to the healthcare system, it does provide a foundation on which to base future studies and to project future care. This chapter uses data from various sources to begin defining not only the prevalence of incontinence, but also its impact on the US healthcare system. At this time, equally important information about the burden of disease on women who are not seeking treatment is not available. The impact of incontinence on the women themselves, their families, their work, and society is also not yet well defined in the literature.

DEFINITION AND DIAGNOSIS

Urinary incontinence is defined by the International Continence Society as "the complaint of

Table 1. Codes used in the diagnosis and management of female urinary incontinence

Females 18 years or older, with one of the following ICD-9 diagnosis codes, but not a coexisting 952.XX or 953.XX code:	
596.51	Hypertonicity of bladder
596.52	Low bladder compliance
596.59	Other functional disorder of bladder
599.8	Other specified disorders of urethra and urinary tract
599.81	Urethral hypermobility
599.82	Intrinsic (urethral) sphincter deficiency (ISD)
599.83	Urethral instability
599.84	Other specified disorders of urethra
625.6	Stress incontinence, female
788.3	Urinary incontinence
788.30	Urinary incontinence unspecified
788.31	Urge incontinence
788.33	Mixed incontinence, male, female
788.34	Incontinence without sensory awareness
788.37	Continuous leakage
Fistulae	
596.1	Intestinovesical fistula
596.2	Vesical fistula not elsewhere classified
619.1	Digestive-genital tract fistula, female
619.0	Urinary-genital tract fistula, female
Spinal cord injury-related incontinence	
(When associated with other ICD-9 diagnosis codes for spinal cord injury 952.XX or 953.XX)	
344.61	Cauda equina syndrome with neurogenic bladder
596.51	Hypertonicity of bladder (specified as overactive bladder in 2001; included if associated with diagnosis code 952.XX)
596.52	Low compliance bladder
596.54	Neurogenic bladder, NOS
596.55	Detrusor sphincter dyssynergia
596.59	Other functional disorder of bladder
599.8	Other specified disorders of urethra and urinary tract
599.84	Other specified disorders of urethra
625.6	Stress incontinence female
788.3	Urinary incontinence
788.30	Urinary incontinence, unspecified
788.31	Urge incontinence
788.32	Stress incontinence male
788.33	Mixed incontinence, male and female
788.34	Incontinence without sensory awareness
788.37	Continuous leakage
788.39	Other urinary incontinence

any involuntary leakage of urine" (2). This supplants the group's previous long-held definition, in which the diagnosis of incontinence required that the leakage be a social or hygienic problem. The less restrictive definition is likely to capture more individuals who experience incontinence, including the many women who may leak daily but do not describe leakage as a social or hygienic problem. A diagnosis of urinary incontinence can be based on the patient's symptoms, the sign of incontinence noted during physical examination, or diagnostic urodynamic testing. Table 1 lists ICD-9 codes commonly used to identify urinary incontinence.

The International Continence Society further categorizes types of incontinence, as well as other bladder symptoms. *Stress urinary incontinence* is the complaint of involuntary leakage on effort or exertion or on sneezing or coughing. Stress urinary incontinence also describes the sign, or observation, of leakage from the urethra synchronous with coughing or exertion. When stress incontinence is confirmed during urodynamic testing by identifying leakage from the urethra coincident with increased abdominal pressure (for example, during a cough or sneeze) but in the absence of a bladder contraction, the diagnosis of *urodynamic stress incontinence* is made.

Urge urinary incontinence is the complaint of involuntary leakage accompanied by or immediately preceded by an urge to urinate and may be further defined with urodynamic investigation. Conventional urodynamic studies take place in a laboratory and involve filling the bladder with a liquid, then assessing bladder function during filling and emptying. If during urodynamic testing the patient demonstrates either spontaneous or provoked involuntary detrusor contractions while filling, she is said to have *detrusor overactivity*. If a relevant neurologic condition exists, the detrusor overactivity is further categorized as *neurogenic*; when no such condition is identified, the overactivity is termed *idiopathic*. These terms replace the previously used *detrusor hyperreflexia* and *detrusor instability*. Many women with urge incontinence do not manifest detrusor overactivity on urodynamic testing. This may be due in part to the fact that such testing, which lasts approximately an hour, is merely a snapshot of the patient's overall bladder function. Ambulatory urodynamic studies can also be performed to document the patient's leakage during everyday activities; such studies identify more detrusor contractions during filling than do conventional ones. Nonetheless, treatment for urge incontinence is often based on implicit clinical assessment because of the low predictive value of a negative test.

Other diagnostic tests may be used to help characterize incontinence and its severity. A pad test quantifies the volume of urine lost by weighing a perineal pad before and after some type of leakage provocation. This type of test has also been used in attempts to distinguish continent from incontinent women. Pad tests can be divided into short-term tests, usually performed under standardized office conditions, and long-term tests, usually performed at home for 24 to 48 hours. Short-term pad tests are generally performed with a symptomatically full bladder or with a certain volume of saline instilled into the bladder before the patient begins a series of exercises.

A voiding diary, or bladder chart, is a record maintained by the patient of her urinary frequency and leakage, voided volumes, and fluid intake over a 3- to 7-day period. This noninvasive test provides useful information about bladder capacity, type of incontinence symptoms, diurnal versus nocturnal voiding patterns, and appropriateness of fluid intake.

PREVALENCE AND INCIDENCE

As noted above, a wide range in the prevalence of urinary incontinence has been reported. One compilation of such studies (3) indicates that approximately 50% of adults report "any" incontinence, while 5% to 25% note leakage at least weekly, and 5 to 15% note it daily or most of the time (Table 2). Rates of incontinence severity patterns are depicted in Figure 1. The rate of urge incontinence tends to rise with age, while the rate of stress incontinence decreases somewhat in the oldest age groups, possibly due to lower activity levels (Figure 2). In a large population of Norwegian women, the rate of stress incontinence peaked at approximately 60% in women 40 to 49 years of age; urge incontinence began to rise in women 50 to 59 years of age and peaked at roughly 20% in women between 80 and 89 years of age (4). Reasons for the divergence of estimates include variations in definitions, sampling methodologies, response rates, and question formats (5).

Table 2. Prevalence of urinary incontinence by frequency and gender in older adults, proportion (counts)

Study	Age	Frequency	Prevalence				F/M
			Women		Men		Ratio
Thomas, 1980	65 +	"ever"	25.80%	(403/1562)	15.30%	(169/1102)	1.7
Rekers, 1992	65–79	"ever"	19.70%	(50/254)			
Hellstrom, 1990	85 +	"ever"	34.70%	(191/551)	18.40%	(49/266)	1.9
Milsom, 1993	66 +	"ever"	22.70%	(962/4238)			
Brockelhurst, 1993	60 +	"ever"	16.80%	(141/840)	12.80%	(90/701)	1.3
Lara, 1994	50 +	"ever"	50.70%	(71/140)			
Sommer, 1990	60–79	"ever"	44.90%	(62/138)			
Sandvik, 1993 & Saim, 1995	60 +	"ever"	31.5%*	(NR)			
Wetle, 1995	65 +	"ever difficulty"	44.40%	(1045/2360)	34.10%	(494/1449)	1.3
Nygaard, 1996	65 +	"ever difficulty"	55.10%	(1116/2025)			
Diokno, 1986	60+	1+ / 12 months	37.70%	(434/1150)	18.90%	(152/805)	2.0
Yarnell, 1979	65 +	1+ / 12 months	16.90%	(37/219)	10.70%	(18/169)	1.6
Yarnell, 1981	65 +	1+ / 12 months	49.60%	(89/180)			
Holst, 1988	65 +	1+/12 months	36.50%	(66/181)			
Milne, 1972 & Milne, 1971	62 +	"current"	41.50%	(114/272)	25.10%	(54/215)	1.7
Campbell, 1985	80 +	"current"	22.10%	(64/290)	21.60%	(29/134)	1.0
Hunter, 1996	50 +	"current"			6.00%	(120/2002)	
Nakanishi, 1997	65 +	"occasionally or more often"	9.70%	(82/842)	9.80%	(55/563)	1.0
Brockelhurst, 1993	60 +	1+ / 2 months	10.20%	(86/840)	5.30%	(37/701)	1.9
Diokno, 1986	60 +	1+ / month	21.70%	(250/1150)	10.40%	(84/805)	2.0
Brown, 1996	65 +	1+ / month	41.30%	(3285/7949)			
Thomas, 1980	65 +	2+ / month	11.40%	(178/1562)	6.90%	(76/1102)	1.7
Brockelhurst, 1993	60 +	2+ / month	10.20%	(86/840)	5.30%	(37/701)	1.9
Holst, 1988	65 +	2+ / month	21.50%	(39/181)			
Diokno, 1986	60 +	1+ / week	12.60%	(145/1150)	5.50%	(44/805)	2.4
Brockelhurst, 1993	60 +	1+ / week	8.30%	(70/840)	3.70%	(26/701)	2.2
Hellstrom, 1990	85 +	1+ / week	27.00%	(149/551)	15.00%	(40/266)	1.8
Rekers, 1992	65–79	1+ / week	6.30%	(16/254)			
Kok, 1992	60 +	2+ / week	22.90%	(164/715)			
Campbell, 1986	80 +	3+ / week	5.10%	(15/290)	3.70%	(5/134)	1.4
Wetle, 1995	65 +	"most or all of the time"	8.80%	(208/2360)	5.80%	(84/1449)	1.5
Sommer, 1990	60–79	"often or always"	8.70%	(12/138)			
Nygaard, 1996	65 +	"most or all of the time	8.30%	(168/2025)			
Diokno, 1986	60 +	1+ / day	5.20%	(60/1150)	1.70%	(14/805)	3.1
Hellstrom, 1990	85 +	1+ / day	16.70%	(92/551)	10.50%	(28/266)	1.5
Kok, 1992	60 +	1+ / day	14.00%	(NR)			
Brown, 1996	65 +	1+ / day	14.20%	(1130/7949)			
Nakanishi, 1997	65 +	1+ / day	2.50%	(21/842)	2.10%	(12/563)	1.2

NR, not reported; F, female; M, male.

*Mean of prevalence by 10-year age groups.

SOURCE: Adapted from Thom D, Variation in estimates of urinary incontinence prevalence in the community: effects of differences in definition, population characteristics, and study type, Journal of the American Geriatrics Society, 46, 473–4801, Copyright 1998, with permission from the American Geriatrics Society.

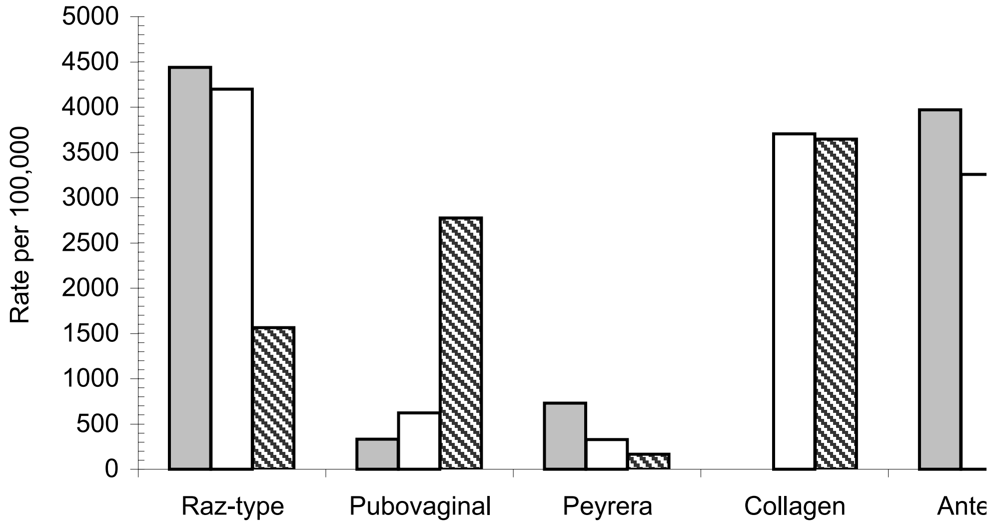

Figure 1. Estimated urge incontinence prevalence rates by age and interview.

Follow-ups III and IV include responses 3 and 6 years after baseline, respectively.

SOURCE: Adapted from Nygaard IE, Lemke JH, Urinary incontinence in rural older women: prevalence, incidence, and remission, Journal of American Geriatrics Society, 44, 1,049–1,054, Copyright 1996, with permission from the American Geriatrics Society.

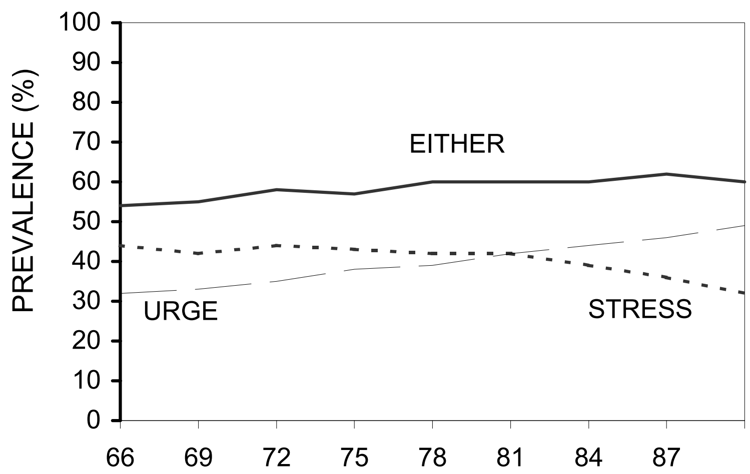

Figure 2. Prevalence of incontinence by age groups at baseline.

Each age represents the midpoint of a 3-year age range. Because of the small number of women above age 90, the graph ends with age range 86-88. "Urge" and "stress" refer to women who answered affirmatively to the urge and stress incontinence questions, respectively. "Either" refers to women who reported any incontinence (either urge or stress).

SOURCE: Adapted from Nygaard IE, Lemke JH, Urinary incontinence in rural older women: prevalence, incidence, and remission, Journal of American Geriatrics Society, 44, 1,049–1,054, Copyright 1996, with permission from the American Geriatrics Society.

Table 3. Prevalence of difficulty controlling bladder among adult women

		Difficulty Controlling Bladder		
	Total	Yes	No	Refused to Answer or Don't Know
Total	23,477,726	8,929,543 (38%)	14,449,905 (62%)	98,278 (0%)
Age at screening				
60–64	5,699,785	2,168,863 (38%)	3,530,922 (62%)	0 (0%)
65–69	4,895,878	1,785,380 (36%)	3,110,498 (64%)	0 (0%)
70–74	4,505,164	1,683,804 (37%)	2,818,651 (63%)	2,709 (0%)
75–79	3,453,472	1,515,900 (44%)	1,873,616 (54%)	63,956 (2%)
80–84	2,981,558	989,003 (33%)	1,967,390 (66%)	25,165 (1%)
85+	1,941,869	786,593 (41%)	1,148,828 (59%)	6,448 (0%)
Race/ethnicity				
Non-Hispanic white	18,729,539	7,662,444 (41%)	11,041,930 (59%)	25,165 (0%)
Non-Hispanic black	1,941,269	386,480 (20%)	1,554,789 (80%)	0 (0%)
Mexican American	649,003	230,567 (36%)	409,279 (63%)	9,157 (1%)
Other Hispanic	1,576,419	468,823 (30%)	1,107,596 (70%)	0 (0%)
Other race	581,496	181,229 (31%)	336,311 (58%)	63,956 (11%)
Education				
Less than high school	8,374,762	2,692,649 (32%)	5,682,113 (68%)	0 (0%)
High school	7,692,149	3,484,970 (45%)	4,207,179 (55%)	0 (0%)
High school+	7,212,158	2,725,611 (38%)	4,461,382 (62%)	25,165 (0%)
Refused	103,678	26,313 (25%)	13,409 (13%)	63,956 (62%)
Don't know	87,647	0 (0%)	85,822 (98%)	1,825 (2%)
Missing	7,332	0 (0%)	0 (0%)	7,332 (100%)
Poverty income ratio[a]				
PIR=0	111,440	31,876 (29%)	79,564 (71%)	0 (0%)
PIR<1	3,145,548	1,116,508 (35%)	2,026,331 (64%)	2,709 (0%)
1.00<=PIR<=1.84	5,520,548	2,193,641 (40%)	3,326,907 (60%)	0 (0%)
PIR>1.84	9,649,331	3,538,606 (37%)	6,085,560 (63%)	25,165 (0%)
Refused	2,090,410	759,112 (36%)	1,331,298 (64%)	0 (0%)
Don't know	1,560,474	741,618 (48%)	817,031 (52%)	1,825 (0%)
Missing	1,399,975	548,182 (39%)	783,214 (56%)	68,579 (5%)

[a]See glossary for definition of poverty income ratio.
The data in this table are based on question KIQ.040: " In the past 12 months, have you had difficulty controlling your bladder, including leaking small amounts of urine when you cough or sneeze?" (Do not include bladder control difficulties during pregnancy or recovery from childbirth.)

SOURCE: National Health and Nutrition Examination Survey, 1999–2000.

Table 4. Frequency of bladder control problems among those who responded "yes" to difficulty controlling bladder

		Frequency of Bladder Control Problems				
	Total	Every Day	Few per Week	Few per Month	Few per Year	Don't Know
Total	8,929,543	3,255,587 (36%)	2,408,421 (27%)	2,016,715 (23%)	1,082,624 (12%)	166,196 (2%)
Age at screening						
60–64	2,168,863	686,213 (32%)	429,351 (20%)	563,017 (26%)	490,282 (23%)	0 (0%)
65–69	1,785,380	475,030 (27%)	511,356 (29%)	479,229 (27%)	172,781 (10%)	146,984 (8%)
70–79	1,683,804	663,681 (39%)	536,511 (32%)	338,233 (20%)	145,379 (9%)	0 (0%)
75–79	1,515,900	575,823 (38%)	448,955 (30%)	286,739 (19%)	204,383 (13%)	0 (0%)
80–84	989,003	456,355 (46%)	233,503 (24%)	258,379 (26%)	21,554 (2%)	19,212 (2%)
85+	786,593	398,485 (51%)	248,745 (32%)	91,118 (12%)	48,245 (6%)	0 (0%)
Race/ethnicity						
Non-Hispanic white	7,662,444	2,759,807 (36%)	1,914,582 (25%)	1,909,818 (25%)	912,041 (12%)	166,196 (2%)
Non-Hispanic black	386,480	212,544 (55%)	74,408 (19%)	45,752 (12%)	53,776 (14%)	0 (0%)
Mexican American	230,567	89,173 (39%)	73,734 (32%)	26,952 (12%)	40,708 (18%)	0 (0%)
Other Hispanic	468,823	77,927 (17%)	315,040 (67%)	7,880 (2%)	67,976 (14%)	0 (0%)
Other Race	181,229	116,136 (64%)	30,657 (17%)	26,313 (15%)	8,123 (4%)	0 (0%)
Education						
Less than high school	2,692,649	1,381,281 (51%)	566,047 (21%)	463,584 (17%)	281,737 (10%)	0 (0%)
High school	3,484,970	1,104,097 (32%)	730,106 (21%)	1,040,720 (30%)	510,224 (15%)	99,823 (3%)
High school+	2,725,611	770,209 (28%)	1,112,268 (41%)	486,098 (18%)	290,663 (11%)	66,373 (2%)
Refused	26,313	0 (0%)	0 (0%)	26,313 (100%)	0 (0%)	0 (0%)
Poverty income ratio[a]						
PIR=0	31,876	0 (0%)	0 (0%)	31,876 (100%)	0 (0%)	0 (0%)
PIR<1	1,116,508	541,675 (49%)	182,029 (16%)	241,012 (22%)	151,792 (14%)	0 (0%)
1.00<=PIR<=1.84	2,193,641	810,902 (37%)	668,567 (30%)	394,473 (18%)	265,876 (12%)	53,823 (2%)
PIR>1.84	3,538,606	988,094 (28%)	1,110,863 (31%)	952,372 (27%)	374,904 (11%)	112,373 (3%)
Refused	759,112	274,391 (36%)	150,098 (20%)	143,238 (19%)	191,385 (25%)	0 (0%)
Don't know	741,618	325,985 (44%)	140,318 (19%)	186,751 (25%)	88,564 (12%)	0 (0%)
Missing	548,182	314,540 (57%)	156,546 (29%)	66,993 (12%)	10,103 (2%)	0 (0%)

[a]See glossary for definition of poverty income ratio.

The data in this table are based on question KIQ.060: "How frequently does this (referring to KIQ.040) occur? Would you say this occurs…every day, a few times a week, a few times a month, or a few times a year?"

SOURCE: National Health and Nutrition Examination Survey, 1999–2000.

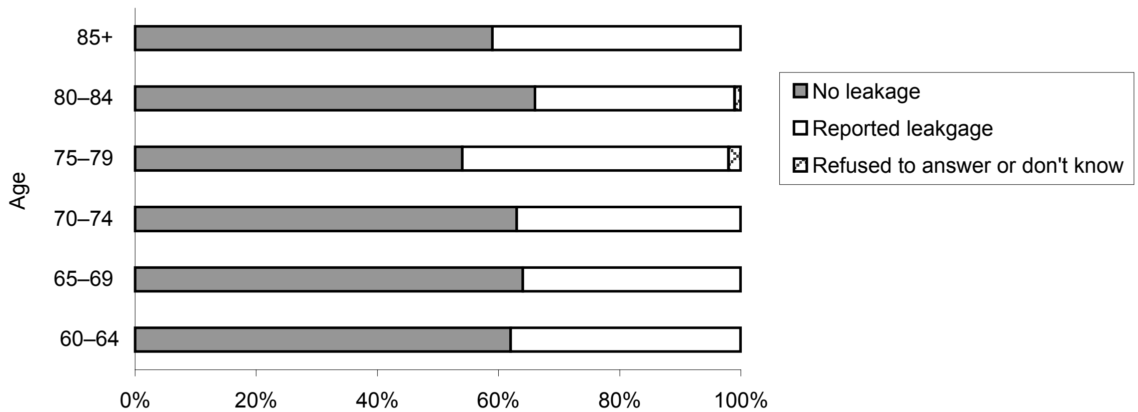

Figure 3a. **Difficulty controlling bladder among female responders.**

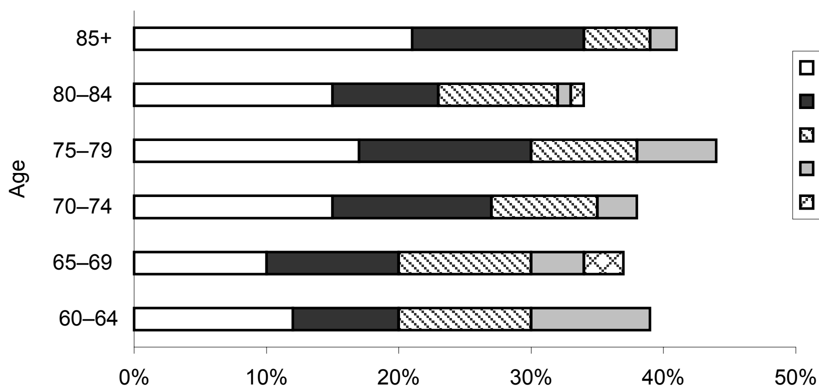

Figure 3b. **Frequency of bladder control problems among female responders who answered "yes" to difficulty controlling bladder.**

SOURCE: National Health and Nutrition Examination Survey, 1999–2001.

Consistent with the Norwegian study, the National Health and Nutrition Examination Survey (NHANES) asked a national sample of community-dwelling adults, "In the past 12 months, have you had difficulty controlling your bladder, including leaking small amounts of urine when you cough or sneeze (exclusive of pregnancy or recovery from childbirth)?" NHANES found the overall prevalence of urinary incontinence in women, as defined in this question, to be 38% in 1999–2000 (Table 3). When broken down by frequency of episodes, 13.7% of all women in NHANES reported daily incontinence, and an additional 10.3% reported weekly incontinence (Table 4). Prevalence was higher in non-Hispanic whites (41%) than in non-Hispanic blacks (20%) or Mexican Americans (36%). The prevalence of daily incontinence increased with age, ranging from 12.2% in all women 60 to 64 years of age to 20.9% in those 85 years of age and over (Figure 3). Women with less than a high school education reported incontinence less often than did those with at least a high school education.

Other large population-based studies have also reported higher rates of urinary incontinence among non-Hispanic whites than in other ethnic or racial groups. In a large cohort of 50- to 69- year-

Table 5. Racial differences in urodynamic diagnoses and measures

	African American (n = 183)	Caucasian (n = 132)	P-value
Diagnosis			
GSI (%)	41 (22)	60 (46)	0.001
Detrusor instability (%)	54 (30)	17 (13)	0.001
Mixed incontinence (%)	29 (16)	14 (11)	0.244
Other (%)	59 (32)	41 (31)	0.902
Measures (mean ± SE)			
Full volume (mL)	279 ± 11	326 ± 14	0.009
MCC (mL)	458 ± 14	536 ± 17	0.001
MUCP (cm H_2O)	68 ± 3	55 ± 3	0.001
MUCP <20 cm H_2O (%)	15 (8)	30 (23)	0.001

GSI, genuine stress incontinence; full volume, volume noted at fullness during filling cystometry; MCC, maximum cystometric capacity; MUCP, maximum urethral closure pressure. Racial comparison of diagnoses by chi^2 or Fisher exact test.

Racial comparison of measures by student t test.

SOURCE: Reprinted from American Journal of Obstetrics and Gynecology, 185, Graham CA, Mallet VT, Race as a predictor of urinary incontinence and pelvic organ prolapse, 116–120, Copyright 2001, with permission from Elsevier.

old women enrolled in the Health and Retirement Survey, non-Hispanic blacks and Hispanics were both 60% less likely to have severe incontinence than were non-Hispanic whites, after adjusting for various comorbidities (6). Similarly, baseline data from the Heart and Estrogen/Progestin Replacement Study showed that non-Hispanic whites were 2.8 times more likely to have weekly stress incontinence than were non-Hispanic blacks, after adjusting for relevant factors (7). This epidemiologic trend appears consistent with laboratory findings as well. Graham and colleagues noted that among women presenting for incontinence treatment, stress incontinence was diagnosed more frequently in Caucasian women, and detrusor overactivity was seen more often in African American women (8). These diagnoses were also consistent with the study's finding that Caucasian women had lower urethral closure pressures than did African American women, while African American women had a lower bladder capacity than Caucasian women (Table 5). A recent analysis of data from the Study of Women's Health Across the Nation (SWAN), which included 3,302 women 42 to 52 years of age provided a closer look at nuances related to race/ethnicity and urinary incontinence (9). African American women with leiomyomata had a 1.81-fold higher risk of urinary incontinence than did Caucasian women, while African American women without fibroids had a decreased risk of urinary incontinence (OR 0.31). Hispanic and Japanese women had a lower risk than did Caucasian women (OR 0.44 and 0.58, respectively). In Chinese women, the risk of incontinence was modified by educational status; the OR of those with less than a college education was 0.35 relative to that of Caucasian women, and 2.53 for those with at least a college education.

Data from the Veterans Health Affairs (VA) were used to estimate the utilization of outpatient care for urinary incontinence among female veterans accessing VA health services. Of all women who received outpatient care in the VA system, urinary incontinence as a percentage of any diagnosis was 2.7% in 1999, 3.6% in 2000, and 3.8% in 2001 (Table 6). These proportions are substantially lower than the rates of daily incontinence reported in population-based surveys, suggesting that the majority of women with incontinence do not seek medical care for it. As expected, the prevalence of medically recognized urinary incontinence increased with age, with the most marked increase occurring between the 25- to 34-year-olds and the 45- to 54- year-olds. Incontinence was more than twice as common among non-Hispanic whites as it was among African Americans and approximately 50% more common among non-Hispanic whites than among Hispanics. Incontinence was most common in the Western region of the United States and least common in the Eastern region, except in 2001, although these differences were not adjusted for differences in age or race/ethnicity.

Less is known about incontinence incidence, remission, and natural history. In prospective cohort studies using a survey design, 10% to 20% of women report remission or recurrence of incontinence over a 1- to 2-year-period (10). Whether this reflects the natural history of incontinence, active intervention, or decreased physical activity (relevant to stress incontinence) is not clear.

Table 6. Frequency of urinary incontinence[a] listed as any diagnosis in female VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	3,780	2,679	5,426	3,597	6,196	3,757
Age						
18–24	23	387	20	348	22	378
25–34	213	796	223	839	237	888
35–44	777	1,882	1,020	2,449	1,052	2,489
45–54	968	3,262	1,531	4,374	1,817	4,440
55–64	469	4,194	697	5,506	827	5,600
65–74	401	4,405	543	5,858	637	5,744
75–84	849	5,412	1,261	6,927	1,440	6,828
85+	80	5,416	131	7,503	164	7,257
Race/ethnicity						
White	2,378	4,212	3,343	5,496	3,665	5,565
Black	406	2,152	511	2,491	562	2,518
Hispanic	83	3,257	102	3,608	117	3,767
Other	31	4,010	42	4,953	45	4,950
Unknown	882	1,412	1,428	2,169	1,807	2,485
Region						
Midwest	715	2,574	1,084	3,713	1,169	3,808
Northeast	672	2,338	862	2,842	1,036	3,162
South	1,354	2,584	2,083	3,682	2,294	3,606
West	1,039	3,228	1,397	4,020	1,697	3,162
Insurance status						
No insurance/self-pay	2,186	2,204	2,978	2,902	3,345	3,084
Medicare/Medicare supplemental	849	5,425	1,467	7,347	1,715	6,819
Medicaid	8	2,614	14	3,070	20	3,697
Private insurance/HMO/PPO	662	2,806	875	3,490	998	3,675
Other insurance	69	3,064	89	3,427	112	3,512
Unknown	6	4,196	3	2,239	6	1,435

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for female urinary incontinence (including stress incontinence and fistulae).

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

RISK FACTORS

Most data on risk factors for urinary incontinence come from clinical trials or cross-sectional studies using survey designs. Some risk factors have been more rigorously studied than others. Hence, the available information has limited generalizability and causality cannot be inferred from it. Bearing these limitations in mind, the literature does suggest that age, pregnancy, childbirth, obesity, functional impairment, and cognitive impairment are associated with increased rates of incontinence or incontinence severity. Some factors pertain more to certain age groups than to others. For example, in older women, childbirth disappears as a significant risk factor, possibly due to increased comorbidities and other intervening factors, such as diabetes, stroke, and spinal cord injury. Other factors about which less is known or findings are contradictory include hysterectomy, constipation, occupational stressors, smoking, and genetics.

TREATMENT

Fewer than half of the women with urinary incontinence report seeking medical care (11). Johnson and colleagues (12) found that the incontinent people most likely to contact a medical doctor are those who use pads, those who have large volume accidents, those who have impairment in activities of daily living; also, men are more likely to seek medical care than women are (Table 7). Many incontinent people practice behavioral modifications such as limiting trips, fluids, and routine activities. These restrictions are particularly striking in women with concomitant fecal incontinence (Table 8).

Most treatment for urge incontinence is nonsurgical. Common therapeutic modalities include pharmacologic treatment, physiotherapy, biofeedback,

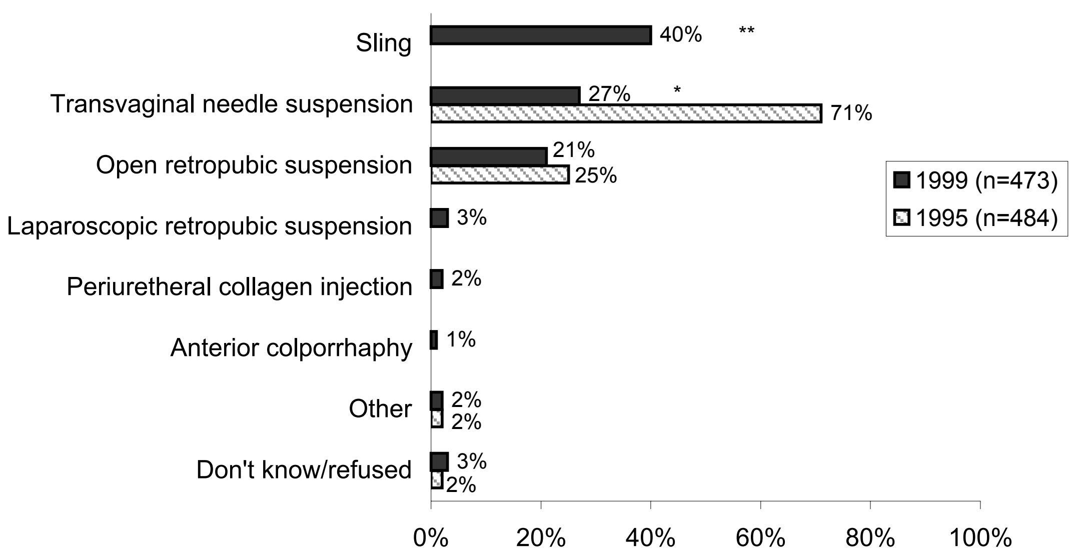

Figure 4. Most common surgical treatments in women with stress urinary incontinence associated with hypermobility, as indicated by practitioners treating females with urinary incontinence.

***Significantly lower than 1995 (p < 0.05)**
****Significantly higher than any other treatment and 1995 (p < 0.05)**

SOURCE: Adapted from O'Leary MP, Gee WF, Holtgrewe HL, Blute ML, Cooper TP, Miles BJ, Nellans RE, Thomas R, Painter MR, Meyer JJ, Naslund MJ, Gormley EA, Blizzard R, Fenninger RB, 1999 American Urological Association Gallup Survey: changes in physician practice patterns, treatment of incontinence and bladder cancer, and impact of managed care, Journal of Urology, 164, 1,311–1,316, Copyright 2000, with permission from Lippincott Williams & Wilkins.

Table 7. Relationship between disposable pad use and contacting an MD among subjects reporting urinary incontinence

	Contacting MD	
Factor	**Bivariate Odds Ratio (95% CI)**	**Multivariate Odds Ratio (95% CI)**
Disposable Pad Usage		
Non-user	1.0	1.0
User	2.81 (2.05–3.85)	3.02 (1.87–4.87)
Gender		
Female	1.0	1.0
Male	1.73 (1.28–2.36)	2.51 (1.58–4.01)
Age group		
70–79	1.0	1.0
80–89	1.12 (0.84–3.28)	1.12 (0.71–1.78)
90+	1.50 (1.00–2.24)	0.83 (0.46–1.51)
Severity of urinary incontinence		
Mild-Mod	1.0	
Severe	2.77 (2.00–3.86)	NS
How often have difficulty holding		
Less than 1/wk	1.0	
More than 1/wk	1.60 (1.42–1.81)	NS
Ever leak/lose urine with cough/laugh		
No	1.0	
Yes	1.05 (0.76–1.44)	NS
How often lose urine completely		
Never	1.0	1.0
Sometimes	1.99 (1.42–2.80)	1.90 (1.18–3.07)
Often	3.53 (2.01–6.19)	2.45 (1.00–6.00)
Mobility ADL		
No impairment	1.0	
Impairment	3.48 (2.28–5.29)	NS
Instrumental ADL		
Not impaired	1.0	1.0
Impairment	3.07 (2.08–4.54)	3.22 (1.83–5.68)
Basic ADL		
Not impaired	1.0	1.0
Impairment	1.48 (1.00–2.18)	0.38 (0.19–0.78)
Bowel incontinence		
None	1.0	
Weekly	2.77 (2.00–3.86)	NS

NS, not significant; ADL, activity of daily living.

95% confidence intervals for age and gender may include 1.0 for odds ratio. In the case of bivariate analysis, the criterion was to include variables significant at $\alpha = 0.10$.

For multivariate analysis, age and gender variables were forced into all final models because they were the stratification variables of the sample.

SOURCE: Reprinted from Johnson TM, Kincade JE, Bernard SL, Busby-Whitehead J, DeFriese GH, Self-care practices used by older men and women to manage urinary incontinence: Results from the national follow-up survey on self-care and aging, Journal of the American Geriatrics Society, 48, 894–902, Copyright 2000, with permission from the American Geriatrics Society.

Table 8. Estimates of self-care practice for those with urinary incontinence, by presence of fecal incontinence, severity of urinary incontinence, and gender

	All UI (95% CI)	UI without Fecal Incontinence[a] (95% CI)	UI with Fecal Incontinence (95% CI)	Mild or Moderate UI (95% CI)	Severe UI (95% CI)	Women with UI (95% CI)	Men with UI (95% CI)
In the last 12 months have you used:							
Disposable pads	36.8% (31.0–42.7)	33.6% (28.2–38.9)	45.2% (19.6–70.9)	27.7% (22.4–32.9)	60.1% (45.9–74.3)	44.5% (36.9–52.1)	15.1% (8.1–22.1)
Laundry service	2.3% (0.8–3.8)	2.5% (0.7–4.1)	1.7% (0–4.4)	1.7% (0.4–3.1)	3.9% (0–8.5)	1.6% (0.4–2.8)	4.2% (0–8.8)
Plastic sheets	11.2% (7.3–15.1)	9.5% (6.1–12.8)	39.6% (19.3–59.9)	7.1% (3.0–11.2)	20.6% (10.4–30.8)	11.3% (7.1–15.4)	11.0% (5.0–17.0)
Changed day-to-day routine activities:							
Limited trips	27.6% (19.6–35.5)	21.4% (16.7–26.0)	56.2% (37.5–74.9)	15.2% (10.6–19.9)	55.8% (40.4–71.2)	25.6% (17.0–34.2)	33.0% (22.4–43.7)
Limited fluids	36.6% (30.3–43.0)	32.6% (27.9–37.2)	57.6% (40.3–74.9)	29.3% (24.2–34.4)	55.3% (39.6–71.0)	39.4% (31.7–47.0)	28.5% (19.5–37.6)
Bladder exercise	11.7% (7.8–15.5)	12.5% (8.7–16.3)	8.1% (0–20.0)	10.4% (7.0–13.9)	15.9% (6.1–25.8)	14.2% (9.7–18.9)	4.3% (1.0–7.7)
Contacted an MD	39.8% (32.2–47.4)	34.5% (29.0–40.2)	62.9% (43.6–82.2)	31.2% (25.3–37.0)	59.2% (44.8–73.6)	37.1% (28.9–45.6)	47.4% (35.8–59.0)
Has someone helped you manage by:							
Changing disposable pads	15.3% (8.3–22.3)	11.3% (5.0–17.7)	60.1% (26.2–93.9)	12.9% (5.0–20.8)	16.4% (3.1–29.7)	11.4% (4.8–18.0)	47.6% (20.8–74.3)
Any assistance[b]	23.2% (18.4–28.0)	21.2% (17.1–25.4)	63.8% (43.6–84.2)	18.8% (13.7–24.0)	34.3% (20.6–47.9)	21.1% (15.6–26.7)	31.7% (22.7–40.6)

[a] Excludes all subjects reporting fecal incontinece. All other categories may include those with dual incontinence (maximum of 8% of total sample).

[b] Any assistance includes receiving diet and exercise advice, help with changing bedding, help with doing laundry, assistance in using the bathroom, help with a bedpan or urinal.

SOURCE: Reprinted from Johnson TM, Kincade JE, Bernard SL, Busby-Whitehead J, DeFriese GH, Self-care practices used by older men and women to manage urinary incontinence: Results from the national follow-up survey on self-care and aging, Journal of the American Geriatrics Society, 48, 894–902, Copyright 2000, with permission from the American Geriatrics Society.

Table 9. Age-specific incidence[a] (annual procedure rate) of surgically managed prolapse and incontinence per 1000 woman-years

Age Group (y)	Population of Women at Risk	All Cases (n = 384)	POP Only (n = 152)	UI Only (n = 138)	POP + UI (n = 82)
20–29	23,770	0.08	0.04	0.04	
30–39	30,358	0.96	0.30	0.43	0.23
40–49	35,828	2.68	0.87	1.23	0.59
50–59	24,242	3.30	1.24	1.24	0.83
60–69	16,231	5.24	2.28	1.60	1.36
70–79	12,236	6.62	3.43	1.72	1.47
≥ 80	6,889	1.60	0.73	0.44	0.44
Total	149,554	2.63			

POP, pelvic organ prolapse; UI, urinary incontinence.

[a]Includes primary and repeat procedures.

SOURCE: Reprinted with permission from the American College of Obstetricians and Gynecologists (Obstetrics and Gynecology, 1997, 89, 501–506).

bladder retraining, and electrical stimulation. For women with intractable, severe urge incontinence, direct neuromodulation of the sacral spinal cord is an increasingly popular option. Surgical therapy designed to increase bladder capacity and decrease contractility is rarely used.

In contrast, surgery is a mainstay of therapy for stress urinary incontinence. Surgeries performed frequently for stress incontinence in the past —anterior colporrhaphies and needle suspension procedures— have more recently been supplanted by retropubic urethropexies, pubovaginal slings (using various types of sling materials), and collagen injections. Based on available evidence that the long-term (3 to 5 years) success rate of anterior colporrhaphy and needle suspension procedures is significantly lower than that of the other two procedures, the Agency for Healthcare Research and Quality (AHRQ), (13) and the American Urological Association (14) have both taken the position that retropubic urethropexies and pubovaginal slings are the procedures of choice for stress incontinence. This trend is seen clearly in a study describing the trends in surgical management by American urologists between 1995 and 1999 (15) (Figure 4).

Nonsurgical therapies are also prominent in the treatment of women with stress urinary incontinence. The primary modality used is pelvic muscle rehabilitation ("Kegel exercises"). Vaginal and urethral devices, bladder training, and biofeedback are also frequently used. In the near future, new pharmacologic agents will be available as well.

While nonsurgical therapies for urge and stress urinary incontinence render only a minority of women completely dry, more than half of the women who participate in trials that assess such therapies report at least a 50% improvement in incontinence episodes. There is Level 1 evidence to support the use of pelvic muscle rehabilitation, bladder training, and anticholinergic therapy in women with some types of urinary incontinence. However, the literature on large, well-designed trials that are generalizable to the population seeking care is limited. Data are lacking on the long-term follow-up of nonsurgical treatment.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Surgical Treatment

Surgical treatment for urinary incontinence can be more easily tracked in existing databases than can non-surgical management. Surgical therapy accounts for a considerable proportion of the cost related to incontinence. Although only a small fraction of all women with urinary incontinence seek surgical intervention, the number of women treated with surgery is substantial. Using a large managed-care database, Olsen and colleagues (1997) reported an 11.1% lifetime risk of undergoing a single operation for urinary incontinence or pelvic organ prolapse by age 80 (Table 9) (16). Using data from the 1998 National Hospital Discharge Survey and the 1998 National Census, Waetjen and colleagues (2003) calculated that approximately 135,000 women in the United States had inpatient surgery for stress urinary incontinence in 1998 (17).

Data from the Healthcare Cost and Utilization Project (HCUP) indicate that the annual rate of hospitalizations for a primary diagnosis of urinary incontinence remained stable at 51 to 54 per 100,000 between 1994 and 1998, then dropped to 44 per 100,000 in 2000 (Table 10). It is unclear whether this drop reflects an actual trend, potentially attributable to newer ambulatory surgical techniques. The annual rate of hospitalizations was higher for women 45 to 84 years of age, peaking in the 65 to 74 age group at 108

Table 10. Inpatient hospital stays[a] by adult females with urinary incontinence listed as primary diagnosis, count, rate[b] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[c,d]	49,338	51 (48–54)	54,527	54 (51–58)	53,226	52 (48–56)	46,470	44 (41–47)
Age								
18–24	211	1.7 (1.1–2.3)	*	*	*	*	*	*
25–34	2,312	11 (10–13)	2,112	10 (8.9–12)	2,176	11 (10–12)	1,770	9.2 (8.0–10)
35–44	8,828	43 (39–47)	9,442	43 (40–47)	9,104	41 (37–44)	8,480	37 (34–41)
45–54	12,880	88 (81–94)	15,481	95 (89–102)	14,589	84 (77–90)	12,365	66 (61–71)
55–64	10,187	96 (88–104)	10,952	100 (92–107)	11,975	103 (95–112)	10,213	83 (76–90)
65–74	10,665	108 (99–117)	11,328	113 (104–121)	10,419	105 (97–114)	8,735	90 (81– 98)
75–84	3,908	67 (60–73)	4,585	72 (64–79)	4,322	64 (58–70)	4,360	63 (56–71)
85+	347	18 (14–23)	518	27 (19–34)	486	25 (20–31)	444	21 (16–26)
Race/ethnicity								
White	34,245	47 (44–50)	37,576	50 (47–53)	35,716	47 (44–51)	30,434	40 (37–43)
Black	1,266	11 (8.4–14)	1,426	12 (9–14)	1,483	12 (9.4–14)	1,119	8.7 (7.3–10)
Asian/Pacific Islander	260	9.5 (6.6–12)	220	6.5 (4.4–8.5)	307	8.1 (5.5–11)	276	6.8 (4.7–9.0)
Hispanic	1,965	24 (20–28)	2,510	28 (22–34)	2,262	23 (19–27)	2,869	27 (23–31)
Region								
Midwest	12,123	53 (46–59)	11,916	51 (45–57)	11,999	50 (44–57)	10,420	44 (37–50)
Northeast	6,809	34 (29–38)	8,839	44 (38–50)	8,380	41 (34–49)	8,051	39 (32–46)
South	18,024	55 (49–61)	22,237	62 (56–69)	21,300	59 (52–65)	17,741	48 (43–53)
West	12,381	61 (53–69)	11,535	55 (47–62)	11,547	53 (45–60)	10,258	44 (37–51)
MSA								
Rural	8,272	34 (29–40)	9,356	41 (36–47)	9,961	43 (37–50)	7,307	32 (27–37)
Urban	40,810	57 (53–61)	44,881	58 (54–62)	42,906	54 (50–58)	39,095	48 (44–52)
Discharge Status								
Routine	46,483	48 (45–51)	51,370	51 (48–55)	50,372	49 (46–53)	44,518	42 (39–46)
Short-term	*	*	*	*	*	*	*	*
Skilled nursing facility	255	0.3 (0.2–0.4)	294	0.3 (0.2–0.4)	…	…	…	…
Intermediate care	*	*	*	*	…	…	…	…
Other facility	*	*	*	*	579	0.6 (0.4–0.7)	347	0.3 (0.2–0.4)
Home healthcare	2,202	2.3 (1.9–2.6)	2,571	2.6 (2.2–3.0)	2,184	2.1 (1.8–2.5)	1,518	1.4 (1.2–1.7)
Against medical advice	*	*	*	*	*	*	*	*
Died	*	*	*	*	*	*	*	*

… data not available.

*Figure does not meet standard of reliability or precision.

MSA, metropolitan statistical area.

[a]Excludes hospitalizations associated with a primary gynecological diagnosis (e.g., pelvic organ prolapse).

[b]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[c]Counts may not add to totals because of rounding.

[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 11. Inpatient stays by female Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	16,160	82 (80–83)	19,840	98 (97–100)	17,700	93 (92–94)
Total < 65	1,240	52 (49–55)	2,520	94 (90–97)	2,520	91 (87–94)
Total 65+	14,920	86 (84–87)	17,320	99 (98–100)	15,180	93 (92–95)
Age						
65–74	9,780	106 (104–109)	11,300	126 (123–128)	9,320	118 (116–120)
75–84	4,380	74 (72–76)	5,220	87 (85–90)	5,100	87 (85–90)
85–94	760	37 (34–39)	740	33 (31–36)	700	31 (29–34)
95+	0	0	60	21 (16–26)	60	19 (15–24)
Race/ethnicity						
White	14,820	88 (87–90)	18,520	107 (105–108)	16,540	102 (101–104)
Black	460	27 (25–30)	640	35 (32–38)	600	34 (31–37)
Asian	…	…	20	21 (12–31)	120	68 (56–80)
Hispanic	…	…	160	80 (67–92)	260	71 (62–79)
N. American Native	…	…	20	124 (68–179)	40	153 (107–199)
Region						
Midwest	4,940	98 (96–101)	5,200	101 (98–104)	4,780	97 (94–100)
Northeast	2,020	45 (43–47)	2,640	59 (57–61)	2,340	60 (57–62)
South	5,840	84 (81–86)	7,880	109 (107–111)	7,540	107 (105–110)
West	3,300	116 (112–120)	3,880	136 (131–140)	2,980	110 (106–114)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

per 100,000 (Figure 5). Hospitalizations were most common in women residing in the South and West and least common in women living in the Northeast. Women living in urban areas had a higher rate of hospitalizations than did those in rural areas. Most of the hospitalizations for urinary incontinence were probably for surgical treatments.

The number of hospitalizations in Table 10 represents roughly one-half of the number of incontinence procedures reported by Waetjen, et. al. This is most likely due to the fact that Waetjen included inpatient stays in which the primary diagnosis was gynecological (such as pelvis organ prolapse) and in whom an incontinence procedure was done in concert with other procedures to repair the primary gynecological problem. Future analyses will address this issue.

Similar trends for older women were found in Medicare (Table 11) and HCUP (Table 10). The rate of inpatient stays for urinary incontinence for older women enrolled in Medicare (those 65+) ranged from 86 to 99 per 100,000 annually, with women between 65 and 74 more likely than the other age groups to be hospitalized. Geographic and racial/ethnic distributions were similar to those found in HCUP and significant differences among racial/ethnic groups were also noted.

Among women with commercial health insurance, the rate of inpatient hospitalizations for incontinence procedures (primary or any procedure) ranged from 123 per 100,000 women in 1994 to 114 per 100,000 in 2000 (Table 12). Most of these procedures were performed in conjunction with other surgical procedures and are thus listed as any procedure.

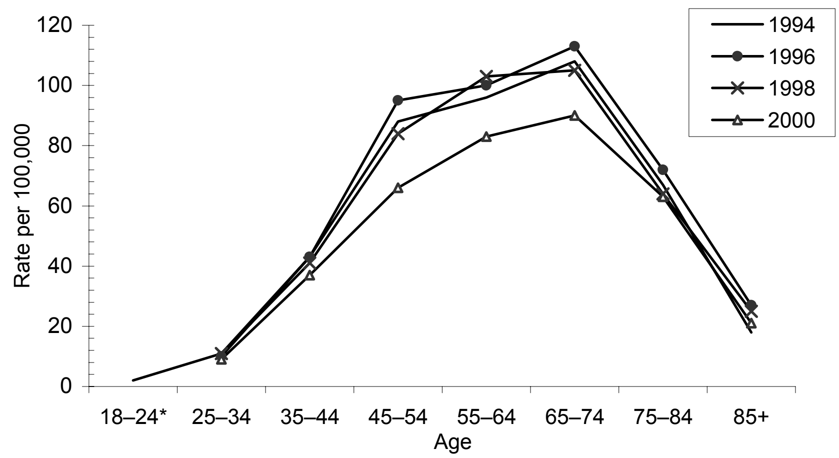

Figure 5. Inpatient hospital stays by females with urinary incontinence listed as primary diagnosis, by age and year.

***Figure does not meet standard for reliability or precision.**

SOURCE: Healthcare Cost and Utilization Project, 1994, 1996, 1998, 2000.

Table 12. Inpatient procedures for females with urinary incontinence having commercial health insurance, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	As Primary Procedure							
Total	230	59	307	53	355	40	334	33
Age								
18–24	0	*	2	*	0	*	0	*
25–34	18	*	16	*	14	*	25	*
35–44	62	54	66	39	100	39	77	27
45–54	97	120	134	106	136	66	116	47
55–64	42	112	79	138	94	95	96	79
65–74	9	*	9	*	10	*	18	*
75–84	1	*	1	*	1	*	2	*
85+	1	*	0	*	0	*	0	*
	As Any Procedure							
Total	483	123	749	130	1,034	115	1,167	114
Age								
18–24	0	*	3	*	2	*	0	*
25–34	38	38	48	34	72	35	74	33
35–44	170	147	253	151	319	125	348	124
45–54	187	232	301	238	407	197	443	180
55–64	72	191	123	214	203	205	249	204
65–74	14	*	18	*	26	*	49	264
75–84	1	*	3	*	5	*	3	*
85+	1	*	0	*	0	*	1	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar years for females in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 13. Trends in mean inpatient length of stay (days) for adult females hospitalized with urinary incontinence listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	3.1	2.6	2.4	2.1
Age				
18–24	2.7	*	*	*
25–34	2.9	2.5	2.2	2.1
35–44	3.0	2.4	2.3	2.1
45–54	3.1	2.5	2.3	2.1
55–64	3.0	2.5	2.3	2.1
65–74	3.3	2.7	2.5	2.1
75–84	3.7	2.9	2.7	2.7
85+	3.9	3.5	2.7	2.9
Race/ethnicity				
White	3.2	2.6	2.3	2.1
Black	3.2	2.7	2.5	2.3
Asian/Pacific Islander	2.7	2.7	2.1	2.2
Hispanic	3.1	2.6	2.5	2.4
Other	3.3	2.5	2.5	2.1
Region				
Midwest	3.1	2.6	2.4	2.1
Northeast	3.7	2.8	2.3	2.0
South	3.2	2.6	2.4	2.2
West	2.7	2.3	2.4	2.2
MSA				
Rural	3.4	2.6	2.3	2.4
Urban	3.1	2.5	2.4	2.1
Discharge status				
Routine	3.1	2.5	2.3	2.1
Short-term	*	*	*	*
Skilled nursing facility	5.0	4.5	…	…
Immediate care	*	*	…	…
Other facility	*	*	5.4	6.6
Home healthcare	3.9	3.3	3.0	2.8
Against medical advice	*	*	*	*
Died	*	*	*	*

….data not available.
*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Hospitalizations for incontinence surgeries as primary procedures ranged from 59 per 100,000 women in 1994 to 33 per 100,000 in 2000. These data suggest a trend toward decreasing numbers of inpatient surgeries for incontinence; if this trend is substantiated in future years, it may reflect either the increased emphasis on nonsurgical treatment for urinary incontinence that followed the dissemination of the AHRQ guidelines or increased utilization of ambulatory incontinence surgeries.

Consistent with decreasing lengths of inpatient stay for other conditions during the past decade, length of stay for women with urinary incontinence as their primary discharge diagnosis decreased steadily, from 3.1 days in 1994 to 2.1 days in 2000 (Table 13). Women in the oldest age groups were hospitalized longer than were those younger than 75. For example, in 2000, length of stay remained stable at 2.1 days in women between 18 and 74 years of age, and varied from 2.7 to 2.9 days in women older than 75. Length of stay was similar across racial/ethnic groups and regions of the country.

Surgical Procedures

In 1998, the most commonly performed surgical procedures for female urinary incontinence were collagen injections, pubovaginal slings, and anterior urethropexies (Table 14). Because anterior colporrhaphies may be performed for either urinary incontinence (a condition for which they are not a currently recommended treatment) or anterior pelvic organ prolapse (cystocele), rates for this procedure are not described. A striking decrease was seen in both Raz and Peyrera needle suspension procedures between 1992 and 1998: Raz procedures decreased from 4,364 per 100,000 women in 1992 to 1,564 per 100,000 in 1998, while Peyrera procedures were done too infrequently by 1998 to be detected in the data. Concomitantly, pubovaginal slings increased from 621 per 100,000 women in 1995 to 2,776 per 100,000 in 1998. The number of women undergoing anterior urethropexy decreased, though less dramatically, from 3,941 per 100,000 women in 1992 to 2,364 per 100,000 in 1998.

Despite an increase in cesarean deliveries and complex laparoscopic pelvic surgeries (two major sources of urogenital fistulae) during the time frame studied, national hospitalization data showed no

Table 14. Surgical procedures used to treat urinary incontinence among female adult Medicare beneficiaries, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	18,820	10,475	32,880	13,096	36,400	11,033
Anterior urethropexy, (e.g., MMK)	7,080	3,941	8,180	3,258	7,800	2,364
Ambulatory surgery center	160	89	360	143	580	176
Inpatient	6,720	3,740	7,740	3,082	7,200	2,182
Hospital outpatient	60	33	0	0	0	0
Physician office	140	78	80	32	20	6
Raz-type suspension	7,840	4,364	10,540	4,198	5,160	1,564
Ambulatory surgery center	360	200	600	239	720	218
Inpatient	7,400	4,119	9,780	3,895	4,400	1,333
Hospital outpatient	20	11	0	0	0	0
Physician office	60	33	160	64	40	12
Laparoscopic repair	0	0	0	0	0	0
Ambulatory surgery center	0	0	0	0	0	0
Inpatient	0	0	0	0	0	0
Hospital outpatient	0	0	0	0	0	0
Physician office	0	0	0	0	0	0
Collagen injection	0	0	9,300	3,704	12,040	3,649
Ambulatory surgery center	0	0	7,900	3,146	9,120	2,764
Inpatient	0	0	220	88	140	42
Hospital outpatient	0	0	300	119	360	109
Physician office	0	0	880	350	2,420	733
Hysterectomy with colpo-urethropexy	1,920	1,069	2,220	884	1,480	449
Ambulatory surgery center	0	0	0	0	0	0
Inpatient	1,920	1,069	2,220	884	1,480	449
Hospital outpatient	0	0	0	0	0	0
Physician office	0	0	0	0	0	0
Pubovaginal sling	640	356	1,560	621	9,160	2,776
Ambulatory surgery center	80	45	140	56	1,240	376
Inpatient	540	301	1,400	558	7,800	2,364
Hospital outpatient	0	0	0	0	0	0
Physician office	20	11	20	8	120	36
Peyrera procedure	1,280	712	820	327	540	164
Ambulatory surgery center	0	0	20	8	60	18
Inpatient	1,280	712	800	319	480	145
Hospital outpatient	0	0	0	0	0	0
Physician office	0	0	0	0	0	0
Kelly plication	60	33	260	104	220	67
Ambulatory surgery center	0	0	0	0	0	0
Inpatient	60	33	260	104	220	67
Hospital outpatient	0	0	0	0	0	0
Physician office	0	0	0	0	0	0

[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 female adult Medicare beneficiaries with a diagnosis of urinary incontinence.
NOTE: Confidence intervals could not be calculated because of multiple data sources.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient File, 1992, 1995, 1998.

Table 15. Inpatient hospital stays for adult females with urinary incontinence caused by urinary fistulae listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	6,689	6.9 (6.4–7.5)	7,589	7.6 (7.0–8.1)	6,813	6.7 (6.2–7.2)	7,031	6.7 (6.2–7.2)
Age								
18–24	294	2.4 (1.6–3.1)	217	1.7 (1.2–2.3)	186	1.5 (0.9–2.0)	*	*
25–34	1,133	5.5 (4.7–6.4)	1,037	5.1 (4.2–5.9)	787	4.0 (3.2–4.7)	791	4.1 (3.4–4.8)
35–44	1,054	5.2 (4.1–6.2)	1,278	5.9 (4.9–6.8)	1,186	5.3 (4.5–6.1)	1,268	5.6 (4.9–6.3)
45–54	732	5.0 (4.0–6.0)	894	5.5 (4.5–6.6)	922	5.3 (4.4–6.2)	1,216	6.5 (5.5–7.5)
55–64	828	7.8 (6.5–9.1)	948	8.6 (7.2–10)	852	7.4 (6.1–8.6)	895	7.3 (6.1–8.5)
65–74	1,257	13 (11–14)	1,424	14 (12–16)	1,204	12 (10–14)	1,133	12 (10–13)
75–84	1,021	17 (15–20)	1,366	21 (18–24)	1,194	18 (15–20)	1,131	16 (14–19)
85+	370	20 (15–24)	425	22 (17–27)	483	25 (19–31)	452	22 (17–26)
Race/ethnicity								
White	4,312	5.9 (5.4–6.4)	4,932	6.6 (6.0–7.1)	4,048	5.4 (4.8–5.9)	4,071	5.3 (4.8–5.8)
Black	482	4.2 (3.2–5.1)	675	5.6 (4.3–6.9)	533	4.3 (3.3–5.3)	565	4.4 (3.5–5.3)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	253	3.1 (2.1–4.0)	331	3.7 (2.3–5.0)	331	3.4 (2.2–4.6)	361	3.4 (2.5–4.3)
Region								
Midwest	1,861	8.1 (6.9–9.3)	2,038	8.7 (7.2–10)	1,701	7.2 (5.8–8.6)	1,676	7.0 (6.1–8.0)
Northeast	1,380	6.8 (5.8–7.8)	1,500	7.5 (6.4–8.6)	1,177	5.8 (4.9–6.7)	1,488	7.2 (6.1–8.3)
South	2,246	6.8 (6.0–7.7)	2,842	8.0 (7.0–8.9)	2,768	7.6 (6.8–8.4)	2,617	7.0 (6.2–7.9)
West	1,202	5.9 (4.8–7.0)	1,208	5.7 (4.8–6.7)	1,167	5.3 (4.4–6.2)	1,250	5.4 (4.6–6.2)

*Figure does not meet standard of reliability or precision.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races and missing or unavailable race and ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 16. Total physician office visits by adult females with urinary incontinence, count, rate[a] (95% CI)

Year	Primary Diagnosis Count	Primary Diagnosis Rate		Any Diagnosis Count	Any Diagnosis Rate	
1992	451,704	468	(252–683)	815,832	845	(480–1,210)
1994	549,827	571	(388–753)	1,048,115	1,088	(791–1,384)
1996	937,275	934	(600–1,267)	1,402,830	1,398	(992–1,803)
1998	1,332,053	1,302	(899–1,705)	2,004,851	1,960	(1,424–2,495)
2000	1,159,877	1,107	(722–1,490)	1,932,768	1,845	(1,313–2,375)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.
SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

increase in hospitalizations for urinary incontinence due to fistulae (Table 15). This rate remained steady at 6.7 to 7.6 per 100,000 women between 1994 and 2000. However, although the rate is low, 7,000 hospitalizations for incontinence due to fistulae are estimated to occur each year nationwide, suggesting that further attention should be paid to prevention.

Outpatient Care

Outpatient and Emergency Room Visits

While the rate of hospitalizations for incontinence surgeries decreased, outpatient visits for urinary incontinence more than doubled between 1992 and 2000 for women both with and without Medicare. Physician visits with urinary incontinence listed as any reason for the visit climbed from 845 per 100,000 women in 1992 to 1,845 per 100,000 in 2000, according to National Ambulatory Medical Care Survey (NAMCS) data (Table 16). Similarly, visits for which incontinence was the primary reason rose from 468 per 100,000 in 1992 to 1,107 per 100,000 in 2000. Office visits for incontinence by women ages 65 and over enrolled in Medicare rose from 1,371 per 100,000 in 1992 to 2,937 per 100,000 in 1998 (Table 17). While the reason for this increase is unknown, at least two potentially related events occurred. AHRQ published its first clinical practice guidelines on urinary incontinence in 1992; these were widely promulgated and may have led to more visits. Second, several new anticholinergic medications for urge incontinence were approved during the late 1990s. The releases of the first new medications for incontinence in several decades were accompanied by major direct-to-consumer advertising campaigns. Thus visits may also have increased because more women became aware that treatment existed. However, this illustrates the difficulty in comparing rates across data sets. Table 3 shows that 38% of elderly women report having UI. Table 8 suggests that 40% of women with UI report seeing a physician. However, in 1998, only 3% of Medicare female beneficiaries had a physician visit for UI. Thus it would appear that people over-report seeing a doctor, UI is under-reported on billing data, or some combination of the two.

Not surprisingly, given the nonemergent nature of urinary incontinence, few women seek emergency room care for it. Only 11 per 100,000 women ages 65 and older enrolled in Medicare were evaluated in emergency room settings for this disorder in 1998.

Ambulatory Surgery

Ambulatory surgical center visits for female urinary incontinence also increased, particularly in women younger than 65. Among those with commercial health insurance, the rate of such visits increased from 15 per 100,000 in 1994 to 34 per 100,000 in 2000 (Table 18). A steady increase was seen in middle-aged women; the rate of ambulatory surgical visits by women 55 to 64 years of age increased from 61 per 100,000 in 1996 to 69 per 100,000 in 1998 and 77 per 100,000 in 2000. Older women also had more ambulatory surgical visits; the rate of such visits by women 65 and older enrolled in Medicare in 1998 was 142 per 100,000 (Table 19). The increased rate of ambulatory surgery is probably due to the wider use of endoscopic injections such as collagen to treat urinary incontinence in women. Collagen for this purpose was not available in 1992, but by 1995

Table 17. Physician office visits by female Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	257,740	1,301 (1,296–1,306)	393,680	1,951 (1,945–1,957)	522,240	2,741 (2,733–2,748)
Total < 65	18,780	786 (775–797)	32,280	1,201 (1,188–1,214)	44,200	1,591 (1,577–1,606)
Total 65+	238,960	1,371 (1,366–1,377)	361,400	2,066 (2,059–2,073)	478,040	2,937 (2,928–2,945)
Age						
65–74	118,140	1,285 (1,278–1,293)	177,840	1,976 (1,967–1,985)	214,960	2,720 (2,709–2,732)
75–84	93,340	1,583 (1,572–1,593)	139,240	2,326 (2,314–2,338)	200,720	3,436 (3,421–3,451)
85–94	26,640	1,283 (1,268–1,299)	42,260	1,901 (1,883–1,918)	59,820	2,689 (2,668–2,710)
95+	840	326 (304–348)	2,060	728 (696–759)	2,540	819 (787–850)
Race/ethnicity						
White	236,320	1,408 (1,402–1,414)	363,440	2,094 (2,088–2,101)	480,900	2,972 (2,964–2,981)
Black	11,020	654 (641–666)	16,520	898 (884–912)	23,040	1,306 (1,289–1,323)
Asian	…	…	1,260	1,335 (1,262–1,408)	2,660	1,503 (1,447–1,560)
Hispanic	…	…	3,120	1,553 (1,499–1,607)	7,160	1,948 (1,903–1,993)
N. American Native	…	…	320	1,980 (1,764–2,197)	300	1,150 (1,020–1,281)
Region						
Midwest	66,100	1,317 (1,307–1,327)	99,840	1,936 (1,924–1,948)	134,480	2,726 (2,712–2,740)
Northeast	50,440	1,113 (1,103–1,123)	74,920	1,667 (1,655–1,679)	89,600	2,287 (2,272–2,302)
South	94,740	1,356 (1,347–1,364)	149,500	2,069 (2,059–2,080)	206,340	2,940 (2,928–2,953)
West	45,000	1,578 (1,564–1,593)	66,900	2,336 (2,319–2,354)	88,700	3,264 (3,243–3,285)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 18. Visits to ambulatory surgery centers for urinary incontinence procedures listed as any procedure by adult females having commercial health insurance, count[a], rate[b] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	60	15	185	32	278	31	351	34
Age								
18–24	0	*	1	*	1	*	0	*
25–34	3	*	7	*	15	*	19	*
35–44	17	*	45	27	71	28	91	32
45–54	25	*	80	63	103	50	128	52
55–64	11	*	35	61	68	69	94	77
65–74	3	*	11	*	17	*	14	*
75–84	0	*	2	*	3	*	4	*
85+	1	*	4	*	0	*	1	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for adult females in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 19. Visits to ambulatory surgery centers by female Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	11,580	58 (57–60)	24,680	122 (121–124)	25,820	135 (134–137)
Total < 65	1,140	48 (45–50)	2,260	84 (81–88)	2,740	99 (95–102)
Total 65+	10,440	60 (59–61)	22,420	128 (126–130)	23,080	142 (140–144)
Age						
65–74	5,900	64 (63–66)	11,880	132 (130–134)	10,780	136 (134–139)
75–84	3,800	64 (62–66)	8,420	141 (138–144)	9,680	166 (162–169)
85–94	720	35 (32–37)	2,080	94 (90–98)	2,500	112 (108–117)
95+	20	7.8 (4.3–11)	40	14 (9.9–18)	120	39 (32–45)
Race/ethnicity						
White	10,460	62 (61–64)	23,120	133 (132–135)	24,480	151 (149–153)
Black	600	36 (33–38)	900	49 (46–52)	860	49 (46–52)
Asian	…	…	60	64 (48–79)	80	45 (35–55)
Hispanic	…	…	60	30 (22–37)	240	65 (57–73)
N. American Native	…	…	40	248 (173–322)	…	…
Region						
Midwest	4,100	82 (79–84)	8,620	167 (164–171)	8,360	169 (166–173)
Northeast	2,400	53 (51–55)	4,500	100 (97–103)	4,820	123 (120–126)
South	4,120	59 (57–61)	9,580	133 (130–135)	10,160	145 (142–148)
West	960	34 (32–36)	1,960	68 (65–71)	2,480	91 (88–95)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,0000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

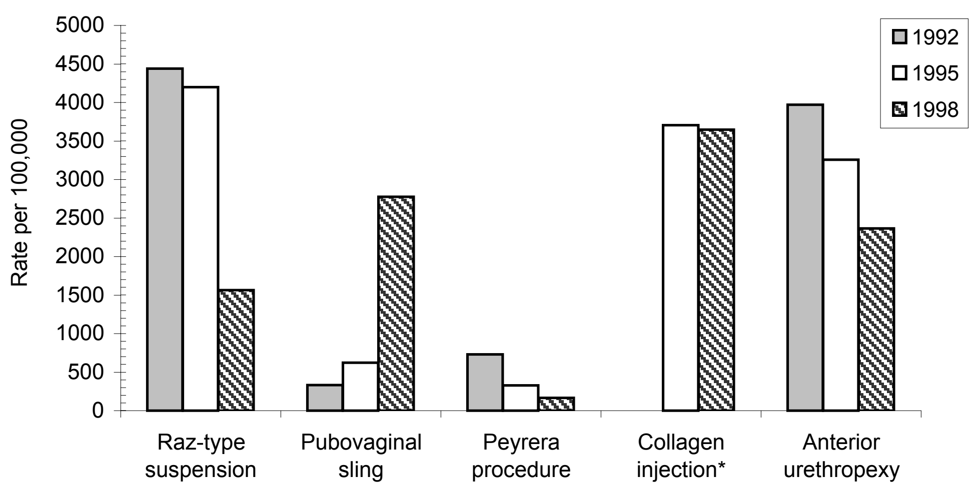

Figure 6. Rate of surgical procedures used to treat urinary incontinence among female Medicare beneficiaries.

***Collagen injection introduced in 1993.**

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

3,704 per 100,000 women enrolled in Medicare were undergoing this therapy. This rate has since plateaued (Table 14 and Figure 6).

Nursing Home Care

Incontinence is particularly a problem in the frail elderly and is exacerbated by dementia, functional limitations, and comorbid conditions. In the United States, identification of incontinence by the Minimum Data Set (developed by the US Health Care Financing Administration) within 14 days of nursing home admission is mandated (18).

According to data collected by the National Nursing Home Survey (NNHS), the rate of women in nursing homes with an admitting or current diagnosis of urinary incontinence has remained fairly stable; the most recent estimate (for 1999) is 1,366 per 100,000. The rate is very similar across age groups of nursing home residents (Table 20). Few female nursing home residents with urinary incontinence have indwelling urethral catheters or ostomies (9,495 per 100,000 in 1999) (Table 21); however, fully half require another person's assistance when using the toilet.

Urinary incontinence is regarded as an important risk factor for nursing home admission. Research has indicated that a significant proportion of those admitted to nursing homes are incontinent of urine at the time of their admission (19, 20). After adjustment for age, cohort factors, and comorbid conditions, Thom found that the relative risk of admission to a nursing home is two times greater for incontinent women (21).

The sharp divergence of the NNHS data from published studies on the prevalence of incontinence in nursing homes compels us to pay particular attention to the method of collecting information on incontinence in nursing home residents. According to NNHS data, only 1% to 2% of nursing home patients have an admitting or current diagnosis of urinary incontinence, a finding that highlights the limitations of using administrative data to study the prevalence of incontinence. When queries about bladder function are expanded to include assistance needed from nursing home staff, a high prevalence of bladder dysfunction becomes apparent. Over half of all female nursing home residents are reported to have "difficulty controlling urine," and over half need assistance in using the toilet (Table 22). Thus, when interpreting incontinence prevalence rates, great care must be taken to clarify the definition of incontinence used.

ECONOMIC IMPACT

Medical expenditures for urinary incontinence among female Medicare beneficiaries (65 years of age and older) nearly doubled between 1992 and 1998 from $128.1 million to $234.4 million, primarily due to increased aggregate costs for physician office visits and ambulatory surgery (Table 23). At the same time, inpatient costs increased only modestly between 1992

Table 20. Female nursing home residents with an admitting or current diagnosis of urinary incontinence, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Total	13,915	1,237 (949–1,524)	20,679	1,789 (1,435–2,143)	15,979	1,366 (1,050–1,681)
Age						
≤74	2,443	1,435 (605–2,265)	2,408	1,334 (610–2,058)	2,627	1,389 (588–2,190)
75–84	4,159	1,131 (662–1,601)	9,029	2,428 (1,679–3,176)	5,668	1,540 (972–2,107)
85+	7,313	1,245 (846–1,644)	9,242	1,531 (1,085–1,978)	7,685	1,254 (823–1,685)
Race						
White	13,397	1,340 (1,022–1,658)	17,962	1,779 (1,403–2,155)	15,075	1,509 (1,148–1,869)
Other	518	421 (0–905)	2,717	1,969 (858–3,080)	904	554 (58–1,051)

[a]Rate per 100,000 nursing home residents in the same demographic stratum.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 21. Special needs of female nursing home residents with urinary incontinence, count, rate[a] (95% CI)

	1995		1997		1999	
Category	**Count**	**Rate**	**Count**	**Rate**	**Count**	**Rate**
Has an indwelling foley catheter or ostomy						
Yes	1,435	10,316 (2,864–17,768)	2,423	11,718 (5,311–18,125)	1,517	9,495 (2,892–16,099)
No	12,479	89,684 (82,232–97,136)	18,256	88,282 (81,875–94,689)	14,462	90,505 (83,901–97,108)
Requires assistance using the toilet						
Yes	9,847	70,766 (59,831–81,702)	14,237	68,846 (59,267–78,424)	8,898	55,684 (43,783–67,586)
No	2,475	17,789 (8,437–27,141)	2,794	13,511 (6,777–20,245)	3,234	20,238 (10,842–29,634)
Question skipped for allowed reason	1,592	11,444 (3,978–18,910)	3,405	16,464 (8,416–24,513)	3,847	24,077 (13,340–34,814)
Question left blank	0	0	244	1,179 (0–3,513)	0	0
Requires assistance from equipment when using the toilet						
Yes	3,214	23,095 (12,895–33,295)	4,464	21,587 (13,465–29,709)	2,821	17,653 (9,041–26,266)
No	6,472	46,513 (34,604–58,422)	9,056	43,793 (33,744–53,842)	5,876	36,771 (25,354–48,188)
Question skipped for allowed reason	4,068	29,234 (18,298–40,169)	6,199	29,976 (20,499–39,452)	7,081	44,316 (32,414–56,217)
Question left blank	161	1,159 (0–3,472)	960	4,644 (134–9,154)	201	1,260 (0–3,771)
Requires assistance from another person when using the toilet						
Yes	9,619	69,132 (58,007–80,256)	14,000	67,698 (58,032–77,365)	8,675	54,292 (42,379–66,205)
No	227	1,635 (0–4,884)	0	0	223	1,393 (0–4,164)
Question skipped for allowed reason	4,068	29,234 (18,298–40,169)	6,199	29,976 (20,499–39,452)	7,081	44,316 (32,414–56,217)
Question left blank	0	0	481	2,326 (0–5,563)	0	0
Has difficulty controlling urine						
Yes	10,695	76,859 (66,543–87,176)	15,255	73,772 (64,947–82,597)	13,648	85,412 (77,364–93,460)
No	2,266	16,287 (7,085–25,489)	3,966	19,176 (11,322–27,031)	1,786	11,180 (3,928–18,432)
Question skipped for allowed reason	954	6,854 (895–12,812)	1,458	7,052 (1,886–12,217)	545	3,408 (0–7,333)

[a] Rate per 100,000 adult female nursing home residents with urinary incontinence in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 22. Special needs of female nursing home residents regardless of continence status, count, rate[a] (95% CI)

Category	1995 Count	1995 Rate	1997 Count	1997 Rate	1999 Count	1999 Rate
Has indwelling foley catheter or ostomy						
Yes	101,827	9,050 (8,281–9,819)	90,855	7,859 (7,151–8,566)	96,151	8,218 (7,484–8,951)
No	1,020,886	90,732 (89,954–91,510)	1,061,282	91,796 (91,072–92,520)	1,064,024	90,937 (90,162–91,712)
Question left blank	2,450	218 (89–347)	3,997	346 (182–510)	9,890	845 (571–1,120)
Requires assistance using the toilet						
Yes	659,035	58,572 (57,256–59,888)	652,615	56,448 (55,131–57,765)	670,006	57,262 (55,935–58,590)
No	286,946	25,503 (24,334–26,671)	280,242	24,240 (23,104–25,375)	273,104	23,341 (22,202–24,480)
Question skipped for allowed reason	173,839	15,450 (14,484–16,417)	216,408	18,718 (17,680–19,756)	218,971	18,714 (17,670–19,759)
Question left blank	5,343	475 (297–652)	6,870	594 (394–794)	7,983	682 (430–935)
Requires assistance from equipment when using the toilet						
Yes	182,812	16,248 (15,274–17,221)	180,518	15,614 (14,659–16,569)	178,305	15,239 (14,293–16,185)
No	460,230	40,903 (39,592–42,215)	433,640	37,508 (36,220–38,795)	467,351	39,942 (38,631–41,254)
Question skipped for allowed reason	460,785	40,953 (39,639–42,267)	496,649	42,958 (41,643–44,272)	492,075	42,055 (40,732–43,379)
Question left blank	21,336	1,896 (1,536–2,257)	45,327	3,921 (3,391–4,450)	32,334	2,763 (2,303–3,224)
Requires assistance from another person when using the toilet						
Yes	652,088	57,955 (56,636–59,274)	640,137	55,369 (54,048–56,689)	661,927	56,572 (55,242–57,901)
No	6,109	543 (345–741)	8,603	744 (511–977)	6,800	581 (384–779)
Question skipped for allowed reason	460,785	40,953 (39,639–42,267)	496,649	42,958 (41,643–44,272)	492,075	42,055 (40,732–43,379)
Question left blank	6,180	549 (357–741)	10,745	929 (681–1,178)	9,263	792 (527–1,056)
Has difficulty controlling urine						
Yes	633,123	56,269 (54,943–57,596)	672,699	58,185 (56,875–59,496)	685,747	58,608 (57,288–59,927)
No	424,287	37,709 (36,411–39,006)	422,839	36,574 (35,293–37,854)	422,162	36,080 (34,793–37,367)
Question skipped for allowed reason	64,822	5,761 (5,124–6,398)	57,080	4,937 (4,370–5,504	55,713	4,761 (4,201–5,322)
Question left blank	2,931	260 (114–407)	3,517	304 (154–454)	6,444	551 (323–778)

[a]Rate per 100,000 adult female nursing home residents in the NNHS for that year.

SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

and 1995, then decreased slightly in 1998 (Figure 7). Table 24 illustrates that, as with Medicare, during the 1990s expenditures in the general population shifted to the outpatient setting. This change in venue probably reflects the general shift of surgical procedures to the outpatient setting, as well as the advent of new procedures, such as periurethral collagen injections, which do not require hospital admission. In addition, the increase in awareness of incontinence and the marketing of new drugs for its treatment may have increased the number of office visits.

While claims-based costs are substantial, others have projected the aggregate cost of UI to be even higher. In one estimation model that included women and men, the aggregate cost of urinary incontinence in the United States in 1995—including diagnostic testing, medical and surgical therapy, medications, routine care, hospitalization, skin irritation, related infections and falls, and other factors—was estimated to be $26.3 billion, almost one-fourth of which was borne by patients themselves as part of routine care (22) (Table 25).

Using diagnostic algorithms, disease prevalence data, reimbursement costs, and sensitivity analyses, Wilson et al. (1) estimated the annual direct cost of urinary incontinence in women to be $12.4 billion in

Table 23. Expenditures for female Medicare beneficiaries age 65 and over for treatment of urinary incontinence, by site of service (% of total)

	Year					
	1992		1995		1998	
Total	$128,100,000		$198,700,000		$234,400,000	
Inpatient	$90.500,000	(70.6%)	$110,900,000	(55.8%)	$110,100,000	(47.0%)
Outpatient						
Physician Office	$25.700,000	(20.1%)	$46,400,000	(23.4%)	$75,900,000	(32.4%)
Hospital Outpatient	$2,200,000	(1.7%)	$3,500,000	(1.8%)	$5,000,000	(2.1%)
Ambulatory Surgery	$9,300,000	(7.2%)	$36,800,000	(18.5%)	$42,800,000	(18.2%)
Emergency room	$400,000	(0.3%)	$1,100,000	(0.6%)	$600,000	(0.2%)

NOTE: Percentages may not add to 100% because of rounding.

SOURCE: Centers for Medicare and Medicaid Services Claims, 1992, 1995, 1998.

Table 24. Expenditures for female urinary incontinence and share of costs, by site of service (% of total)

	Year							
	1994		1996		1998		2000	
Total[a]	$324,600,000		$426,700,000		$485,700,000		$452,800,000	
Inpatient	$295,100,000	(90.9%)	$346,000,000	(81.1%)	$357,500,000	(73.6%)	$329,200,000	(72.7%)
Physician Office	$29,500,000	(9.1%)	$80,600,000	(18.9%)	$128,200,000	(26.4%)	$123,600,00	(27.3%)
Hospital Outpatient	*		*		*		*	
Emergency Room	*		*		*		*	

*Unweighted counts too low to yield reliable estimates.

[a]Total unadjusted expenditures exclude spending on outpatient prescription drugs for the treatment of urinary incontinence. Average drug spending for incontinence-related conditions (both male and female) is estimated at $82 million to $102 million annually for the period 1996 to 1998.

NOTE: Percentages may not add to 100% because of rounding.

SOURCES: National Ambulatory and Medical Care Survey, National Hospital Ambulatory Medical Care Survey, Healthcare Cost and Utilization Project, Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

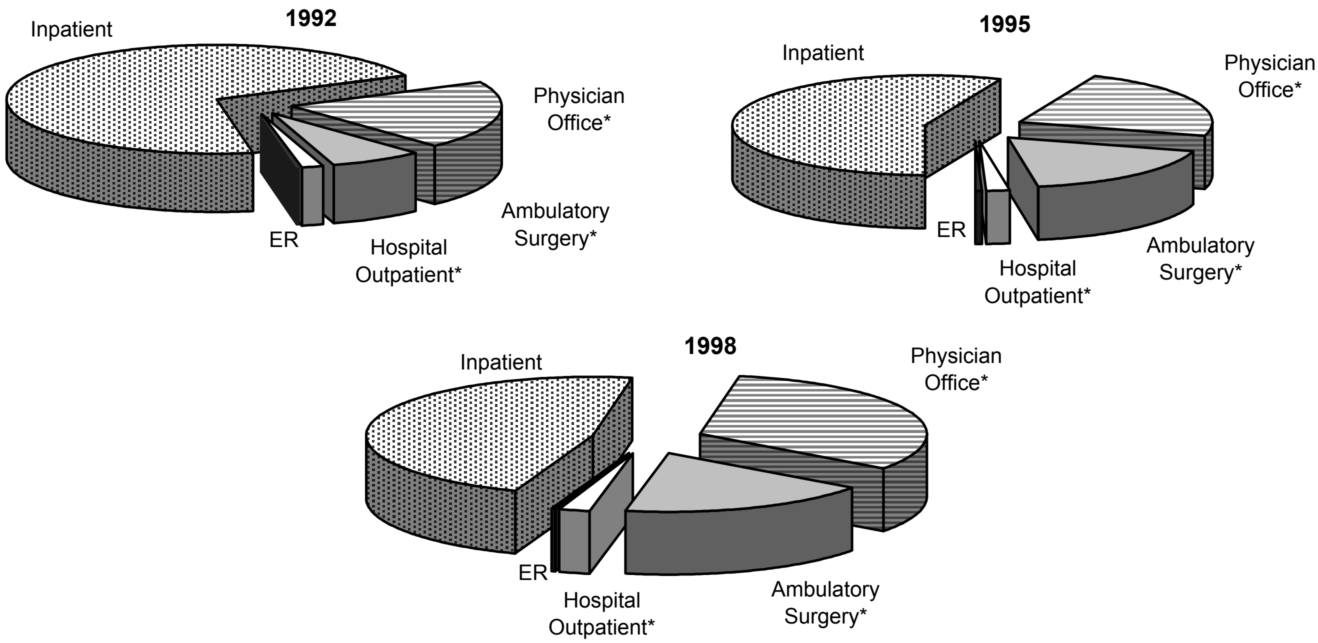

Figure 7. Expenditures for female Medicare benefiiciaries age 65 and over for the treatment of urinary incontinence (in millions of $).

***Constitute outpatient services.**

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

1995 (Table 26). The largest cost category was routine care, which accounted for 70% of all costs.

In a multivariate analysis controlling for age, gender, work status, median household income, urban vs rural residence, medical and drug plan characteristics, and comorbid conditions, the presence of urinary incontinence was associated with more than twice the annual expenditures per person per year compared to those without this condition (Table 27).

The indirect costs for urinary incontinence are estimated by measurements of work lost (Tables 28 and 29). Among all workers with urinary incontinence, 23% of women missed work, while only 8% of men did so. Average annual work absence for women totaled 28.7 hours for both inpatient (7.1 hours) and outpatient (21.6 hours) services. Although women and men had similar numbers of outpatient visits for urinary incontinence, average work loss associated with outpatient care was greater for women (Table 29), probably because of the availability of outpatient procedures for women.

RECOMMENDATIONS

Classification and Coding

Existing databases allow researchers to describe trends in incontinence surgery and hospitalization more accurately than trends in outpatient visits or treatment in nursing homes. Urinary incontinence may be coded as stress incontinence, urge incontinence, mixed incontinence, intrinsic sphincter deficiency, frequency, nocturia, or other terms. Visits during which patients return for follow-up after treatment are also often coded as visits for incontinence, even if the symptom has resolved. While providers can be urged to code more diligently, administrative databases alone will never yield the degree of clinical accuracy needed to create a comprehensive picture of urinary incontinence and its impact on women

Table 25. Costs of urinary incontinence in 1995 (in millions of $)

Cost Factor	
Diagnostic costs	
Community[a]	380.7
Institution[b]	12.8
Treatment Costs	
Behavioral	
Community	60.0
Institution	4.0
Pharmacologic	
Community	8.5
Institution	0.8
Surgical	
Community	613.8
Institution	41.2
Routine care costs	
Community	7,146.2
Institution	4,259.7
Incontinence consequences costs	
Skin irritation	
Community	282.8
Institution	136.3
Urinary tract infections	
Community	346.1
Institution	3,835.5
Falls	
Community	56.7
Institution	1.7
Additional admissions to institutions	2,172.1
Longer hospitalization periods	6,229.1
Total direct costs	25,588.0
Indirect costs (value of home care services)	704.4
Total costs of urinary incontinence	26,292.4
Cost per person with urinary incontinence	3,565.1

[a]Non-institutionalized older adults.

[b]Older adults living in an institution.

SOURCE: Reprinted from Urology, 51, Wagner TH, Hu T, Economic costs of urinary incontinence in 1995, 355–361, Copyright 1998, with permission from Elsevier Science.

in the United States. Although hospitalizations are more rigorously coded, there is often a substantial lag between the adoption of new surgical procedures and the establishment of new reimbursement codes, making tracking of trends difficult. Further, surgical codes are often not specific enough for use in health services or clinical research. For example, many types of pubovaginal slings are represented by one code. Despite these limitations, administrative databases do allow investigators to paint broad-brush pictures of the overall picture of urinary incontinence in American women. More specific cohort studies are essential to provide the details.

Future Studies

Given the large number of women affected by urinary incontinence, future studies focusing on both prevention and treatment are vital. Longitudinal studies are needed to delineate the risk factors for urinary incontinence and fistulae in women in different age groups. Such long-term prospective cohort studies, as well as randomized trials, can help determine which factors are amenable to intervention and whether such intervention can change continence status. Well-designed studies are needed to evaluate the effect of child-bearing practices on urinary incontinence and other pelvic floor disorders, particularly in younger women. Many studies of urinary incontinence treatment have very narrow inclusion criteria and do not reflect the general population of incontinent women. More population-based studies are needed. In addition, the inclusion criteria should be broadened in future randomized trials, particularly those of pharmacologic agents, to make the trial results more relevant. Long-term follow-up studies are needed to improve understanding of the longevity of therapeutic effectiveness for incontinence, particularly in patients who have had surgery.

Table 26. Costs of urinary incontinence by age group, residence, and gender[a]

	Elderly[b]		Middle-Age[b]	Younger[b]	
Variable	Community Dwelling	Institutionalized	Community Dwelling		Total Cost
Total cost	5,269 (32)	5,500 (34)	2,518 (15)	2,964 (18)	16,252 (100)
Women	3,734 (30)	3,851 (31)	2,245 (18)	2,598 (21)	12,428 (76)
Men	1,535 (40)	1,650 (43)	273 (7)	366 (10)	3,824 (24)
Cost by category[c]					
Routine care	4,174 (79)	2,830 (51)	1,799 (71)	2,533 (85)	11,336 (70)
Women	2,922 (70)	1,981 (70)	1,576 (88)	2,199 (87)	8,678 (77)
Men	1,252 (30)	849 (30)	223 (12)	334 (13)	2,658 (23)
Nursing home admissions	0 (0)	2,410 (44)	0 (0)	0 (0)	2,410 (15)
Women	0 (0)	1,687 (70)	0 (0)	0 (0)	1,687 (70)
Men	0 (0)	723 (30)	0 (0)	0 (0)	723 (30)
Treatment	312 (6)	126 (2)	530 (21)	324 (11)	1,292 (8)
Women	274 (88)	88 (70)	503 (95)	306 (94)	1,171 (91)
Behavioral therapy	8 (3)	88 (100)	4 (1)	6 (2)	106 (9)
Surgery	224 (82)	0 (0)	476 (95)	268 (88)	968 (83)
Pharmacologic therapy	42 (15)	0 (0)	23 (4)	32 (10)	97 (8)
Men	38 (12)	38 (30)	27 (5)	19 (6)	122 (9)
Behavioral therapy	2 (5)	38 (100)	0.4 (1)	0.6 (3)	41 (34)
Surgery	24 (63)	0 (0)	25 (92)	15 (79)	64 (52)
Pharmacologic therapy	12 (32)	0 (0)	2 (7)	3 (16)	17 (14)
Complications	699 (13)	132 (4)	152 (4)	56 (1)	1,039 (7)
Women	479 (69)	93 (70)	134 (89)	49 (88)	755 (73)
Skin irritation	238 (50)	56 (60)	64 (47)	0 (0)	358 (47)
UTI	113 (23)	26 (28)	35 (26)	49 (100)	223 (30)
Falls	128 (27)	11 (12)	34 (25)	0 (0)	173 (23)
Men	220 (31)	39 (30)	19 (11)	7 (13)	285 (27)
Skin irritation	102 (46)	24 (62)	9 (47)	0 (0)	135 (47)
UTI	63 (28)	10 (26)	5 (26)	7 (13)	85 (30)
Falls	55 (25)	5 (13)	5 (26)	0 (0)	65 (23)
Diagnoses and evaluation	84 (2)	3 (0.1)	36 (1)	51 (1)	174 (1)
Women	59 (70)	2 (70)	32 (89)	44 (86)	137 (79)
Men	25 (30)	1 (30)	4 (11)	7 (14)	37 (21)

UTI, urinary tract infection.

[a]Costs presented in millions 1995 US dollars. Percents may not add to 100% because of rounding.

[b]Elderly includes people ≥ 65 years old; middle-age includes people 40-64 years old; younger includes people 15-39 years old.

[b]Results shown indicate costs and % of total cost by age group in major cost categories. Cost and % of major cost category are shown for gender, complication type, and/or treatment type.

SOURCE: Reprinted with permission from the American College of Obstetricians and Gynecologists (Obstetrics and Gynecology, 2001, 98, 398–406.

Table 27. Estimated annual expenditures of privately insured employees with and without a medical claim for urinary incontinence (UI) in 1999[a]

	Annual Expenditures (per person)			
	Persons without UI (N=277,803)	Persons with UI (N=1,147)		
	Total	Total	Medical	Rx Drugs
Total	$3,204	$7,702	$6,099	$1,604
Age				
18–44	$2,836	$7,361	$5,993	$1,369
45–54	$3,305	$8,442	$6,695	$1,747
55–64	$3,288	$7,247	$5,623	$1,623
Gender				
Male	$2,813	*	*	*
Female	$3,933	*	*	*
Region				
Midwest	$3,086	$8,500	$6,861	$1,639
Northeast	$3,085	$7,236	$5,502	$1,734
South	$3,416	$8,329	$6,851	$1,477
West	$3,237	$8,082	$7,118	$964

Rx, prescription.

*Figure does not meet standard for reliability or precision.

[a]The sample consists of primary beneficiaries aged 18 to 64 with employer-provided insurance, who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.

SOURCE: Ingenix, 1999.

Table 28. Average annual work loss of persons treated for urinary incontinence (95% CI)

			Average Work Absence (hrs)		
Gender	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
Male	51	8%	0	2.3 (0–5.0)	2.3 (0–5.0)
Female	319	23%	7.1 (1.7–12.6)	21.6 (11.3–31.9)	28.7 (14.9–42.5)

[a]Individuals with an inpatient or outpatient claim for urinary incontinence and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: MarketScan, 1999.

Table 29. Average work loss associated with a hospitalization or an ambulatory care visit for treatment of urinary incontinence (95% CI)

	Inpatient Care		Outpatient Care	
Gender	**Number of Hospitalizations[a]**	**Average Work Absence (hrs)**	**Number of Outpatient Visits**	**Average Work Absence (hrs)**
Male	*	*	82	1.4 (0.1–2.7)
Female	*	*	625	11.0 (7.5–14.6)

*Figure does not meet standard for reliability or precision.
[a]Unit of observation is an episode of treatment. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.
SOURCE: MarketScan, 1999.

REFERENCES

1. Wilson L, Brown JS, Shin GP, Luc KO, Subak LL. Annual direct cost of urinary incontinence. Obstet Gynecol 2001;98:398-406.
2. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Am J Obstet Gynecol 2002;187:116-26.
3. Thom D. Variation in estimates of urinary incontinence prevalence in the community: effects of differences in definition, population characteristics, and study type. J Am Geriatr Soc 1998;46:473-80.
4. Hannestad YS, Rortveit G, Sandvik H, Hunskaar S. A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study. Epidemiology of Incontinence in the County of Nord-Trondelag. J Clin Epidemiol 2000;53:1150-7.
5. Hunskaar S, Burgio K, Diokno AC, Herzog AR, Hjalmas K, Lapitan MC. Epidemiology and natural history of urinary incontinence (UI). In: Abrams P, Cardozo L, Khoury S, Wein A, eds. Incontinence 2nd International Consultation on Incontinence. 2nd ed. Plymouth: Plymbridge Distributors Ltd., 2002:165-201.
6. Nygaard I, Turvey C, Burns TL, Crischilles E, Wallace R. Urinary incontinence and depression in middle-aged United States women. Obstet Gynecol 2003;101:149-56.
7. Brown JS, Grady D, Ouslander JG, Herzog AR, Varner RE, Posner SF. Prevalence of urinary incontinence and associated risk factors in postmenopausal women. Heart & Estrogen/Progestin Replacement Study (HERS) Research Group. Obstet Gynecol 1999;94:66-70.
8. Graham CA, Mallett VT. Race as a predictor of urinary incontinence and pelvic organ prolapse. Am J Obstet Gynecol 2001;185:116-20.
9. Sampselle CM, Harlow SD, Skurnick J, Brubaker L, Bondarenko I. Urinary incontinence predictors and life impact in ethnically diverse perimenopausal women. Obstet Gynecol 2002;100:1230-8.
10. Herzog AR, Diokno AC, Brown MB, Normolle DP, Brock BM. Two-year incidence, remission, and change patterns of urinary incontinence in noninstitutionalized older adults. J Gerontol 1990;45:M67-74.
11. Kinchen KS, Burgio K, Diokno AC, Fultz NH, Bump R, Obenchain R. Factors associated with women's decisions to seek treatment for urinary incontinence. J Womens Health (Larchmt) 2003;12:687-98.
12. Johnson TM, 2nd, Kincade JE, Bernard SL, Busby-Whitehead J, DeFriese GH. Self-care practices used by older men and women to manage urinary incontinence: results from the national follow-up survey on self-care and aging. J Am Geriatr Soc 2000;48:894-902.
13. Agency for Health Care Policy and Research, HHS, PHS. Urinary Incontinence in Adults: Clinical Practice Guideline. AHCPR Pub. 92-0038 1992.
14. Leach GE, Dmochowski RR, Appell RA, Blaivas JG, Hadley HR, Luber KM, Mostwin JL, O'Donnell PD, Roehrborn CG. Female Stress Urinary Incontinence Clinical Guidelines Panel summary report on surgical management of female stress urinary incontinence. The American Urological Association. J Urol 1997;158:875-80.
15. O'Leary MP, Gee WF, Holtgrewe HL, Blute ML, Cooper TP, Miles BJ, Nellans RE, Thomas R, Painter MR, Meyer JJ, Naslund MJ, Gormley EA, Blizzard R, Fenninger RB. 1999 American Urological Association Gallup Survey: changes in physician practice patterns, treatment of incontinence and bladder cancer, and impact of managed care. J Urol 2000;164:1311-6.
16. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-6.
17. Waetjen LE, Subak LL, Shen H, Lin F, Wang TH, Vittinghoff E, Brown JS. Stress urinary incontinence surgery in the United States. Obstet Gynecol 2003;101:671-6.
18. Resident assessment instrument training manual and resource guide. Massachusetts: Elliot Press, 1991.
19. Ouslander JG. Urinary incontinence in nursing homes. J Am Geriatr Soc 1990;38:289-91.
20. Coward RT, Horne C, Peek CW. Predicting nursing home admissions among incontinent older adults: a comparison of residential differences across six years. Gerontologist 1995;35:732-43.
21. Thom DH, Haan MN, Van Den Eeden SK. Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality. Age Ageing 1997;26:367-74.
22. Wagner TH, Hu TW. Economic costs of urinary incontinence in 1995. Urology 1998;51:355-61.

CHAPTER 6

Urinary Incontinence in Men

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Urinary Incontinence in Men

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INTRODUCTION

While urinary incontinence (UI) is widely thought of as a condition affecting women, it also affects men of all ages, including 17% of an estimated 3.4 million men over the age of 60 in the United States. The prevalence of UI increases with advancing male age, and rose over time during the 1990s. Ethnicity plays less of a role in UI prevalence estimates for men than it does for women.

Risk factors for UI in both men and women include stroke, dementia, recurrent cystitis, bladder cancer, stool impaction, reduced mobility, diabetes, chronic cough, medications, and aging. However, specific to men is incontinence secondary to benign and malignant prostatic diseases and their treatments. Up to 30% of patients who have had a radical prostatectomy experience some degree of incontinence afterwards.

UI in elderly men creates a substantial burden on healthcare resources, the largest impact being felt in doctors' offices, followed by outpatient services and surgeries. During the 1990s, rates of physician office visits increased, but the burden of male UI is greatest in nursing homes, where more than half of the male residents report difficulty controlling their urine and require assistance using the toilet, either from equipment (14.8%) or from another person (52%).

The direct economic burden for UI in men is estimated to be $3.8 billion per year (1). The annual medical expenditures of persons with UI are more than twice those of persons without UI, $7,702 vs $3,204. Patients themselves bear a significant proportion of the direct costs of incontinence, including the costs of pads, condom drainage catheters, indwelling foley catheters, and external devices such as Cunningham clamps. Annual costs to all individuals living at home have been estimated to be $7.1 billion (2).

DEFINITION AND DIAGNOSIS

Urinary incontinence is defined as the complaint of any involuntary leakage of urine (3). It is sometimes grouped with other voiding complaints known collectively as lower urinary tract symptoms (LUTS). LUTS are subjective in nature and hence can be voluntarily self-reported or elicited during a medical history.

Recognized clinical subtypes of UI are defined on the basis of their presumed underlying etiology. An international standard for definitions of incontinence subtypes was set by the International Continence Society (ICS) in 1990 (4) and was updated in 2003 (3).

Stress incontinence is the involuntary leakage of urine on effort or exertion, sneezing, or coughing. *Urge incontinence* is the involuntary leakage of urine accompanied by, or immediately preceded by, urgency. Patients describe this type of incontinence as difficulty in holding their urine until they are able to reach a toilet. *Mixed incontinence* involves components of both stress- and urgency-related leakage. *Continuous incontinence* is constant leakage, usually associated with a fistula; it occurs only rarely in males. *Enuresis* refers to any involuntary loss of urine and should be distinguished from *nocturnal enuresis,* or urinary loss during sleep.

Table 1. Codes used in the diagnosis and management of male urinary incontinence

Males 18 years or older, with any one of the following ICD-9 codes, but not a coexisting 952.XX or 953.XX code:	
788.3	Urinary incontinence
788.3	Urinary incontinence unspecified
788.33	Mixed incontinence, male and female
788.34	Incontinence without sensory awareness
788.37	Continuous leakage
599.8	Other specified disorders of urethra and urinary tract
599.81	Urethral hypermobility
599.82	Intrinsic (urethral) sphincter deficiency (ISD)
599.83	Urethral instability
599.84	Other specified disorders of urethra
788.31	Urge incontinence
596.59	Other functional disorder of bladder
596.52	Low bladder compliance
596.51	Hypertonicity of bladder
Post-radical prostatectomy incontinence	
Males 18 years or older, with at least one of the above codes and at least one of the following prostatectomy codes:	
ICD-9 Procedure Codes	
60.5	Radical prostatectomy
CPT Codes	
55840	Prostatectomy, retropubic radical, with or without nerve sparing
55842	Prostatectomy, retropubic radical, with or without nerve sparing
55845	Prostatectomy, retropubic radical, with or without nerve sparing
Spinal cord injury-related incontinence	
Males 18 years or older, with a diagnosis code for spinal cord injury 952.XX or 953.XX and at least one of the following ICD-9 codes	
344.61	Cauda equina syndrome with neurogenic bladder
596.51	Hypertonicity of bladder (specified as overactive bladder in 2001; included if associated with diagnosis code 952.XX)
596.52	Low compliance bladder
596.54	Neurogenic bladder, NOS
596.55	Detrusor sphincter dyssynergia
596.59	Other functional disorder of bladder
599.8	Other specified disorders of urethra and urinary tract
599.84	Other specified disorders of urethra
625.6	Stress incontinence, female
788.3	Urinary incontinence
788.31	Urge incontinence
788.32	Stress incontinence, male
788.33	Mixed incontinence, male and female
788.34	Incontinence without sensory awareness
788.37	Continuous leakage
788.39	Other urinary incontinence

Some of the 5-digit ICD-9 codes (Table 1) related to incontinence are based on the underlying mechanisms as demonstrated during urodynamic testing. In general, definitions are divided into those seen during filling and those seen during emptying, the two phases of the bladder cycle. Abnormalities during the filling phase include detrusor instability, detrusor hyperreflexia, and abnormalities of bladder compliance. The observation of involuntary detrusor contractions during filling cystometry is called *detrusor instability* in the absence of a neurologic lesion and *detrusor hyperreflexia* in the presence of a neurologic lesion. *Detrusor sphincter dyssynergia* (DSD), an abnormality during the emptying phase of the bladder, refers to simultaneous contraction of the detrusor and involuntary contraction of the urethral and/or periurethral striated muscle in a patient with neurologic disease.

Recently, the terminology for urodynamic definitions associated with incontinence was modified to conform to the International Classification of Functioning, Disability and Health (ICFDH-2) and the ICD-10 (5). The terms *detrusor instability* and *detrusor hyperreflexia* were replaced. When involuntary detrusor contractions occur during filling cystometry, they are classified as *detrusor overactivity*. If the patient has incontinence at the time of the detrusor overactivity, the term *detrusor overactivity incontinence* is used. If a relevant neurogenic condition is present, the more specific term neurogenic detrusor overactivity is used; otherwise, *idiopathic detrusor overactivity* is used.

Urinary incontinence may be a sign or a symptom. As a symptom, UI may be self-reported or recorded by a third party such as a healthcare professional or researcher. On rare occasions, patients who report UI as a symptom do not actually have the condition. Perspiration, for example, may mimic UI in men. As such, determining the presence of incontinence by questioning alone is inherently problematical. Because patient reports of severity are subjective, the disorder is difficult to quantify unless specific, standardized questions are posed.

As a clinical sign, UI may be demonstrated during physical examination, cystoscopy, urodynamics, or videourodynamics, or by pad testing. In males, physical examination may reveal clues to the etiology of the underlying condition, but only rarely is the actual sign of incontinence seen. Indirect indicators include soiled clothing, the use of a variety of types of incontinence protection devices, and abnormalities presenting during the neurologic examination, which should include a careful digital rectal examination and assessment of anal sphincter tone. At the time of cystoscopy, abnormalities of the urethral sphincter may be seen in men who have previously undergone prostatectomy, but these abnormalities are not definitive for the diagnosis. Rarely, a urethrocutaneous or rectourethral fistula is observed. Both urodynamics and videourodynamics can provide definitive diagnoses and quantitative measures of the amount of urinary loss under standardized conditions, including volume of urine in the bladder, physical posture, and physical activity. Pad testing is performed by instilling a standardized volume of liquid into the bladder, placing an incontinence pad in the patient's undergarments, and having the patient undergo a standardized sequence of physical activities. The pad is then weighed to quantify the leakage.

A wide range of survey questions can be used to collect data concerning UI. General questions may be as simple as, "Do you have or have you ever had loss of urinary control?" More specific questions are used to elicit the underlying etiology of UI. An affirmative answer to the question, "Do you ever leak or lose urine when you cough, laugh, or sneeze?" may indicate stress incontinence; the answer to, "How often do you have difficulty holding your urine until you can get to a toilet?" may indicate urge incontinence (6).

PREVALENCE AND INCIDENCE

Although the epidemiology of UI has not been investigated in men as thoroughly as in women, most studies show that the male-to-female ratio is about 1:2. The type, age distribution, and risk factors differ greatly between the genders (7). Estimates of UI prevalence are obtained primarily from responses to survey questions, and the way the questions are worded affects the prevalence estimate (see above). Because UI can be an intermittent condition, the length of time the patient is asked to consider may alter response rates. For example, "Do you have or have you ever had UI?" may elicit a different response than "Over the last 12 months have you experienced loss of urinary control?" In-person interviews tend to yield higher prevalence rates than do self-reported questionnaires. The prevalence of UI varies by patient age, gender, and language.

When UI prevalence is estimated using ICD-9 codes, several additional issues should be kept in mind. The 5-digit ICD-9 codes used for the National Ambulatory Medical Care Survey (NAMCS), Medstat, Healthcare Care Utilization Project (HCUP), Medicare, and Ingenix datasets may be used to divide incontinence into five groups: tologic BPH;

- detrusor instability/overactive bladder/ urge incontinence,
- traumatic/iatrogenic incontinence (e.g., following radical prostatectomy),
- spinal-cord-related incontinence,
- nocturnal enuresis, and
- other (fistula, neuropathic bladder, nonorganic causes).

In addition, the following caveats should be noted when considering the data presented in this chapter:

- There is no specific category for overflow incontinence secondary to outlet obstruction in men, related to prostate or urethral disease. The closest match for this subtype is 788.39 (overflow neurogenic, paradoxical).
- To identify males with post-radical prostatectomy incontinence, one needs to use codes for incontinence and prostatectomy. In addition, a man may have stress incontinence due to traumatic injury or to prostatectomy for benign prostate disease. There is no specific code for these rare conditions.
- Urodynamic testing would be required for certain 5-digit codes (e.g., 596.59 for detrusor instability); however, the clinical management of individual patients may not involve urodynamic testing.
- Because the Medical Expenditure Panel Survey (MEPS) database uses only 3-digit ICD-9 codes, it lacks the specificity necessary to stratify by subtypes of UI.
- Of all the urological conditions examined in this project, UI is among the least likely to result in a contact with the medical community. While 17% of aged men report some UI, medical care utilization rates are typically less than 1%.

Pooled data from 21 international population-based surveys (Table 2), stratified for age, gender, and frequency of incontinence, indicate that the prevalence of lifetime incontinence among older men is 11% to 34% (median 17%, pooled mean 22%), while the prevalence of daily incontinence is 2% to 11% (median 4%, pooled mean 5%). The prevalence of lifetime incontinence was significantly lower among middle-aged and younger men, ranging from 3% to 5% (median 4%, pooled mean, 5%) (8).

Langa et al. reported a prevalence of 13% in community-dwelling older people (9). These people responded affirmatively when asked, "During the last 12 months, have you lost any amount of urine beyond your control?" This time frame is similar to that in the NHANES question.

As in Thom's study, National Health and Nutrition Examination Survey (NHANES) data

Table 2. Summary prevalences of urinary incontinence (UI) by age, gender, and frequency

	Ever UI			Daily UI		
	Range	Median	Mean[a]	Range	Median	Mean[a]
Group	%	%	%	%	%	%
Older women	17–55	35	34	3–7	14	12
Older men	11–34	17	22	2 –11	4	5
Younger women	12–42	28	25	...	...	...
Younger men	3–5	4	5	...	...	...

...data not available.

[a]Calculated using numerator and denominator data from each available study.

SOURCE: Reprinted from Thom D, Variation in estimates of urinary incontinence prevalence in the community: effects of differences in definition, population characteristics, and study type, Journal of American Geriatrics Society, 46, 473-480, Copyright 1998, with permission from the American Geriatrics Society.

Table 3. Prevalence of difficulty controlling bladder among adult men

		Difficulty Controlling Bladder		
	Total	Yes	No	Refused to Answer or Don't Know
Total	18,231,934	3,131,814 (17%)	15,054,506 (83%)	45,614 (0%)
Age at screening				
60–64	5,037,678	546,559 (11%)	4,491,119 (89%)	0 (0%)
65–69	4,731,187	518,157 (11%)	4,213,030 (89%)	0 (0%)
70–74	3,320,840	630,898 (19%)	2,675,986 (81%)	13,956 (0%)
75–79	2,748,396	750,478 (27%)	1,988,932 (72%)	8,986 (0%)
80–84	1,478,414	399,774 (27%)	1,078,640 (73%)	0 (0%)
85+	915,419	285,948 (31%)	606,799 (66%)	22,672 (2%)
Race/ethnicity				
Non-Hispanic white	14,790,935	2,395,212 (16%)	12,395,723 (84%)	0 (0%)
Non-Hispanic black	1,436,582	296,022 (21%)	1,122,588 (78%)	17,972 (1%)
Mexican American	559,680	81,134 (14%)	478,546 (86%)	0 (0%)
Other race	429,299	142,015 (33%)	273,598 (64%)	13,686 (3%)
Other Hispanic	1,015,438	217,431 (21%)	784,051 (77%)	13,956 (1%)
Education				
Less than high school	6,072,264	1,214,224 (20%)	4,840,068 (80%)	17,972 (0%)
High school	4,516,092	698,919 (15%)	3,817,173 (85%)	0 (0%)
High school+	7,572,244	1,198,317 (16%)	6,373,927 (84%)	0 (0%)
Refused	25,054	11,368 (45%)	0 (0%)	13,686 (55%)
Don't know	46,280	8,986 (19%)	23,338 (50%)	13,956 (30%)
Poverty income ratio[a]				
Missing	631,305	111,353 (18%)	505,996 (80%)	13,956 (2%)
PIR=0	22,159	12,082 (55%)	10,077 (45%)	0 (0%)
PIR<1	1,806,996	440,261 (24%)	1,366,735 (76%)	0 (0%)
1.00<=PIR<=1.84	3,408,381	653,095 (19%)	2,755,286 (81%)	0 (0%)
PIR>1.84	9,404,848	1,458,110 (16%)	7,946,738 (84%)	0 (0%)
Refused	1,858,169	324,042 (17%)	1,511,455 (81%)	22,672 (1%)
Don't know	1,100,076	132,871 (12%)	958,219 (87%)	8,986 (1%)

[a]See glossary for definition of poverty income ratio.

The data in this table are based on question KIQ.040: "In the past 12 months, have you had difficulty controlling your bladder, including leaking small amounts of urine when you cough or sneeze?"

SOURCE: National Health and Nutrition Examination Survey, 1999–2000.

Table 4. Frequency of bladder control problems among those who responded "yes" to difficulty controlling bladder

	Total	Every Day	Few per Week	Few per Month	Few per Year	Don't Know
Total	3,131,814	1,307,755 (42%)	747,906 (24%)	577,835 (18%)	459,015 (15%)	39,303 (1%)
Age at screening						
60–64	546,559	187,452 (34%)	204,858 (37%)	48,555 (9%)	105,694 (19%)	0 (0%)
65–69	518,157	172,945 (33%)	153,221 (30%)	104,208 (20%)	87,783 (17%)	0 (0%)
70–74	630,898	299,011 (47%)	111,501 (18%)	118,464 (19%)	100,100 (16%)	1,822 (0%)
75–79	750,478	377,370 (50%)	101,664 (14%)	176,165 (23%)	86,293 (11%)	8,986 (1%)
80–84	399,774	137,186 (34%)	134,527 (34%)	60,591 (15%)	54,106 (14%)	13,364 (3%)
85+	285,948	133,791 (47%)	42,135 (15%)	69,852 (24%)	25,039 (9%)	15,131 (5%)
Race/ethnicity						
Non-Hispanic white	2,395,212	1,039,490 (43%)	505,540 (21%)	418,365 (17%)	403,322 (17%)	28,495 (1%)
Non-Hispanic black	296,022	111,731 (38%)	106,168 (36%)	35,532 (12%)	33,605 (11%)	8,986 (3%)
Mexican American	81,134	47,757 (59%)	17,210 (21%)	6,213 (8%)	8,132 (10%)	1,822 (2%)
Other race	142,015	37,697 (27%)	63,131 (44%)	41,187 (29%)	0 (0%)	0 (0%)
Other Hispanic	217,431	71,080 (33%)	55,857 (26%)	76,538 (35%)	13,956 (6%)	0 (0%)
Education						
Less than high school	1,214,224	423,490 (35%)	386,717 (32%)	244,357 (20%)	157,838 (13%)	1,822 (0%)
High school	698,919	245,562 (35%)	137,414 (20%)	184,242 (26%)	118,337 (17%)	13,364 (2%)
High school+	1,198,317	627,335 (52%)	223,775 (19%)	149,236 (12%)	182,840 (15%)	15,131 (1%)
Refused	11,368	11,368 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Don't know	8,986	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8,986 (100%)
Poverty income ratio[a]						
PIR=0	12,082	0 (0%)	0 (0%)	12,082 (100%)	0 (0%)	0 (0%)
PIR<1	440,261	144,297 (33%)	112,216 (25%)	123,240 (28%)	58,686 (13%)	1,822 (0%)
1.00<=PIR<=1.84	653,095	262,660 (40%)	170,625 (26%)	116,420 (18%)	88,259 (14%)	15,131 (2%)
PIR>1.84	1,458,110	640,720 (44%)	356,276 (24%)	193,356 (13%)	254,394 (17%)	13,364 (1%)
Refused	324,042	156,956 (48%)	47,695 (15%)	72,079 (22%)	47,312 (15%)	0 (0%)
Don't know	132,871	86,722 (65%)	11,890 (9%)	14,909 (11%)	10,364 (8%)	8,986 (7%)
Missing	111,353	16,400 (15%)	49,204 (44%)	45,749 (41%)	0 (0%)	0 (0%)

[a]See glossary for definition of poverty income ratio.

The data in this table are based on question KIQ.060: "How frequently does this (referring to KIQ.040) occur? Would you say this occurs…every day, a few times a week, a few times a month, or a few times a year?"

SOURCE: National Health and Nutrition Examination Survey, 1999–2000.

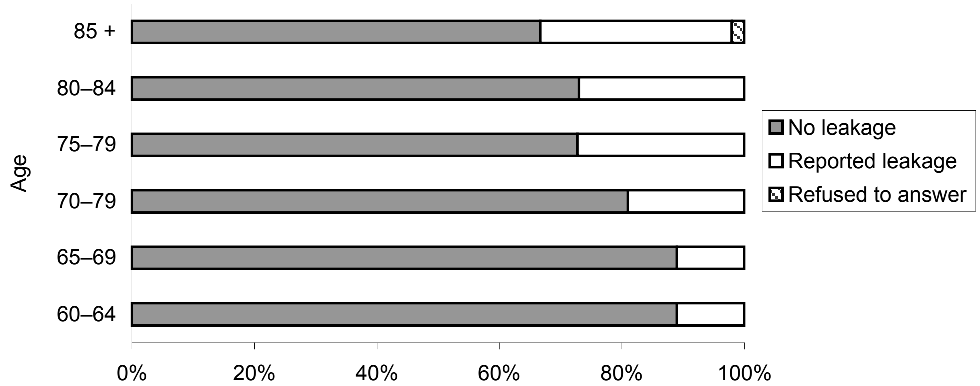

Figure 1a. **Difficulty controlling bladder among male responders.**

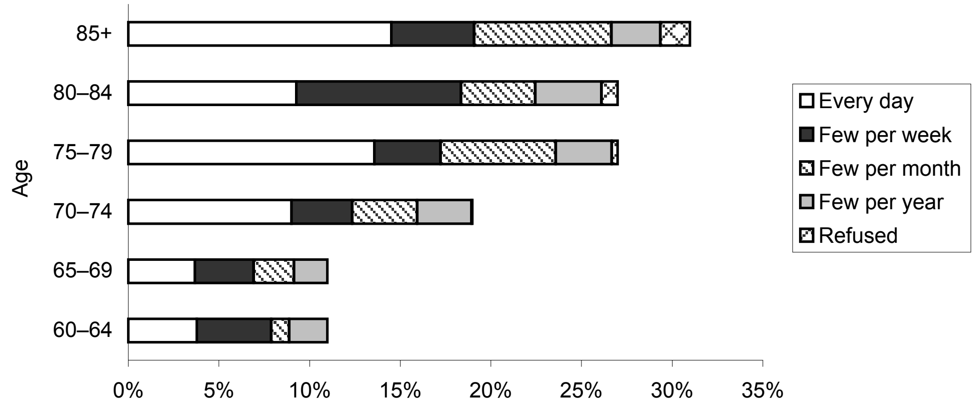

Figure 1b. **Frequency of bladder control problems among male responders who answered "yes" to difficulty controlling bladder.**

SOURCE: National Health and Nutrition Examination Survey, 1999–2001.

suggest that 17% of males older than 60 experience UI (Table 3 and Figure 1a). These men answered affirmatively when asked, "In the past 12 months, have you had difficulty controlling your bladder, including leaking small amounts of urine when you cough or sneeze?" NHANES data indicate a trend of increasing prevalence of UI with increasing age in males. Of the 17% of men reporting UI, 42% indicated that it occurred on a daily basis, while 24% indicated that it occurred weekly (Table 4 and Figure 1b). The 7% prevalence of daily UI in men over 60 (17% of 42%) is similar to the 4% of older men who reported daily episodes in the pooled data reported by Thom (8). The severity of UI based on the frequency of incontinence episodes among younger males is not well documented. The utilization data in this chapter are not entirely consistent with this citation.

Based on a prevalence rate of 17% (Table 3) and data from the 2001 US Census Bureau's intercensal population estimates, it is estimated that almost 3.4 million American men over the age of 60 have UI (US Census).

MORTALITY

In univariate analyses without adjustment for comorbidities or other potential confounding factors, UI is associated with an increased risk of death among elderly men living in both community and nursing home settings (10, 11). The magnitude of increased relative risk of death is variable and is related to the severity of the incontinence and the overall health and functional status of the patient. Applying univariate hazard ratios for mortality in large population studies revealed an increased risk of mortality in the elderly associated with the degree of incontinence: the relative risk of dying is 2.27 for mild UI, 2.96 for moderate UI, and 5.94 for severe UI, compared with continent controls over a 42-month period (11).

The association observed between UI and death is not likely to be causal because of the impact of advanced age, poor general health, and psychosocial factors. When population studies are subjected to more rigorous multivariate analysis and confounders are taken into consideration, the impact of mild to moderate incontinence on mortality is greatly reduced—in fact, it is statistically insignificant in some studies. However, severe incontinence remains as an independent risk factor for mortality. Specifically, elderly men with incontinence had 50% greater mortality than continent men after adjustment for age alone, but only a 20% greater risk of mortality after additional adjustment for comorbid conditions (12). Therefore, the relationship between mortality and UI is thought to be due in large part to a reduction in general health and increased frailty in the elderly. Daily preventive health measures and the use of routine health screenings are independent predictors of survival in elderly incontinent individuals after age, health status, and psychosocial factors have been controlled for (6).

While epidemiologic studies of mortality in the incontinent have focused on the elderly population, an important consideration is the relative overrepresentation in the younger male population of individuals with neurogenic bladders due to spinal cord injury. The relative risk of mortality in incontinent vs continent younger men is not well documented.

Risk Factors for Urinary Incontinence in Men	
Physical Attributes	**Pharmaceutical Agents**
Age	Benzodiazepines
Obesity	Antidepressants
Race	Antipsychotics
Immobility	Diuretics
Previous transurethral surgery	Antiparkinsonian medications
Previous radical prostatectomy	Narcotic analgesics
	Alpha antagonists
Neurologic disease (e.g., stroke)	Alpha agonists
	Calcium channel blockers
Spinal cord injury	ACE inhibitors
Cognitive impairment	Antianxiety/hypnotics
Social Habits	**Reversible Factors**
Smoking	Urinary tract infection
Alcohol	Pharmaceuticals
Caffeine	Psychological
	Exessive urine production (polyuria or nocturia)
	Stool impaction

RISK FACTORS

Continence in males results from a combination of factors, including appropriate function of the bladder and sphincter mechanisms. Since the function of these anatomic structures is neurologically regulated, diseases that affect the central or peripheral nervous systems may increase the risk of UI. Environmental factors, cognitive status, mobility, medications and social habits can also influence continence status. Risk factors for UI can be categorized as physical attributes, pharmaceutical agents, social habits, and reversible factors.

As noted above, the prevalence of UI increases with *increasing age*, particularly in those over 65. Age-related physical changes within the detrusor itself include more unstable bladder contractions, more residual urine, and less bladder contractility (13). Overall, the multifactorial elements of aging, including modified pharmacokinetics and associated physical comorbidities, may convert a continent patient to an incontinent one. For example, as men age, the prostate gland enlarges due to benign or malignant disease. Additional physical attributes such as age, mobility, previous prostatic surgery, neurologic disease, spinal cord injury, and delirium may also contribute to loss of continence. Obesity and race are cited as risk factors for UI in women, but data on these factors specific to men are lacking.

A history of prostate cancer treatment, including radiation or radical prostatectomy, is known to confer an increased risk of incontinence, as has been reported by many researchers since the mid-1990s. Radical prostatectomy involves extensive dissection near the bladder neck and external sphincter, both of which contribute to continence in men. Prostate radiation (external beam or brachytherapy) may affect the same structures and may also cause damage to the bladder itself, leading to incontinence from an overactive detrusor.

Restricted mobility (due, e.g., to bedrails, trunk restraints, or chair restraints) limits access to toilet facilities and hence increases the risk of UI (14).

Because the central nervous system has both excitatory and inhibitory effects on the bladder, a variety of central neurological diseases can cause incontinence. Most notably, stroke confers an increased risk of UI. In one large population-based study, nearly 50% of stroke patients had UI. This proportion falls to about 20% in patients surviving for at least six months after a stroke (15).

While somewhat controversial, alcohol and caffeine intake have been implicated as risk factors for UI, although almost no data on male subjects are available.

Because elderly patients have altered pharmacodynamics and pharmacokinetics, certain drugs that affect cognition may impact bladder function primarily or may lead to increased urine output, thus contributing to the risk of UI (14). For example, benzodiazepine use has been reported to increase the risk of UI by 45% (OR, 1.44; 95% CI, 1.12–1.83) (16). Selective serotonin reuptake inhibitors have been similarly implicated (17).

NATURAL HISTORY

Cross-sectional studies have found that the prevalence of UI in men increases with age in a roughly linear fashion. Most studies have found a predominance of urge incontinence (40%–80%), followed by mixed incontinence (10%–30%) and stress incontinence (<10%). Stress incontinence becomes more common as men age, probably as a result of surgery for prostate enlargement and prostate cancer. For example, up to 34% of men report persistent UI following a radical prostatectomy (18).

Relatively little information is available on the incidence of UI in men, but what there is suggests that it is a surprisingly dynamic condition. One population-based study of men and women 60 and older found the one-year incidence of new UI in men (most of which was classified as mild) to be 10%, (19). The annual rate of remission was about 30%. These figures probably reflect the important role of reversible causes of male UI, including benign prostatic hyperplasia, urinary tract infections, and constipation.

Table 5. Inpatient hospital stays by males with urinary incontinence listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	1,431	2.1 (1.4–1.9)	1,529	1.7 (1.4–2.0)	1,490	1.6 (1.4–1.8)	1,332	1.4 (1.2–1.6)
Region								
Midwest	397	2.1 (1.4–2.4)	285	1.3 (0.6–2.0)	435	2.0 (1.4–2.6)	334	1.5 (1.0–1.9)
Northeast	338	2.1 (1.3–2.5)	366	2.0 (1.4–2.6)	304	1.7 (1.2–2.2)	324	1.8 (1.2–2.4)
South	393	1.1 (0.9–1.7)	640	2.0 (1.4–2.6)	527	1.6 (1.2–1.9)	459	1.4 (1.0–1.7)
West	302	2.1 (0.8–2.3)	238	1.2 (0.8–1.6)	225	1.1 (0.8–1.4)	215	1.0 (0.6–1.4)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 6. Inpatient stays by male Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	1,520	10 (9.8–11)	1,680	11 (11–12)	1,620	11 (11–12)
Total < 65	60	1.9 (1.5–2.4)	160	4.6 (3.9–5.4)	140	4.1 (3.4–4.7)
Total 65+	1,460	13 (12–13)	1,520	13 (12–14)	1,480	13 (13–14)
Age						
65–74	700	9.7 (9.0–10)	640	8.9 (8.2–9.6)	620	9.6 (8.9–10)
75–84	580	16 (15–18)	640	17 (16–19)	760	21 (19–22)
85–94	160	20 (17–23)	200	24 (20–27)	100	12 (9.2–14)
95+	20	26 (14–37)	40	49 (34–63)	0	0
Race/ethnicity						
White	1,320	11 (10–11)	1,480	11 (11–12)	1,440	12 (11–12)
Black	120	9.4 (7.8–11)	80	5.8 (4.5–7.1)	120	9.0 (7.4–11)
Asian	…	…	0	0	0	0
Hispanic	…	…	60	30 (23–38)	40	12 (8.3–16)
N. American Native	…	…	0	0	0	0
Region						
Midwest	420	11 (10–12)	620	16 (15–17)	660	18 (16–19)
Northeast	320	10 (9.0–11)	120	3.8 (3.1–4.4)	280	10 (8.9–11)
South	420	8.0 (7.3–8.8)	700	13 (12–14)	500	9.3 (8.5–10)
West	340	15 (14–17)	200	8.6 (7.4–9.8)	160	7.2 (6.0–8.3)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other race, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Table 5 shows rates of inpatient hospitalizations among men having UI as the primary diagnosis. Data from the HCUP inpatient sample indicate that the overall rate was steady at 1.4 to 2.1 per 100,000, with no meaningful change from 1994 through 2000. The rate remained low across all geographic regions. This is consistent with clinical experience that UI does not typically lead to hospital admission, except for surgical correction of the condition. Estimates of inpatient hospitalizations through the 1990s in the Medicare (CMS) population are presented in Table 6. The overall rate of inpatient hospital stays for men ≥65 years of age with UI was stable at 13 per 100,000 male Medicare beneficiaries. The rate for men <65 years of age in the Medicare population fluctuated more, probably as a result of peculiarities of data on the disabled population. Caucasian males had higher inpatient hospitalization rates than did African American males. Asian and Hispanic men were not identified as specific populations until 1995, and their relatively low counts make interpretation of the corresponding rates difficult.

Consistent with larger secular trends, lengths of stay (LOS) of men with UI as a primary diagnosis decreased between 1994 and 2000 (Table 7). Sample sizes for the non-whites and those younger than 55 were too small to produce reliable estimates for those demographic categories. LOS declined across all regions from 1994 to 1996, the shortest mean LOS being 2.0 days in the West. Increasing market pressure from managed care during that time may have contributed to this trend. There was wide variation in inpatient

Table 7. Trends in mean inpatient length of stay (days) for adult males hospitalized with urinary incontinence listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	3.7	2.8	3.0	3.2
Age				
18–24	*	*	*	*
25–34	*	*	*	*
35–44	*	*	*	*
45–54	*	*	*	*
55–64	2.8	2.1	3.0	2.8
65–74	3.3	2.3	2.0	2.9
75–84	4.3	3.6	3.4	3.2
85+	*	*	*	*
Race/ethnicity				
White	3.9	2.9	3.2	3.1
Black	*	*	*	*
Hispanic	*	*	*	*
Asian/Pacific Islander	*	*	*	*
Other	*	*	*	…
Region				
Midwest	3.2	2.2	3.1	3.3
Northeast	5.1	2.8	4.0	2.5
South	3.8	3.5	2.6	2.9
West	2.7	2.0	2.5	4.5
MSA				
Rural	3.8	4.2	2.3	4.3
Urban	3.7	2.7	3.2	3.0
Discharge status				
Routine	3.0	2.5	2.5	2.6
Skilled nursing facility	*	*	…	…
Intermediate care	*	*	…	…
Other facility	*	*	6.2	*
Home health	*	*	*	*
Against medical advice	*	*	*	*
Died	*	*	*	*

… data not available.

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

LOS for men with UI in rural areas. In 1994, mean LOS in rural hospitals (3.8 days) was similar to that in urban hospitals; in 1996, it increased to 4.2 days, then it declined to 2.3 days in 1998; it then increased to a high of 4.3 days in 2000, 1.3 days longer than for urban sites. In urban hospitals, there was a general downward trend in LOS, to 3.0 days in 2000. The diffusion of managed care from urban to rural areas through the 1990s may explain these observations.

Outpatient Care

According to data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) for 1994, 1996, 1998, and 2000 (Table 8), 0.1% of all hospital outpatient visits by men over the age of 18 were associated with UI as any listed diagnosis. Because the counts for this diagnosis were so low, the 1994, 1996, 1998, and 2000 data were collapsed to yield a rate of 90 per 100,000 for the four years combined (or 22.5 per 100,000 annually). Hospital outpatient visit rates for men with UI listed as the primary diagnosis were about 10 per 100,000 annually.

As expected, the rate of outpatient visits for men with UI (Table 9) is far greater than that for inpatient visits by men (Table 6) both under and over age 65. The rates increased for men in all groups from 1992 to 1998. Outpatient visits by men over age 65 with UI were 2.8 times more frequent than inpatient visits (hospitalizations) in 1992 and were 5.2 times more frequent by 1998. Men 75 to 84 years of age had the highest outpatient visit rates, 59 per 100,000 in 1992 and 85 per 100,000 in 1995. The difference in Medicare outpatient vs inpatient services for men with UI under age 65 is even more striking. Outpatient visits were 10 times more frequent than inpatient visits in 1992 and 11.4 times more frequent in 1998. Regional Medicare data indicate that outpatient visit rates in 1992 ranged from 2.9 to 4.4 times the rate of inpatient visits. By 1998, outpatient visit rates were 4.1 to 9.6 times higher than inpatient visit rates for all regions. In 1998 (the most recent year for which data are available), the South had the lowest rate of inpatient visits, 42 per 100,000. In the Midwest, both outpatient and inpatient visit rates increased to a high of 98 per 100,000 in 1998, more than double the rate in the South.

Interestingly, there was an inverse relationship between the rate of outpatient and inpatient services for African American males and that for Caucasian

Table 8. Hospital outpatient visits by adult males with urinary incontinence, (1994–2000) merged, count (95% CI), number of visits, percentage of visits, rate (95% CI)

	4-Year Count (95% CI)	Total No. Visits by Men 18+ 1994–2000	Percent of Visits	4-Year Rate (95% CI)
Primary diagnosis	38,629 (3,361–73,897)	78,399,663	0%	42 (4–80)
Any diagnosis	83,762 (29,850–137,674)	78,399,663	0.1%	90 (32–149)

[a]Rate per 100,000 based on the sum of weighted counts in 1994, 1996, 1998, 2000 over the mean estimated base population across those four years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.
SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

Table 9. Hospital outpatient visits by male Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	5,080	34 (34–35)	8,300	55 (53–56)	9,420	65 (64–66)
Total < 65	900	29 (27–31)	1,620	47 (45–49)	2,040	59 (57–62)
Total 65+	4,180	36 (35–37)	6,680	57 (55–58)	7,380	67 (65–68)
Age						
65–74	1,840	25 (24–27)	2,900	40 (39–42)	2,960	46 (44–48)
75–84	2,080	59 (56–61)	3,120	85 (82–88)	3,080	84 (81–87)
85–94	240	30 (27–34)	620	73 (67–79)	1,300	150 (142–158)
95+	20	26 (14–37)	40	49 (34–63)	40	46 (32–59)
Race/ethnicity						
White	3,840	31 (30–32)	6,200	48 (47–49)	7,320	60 (58–61)
Black	900	71 (66–75)	1,580	114 (108–120)	1,160	87 (82–92)
Asian	…	…	20	27 (15–40)	100	73 (58–88)
Hispanic	…	…	240	121 (106–136)	600	179 (164–193)
N. American Native	…	…	40	199 (139–258)	0	0
Region						
Midwest	1,780	48 (46–50)	2,280	59 (57–62)	3,620	98 (95–101)
Northeast	1,260	40 (38–42)	1,880	59 (56–62)	1,920	69 (66–72)
South	1,060	20 (19–21)	2,260	41 (40–43)	2,280	42 (41–44)
West	980	44 (41–46)	1,880	81 (77–85)	1,580	71 (67–74)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

males. From 1992 to 1998, rates of inpatient visits were consistently higher for Caucasians, while rates of outpatient services were consistently higher for African Americans. The difference was greatest in 1995, when the ratio of outpatient visits for African American males was 2.4 times that for Caucasian males, narrowing to 1.5 in 1998. As with inpatient visits, Hispanic men had a markedly higher rate of outpatient visits—179 per 100,000 in 1998, twice that of African Americans and three times that of Caucasians. These differences may follow from differences in the types of services provided. Surgical therapy for UI in the 1990s was typically provided on an inpatient basis, while nonsurgical therapy was provided on an outpatient basis. Further study is needed to clarify these trends.

Veterans Health Affairs (VA) data, which are based on outpatient medical records rather than population survey data, show a strong trend toward increasing prevalence of medically recognized UI with increasing age in males; the prevalence in men 85 years of age and older is approximately ten times that in men 35 to 44 years of age. Table 10 also demonstrates an increase over time in the prevalence of medically recognized UI in men, from 717 per 100,000 in 1999 to 975 per 100,000 in 2001 (all diagnoses of UI). As expected, the prevalence of medically recognized UI based on ICD-9 codes from office visits is substantially less than that found in the NHANES study, which is population-based. The increase in medically recognized UI between 1999 and 2001 likely reflects an increase in clinical ascertainment of UI, rather than an increase in underlying prevalence. Racial/ethnic differences in prevalence among men are modest compared to the differences among women, although African American men consistently have a slightly higher prevalence than do Caucasians. Racial differences in care-seeking behavior and perceptions of the healthcare system make these data difficult to interpret. Regional differences are slight and vary from year to year without a consistent pattern.

According to Medicare data (Table 11), the rates of physician office visits for male UI increased by 77% between 1992 and 1998, from 395 per 100,000 to 698 per 100,00, for all age groups. Visit rates for men 65 years of age and older increased from 457 per 100,000 to 818 per 100,000, and rates for those under 65 increased from 164 per 100,000 to 314 per 100,000. More detailed examination reveals that there is a trend of increasing rates of physician office visits for each age category in the 65 and older group up to and including the 85 to 94 age group, which had a rate of 1,721 per 100,000 in 1998 (Table 11 and Figure 2). Regionally, physician office visit rates varied less than hospitalization rates, which ranged widely from year to year, even within individual geographic areas.

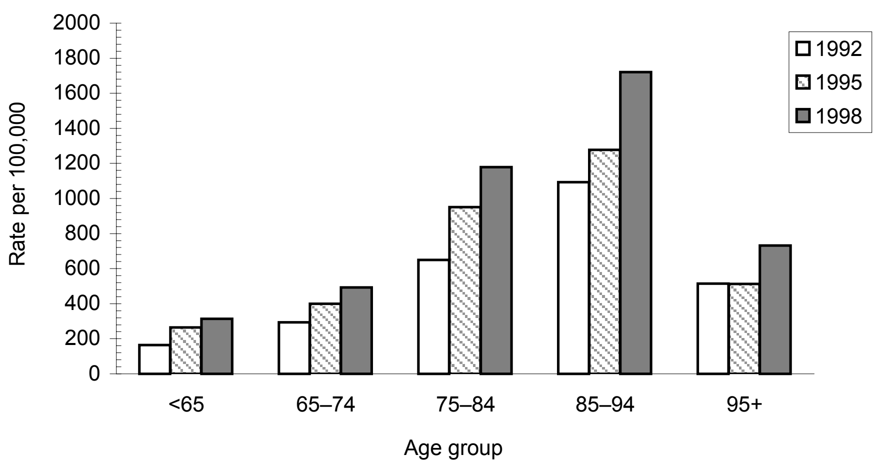

Figure 2. Physician office visits by male Medicare beneficiaries for urinary incontinence, by patient age and year.

SOURCE: Centers for Medicaid and Medicare Serivces, MedPAR, and 5% Carrier File, 1992, 1995, 1998.

Table 10. Frequency of urinary incontinence[a] in male VA patients seeking outpatient care, rate[b]

	1999		2000		2001	
	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis
Total	437	717	525	914	515	975
Age						
18–24	62	77	79	113	87	99
25–34	103	146	117	169	133	178
35–44	148	216	183	275	196	290
45–54	228	336	273	411	280	444
55–64	363	570	416	677	422	707
65–74	538	886	596	1,058	558	1,076
75–84	812	1,400	950	1,748	836	1,723
85+	1,227	2,243	1,489	2,792	1,365	2,908
Race/ethnicity						
White	597	963	696	1,197	688	1,264
Black	691	1,068	833	1,296	876	1,382
Hispanic	492	891	678	1,075	571	1,004
Other	549	899	634	1,129	536	894
Unknown	177	319	237	479	251	586
Region						
Midwest	398	693	484	928	459	937
Northeast	557	874	628	1,006	563	998
South	343	591	450	806	480	930
West	494	767	578	973	584	1,075
Insurance status						
No insurance/self-pay	344	541	408	660	394	690
Medicare/Medicare supplemental	679	1162	768	1,449	726	1,482
Medicaid	538	926	671	1,128	581	1,019
Private insurance/HMO/PPO	432	722	491	828	467	853
Other insurance	322	574	401	699	388	680
Unknown	1,244	2,035	1,076	1,937	416	648

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for male urinary incontinence.

[b]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 11. Physician office visits by male Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	58,240	395 (392–399)	83,800	551 (547–554)	101,080	698 (694–702)
Total < 65	5,080	164 (160–169)	9,080	264 (258–269)	10,780	314 (308–320)
Total 65+	53,160	457 (453–461)	74,720	635 (630–639)	90,300	818 (812–823)
Age						
65–74	21,200	293 (289–297)	28,720	400 (395–404)	31,600	492 (486–497)
75–84	22,920	649 (641–657)	34,740	950 (940–960)	43,160	1,179 (1,168–1,190)
85–94	8,640	1,093 (1,070–1,116)	10,840	1,278 (1,254–1,302)	14,900	1,721 (1,694–1,748)
95+	400	515 (465–565)	420	512 (463–561)	640	732 (676–788)
Race/ethnicity						
White	50,280	405 (402–409)	74,320	572 (568–576)	88,900	727 (722–732)
Black	4,120	323 (313–333)	6,380	461 (449–472)	7,020	526 (514–538)
Asian	…	…	740	1,015 (943–1,088)	940	685 (642–729)
Hispanic	…	…	940	473 (443–504)	2,260	673 (646–701)
N. American Native	…	…	20	99 (55–144)	40	143 (100–186)
Region						
Midwest	15,480	417 (411–424)	20,540	533 (526–540)	23,880	646 (638–654)
Northeast	11,840	373 (367–380)	17,880	562 (554–570)	19,660	707 (698–717)
South	21,180	404 (399–410)	30,440	555 (549–561)	39,760	741 (734–748)
West	8,900	396 (388–404)	13,900	599 (589–609)	16,680	746 (735–757)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

Table 12. Physician office visits by adult males with urinary incontinence, 1992–2000 (merged), count (95% CI), number of visits, percentage of visits, rate (95% CI)

	5-Year Count (95% CI)	Total No. Visits by Men 18+, 1992–2000	% of Visits	5-Year Rate (95% CI)
Primary diagnosis	989,688 (665,142–1,314,234)	1,122,162,099	0.1	1,079 (725–1,433)
Any diagnosis	1,660,627 (1,245,549–2,075,705)	1,122,162,099	0.1	1,811 (1,358–2,263)

[a]Rate per 100,000 based on the sum of weighted counts in 1992, 1994, 1996, 1998, 2000 over the mean estimated base population across those five years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.
SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 13. Visits to ambulatory surgery centers by male Medicare beneficiaries with urinary incontinence listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	3,140	21 (21–22)	7,340	48 (47–49)	5,480	38 (37–39)
Total < 65	340	11 (9.8–12)	680	20 (18–21)	600	17 (16–19)
Total 65+	2,800	24 (23–25)	6,660	57 (55–58)	4,880	44 (43–45)
Age						
65–74	1,320	18 (17–19)	3,680	51 (50–53)	2,460	38 (37–40)
75–84	1,040	29 (28–31)	2,460	67 (65–70)	1,980	54 (52–56)
85–94	440	56 (50–61)	500	59 (54–64)	420	49 (44–53)
95+	0	0	20	24 (13–35)	20	23 (13–33)
Race/ethnicity						
White	2,700	22 (21–23)	6,800	52 (51–54)	4,820	39 (38–41)
Black	200	16 (13–18)	320	23 (21–26)	480	36 (33–39)
Asian	…	…	0	0	60	44 (33–55)
Hispanic	…	…	40	20 (14–26)	20	6.0 (3.3–8.6)
N. American Native	…	…	0	0	0	0
Region						
Midwest	1,280	35 (33–36)	2,200	57 (55–59)	1,720	47 (44–49)
Northeast	640	20 (19–22)	1,700	53 (51–56)	1,140	41 (39–43)
South	960	18 (17–19)	2,880	52 (51–54)	1,860	35 (33–36)
West	260	12 (10–13)	560	24 (22–26)	740	33 (31–35)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

The trend to increasing physician visits was consistent across all geographic regions. In 1998, the highest rate occurred in the West, 746 per 100,000, but this was only 10% higher than the lowest rate, seen in the Midwest. In 1998, the highest utilization of physician office services was for Caucasian males, followed by Asians, Hispanics, and African Americans. According to data from NAMCS for 1992–2000, 0.1% of all office visits to physician offices by males were for UI as the primary diagnosis (Table 12). Because the counts were so low for this diagnosis, the five even years between 1992 and 2000 were collapsed to yield a physician rate of 1,079 per 100,000 for the five years combined (or 216 per 100,000 annually). When the scope of the definition was broadened to include UI as any diagnosis, the proportion remained unchanged, but the visit rate increased to 1,811 per 100,000 for the five years combined (or 362 per 100,000 annually).

Ambulatory surgery visits for men with UI (Table 13) were far less frequent than were physician office visits (Table 11). For men under 65, the rate increased between 1992 and 1995, then decreased to the 1998 level of 17 per 100,000. Likewise, the rate for men over 65 increased between 1992 and 1995, then fell slightly to the 1998 level of 44 per 100,000. This pattern of increasing rates followed by a slight decline was seen across all age groups for men 65 and over.

The pattern of change in rates of ambulatory surgery visits for regions mirrors the trend for age. That is, rates increased across all geographic regions between 1992 and 1995, then decreased for 1998, where the lowest rate, 33 per 100,00, was seen in the West.

Table 14. Special needs of male nursing home residents regardless of continence status, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Has indwelling foley catheter or ostomy						
Yes	50,298	11,961 (10,569–13,352)	53,938	12,141 (10,731–13,552)	51,457	11,266 (9,941–12,591)
No	369,452	87,854 (86,453–89,254)	389,880	87,762 (86,348–89,176)	401,402	87,884 (86,497–89,271)
Question left blank	781	186 (3–368)	430	97 (0–210)	3,883	850 (385–1,315)
Requires assistance using the toilet						
Yes	207,587	49,363 (47,203–51,523)	221,599	49,882 (47,736–52,028)	241,558	52,887 (50,755–55,020)
No	141,870	33,736 (31,689–35,783)	133,378	30,023 (28,069–31,977)	128,251	28,080 (26,154–30,005)
Question skipped for allowed reason	69,267	16,471 (14,863–18,080)	86,814	19,542 (17,809–21,275)	81,977	17,948 (16,308–19,588)
Question left blank	1,807	430 (146–714)	2,459	553 (238–869)	4,956	1,085 (571–1,599)
Requires assistance from equipment when using the toilet						
Yes	57,463	13,664 (12,183–15,145)	59,329	13,355 (11,901–14,809)	67,782	14,840 (13,323–16,357)
No	143,213	34,055 (32,011–36,100)	149,218	33,589 (31,564–35,614)	162,895	35,665 (33,630–37,699)
Question skipped for allowed reason	211,137	50,207 (48,047–52,368)	220,191	49,565 (47,419–51,711)	210,228	46,028 (43,899–48,156)
Question left blank	8,719	2,073 (1,466–2,680)	15,510	3,491 (2,702–4,281)	15,837	3,467 (2,650–4,285)
Requires assistance from another person when using the toilet						
Yes	203,490	48,389 (46,230–50,548)	217,556	48,972 (46,827–51,117)	238,252	52,163 (50,029–54,297)
No	2,350	559 (237–881)	2,571	579 (234–924)	2,690	589 (237–941)
Question skipped for allowed reason	211,137	50,207 (48,047–52,368)	220,191	49,565 (47,419–51,711)	210,228	46,028 (43,899–48,156)
Question left blank	3,554	845 (451–1,239)	3,930	885 (482–1,287)	5,573	1,220 (681–1,759)
Has difficulty controlling urine						
Yes	218,491	51,956 (49,797–54,115)	232,536	52,344 (50,203–54,485)	242,189	53,025 (50,898–55,153)
No	170,988	40,660 (38,537–42,783)	175,090	39,413 (37,325–41,500)	177,128	38,781 (36,709–40,852)
Question skipped for allowed reason	29,338	6,976 (5,881–8,072)	36,416	8,197 (7,028–9,366)	34,206	7,489 (6,406–8,572)
Question left blank	1,715	408 (110–705)	207	47 (0–138)	3,220	705 (255–1,155)

[a]Rate per 100,000 adult male nursing home residents in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

It was not possible to calculate trends in outpatient UI surgery visit rates among ethnic groups because counts were too small to produce reliable estimates. The exception was the rate for Caucasian males, who showed an increase in outpatient surgical visits in 1995, with a subsequent reduction in 1998.

Nursing Home Care

Data from the National Nursing Home Survey (NNHS) for 1995, 1997, and 1999 are shown in Table 14. The burden of UI in the nursing home setting is clear when activities of daily living are considered. In 1999, more than half of the men in nursing homes were reported to have difficulty controlling their urine and required assistance using the toilet; 14.8% required assistance from equipment and 52% required assistance from another person. Eleven percent had either an indwelling foley or an ostomy. There was little change in these parameters over the years studied. In fact, from 1997 to 1999, there was a small increase in the rate of patients requiring assistance from another person to use the toilet.

TREATMENT

In general, treatment options for incontinence are based on the type of incontinence rather than the gender of the patient. For this reason, many studies and reviews include case mixes of men and women (20). The exceptions are in the management of issues related to the prostate gland (e.g., post-radical prostatectomy) and male neurogenic bladder, where treatment addresses the male sphincter. In these areas, where large groups of men have been studied, gender-specific treatment effects are apparent.

Nonpharmaceutical / Nonsurgical

Behavioral therapies, including pelvic floor muscle (PFM) exercises, biofeedback, and bladder training, are the least invasive options and have a low rate of side effects. They may be used both for cognitively impaired/institutionalized patients and for independently living, cognitively aware geriatric patients able to participate in learning new skills. There is a considerable body of scientific evidence supporting the effectiveness of behavioral therapy, but most subjects in those reports are women. Most of the research on conservative treatment of UI in men focuses on post-prostatectomy incontinence.

A recent review of the Cochrane database found only 6 randomized controlled trials of conservative approaches to management of post-prostatectomy incontinence. Studies were moderate in quality, and the authors concluded, "Men's symptoms tend to improve over time, irrespective of management. The value of the various approaches to conservative management of post-prostatectomy incontinence remains uncertain" (21).

PFM exercises, often attributed to Dr Kegel, refer primarily to pelvic muscle training as a means of reducing stress incontinence in women (22). In a randomized controlled trial of PFM exercises in 58 consecutive post-prostatectomy patients with a four-week follow-up, Porru et al. (23) reported more rapid resolution of UI symptoms and significantly better quality of life in the treatment group. A Cochrane review of PFM exercises reported no difference in the occurrence of post-operative UI between patients who had pre-prostate-surgery PFM training and the control group (24, 25). There are no randomized controlled trials in the literature concerning PFM exercises for non-post-operative men (26).

Biofeedback affords patients immediate observed information on performance of muscle contraction, allowing them to adjust their voiding technique accordingly to achieve maximum effect. A randomized, comparative study of biofeedback vs verbal feedback for learning PFM exercises after radical prostatectomy showed no difference in measures of UI at six-month follow-up (27).

Bladder training (a systematic approach to modifying voiding patterns) and prompted voiding (timely reminders to void for people with or without dementia) have also been the subject of Cochrane reviews. Most studies that met review criteria were in women, and no conclusions have been drawn about the benefit of these approaches for men (28, 29).

Results of combinations of strategies in men following prostatectomy are contradictory. Moore et al. (30) studied PFM exercises alone and in combination with electrical stimulation vs no treatment following prostatectomy and found no difference in UI among groups. Van Kampen et al. (31) compared combinations of PFM exercises with initial electrical stimulation and biofeedback vs sham electrical stimulation post-prostatectomy. Patients with urge incontinence also received bladder training. The active treatment group fared better in terms of duration and degree of continence and quality of life. Data for urge incontinence patients were not analyzed separately. In a randomized controlled trial by Vahtera et al. (32) of electrical stimulation followed by biofeedback and PFM exercises vs no treatment in 30 men and 50 women with detrusor hyperreflexia associated with multiple sclerosis, there was a significant improvement in subjective symptoms in the male group only.

Pharmacological

The use of medications for the treatment of stress incontinence in males is anecdotal. Anticholinergic drugs (e.g., oxybutynin and tolterodine) are more effective than placebo in treating overactive bladder syndrome, which may include urgency incontinence. Systematic literature reviews concerning pharmacological treatment of urge incontinence (20) and overactive bladder syndrome with anticholinergic drugs (33, 34) reveal significant symptom improvement. Although these studies involved male subjects, the men were not analyzed separately.

Surgical

Inpatient surgical procedures for male Medicare patients diagnosed with UI decreased from 1,804 per 100,000 men with UI in 1992 to 1,751 per 100,000 in 1995 and then to 1,337 per 100,000 men with UI in 1998. The counts of procedures performed in ambulatory surgical centers more than quadrupled during this same period (Table 15); however, this trend should be interpreted with caution, given the small numbers.

According to data from the Center for Health Care Policy and Evaluation, the rate of surgical correction of UI (including revision or repair of an artificial sphincter) was 4.8 per 100,000 males having commercial health insurance in 2000 (Table 16). Rates for prior years did not reveal counts high enough to make reliable estimates about trends in this population, nor do the data reveal the specific types of surgery done.

Urgency Incontinence/Neurogenic Bladder

Augmentation cystoplasty is performed primarily for neurogenic bladder. Although many subjects in studies of this treatment are male, results are rarely reported by gender (35). There are no randomized controlled trials of augmentation cystoplasty in the literature. Electrostimulation (sacral nerve stimulation, neuromodulation) in men sends sensory

Table 15. Urinary incontinence procedures for male Medicare beneficiaries, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	1,100	2,363	1,640	2,563	1,700	2,274
Operation for correction of incontinence	980	2,105	1,420	2,219	1,440	1,926
Ambulatory surgery center	140	301	280	438	420	562
Inpatient	840	1,804	1,120	1,751	1,000	1,337
Hospital outpatient	0	0	20	31	20	27
Physician office	0	0	0	0	0	0
Revision or repair of prosthetic	120	258	220	344	260	348
Ambulatory surgery center	0	0	40	63	40	53
Inpatient	100	215	160	250	220	294
Hospital outpatient	0	0	20	31	0	0
Physician office	20	43	0	0	0	0

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries diagnosed with urinary incontinence in the same demographic stratum.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

Table 16. Urinary incontinence procedures for males having commercial health insurance in 2000, count[a], rate[b]

	Count	Rate
Total		
Operation for correction of incontinence	48	4.8
Ambulatory surgery	12	*
Inpatient	12	*
Revision/repair of prosthetic		
Ambulatory surgery	21	*
Inpatient	3	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year.
SOURCE: Center for Health Care Policy and Evaluation, 2000.

input through the pudendal nerve to inhibit detrusor activity (36). Electrodes can be placed externally (in the rectum) or can be internally implanted. A review of the literature (5) reported improvement in urge incontinence in as many as 82.5% of subjects, but men and women were not reported separately.

Prevention

Prevention is typically divided into three types of measures: primary (those that prevent onset of a condition), secondary (those that prevent progression of the condition from its preclinical or asymptomatic state to its clinical or symptomatic state), and tertiary (those that impede the progression of a condition or its complications once it is clinically manifest). Primary prevention is most germane to UI. The principal potentially modifiable risk factors for UI in men are prostatectomy (transurethral or radical) and other medical conditions, including stroke, dementia, recurrent cystitis, bladder cancer, stool impaction, reduced mobility, diabetes, chronic cough, and medications (e.g., diuretics and hypnotics) (37).

Because as many as 30% of patients experience some degree of incontinence following radical prostatectomy (18), techniques to minimize the risk of postoperative incontinence are relevant to prevention of the disorder. Physical therapy to strengthen the pelvic floor musculature has been evaluated as primary prevention for patients undergoing prostate cancer in at least two randomized controlled trials, neither of which found a benefit (23, 24). Various surgical and perioperative techniques have also been suggested to reduce the risk of post-prostatectomy UI, including modified apical dissection and construction of a tubularized neourethra (18). Using the SEER-Medicare linked database, Begg et al. (38) described significantly lower rates of UI among men undergoing radical prostatectomy when the procedures were done in high-volume hospitals by high-volume surgeons. Of course, effective efforts to prevent prostate cancer would also decrease the incidence of male incontinence.

The goal of primary prevention for incontinence not associated with prostatectomy is to prevent the conditions believed to increase the risk of UI, including stroke, dementia, diabetes, and chronic lung disease. Modification of additional risk factors may in turn reduce the incidence of UI. Such preventive measures include controlling diabetes, preventing or treating constipation, maximizing mobility, treating symptomatic urinary tract infections, and avoiding medications that contribute to incontinence. There are apparently no studies evaluating such measures; nonetheless, it is logical to recommend them, as they are consistent with good clinical care.

ECONOMIC IMPACT

As baby boomers age, the number of individuals with incontinence rises and the heavy economic burden of UI on society grows. Governments and healthcare institutions are increasingly concerned about the burden of this disease, particularly since UI is one of the leading causes of individuals losing the ability to live independently and having to enter a care facility.

Direct costs of UI are borne by both the health sector and individual patients and their families. Direct costs related to operating costs for the health sector include those of both inpatient and outpatient services, particularly in the areas of supplies, equipment, and health professionals. Some direct health sector costs, such as the cost of supplies and health professionals' time, are *variable*, while others, such as the overhead incurred in running a hospital or clinic, are *fixed*. The vast majority of patients do not seek medical care; it has been estimated that only 2% of individuals living in the community and 5% of those living in institutions sought treatment for UI each year (2). Direct costs borne by the patient include the costs of medication and supplies to protect against incontinence. Padding and incontinence protection devices for men are somewhat different from those for women. Some men use gender-specific protective undergarments, which are often more costly than female garments, and some choose to use condom drainage or an external device such as a penile clamp.

Indirect costs include lost earnings for both the patient and family or friends who provide care. Since the prevalence of UI increases dramatically with age, the working status of the 60+ age group is of particular importance.

Estimating the economic burden of UI is complicated by two factors. First, UI is often not coded as the primary diagnosis, making it difficult to quantify the incremental costs of a hospitalization or ambulatory visit attributable to UI. For example, complications of UI such as skin irritation, urinary tract infections, nursing home placements, and fractures incurred when rushing to the toilet may easily be overlooked in claims-based analyses. Second, relatively few individuals with incontinence receive medical treatment for the condition. As a result, even the most rigorous attempts to quantify the economic costs of UI underestimate the true burden. In this section, we estimate the costs of UI, using claims-based data, supplemented by findings from published studies, recent national surveys, and employer data. Because UI is uncommon in men, costs will be proportionately low compared to UI in women.

Published estimates of national annual expenditures for UI vary widely. One study found that the costs of UI-related conditions for persons age 15 and older exceeded $16.3 billion in 1995 dollars (39). Another study considered only adults 65 and over and reported that UI treatment cost $26.3 billion (2). Both studies included estimates of costs for UI-related medical complications, nursing home stays, and supplies such as pads and laundry, as well as the indirect costs of UI. Although the reasons for this wide discrepancy are not entirely clear, both estimates indicate a substantial economic burden on the American public. The data presented in this chapter address individual components of UI-related costs; hence, they may not be directly comparable to aggregate estimates drawn from the literature.

Table 17. Expenditures for male Medicare beneficiaries for the treatment of urinary incontinence, by site of service, 1998

	Total Annual Expenditures	
Site of Service	Age < 65	Age 65+
Inpatient	*	$11,300,000
Outpatient		
Physician Office	$1,700,000	$15,200,000
Hospital Outpatient	$300,000	$1,300,000
Ambulatory Surgery	$1,300,000	$10,600,000
Emergency Room	$100,000	$600,000
Total	$3,400,000	$39,000,000

*Figure does not meet standard for reliability or precision.
SOURCE: Centers for Medicare and Medicaid Services, 1998.

Direct Costs

A small, but notable, proportion of Medicare expenditures for male UI is accounted for by males under age 65, that is, disabled individuals (Table 17). This is consistent with clinical experience among younger men with spinal cord injury and other neurological disorders that can affect the urinary tract. Among male Medicare beneficiaries age 65 and over, total costs doubled between 1992 and 1995, from $19.1 million to $38.1 million, then remained stable in 1998 (Table 18). Most of the increase occurred in the ambulatory surgery setting, although expenditures for physician office visits also rose substantially. While the amount spent in the inpatient setting rose in absolute terms, it declined from 44% to 29%, consistent with secular trends toward outpatient care in the 1990s (Figure 3).

Given the inherent limitations in deriving treatment costs from claims data, the Urologic Diseases in America analyses used multivariate regression models to estimate the incremental costs associated with a primary diagnosis of UI (Table 19). The study sample consisted of nearly 280,000 primary beneficiaries age 18 to 64 who had employer-provided coverage throughout 1999. Regression models were estimated for annual medical and pharmacy costs per person. The main independent variables included a set of measures to describe medical and drug benefits

Table 18. Expenditures for male Medicare beneficiaries age 65 and over for treatment of urinary incontinence, by site of service (% of total)

	Year					
	1992		1995		1998	
Total	19,100,000		38,100,000		39,000,000	
Inpatient	8,400,000	(43.9%)	10,300,000	(27.0%)	11,300,000	(29.0%)
Outpatient						
Physician Office	6,200,000	(32.5%)	11,000,000	(28.9%)	15,200,000	(39.0%)
Hospital Outpatient	600,000	(3.1%)	2,000,000	(5.2%)	1,300,000	(3.3%)
Ambulatory Surgery	3,300,000	(17.3%)	13,900,000	(36.5%)	10,600,000	(27.2%)
Emergency Room	600,000	(3.1%)	900,000	(2.4%)	600,000	(1.5%)

NOTE: Percentages may not add to 100% because of rounding.

SOURCE: Centers for Medicaid and Medicare Services, 1992, 1995, 1998.

(such as deductibles, co-insurance, and co-payments), patient demographics (age, gender, work status), area characteristics (urban residence, median household income in zip code), and a set of comorbidities derived from the medical claims (binary indicators of 26 disease conditions such as diabetes, asthma, and hypertension). The regression results were used to predict average medical and pharmacy costs for persons with and without a primary diagnosis of UI. Total annual expenditures in 1999 for privately insured adults age 18 to 64 with a primary diagnosis of UI were $7,702, nearly $4,500 more than those for similar individuals without a diagnosis of UI. Nonetheless, the aggregate cost is low, given the relative infrequency of urinary incontinence claims in men.

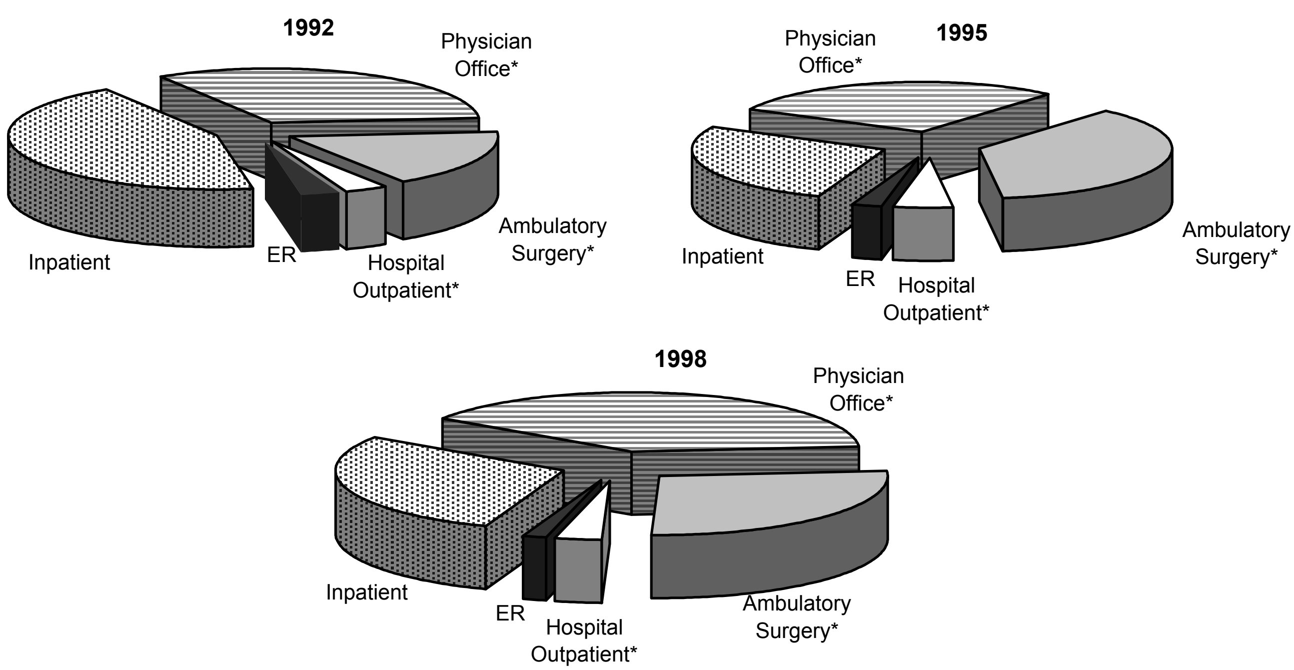

Figure 3. Expenditures of male Medicare beneficiaries age 65 and over for treatment of urinary incontinence (in millions of $).

***Constitute outpatient services.**

SOURCE: Centers for Medicaid and Medicare Serivces, 1992, 1995, 1998.

Table 19. Estimated annual expenditures of privately insured employees with and without a medical claim for urinary incontinence (UI) in 1999[a]

	Annual Expenditures (per person)			
	Persons without UI (N=277,803)	Persons with UI (N=1,147)		
	Total	Total	Medical	Rx Drugs
Total	$3,204	$7,702	$6,099	$1,604
Age				
18–44	$2,836	$7,361	$5,993	$1,369
45–54	$3,305	$8,442	$6,695	$1,747
55–64	$3,288	$7,247	$5,623	$1,623
Gender				
Male	$2,813	*	*	*
Female	$3,933	*	*	*
Region				
Midwest	$3,086	$8,500	$6,861	$1,639
Northeast	$3,085	$7,236	$5,502	$1,734
South	$3,416	$8,329	$6,851	$1,477
West	$3,237	$8,082	$7,118	$964

Rx, prescription.

*Figure does not meet standard for reliability or precision.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.

SOURCE: Ingenix, 1999.

Table 20. Average annual spending and use of outpatient prescription drugs for treatment of urinary incontinence (both male and female), 1996–1998[a]

Drug Name	Number of Rx Claims	Mean Price	Total Expenditures
Alpha-blocker			
Cardura™	378,895	$43.71	
Anticholinergics			
Oxybutynin	485,044	$19.79	$9,599,027
Imipramine (brand)	247,249	$13.13	$3,246,379
Imipramine (generic)	162,184	$6.59	$1,068,790
Ditropan™	130,390	$32.91	$4,291,146
TOTAL	1,403,762		$34,766,829

Rx, prescription.

[a]Estimates include prescription drug claims with a corresponding diagnosis of urinary incontinence and exclude drugs with fewer than 30 claims. Including expenditures on prescription drugs with fewer than 30 claims (unweighted) would increase total drug spending by approximately 83%, to $63.7 million.

SOURCE: Medical Expenditure Panel Survey, 1996–1998.

Although data on pharmaceutical costs are not available by gender, Table 20 presents the relative expenditures for the medications most often used to treat patients with UI. Almost half of the expenditures in 1996–1998 were for alpha-blockers, generally prescribed to older men with bladder outlet obstruction; this suggests that prostate enlargement contributes to both the human and the financial cost of UI. Not surprisingly, most of the actual prescriptions for UI were written for anticholinergic agents. Because these were predominantly generics, they represent a disproportionately small fraction of total drug expenditures in this period. Since 1998, new long-acting agents in this class have been developed and marketed, altering the economic landscape for the pharmaceutical management of individuals with UI.

Additional direct patient costs include those of pads, diapers, condom catheters, indwelling catheters, and penile clamps. Little detailed information on these costs is available; however, they are thought to be substantial, owing in large part to out-of-pocket outlays that aggregate over many years. Wagner and Hu estimated the annual cost of UI-related supplies to be $7.1 billion for individuals in the home setting and $4.3 billion for those in the institutional setting; supplies related to catheterization accounted for $224 million of the total expenditures (2).

Indirect Costs

The indirect financial burden of incontinence also falls on "informal caregivers," i.e., family and friends. Data from the 1993 Asset and Health Dynamics Study of persons over the age of 70 indicate that continent men received 7.4 hours of care per week, increasing to 11.3 hours and 16.6 hours for men with incontinence who did not and did use pads for protection, respectively. The cost of this care was an additional $1,700 per man without pads and $4,000 per man with pads (40).

Relatively little work loss is associated with UI among men, as indicated in 1999 data from Marketscan (Table 21). In fact, of the 51 men in this dataset with claims for UI, only 8% missed work because of it, about three times lower than the rate for women. Because these 51 men represent only 0.4% of the men in the sample, the proportion of men missing work for claims related to UI is only 0.03%. Among those men who missed work, the average annual work absence was only 2.3 hours, all for outpatient services,

Table 21. Average annual work loss of persons treated for urinary incontinence (95% CI)

			Average Work Absence (hrs)		
Gender	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
Male	51	8%	0	2.3 (0–5.0)	2.3 (0–5.0)
Female	319	23%	7.1 (1.7–12.6)	21.6 (11.3–31.9)	28.7 (14.9–42.5)

[a]Individuals with an inpatient or outpatient claim for urinary incontinence and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: MarketScan, 1999.

Table 22. Average work loss associated with a hospitalization or an ambulatory care visit for treatment of urinary incontinence (95% CI)

	Inpatient Care		Outpatient Care	
Gender	Number of Hospitalizations[a]	Average Work Absence (hrs)	Number of Outpatient Visits	Average Work Absence (hrs)
Male	*	*	82	1.4 (0.1–2.7)
Female	*	*	625	11.0 (7.5–14.6)

*Figure does not meet standard for reliability or precision.

[a]Unit of observation is an episode of treatment. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

SOURCE: MarketScan, 1999.

less than one-tenth the number for women. Men had much less time away from work for each outpatient visit than did women (Table 22).

RECOMMENDATIONS

The newly recommended changes in the definition of UI and its subtypes will conform better to the new ICD-10 classification, which should improve the accuracy of coding for UI. Studies are needed on the outcome of UI treatment specifically for men and on the role of ethnicity in both prevalence and the likelihood of seeking treatment. Given the aging population, the impact of UI within nursing home settings calls for further research into prevention, treatment, and management practices that could lessen the impact of UI on both the patients and the healthcare system.

REFERENCES

1. Wilson L, Brown JS, Shin GP, Luc KO, Subak LL. Annual direct cost of urinary incontinence. Obstet Gynecol 2001;98:398-406.
2. Wagner TH, Hu TW. Economic costs of urinary incontinence in 1995. Urology 1998;51:355-61.
3. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, Van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology 2003;61:37-49.
4. Abrams P, Blaivas JG, Stanton SL, Andersen JT, Fowler CJ, Gerstenberg T, Murray K. Sixth report on the standardisation of terminology of lower urinary tract function. Procedures related to neurophysiological investigations: electromyography, nerve conduction studies, reflex latencies, evoked potentials and sensory testing. The International Continence Society Committee on Standardisation of Terminology, New York, May 1985. Scand J Urol Nephrol 1986;20:161-4.
5. Abrams P, Blaivas JG, Fowler CJ, Fourcroy JL, Macdiarmid SA, Siegel SW, Van Kerrebroeck P. The role of neuromodulation in the management of urinary urge incontinence. BJU Int 2003;91:355-9.
6. Johnson TM, 2nd, Kincade JE, Bernard SL, Busby-Whitehead J, DeFriese GH. Self-care practices used by older men and women to manage urinary incontinence: results from the national follow-up survey on self-care and aging. J Am Geriatr Soc 2000;48:894-902.
7. Hunskaar S, Burgio K, Diokno AC, Herzog AR, Hjalmas K, Lapitan MC. Epidemiology and natural history of urinary incontinence (UI). In: Abrams P, Cardozo L, Khoury S, Wein A, eds. Incontinence 2nd International Consultation on Incontinence. 2nd ed. Plymouth: Plymbridge Distributors Ltd., 2002:165-201.
8. Thom D. Variation in estimates of urinary incontinence prevalence in the community: effects of differences in definition, population characteristics, and study type. J Am Geriatr Soc 1998;46:473-80.
9. Langa KM, Fultz NH, Saint S, Kabeto MU, Herzog AR. Informal caregiving time and costs for urinary incontinence in older individuals in the United States. J Am Geriatr Soc 2002;50:733-7.
10. Johnson TM, 2nd, Bernard SL, Kincade JE, Defriese GH. Urinary incontinence and risk of death among community-living elderly people: results from the National Survey on Self-Care and Aging. J Aging Health 2000;12:25-46.
11. Nakanishi N, Tatara K, Shinsho F, Murakami S, Takatorige T, Fukuda H, Nakajima K, Naramura H. Mortality in relation to urinary and faecal incontinence in elderly people living at home. Age Ageing 1999;28:301-6.
12. Thom DH, Haan MN, Van Den Eeden SK. Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality. Age Ageing 1997;26:367-74.
13. Elbadawi A, Diokno AC, Millard RJ. The aging bladder: morphology and urodynamics. World J Urol 1998;16 Suppl 1:S10-34.
14. Brandeis GH, Baumann MM, Hossain M, Morris JN, Resnick NM. The prevalence of potentially remediable urinary incontinence in frail older people: a study using the Minimum Data Set. J Am Geriatr Soc 1997;45:179-84.
15. Nakayama H, Jorgensen HS, Pedersen PM, Raaschou HO, Olsen TS. Prevalence and risk factors of incontinence after stroke. The Copenhagen Stroke Study. Stroke 1997;28:58-62.
16. Landi F, Cesari M, Russo A, Onder G, Sgadari A, Bernabei R. Benzodiazepines and the risk of urinary incontinence in frail older persons living in the community. Clin Pharmacol Ther 2002;72:729-34.
17. Movig KL, Leufkens HG, Belitser SV, Lenderink AW, Egberts AC. Selective serotonin reuptake inhibitor-induced urinary incontinence. Pharmacoepidemiol Drug Saf 2002;11:271-9.
18. Milam DF, Franke JJ. Prevention and treatment of incontinence after radical prostatectomy. Semin Urol Oncol 1995;13:224-37.
19. Herzog AR, Diokno AC, Brown MB, Normolle DP, Brock BM. Two-year incidence, remission, and change patterns of urinary incontinence in noninstitutionalized older adults. J Gerontol 1990;45:M67-74.
20. Haeusler G, Leitich H, van Trotsenburg M, Kaider A, Tempfer CB. Drug therapy of urinary urge incontinence: a systematic review. Obstet Gynecol 2002;100:1003-16.
21. Moore KN, Cody DJ, Glazener CM. Conservative management for post prostatectomy urinary incontinence. Cochrane Database Syst Rev 2001:CD001843.
22. Kegel AH. Progressive resistance exercise in the functional restoration of the perineal muscles. J Am Obstet Gynecol 1948;56:238-248.
23. Porru D, Campus G, Caria A, Madeddu G, Cucchi A, Rovereto B, Scarpa RM, Pili P, Usai E. Impact of early pelvic floor rehabilitation after transurethral resection of the prostate. Neurourol Urodyn 2001;20:53-9.
24. Bales GT, Gerber GS, Minor TX, Mhoon DA, McFarland JM, Kim HL, Brendler CB. Effect of preoperative biofeedback/pelvic floor training on continence in men

undergoing radical prostatectomy. Urology 2000;56:627-30.
25. Hay-Smith J, Herbison P, Morkved S. Physical therapies for prevention of urinary and faecal incontinence in adults. Cochrane Database Syst Rev 2002:CD003191
26. Bo K, Berghmans LC. Nonpharmacologic treatments for overactive bladder-pelvic floor exercises. Urology 2000;55:7-11; discussion 14-6.
27. Floratos DL, Sonke GS, Rapidou CA, Alivizatos GJ, Deliveliotis C, Constantinides CA, Theodorou C. Biofeedback vs verbal feedback as learning tools for pelvic muscle exercises in the early management of urinary incontinence after radical prostatectomy. BJU Int 2002;89:714-9.
28. Eustice S, Roe B, Paterson J. Prompted voiding for the management of urinary incontinence in adults. Cochrane Database Syst Rev 2000:CD002113.
29. Roe B, Williams K, Palmer M. Bladder training for urinary incontinence in adults. Cochrane Database Syst Rev 2000:CD001308.
30. Moore KN, Griffiths D, Hughton A. Urinary incontinence after radical prostatectomy: a randomized controlled trial comparing pelvic muscle exercises with or without electrical stimulation. BJU Int 1999;83:57-65.
31. Van Kampen M, De Weerdt W, Van Poppel H, De Ridder D, Feys H, Baert L. Effect of pelvic-floor re-education on duration and degree of incontinence after radical prostatectomy: a randomised controlled trial. Lancet 2000;355:98-102.
32. Vahtera T, Haaranen M, Viramo-Koskela AL, Ruutiainen J. Pelvic floor rehabilitation is effective in patients with multiple sclerosis. Clin Rehabil 1997;11:211-9.
33. Hay-Smith J, Herbison P, Ellis G, Moore K. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. Cochrane Database Syst Rev 2002:CD003781.
34. Chapple CR. Muscarinic receptor antagonists in the treatment of overactive bladder. Urology 2000;55:33-46; discussion 50.
35. Cetinel B, Demirkesen O, Onder AU, Yaycioglu O, Ismailoglu V, Solok V. Reconstructive surgery in voiding dysfunction: experience with 69 patients. Urology 2000;56:962-6.
36. Plevnik S, Janez J, Vrtachik B, Trsinar B, Vodusek DB. Short-term electrical stimulation: home treatment for urinary incontinence. World J Urol 1986;4:24-26.
37. Fonda D, Resnick NM, Kirschner-Hermanns R. Prevention of urinary incontinence in older people. Br J Urol 1998;82 Suppl 1:5-10.
38. Begg CB, Riedel ER, Bach PB, Kattan MW, Schrag D, Warren JL, Scardino PT. Variations in morbidity after radical prostatectomy. N Engl J Med 2002;346:1138-44.
39. Wilson L, Brown JS, Shin GP, Luc KO, Subak LL. Annual direct cost of urinary incontinence. Obstet Gynecol 2001;98:398-406.
40. Langa KM, Fultz NH, Saint S, Kabeto MU, Herzog AR. Informal caregiving time and costs for urinary incontinence in older individuals in the United States. J Am Geriatr Soc 2002;50:733-7.

CHAPTER 7

Bladder and Upper Tract Urothelial Cancer

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Bladder and Upper Tract Urothelial Cancer

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INTRODUCTION

Urothelial cancers of the urinary tract consist of tumors of the bladder and of the renal pelvis and ureters (upper tracts). Bladder cancer is far more common than upper tract cancers. For purposes of this chapter, we distinguish upper tract urothelial cancers from those of the lower tract. The ICD-9 and CPT codes used for identifying the conditions and related procedures are described in Table 1.

DEFINITION AND DIAGNOSIS

Urothelial malignancies, i.e., transitional cell carcinomas, are believed to represent a field change phenomenon with the possibility of multiple synchronous or metachronous tumors occurring at any point along the urinary tract that is lined by transitional epithelium. Most patients with urothelial cancer present with either microscopic or macroscopic hematuria. Some patients, particularly those with carcinoma *in situ* (CIS), may present with irritative voiding symptoms such as urgency, frequency, and dysuria. On occasion, ureteric obstruction by an upper tract tumor or a bladder tumor may result in flank pain. Tumors arising near the bladder outlet or in the prostatic urethra may present with urinary retention.

Diagnostic evaluation of the upper tracts is typically performed using an intravenous pyelogram, retrograde pyelogram, ultrasound, computed tomography (CT) scan, CT urogram, or some combination thereof. Evaluation of the lower urinary tract is performed by cystoscopy. Voided urine and/or saline bladder wash is performed for cytology. A number of newer tests, including fluorescent *in situ* hybridization (FISH), NMP22, and BTA stat, are now available to augment the diagnostic ability of urine/bladder wash cytology. Many of these newer tests have higher sensitivity but lower specificity than routine cytology and are not universally employed. Once a tumor is visualized in the lower or upper urinary tract, a biopsy is performed to allow evaluation of the grade and extent of tumor (1). Tumors are graded as low or high, while staging is according to the TNM system (Table 2). Bladder tumors that do not clearly invade the muscularis propria (Ta, TIS, T1) are considered "superficial," while those that do invade the muscularis (T2, T3, T4) are considered "invasive," however this classification may be a misleading oversimplification as it implies that superficial tumors are not potentially life-threatening (2). A comparable staging system exists for upper tract tumors. Ureteric tumors are more likely to be invasive and to extend beyond the ureter because of the ureter's thin muscular envelope.

Approximately 90% of all bladder cancers are transitional cell carcinomas (TCCs); the remainder includes squamous cell carcinomas (SCCs) and adenocarcinomas (3). In contrast to TCC, squamous cell carcinoma of the bladder appears to have a higher incidence in African Americans than in Caucasians (4). About 75% of all TCCs of the bladder are stage Ta, TIS, or T1 and have a predilection for local recurrence. Progressive disease develops in about 15% to 25% of patients who initially present with stage Ta, TIS, or T1 TCC of the bladder (3). One in four patients with

Table 1. Codes used in the diagnosis and management of transitional cell carcinoma (TCC)

Upper Tract	
Individuals 40 years or older, with one or more of the following:	
ICD-9 diagnosis codes	
189.1	Malignant neoplasm of renal pelvis
189.2	Malignant neoplasm of ureter
CPT procedure codes	
50234	Nephrectomy with total ureterectomy and bladder cuff; through same incision
50236	Nephrectomy with total ureterectomy and bladder cuff; through separate incision
50548	Laparoscopy, surgical; nephrectomy with total ureterectomy
Lower Tract	
Individuals 40 years or older, with one or more of the following:	
ICD-9 diagnosis codes	
188	Malignant neoplasm of bladder
188.0	Malignant neoplasm of trigone of urinary bladder
188.1	Malignant neoplasm of dome of urinary bladder
188.2	Malignant neoplasm of lateral wall of urinary bladder
188.3	Malignant neoplasm of anterior wall of urinary bladder
188.4	Malignant neoplasm of posterior wall of urinary bladder
188.5	Malignant neoplasm of bladder neck
188.6	Malignant neoplasm of ureteric orifice
188.7	Malignant neoplasm of urachus
188.8	Malignant neoplasm of other specified sites of bladder
188.9	Malignant neoplasm of bladder part, unspecified
189.3	Malignant neoplasm of urethra
233.7	Carcinoma in situ of bladder
ICD-9 procedure codes	
57.4	Transurethral excision or destruction of bladder cancer
57.49	Other transurethral excision or destruction of lesion or tissue of bladder
57.5	Other excision or destruction of bladder tissue
57.59	Open excision or destruction of other lesion or tissue of bladder
57.6	Partial cystectomy
57.71	Radical cystectomy
57.87	Reconstruction of urinary bladder
CPT procedure codes	
51020	Cystotomy or cystostomy; with fulguration and/or insertion of radioactive material
51530	Cystotomy; for excision of bladder tumor
51570	Cystectomy, complete
51575	Cystectomy, complete; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes
51580	Cystectomy, complete, with uretereosigmoidostomy or ureterocutaneous transplantations
51585	Cystectomy, complete, with uretereosigmoidostomy or ureterocutaneous transplantations; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes
51590	Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis
51595	Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes
51596	Cystectomy, complete, with continent diversion, any open technique, using any segment of small and/or large intestine to construct neobladder
51720	Bladder instillation of anticarcinogenic agent (including detention time)
52224	Cystourethroscopy, with fulguration (including cryosurgery or laser surgery) or treatment of MINOR (less than 0.5 cm) lesion(s) with or without biopsy
52234	Cystourethroscopy, with fulguration (including cryosurgery or laser surgery) and/or resection of; SMALL bladder tumor(s) (0.5 to 2.0 cm)
52235	Cystourethroscopy, with fulguration (including cryosurgery or laser surgery) and/or resection of; MEDIUM bladder tumor(s) (2.0 to 5.0 cm)
52240	Cystourethroscopy, with fulguration (including cryosurgery or laser surgery) and/or resection of; LARGE bladder tumor(s)
52250	Cystourethroscopy with insertion of radioactive substance, with or without biopsy or fulguration

bladder cancer presents with invasive TCC, and of these patients, from 20% to 40% may already have lymph node metastases at the time of presentation (3, 5).

RISK FACTORS

The single most important risk factor for urothelial cancers, particularly TCC, is smoking. Other well-described factors include exposure to aniline dyes used in coloring, printing, and rubber industries. Balkan nephropathy, frequent in the Balkan countries, is a known risk factor for upper tract urothelial tumors. A history of radiation or cyclophosphamide chemotherapy can increase the risk of developing bladder cancer, and overuse of the analgesic phenacetin has also been associated with increased risk. Chronic irritation in the form of indwelling foreign bodies such as urethral catheters, recurrent infections, or stones can also increase the risk of squamous cell carcinoma of the bladder. Most of these risk factors hold true for upper tract tumors as well. Prior history or the presence of lower tract TCC is also a risk factor for development of upper tract TCC. Infection with *Schistosoma hematobium*, which results in the deposition of parasitic ova in the bladder mucosa, is well known to be associated with squamous cell carcinoma of the bladder and is particularly common in the Nile delta and other regions of Africa. Pelvic lipomatosis and cystitis glandularis have been associated with adenocarcinoma of the bladder.

TREATMENT

Initial treatment of bladder tumors involves excisional biopsy in the form of a transurethral resection (TURBT). This may require more than one sitting in cases where the tumor is large or the initial sampling is found to be incomplete. In the case of stage Ta but high-grade TCC or of stage TIS or T1, intravesical chemo/immunotherapy is often warranted. This involves placing an agent directly

Table 2. TNM staging system for bladder cancer

Primary tumor (T)	
TX:	Primary tumor cannot be assessed
T0:	No evidence of primary tumor
Ta:	Noninvasive papillary carcinoma
Tis:	Carcinoma in situ (i.e., flat tumor)
T1:	Tumor invades subepithelial connective tissue
T2:	Tumor invades muscle
pT2a:	Tumor invades superficial muscle (inner half)
pT2b:	Tumor invades deep muscle (outer half)
T3:	Tumor invades perivesical tissue
pT3a:	Microscopically
pT3b:	Macroscopically (extravesical mass)
T4:	Tumor invades any of the following: prostate, uterus,vagina, pelvic wall, or abdominal wall
T4a:	Tumor invades the prostate, uterus, vagina
T4b:	Tumor invades the pelvic wall, abdominal wall
Regional lymph nodes (N)	
NX:	Regional lymph nodes cannot be assessed
N0:	No regional lymph node metastasis
N1:	Metastasis in a single lymph node, ≤ 2 cm in greatest dimension
N2:	Metastasis in a single lymph node, > 2 cm but ≤ 5 cm in greatest dimension; or multiple lymph nodes, ≤ 5 cm in greatest dimension
N3:	Metastasis in a lymph node, > 5 cm in greatest dimension
Distant metastasis (M)	
MX:	Distant metastasis cannot be assessed
M0:	No distant metastasis
M1:	No distant metastasis

SOURCE: Adapted from Urinary bladder. In: American Joint Committee on Cancer.: AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, Copyright 2002, 335–340.

Table 3. Estimated new bladder cancer cases in the United States, count, percentage of all new cancers

	1996		1998		2000		2002		2004	
	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent
Total	52,900	(3.9%)	54,400	(4.4%)	53,200	(4.4%)	56,500	(4.4%)	60,240	(4.4%)
Male	38,300	(5.0%)	39,500	(6.3%)	38,300	(6.2%)	41,500	(6.5%)	44,640	(6.4%)
Female	14,600	(2.5%)	14,900	(2.5%)	14,900	(2.5%)	15,000	(2.3%)	15,600	(2.3%)

SOURCE: Cancer Statistics, 1996, 1998, 2000, 2004. American Cancer Society Surveillance Research.

into the bladder through a urethral catheter. The agents most commonly utilized for chemotherapy are Mitomycin, Doxorubicin, and Epirubicin. Bacillus Calmette-Guerin (BCG) is the most frequently used intravesical agent for immunotherapy, with the addition of Interferon in some cases to treat refractory disease (6). BCG is the agent of choice for intravesical therapy in patients with high-grade tumors. In the less common case of tumor invasion into the muscularis propria (stage T2 or T3), patients typically require a radical cystectomy with urinary diversion and regional lymphadenectomy. Cystectomy is the surgical removal of the entire urinary bladder. An ileal conduit involves repurposing a segment of the ileum to divert urine from the ureters to the skin, where it is collected with an external bag. A neobladder, a much more complex form of urinary reconstruction after cystectomy, involves reconfiguring a segment of small and/or large intestine as a continent internal storage pouch for urine. Urethrectomy, surgical removal of the urethra, may also be required.

In males, simultaneous urethrectomy is not routinely performed unless the tumor involves

Table 4. Age-adjusted incidence rates[a] for bladder cancer, 1997–2001, by race/ethnicity, and gender

	Total	Males	Females
Race/ethnicity			
All	20.4	36.1	9.1
White	22.5	39.9	9.8
White Hispanic[b]	10.8	19.1	5.1
White Non-Hispanic[b]	23.4	41.3	10.2
Black	12.6	20.4	7.7
Asian/Pacific Islander	9.6	16.3	4.5
Hispanic	10.5	18.6	5
N. American Native/ Alaska Native	5.6	9.5	…

…data not available

[a]Rates per 100,000 from the 12 SEER areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, and Alaska Native Registry).

[b]Hispanic and Non-Hispanic are not mutually exclusive from Whites, Blacks, Asian Pacific Islanders, and American Indians/ Alaska Natives. Incidence for Hispanics and Non-Hispanics do not include cases from Detroit, Hawaii,and Alaska Native Registry.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/, 2004.

Table 5. Estimated bladder cancer prevalence counts[a] and rates[b] in the United States in 2001

	Count	Rate
All[c]	490,458	173
Males	361,471	260
Females	128,987	89
White[c]	458,586	200
Males	339,089	299
Females	119,497	103
Black[c]	16,563	47
Males	11,239	66
Females	5,324	28
Asian/Pacific Islander[d]	…	...
Males	…	...
Females	…	...
Hispanic[e]	…	...
Males	…	...
Females	…	...

…data not available.

[a]US 2001 cancer prevalence counts are based on 2001 cancer prevalence proportions from the SEER registries and 1/1/2001 US population estimates based on the average of 2000 and 2001 population estimates from the US Bureau of the Census.

[b]Rate per 100,000 based on 2001 cancer prevalence proportions from the SEER registries and 1/1/2001 US population estimates based on the average of 2000 and 2001 population estimates from the US Bureau of the Census.

[c,d,e]Statistics based on b) SEER 9 areas, c) SEER 11 areas, or d) SEER 11 areas excluding Hawaii and Detroit.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/, 2004.

Table 6. Survival rates (%) for bladder cancer (invasive and *in situ*), by race/ethnicity, gender, diagnosis year, stage, and age

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
5-Yr Survival Rates									
Year of Diagnosis									
1960–1963[a]	…	…	…	53	53	53	24	24	24
1970–1973[a]	…	…	…	61	61	60	36	38	27
1974–1976[b]	73	74	70	74	75	72	48	55	37[d]
1977–1979[b]	75	77	71	76	77	73	55	63	39[d]
1980–1982[b]	78	79	75	79	80	76	59	63	49[d]
1983–1985[b]	78	79	73	78	80	75	60	65	51[d]
1986–1988[b]	80	82	75	81	82	76	63	68	52[d]
1989–1991[b]	81	84	74	82	84	76	62	66	56
1992–1994[b]	82	84	75	82	85	76	64	69	55
1995–2000[b]	82[c]	84[c]	76[c]	83[c]	85[c]	77[c]	62[c]	68[c]	52[c]
1995–2000[b]									
All stages	82	84	76	82	85	77	62	68	52
Localized	94	95	91	95	96	92	82	86	75[d]
Regional	49	51	44	50	52	44	39	43[d]	34[d]
Distant	5.5	6.8	3.2	5	5.8	3.7	5.3	7.0[d]	...
Unstaged	60	64	50	62	65	51[d]	37[d]	46[d]	19[d]
5-Yr Survival Rates, 1995–2000[b]									
Age at Diagnosis									
< 45	90	91	87	92	93	90	76[d]	81[d]	...
45–54	87	88	83	88	89	84	71[d]	73[d]	67[d]
55–64	85	86	80	86	87	82	63[d]	71[d]	47[d]
65–74	82	84	77	83	85	79	58	67[d]	43[d]
75+	75	78	70	76	79	70	56[d]	54[d]	58[d]
< 65	86	87	82	87	88	84	68	73	54[d]
65+	79	82	73	80	83	74	57	62	51[d]

…data not available.

[a]Rates are based on End Results data from a series of hospital registries and one population-based registry.

[b]Rates are from the SEER 9 areas. They are based on data from population-based registries in Connecticut, New Mexico, Utah,Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound and San Francisco-Oakland. Rates are based on follow-up of patients into 2001.

[c]The difference in rates between 1974–1976 and 1995–2000 is statistically significant (p<.05).

[d]The standard error of the survival rate is between 5 and 10 percentage points.

[e]The standard error of the survival rate is greater than 10 percentage points.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/, 2004.

the urethra. In females, urethrectomy is typically performed concomitantly, unless a neobladder is planned. In select cases of muscle-invasive disease, a bladder-preserving approach employing systemic chemotherapy and radiation may be therapeutic. Management of metastatic bladder cancer typically relies on systemic combination chemotherapy with any of several common regimens, most frequently Gemcitabine and Cisplatin (GC) or Methotrexate, Vinblastine, Adriamycin, and Cisplatin (MVAC). The former regimen is less toxic, but both appear to have similar efficacy in the metastatic setting.

Treatment of upper tract TCC relies on local resection of stage Ta, TIS, or T1 disease in the form of either a biopsy or a curative resection, particularly for low-grade/stage tumors. On occasion, laser fulguration of a biopsy-confirmed, stage Ta, or T1 TCC of the ureter or renal pelvis may be performed. Ureteric tumors can effectively be treated with excision of a segment of the diseased ureter, particularly if the tumor is situated in the distal third. More proximally located tumors may require excision of the kidney and ureter. Excision of tumors of the renal pelvis routinely requires a nephroureterectomy. Locally extensive or

Table 7. Age-adjusted death rates[a] for bladder cancer, by year, race/ethnicity, and gender

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
Year of Death									
1975	5.5	9.8	2.8	5.6	10.1	2.7	5.0	6.9	3.6
1976	5.6	9.8	2.9	5.6	10.0	2.8	5.3	7.8	3.5
1977	5.5	9.7	2.9	5.6	9.9	2.8	5.2	7.6	3.6
1978	5.4	9.5	2.9	5.5	9.8	2.8	4.9	7.2	3.4
1979	5.2	9.3	2.7	5.3	9.6	2.7	5.0	7.6	3.3
1980	5.2	9.2	2.7	5.2	9.5	2.7	4.7	6.2	3.7
1981	5.1	9.0	2.7	5.1	9.3	2.6	4.9	7.2	3.4
1982	5.0	8.9	2.6	5.0	9.2	2.5	4.9	6.8	3.6
1983	4.9	8.8	2.5	4.9	9.0	2.5	4.7	7.2	3.2
1984	4.7	8.5	2.5	4.8	8.7	2.4	4.7	6.9	3.4
1985	4.7	8.4	2.4	4.7	8.7	2.4	4.5	6.9	3.0
1986	4.5	8.1	2.4	4.6	8.4	2.3	4.2	5.8	3.3
1987	4.4	7.9	2.3	4.5	8.1	2.3	4.4	6.5	3.1
1988	4.4	7.8	2.4	4.5	8.0	2.3	4.3	5.9	3.3
1989	4.5	8.0	2.4	4.5	8.2	2.3	4.6	7.0	3.2
1990	4.5	8.0	2.4	4.6	8.2	2.4	4.4	6.4	3.2
1991	4.4	7.9	2.3	4.5	8.1	2.3	4.4	6.6	3.1
1992	4.5	7.9	2.4	4.5	8.1	2.4	4.3	6.7	3.1
1993	4.5	8.1	2.3	4.5	8.3	2.3	4.2	6.4	2.9
1994	4.5	7.9	2.4	4.5	8.1	2.4	4.3	6.4	3.2
1995	4.4	7.8	2.3	4.4	8.1	2.2	4.0	5.8	3.1
1996	4.4	7.8	2.4	4.5	8.1	2.3	4.2	5.9	3.1
1997	4.4	7.6	2.4	4.5	7.9	2.4	4.0	5.9	3.0
1998	4.4	7.7	2.3	4.5	8.0	2.3	3.9	5.6	3.0
1999	4.4	7.7	2.3	4.5	7.9	2.2	4.0	5.8	3.0
2000	4.3	7.6	2.3	4.5	7.9	2.3	3.7	5.7	2.7
2001	4.3	7.5	2.2	4.5	7.9	2.2	3.7	5.1	2.9

[a]Rates are per 100,000 and are age-adjusted to the 2000 United States standard population.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

metastatic upper tract tumors also routinely require systemic combination chemotherapy using regimens similar to those employed for TCC of the bladder.

The management approach to squamous cell carcinoma arising in the bladder or upper tracts is similar to that described for TCC. Adenocarcinomas and squamous cell carcinomas are less responsive to chemotherapy than TCCs and are more likely to present with invasive or extensive disease. Hence, prognosis following treatment of these tumors is typically not as good as that following treatment of TCC. Some patients develop adenocarcinomas arising from the urachus at the dome of the bladder. These tumors can be treated with partial cystectomy, thereby preserving the bladder and promising a reasonably good outcome (7).

PREVALENCE AND INCIDENCE

Bladder cancer is the fourth most common cancer in men and the eighth most common cancer in women in the United States (8). It was estimated that in 2006, 64,420 new cases of bladder cancer woud be diagnosed, and 13,060 people would die of the disease (8). The number of newly diagnosed cases of bladder cancer in both sexes has been steadily increasing over the past decade (Table 3). The observed increase in incidence could be due to more assiduous diagnostic workup of individuals who present with hematuria and irritative voiding symptoms. Development of guidelines for workup of microhematuria and for improved physician and patient education has also probably contributed to observed increases in detection rates.

Table 8. Inpatient stays by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	68,980	198 (191–204)	198	55,720	157 (152–163)	157	47,400	141 (136–147)	141	49,260	140 (134–145)	140
Total < 65	2,620	47 (39–55)		2,020	33 (27–39)		2,520	41 (33–48)		2,440	35 (28–41)	
Total 65+	66,360	226 (218–234)		53,700	183 (177–190)		44,880	164 (157–171)		46,820	166 (159–173)	
Age												
65–69	12,940	143 (132–155)		8,220	97 (88–107)		6,280	86 (76–95)		6,940	92 (83–102)	
70–74	15,820	208 (194–223)		12,900	167 (154–180)		10,220	146 (133–159)		8,460	122 (110–133)	
75–79	15,420	269 (250–288)		12,540	220 (203–237)		10,580	187 (171–203)		11,340	190 (174–205)	
80–84	11,980	316 (291–341)		9,700	246 (224–267)		9,460	246 (224–268)		10,140	250 (228–271)	
85–89	6,800	330 (295–365)		6,680	307 (275–340)		5,380	246 (217–276)		7,080	304 (272–336)	
90–94	2,620	314 (260–368)		2,920	325 (272–377)		2,300	254 (207–300)		2,220	233 (189–276)	
95–97	560	297 (187–407)		500	263 (160–367)		460	227 (134–320)		400	205 (115–294)	
98+	220	146 (60–233)		240	137 (59–214)		200	102 (39–166)		240	111 (48–173)	
Gender												
Male	52,020	349 (336–363)	357	41,420	272 (260–284)	277	35,200	243 (232–254)	248	37,280	242 (231–253)	247
Female	16,960	85 (79–90)	79	14,300	71 (66–76)	67	12,200	64 (59–69)	60	11,980	60 (56–65)	56
Race/ethnicity												
White	61,240	207 (200–215)	207	50,320	166 (159–172)	166	42,280	149 (142–155)	148	44,540	149 (142–155)	148
Black	4,100	138 (119–157)	132	3,580	111 (95–127)	109	3,400	110 (93–126)	108	3,020	89 (74–103)	93
Asian	…	…	…	40	24 (0–57)	12	280	89 (42–136)	102	260	55 (25–84)	55
Hispanic	…	…	…	320	80 (41–119)	85	640	91 (59–123)	94	660	83 (55–111)	91
N. American Native	…	…	…	20	55 (0–163)	110	20	37 (0–109)	37	80	120 (3.0–237)	120
Region												
Midwest	15,780	181 (168–193)	179	12,700	141 (130–152)	138	11,780	136 (125–147)	138	12,600	143 (132–155)	144
Northeast	21,840	284 (267–300)	277	17,700	231 (215–246)	228	13,080	195 (180–210)	190	12,220	177 (163–191)	172
South	22,160	181 (171–192)	185	17,720	139 (130–149)	140	16,460	133 (124–142)	135	17,660	133 (124–142)	137
West	8,520	156 (141–170)	158	7,180	139 (124–153)	144	5,500	111 (98–124)	109	6,340	117 (104–130)	114

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 9. Inpatient hospital stays for lower tract transitional cell carcinoma listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	95,972	98 (93–103)	98	85,057	81 (77–85)	81	76,720	70 (65–74)	70	72,776	63 (60–66)	63
Age												
40–54	7,120	15 (14–16)		6,450	12 (11–13)		6,269	11 (10–13)		6,497	11 (10–12)	
55–64	13,250	66 (61–70)		10,895	52 (48–56)		10,326	47 (42–51)		9,780	42 (39–45)	
65–74	31,002	175 (165–184)		26,075	143 (135–151)		22,887	128 (117–138)		20,601	116 (109–122)	
75–84	32,175	333 (314–352)		29,564	278 (265–292)		26,015	230 (217–244)		24,877	212 (201–223)	
85+	12,425	447 (418–476)		12,075	431 (404–459)		11,224	387 (359–414)		11,021	353 (332–374)	
Gender												
Male	70,750	155 (147–164)	174	62,376	128 (121–134)	145	55,792	108 (101–116)	121	52,618	98 (93–102)	109
Female	25,223	48 (45–51)	44	22,665	40 (38–43)	37	20,928	36 (33–38)	33	20,149	33 (31–35)	31
Region												
Midwest	20,664	89 (80–98)	89	18,997	16 (70–82)	75	17,465	68 (64–73)	66	16,734	63 (58–68)	64
Northeast	28,572	135 (120–149)	131	25,560	119 (106–132)	115	22,495	101 (81–121)	98	20,110	88 (80–96)	82
South	32,911	99 (91–107)	99	28,012	76 (71–81)	76	25,131	64 (60–69)	65	24,849	60 (55–66)	60
West	13,825	68 (60–75)	70	12,489	58 (53–63)	61	11,629	50 (45–55)	53	11,083	45 (41–50)	48
MSA												
Rural	14,385	54 (47–61)	50	12,323	49 (44–54)	47	10,206	39 (35–43)	36	10,564	39 (35–43)	36
Urban	81,332	114 (107–120)	117	72,578	91 (86–96)	93	66,243	79 (73–85)	81	62,162	71 (67–74)	72

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population, 40 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 10. Visits to ambulatory surgery centers by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	67,320	193 (186–199)	193	85,820	242 (235–250)	242	84,820	253 (245–261)	253	90,820	257 (250–265)	257
Total < 65	1,440	26 (20–32)		2,580	42 (35–49)		3,640	59 (50–67)		3,620	51 (44–59)	
Total 65+	65,880	224 (217–232)		83,240	284 (276–293)		81,180	297 (288–306)		87,200	309 (300–318)	
Age												
65–69	15,400	171 (159–183)		15,820	187 (174–200)		15,260	208 (193–223)		13,820	184 (170–197)	
70–74	18,100	238 (223–254)		23,380	303 (285–320)		20,280	290 (272–307)		23,080	332 (313–351)	
75–79	15,820	276 (256–295)		18,740	329 (308–350)		20,780	367 (345–389)		24,540	411 (388–434)	
80–84	10,000	264 (241–287)		16,340	414 (385–442)		15,240	396 (368–425)		15,480	381 (354–408)	
85–89	4,500	218 (190–247)		7,080	326 (292–360)		7,520	344 (310–379)		8,000	343 (310–377)	
90–94	1,500	180 (139–220)		1,620	180 (141–219)		1,760	194 (154–235)		1,960	205 (165–246)	
95–97	360	191 (103–279)		180	95 (33–157)		320	158 (81–236)		220	113 (46–179)	
98+	200	133 (51–216)		80	46 (1.1–90)		20	10 (0–30)		100	46 (5.5–87)	
Gender												
Male	47,740	320 (308–333)	322	60,740	399 (385–413)	406	60,280	416 (402–431)	422	65,700	426 (412–441)	431
Female	19,580	98 (92–104)	97	25,080	124 (117–131)	119	24,540	129 (122–136)	124	25,120	127 (120–134)	123
Race/ethnicity												
White	62,120	210 (203–218)	210	80,820	266 (258–274)	266	79,640	280 (272–289)	280	84,620	282 (274–291)	282
Black	2,000	67 (54–81)	64	3,060	95 (80–110)	96	2,940	95 (80–110)	97	3,740	110 (94–125)	113
Asian	…	…	…	180	108 (37–178)	132	400	127 (72–183)	121	440	93 (54–131)	97
Hispanic	…	…	…	280	70 (33–107)	75	540	77 (48–106)	82	640	81 (53–108)	83
N. American Native	…	…	…	40	110 (0–262)	110	20	37 (0–109)	37	20	30 (0–88)	30
Region												
Midwest	21,200	243 (228–258)	235	28,020	311 (295–327)	304	25,940	301 (284–317)	302	27,900	317 (301–334)	320
Northeast	16,140	210 (195–224)	212	21,620	282 (265–298)	281	22,380	334 (315–354)	337	22,100	320 (301–339)	317
South	22,120	181 (170–192)	183	26,900	212 (200–223)	215	27,760	224 (212–236)	224	30,940	233 (222–245)	235
West	7,820	143 (129–157)	146	9,220	178 (162–194)	183	8,620	174 (158–190)	168	9,520	176 (160–192)	171

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 11. Physician office visits by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	249,920	716	(703–728)	716	327,240	924	(910–938)	924
Total < 65	6,740	122	(109–135)		9,320	152	(138–166)	
Total 65+	243,180	828	(813–842)		317,920	1.086	1,069–1,103)	
Age								
65–69	49,720	551	(530–573)		63,080	746	(720–772)	
70–74	66,620	877	(848–907)		84,000	1,087	(1,054–1,120)	
75–79	60,460	1,053	(1,016–1,091)		75,820	1,331	(1,289–1,374)	
80–84	42,200	1,113	(1,066–1,160)		58,360	1,478	(1,425–1,531)	
85–89	18,160	881	(824–938)		28,500	1,312	(1,244–1,379)	
90–94	5,060	606	(532–681)		7,060	785	(704–867)	
95–97	820	435	(302–567)		800	422	(291–552)	
98+	140	93	(24–162)		300	171	(84–258)	
Gender								
Male	181,740	1,220	(1195–1,245)	1,233	241,280	1,585	(1,557–1,613)	1,609
Female	68,180	341	(329–352)	331	85,960	426	(413–439)	408
Race/ethnicity								
White	229,760	778	(764–792)	774	303,740	1,001	(985–1,017)	1,004
Black	9,220	311	(283–339)	302	11,360	352	(323–381)	359
Asian	…	...		…	1,580	945	(737–1,152)	1,124
Hispanic	…	...		…	2,960	741	(622–860)	666
N. American Native	…	...		…	40	110	(0–262)	165
Region								
Midwest	57,880	663	(639–687)	661	73,120	811	(785–838)	824
Northeast	66,320	861	(832–890)	868	87,680	1,143	(1,109–1,176)	1,124
South	89,680	734	(712–755)	730	114,360	900	(876–923)	897
West	33,540	613	(584–642)	613	49,380	953	(915–990)	964

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Table 11 (continued). Physician office visits by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	323,140	964	(949–978)	964	368,200	1,044	(1,029–1,059)	1,044
Total < 65	11,200	180	(165–195)		11,520	163	(150–177)	
Total 65+	311,940	1,142	(1,124–1,160)		356,680	1,264	(1,246–1,283)	
Age								
65–69	57,120	780	(751–808)		58,960	783	(755–811)	
70–74	82,980	1,185	(1,149–1,221)		89,680	1,289	(1,252–1,327)	
75–79	75,640	1,136	(1,294–1,379)		98,020	1,640	(1,595–1,686)	
80–84	57,400	1,493	(1,439–1,547)		62,300	1,534	(1,480–1,587)	
85–89	29,540	1,353	(1,284–1,421)		36,200	1,554	(1,483–1,625)	
90–94	8,060	889	(802–975)		9,200	964	(876–1,052)	
95–97	1,040	514	(375–653)		1,680	859	(676–1,043)	
98+	160	82	(25–139)		640	295	(193–397)	
Gender								
Male	235,860	1,629	(1,600–1,658)	1,656	268,560	1,742	(1712–1771)	
Female	87,280	458	(444–472)	437	99,640	502	(488–516)	
Race/ethnicity								
White	300,860	1,059	(1,042–1,076)	1,060	341,640	1,140	(1,123–1,157)	1,136
Black	10,380	335	(306–364)	331	13,040	383	(353–412)	380
Asian	2,540	809	(669–949)	643	2,040	430	(346–513)	463
Hispanic	3,520	501	(427–574)	549	3,040	382	(322–443)	393
N. American Native	40	74	(0–176)	74	360	540	(291–789)	630
Region								
Midwest	75,400	874	(846–901)	900	85,640	974	(945–1,003)	991
Northeast	82,480	1,232	(1,194–1,269)	1,221	90,880	1,315	(1,277–1,353)	1,283
South	118,740	959	(934–983)	967	133,140	1,004	(980–1,028)	1,005
West	42,980	868	(831–904)	810	55,140	1,021	(983–1,059)	1,029

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 12. Hospital outpatient visits by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	32,860	94	(90–99)	94	36,720	104	(99–108)	104
Total < 65	1,160	21	(16–26)		1,680	27	(22–33)	
Total 65+	31,700	108	(103–113)		35,040	120	(114–125)	
Age								
65–69	7,320	81	(73–89)		5,720	68	(60–75)	
70–74	7,780	102	(92–113)		10,640	138	(126–149)	
75–79	7,720	135	(121–148)		9,100	160	(145–174)	
80–84	5,380	142	(125–159)		5,540	140	(124–157)	
85–89	2,160	105	(85–125)		2,980	137	(115–159)	
90–94	1,000	120	(87–153)		960	107	(77–137)	
95–97	180	95	(33–158)		60	32	(0–67)	
98+	160	106	(33–180)		40	23	(0–54)	
Gender								
Male	23,800	160	(151–169)	163	26,780	176	(167–185)	177
Female	9,060	45	(41–49)	43	9,940	49	(45–54)	48
Race/ethnicity								
White	30,320	103	(97–108)	102	33,280	110	(104–115)	109
Black	1,760	59	(47–72)	60	1,920	60	(48–71)	63
Asian	…	...		…	40	24	(0–57)	24
Hispanic	…	...		…	360	90	(49–132)	65
N. American Native	…	...		…	0	0		0
Region								
Midwest	11,720	134	(123–145)	119	11,540	128	118–139)	125
Northeast	9,340	121	(110–132)	131	12,700	165	(153–178)	177
South	6,800	56	(50–62)	58	7,660	60	(54–66)	57
West	4,440	81	(70–92)	87	4,640	90	(78–101)	87

Continued on next page

Table 12 (continued). Hospital outpatient visits by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	31,460	94	(89–98)	94	32,700	93	(88–97)	93
Total < 65	2,100	34	(27–40)		1,380	20	(15–24)	
Total 65+	29,360	107	(102–113)		31,320	111	(106–116)	
Age								
65–69	5,400	74	(65–82)		6,020	80	(71–89)	
70–74	8,840	126	(114–138)		6,880	99	(88–109)	
75–79	6,480	114	(102–127)		8,440	141	(128–155)	
80–84	5,360	139	(123–156)		6,280	155	(138–172)	
85–89	2,920	134	(112–155)		3,100	133	(112–154)	
90–94	200	22	(8–36)		400	42	(24–60)	
95–97	160	79	(24–134)		180	92	(32–152)	
98+	0	0			20	9	(0–27)	
Gender								
Male	23,660	163	(154–173)	167	22,640	147	(138–155)	149
Female	7,800	41	(37–45)	38	10,060	51	(46–55)	49
Race/ethnicity								
White	27,120	95	(90–101)	95	28,960	97	(92–102)	97
Black	2,300	74	(61–88)	72	2,520	74	(61–87)	77
Asian	360	115	(62–167)	89	20	4	(0–12)	4.2
Hispanic	840	119	(83–156)	122	460	58	(34–82)	55
N. American Native	20	37	(0–109)	0	0	0		0
Region								
Midwest	10,120	117	(107–127)	118	11,720	133	(123–144)	133
Northeast	8,460	126	(114–138)	129	7,140	103	(93–114)	100
South	7,300	59	(53–65)	57	7,380	56	(50–61)	57
West	5,040	102	93(89–114)	99	6,260	116	(103–129)	116

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

The incidence of bladder cancer is higher in individuals over 65 years of age; it is higher in Caucasians than in African Americans, and it is lowest among Native Americans (Table 4). Based on analysis of data from the Surveillance, Epidemiology, and End Results Program (SEER), 490,458 cases of bladder cancer were recorded in 2001 (Table 5). The lifetime risk of bladder cancer is 3.5% for males and 1.13% for females (9). There appears to be regional variation in the incidence of bladder cancer, with the highest rates in the United States being observed in the Northeast (10). There are also variations in stage, grade, age at diagnosis, insurance status, and duration of symptoms between Caucasians and African Americans (11).

When considering epidemiologic data, it is important to recognize the difference between mortality, the deaths in the general population due to the specific disease, and survival, which is limited to the patient cohort with the disease. Overall, survival of patients with bladder cancer has been steadily improving over the past four decades. While much of this gain could be the result of improvements in treating low-grade/stage disease and CIS, it appears that age-adjusted death rates have declined even in patients with invasive disease. Recent estimates indicate an overall five-year survival rate of 82% for all stages combined (Table 6). Survival rates are lower in those with metastatic disease, with only 6% of patients with distant disease surviving five years. The mortality rate decreased slightly from 5.5 to 4.3 per 100,000 persons between 1975 and 2001 (Table 7). Survival is highest among Caucasian males with

Table 13. Physician office visits for lower transitional cell carcinoma listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000			
	Count	5-Year Rate	Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	3,470,336	3,303 (2,767–3,840)	661	3,307
Age				
40–54	*	*	*	
55–64	483,264	2,240 (1,395–3,085)	448	
65–74	1,288,579	7,146 (5,145–9,147)	1,429	
75+	1,499,740	11,185 (8,381–13,989)	2237	
Gender				
Male	2,426,291	4,958 (4,000–5,915)	992	5,511
Female	1,044,045	1,860 (1,301–2,419)	372	1,740
Race/ethnicity				
White	3,272,437	3,899 (3,243–4,556)	780	3,712
Other	*	*	*	*
Region				
Midwest	886,818	3,597 (2,379–4,816)	719	3,526
Northeast	1,124,935	5,174 (3,741–6,608)	1,035	5,087
South	1,002,385	2,724 (1,906–3,542)	545	2,702
West	456,198	2,086 (1,171–3,001)	417	2,251
MSA				
MSA	2,930,282	3,727 (3,075–4,379)	745	3,744
Non-MSA	540,054	2,043 (1,153–2,932)	409	2,019

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population, 40 years and older.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 14. Physician office visits for lower transitional cell carcinoma listed as any diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	Count	Rate	Age-Adjusted Rate
Total			
1992	797,128	820 (552–1,088)	820
1994	554,627	565 (385–746)	565
1996	746.759	712 (437–987)	712
1998	607,555	552 (302–802)	552
2000	764,267	665 (452–877)	665

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population, 40 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 15. Physician office visits for lower tract transitional cell carcinoma listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], rate per visits[c] (95% CI)

	1992–2000			
Physician Specialty	Count	5-Year Rate	Annualized Rate	Rate
Total	3,470,336	3,303 (2,767–3,840)	661	100,000 (83,751–116,249)
Urology	2,385,136	2,270 (1,936–2,605)	454	68,729 (58,605–78,854)
All Other	1,085,200	1,033 (618–1,448)	207	31,271 (18,707–43,835)

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US 40 years of age and above civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Rate per 100,000 adults 40+ years visits is based on estimated number of visits for lower tract TCC in NAMCS 1992–2000.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

localized disease (Table 6). This may be due to earlier presentation, better access to care, or better post-intervention social support for Caucasian patients. Currently available data are insufficient to support any conclusions in this regard. Bladder cancer patients younger than 65 years of age also tend to have better five-year survival rates, while those older than 75 tend to have the lowest survival rates. Survival rates for upper tract cancers have also been improving (12), but precise population-based estimates are not available because these cancers are often grouped with tumors of the renal parenchyma (kidney cancer).

LOWER TRACT UROTHELIAL CANCER

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

The frequency of inpatient care for lower tract urothelial cancer has decreased in both Medicare and non-Medicare populations. The decrease has been observed in both genders and in Caucasians and African Americans. The rate of inpatient stays is highest in the Northeast and among patients 80 to 89 years of age (Table 8). According to data from the Healthcare Cost and Utilization Project (HCUP), the rate of inpatient stays is also higher in urban areas (Table 9).

Outpatient Care

Ambulatory Surgery

Medicare and non-Medicare data indicate an increasing frequency of ambulatory surgical and outpatient care for patients with bladder cancer, while the frequency of inpatient care is declining correspondingly (Tables 10 and 11). The overall rate of ambulatory surgery visits by Medicare patients increased for the entire population (Table 10) and for individuals of all races with sufficient counts from which to draw conclusions. Hospital outpatient visits by Medicare patients increased from 1992 to 1995 and then began to decline (Table 12). This pattern was observed in males and in all racial groups except African Americans.

Physician Office Visits

Physician office visit rates for non-Medicare patients appear to vary by region and are higher in males and in older patients (Table 13). Nationwide, patients of all ages with bladder cancer made 764,267 visits to physicians' offices in 2000; Medicare beneficiaries made 368,200 office visits in 2001 (Tables 14 and 11). A majority of these visits (68%) were to urologists (Tables 15 and 16). SEER data suggest that the largest proportion of office visits within 12 months following diagnosis were made by patients with stage I disease, though the actual rate of visits increased concomitantly with disease stage (Table 17). There were no gender- or race-based differences in the rate of office visits, but patients 65 to 75 years of age had significantly higher rates of visits than did older individuals. Among patients with a specific bladder-cancer-related office visit within 12 months of diagnosis, 92% went to urologists, 8% went to medical oncologists, and 18% went to internists (Table 16). The proportion of patients visiting a medical oncologist increased appropriately with increasing disease stage, although only 36% of those with stage IV disease did so (Table 16). Even if it is assumed that visits to internists and physicians of unlisted specialty were visits to medical oncologists, a substantial fraction of patients with stage III and IV disease would not have visited a physician who could treat them with potentially beneficial combination systemic chemotherapy. The pattern of distribution of office visits between urologists, medical oncologists, internists, and other specialists remained fairly similar across age, gender, and racial groups (Table 16).

Physician Office-Based Diagnostic Testing/ Procedures

Commonly performed office-based procedures for the evaluation and surveillance of bladder cancer include urinalysis to identify hematuria, urine cytology, and office cystoscopy. With improved instrumentation and easier availability of flexible cystoscopes, cystoscopy is now routinely performed under local anesthesia in the office. Patients with low-stage bladder cancer (Ta, TIS, T1) require an intensive surveillance regimen that typically consists of office urinalysis, cytology, and cystoscopy at three-month intervals for the first two years, six-month intervals for the next three years, and yearly thereafter. According

Table 16. Distribution of outpatient visits for lower tract transitional cell carcinoma in the year following diagnosis, by physician specialty

	Number of patients with Lower Tract TCC**	% of patients with urology office visit	% of patients with oncology office visit	% of patients with internal medicine office visit	% of patients with radiation oncology office visit	% of patients with other specialty office visit	% of patients with unknown specialty office visit
Total	23,588	92% (92%–92%)	8% (8%–9%)	18% (18%–19%)	1% (1%–1%)	4% (4%–5%)	10% (9%–10%)
Gender							
Male	16,921	93% (92%–93%)	8% (8%–8%)	17% (16%–18%)	1% (1%–1%)	4% (4%–5%)	10% (9%–10%)
Female	6,667	91% (90%–91%)	10% (9%–10%)	21% (20%–22%)	1% (1%–2%)	5% (5%–6%)	9% (9%–10%)
Age							
65–75	11,876	93% (92%–93%)	9% (8%–9%)	18% (17%–18%)	1% (1%–1%)	5% (4%–5%)	10% (9%–10%)
76–85	9,263	92% (91%–93%)	9% (8%–9%)	18% (17%–19%)	1% (1%–2%)	5% (4%–5%)	10% (9%–10%)
86–95	2,358	90% (89%–91%)	6% (5%–7%)	19% (18%–21%)	2% (1%–2%)	4% (3%–5%)	9% (8%–11%)
96+	91	88% (81%–95%)	*	16% (9%–24%)	*	*	*
Race/ethnicity							
White	21,699	92% (92%–93%)	8% (8%–9%)	18% (17%–18%)	1% (1%–1%)	4% (4%–5%)	9% (9%–10%)
Black	883	87% (85%–89%)	11% (9%–13%)	22% (20%–25%)	1% (1%–2%)	5% (4%–7%)	17% (14%–19%)
Hispanic	164	93% (89%–97%)	*	17% (11%–23%)	*	*	13% (8%–18%)
Asian	409	92% (89%–94%)	8% (5%–10%)	24% (20%–28%)	*	5% (3%–8%)	11% (8%–14%)
N. American Native	20	*	*	*	*	*	*
Other	315	88% (84%–91%)	10% (7%–13%)	24% (19%–29%)	3% (1%–6%)	7% (4%–10%)	8% (5%–11%)
Unknown	98	85% (78%–92%)	*	22% (14%–31%)	0%	*	*
Stage							
Stage 1	17,164	94% (94%–95%)	3% (3%–3%)	14% (13%–15%)	0%	3% (2%–3%)	7% (7%–8%)
Stage 2	2,296	88% (87%–90%)	20% (18%–22%)	28% (27%–30%)	3% (3%–4%)	10% (8%–11%)	15% (13%–16%)
Stage 3	1,366	88% (86%–89%)	25% (23%–28%)	30% (28%–32%)	4% (3%–5%)	10% (8%–11%)	18% (16%–20%)
Stage 4	1,749	79% (77%–81%)	36% (34%–38%)	34% (32%–37%)	4% (3%–5%)	11% (10%–13%)	21% (19%–22%)
Unknown	1,013	88% (86%–90%)	8% (6%–10%)	18% (16%–21%)	1% (1%–2%)	4% (3%–5%)	10% (8%–12%)

*Figure does not meet standard for reliability or precision.

** Excludes 10,254 patients with no lower tract TCC related office visits in the 12 months following diagnosis.

Bladder Cancer patients 65 and older, diagnosed in 1991 though 1999, with at least 1 lower tract TCC related outpatient visit.

SOURCE: SEER, 1991–2000.

Table 17. Physician office visits for lower tract transitional cell carcinoma in the 12 months following diagnosis

	Base Population	Count of Visits	Rate per 100,000 patients with lower tract TCC
Total	33,842	141,748	418,852 (412,261–425,444)
Gender			
Male	24,492	103,481	422,509 (414,725–430,294)
Female	9,350	38,267	409,273 (396,890–421,656)
Age			
65–75	16,412	77,231	470,576 (460,215–480,938)
76–85	13,353	53,821	403,063 (393,165–412,961)
86–95	3,864	10,387	268,815 (255,314–282,316)
96+	213	309	145,070 (103,165–186,976)
Race/ethnicity			
White	30,786	129,425	420,402 (413,506–427,298)
Black	1,456	5,877	403,640 (368,101–439,179)
Hispanic	279	922	330,466 (275,938–384,994)
Asian	593	2,859	482,125 (436,469–527,780)
N. American Native	30	114	380,000 (186,494–573,506)
Other	534	2,106	394,382 (338,106–450,658)
Unknown	164	445	271,341 (210,169–332,514)
AJCC Stage			
Stage 1	23,687	95,046	401,258 (394,582–407,935)
Stage 2	3,212	15,755	490,504 (465,765–515,244)
Stage 3	1,850	9,498	513,405 (478,590–548,221)
Stage 4	2,725	16,242	596,037 (556,836–635,238)
Unknown	2,368	5,207	219,890 (200,731–239,050)

Lower tract TCC patients 65 and older, diagnosed in 1991 through 1999, with at least one CMS claim in the 12 months after diagnosis.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/, 2004.

to data from the National Ambulatory Medical Care Survey (NAMCS), 54% of patients with a diagnosis of lower tract TCC underwent urinalysis during their office visits, while 21% underwent cystoscopy (Table 18).

Data regarding urine cytology were not available in NAMCS, but cytology testing was used very infrequently in Medicare beneficiaries with bladder cancer. Although the rate of use of such testing has increased steadily over the past decade, only 3.3% of patients underwent cytology in 2001 (Table 19). The rate did not vary significantly among age groups, genders, or racial groups. There was some variation by geographic region, with the highest rates observed

Table 18. Use of specific investigations at physician office visits for lower tract transitional cell carcinoma listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], rate per visits[c] (95% CI)

	1992–2000					
	Count	5-Year Rate		Annualized Rate	Rate	
Total	3,470,336	3,303	(2,767–3,840)	661	100,000	(83,751–116,249)
with urinalysis performed	1,860,763	1,771	(1,423–2,119)	354	53,619	(43,075–64,163)
with cystoscopy performed	724,041	689	(515–863)	138	20,864	(15,594–26,134)

[a]Rate per 100,000 is based on 1992–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, demographic for relevant categories of US adult 40+ civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Rate per 100,000 adult 40+ visits is based on estimated number of visits for lower tract TCC in NAMCS 1992–2000.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

in the West and the lowest rates observed in the Northeast in 2001. Until 2001, the highest rates of urine cytology were observed in the Midwest, where rates were almost twice those of the next highest region, the South. Regional variations have not been consistent over the years. The very low frequency of cytology testing may reflect a lack of accurate documentation, the use of bladder washing as opposed to routine voided cytology, or billing to non-Medicare insurers. Regional variations may be due to differences in availability of cytopathologists and other resources or differential use of testing resources (cytology) by physicians in general as opposed to those used only by urologists (cystoscopy). In 2001, cytology rates were also lowest among African Americans.

Cystoscopy is by far the most common procedure in patients with bladder cancer. The use of cystoscopy concomitantly with an office visit by bladder cancer patients appears to be steadily increasing over time (Table 20). The rates of cystoscopy were lower among African Americans than among Caucasians, although this gap gradually narrowed over the time period analyzed. These data are consistent with those reported by Schrag et al. (13) using SEER-Medicare data. Schrag et al. observed that only 40% of all patients with non-muscle-invasive bladder cancer underwent surveillance at a frequency they considered standard, i.e., cystoscopy at each six-month interval in the first three years following initial diagnosis. They also observed that reaching 75 years of age, living in a low-income area, low-grade tumor, and higher comorbidity level were associated with less-intense surveillance. The increase in cystoscopy use has been facilitated by increased availability of flexible cystoscopic equipment. Retrograde pyelography is very infrequently performed in the office setting; rates of 436 to 663 per 100,000 Medicare patients with a bladder cancer diagnosis were noted over a 10-year period (Table 21). In the most recent three years for which data were available, there was actually a steady decline in office-performed retrograde pyelograms. This may reflect increased use of ambulatory surgery centers or hospitals for performing this procedure. The observed regional variations in the frequency of office-based ancillary diagnostic tests may also be affected by reimbursement rates, insurance payor mix, and patient demographics.

Physician Office Tests Used for Staging Evaluation

While the standard staging algorithm to evaluate extent of disease is as described earlier in this chapter, various combinations of tests can be utilized to assess stage. Evolving technology and test availability may influence the rate of usage of a particular test. The number of patients undergoing CT scanning prior to radical cystectomy has increased among Medicare beneficiaries over the four index years of observation, which span the decade from 1992 to 2001. Most of this increase was observed among Caucasians; almost no change was seen in African Americans (Table 22). Although CT is commonly used prior to surgery in those with muscle-invasive disease, the rates in Table 22 were computed per 100,000 patients with a diagnosis of bladder cancer, not just in those with invasive disease who would require additional imaging to assess disease stage. Racial variations in stage at presentation may explain variations in utilization of staging modalities. The increase in the use of CT scanning over the observation period, accompanied by a corresponding decline in the use of intravenous pyelogram after a peak in 1995, suggests that intravenous pyelograms (IVPs) may be largely being replaced by CT scans for upper tract evaluation in these patients. Medicare data indicate that magnetic resonance imaging (MRI) scanning is utilized very infrequently in staging patients with bladder cancer. While the rate of MRI scanning in patients with bladder cancer was 157 per 100,000 in 2001, the rate for CT scanning was 8,955 per 100,000. The MRI utilization rate gradually declined after a sharp increase in 1995. The frequency of utilization of bone scanning in patients with bladder cancer increased from 2.9% (2,922 per 100,000) in 1992 to 3.9% (3,928 per 100,000) in 2001. The absolute count of bone scans only in patients prior to cystectomy has also shown a gradual increase across all age groups except those 70 to 74 years of age and in all regions and all racial groups.

Outpatient VA Care

Data from the VA system indicate a decrease in the rate of affected patients from 1998 to 2003 (Table 23). More males than females with a diagnosis of lower tract were seen at VA facilities.

Table 19. Use of urine cytology in the physician office setting among Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	3,540	1,396	(1,110–1,682)		5,640	2,198	(1,858–2,537)	
Age								
65–69	740	1,508	(897–2,119)		1,440	3,216	(2,250–4,182)	
70–74	940	1,448	(913–1,982)		1,300	1,984	(1,340–2,628)	
75–79	980	1,578	(852–2,303)		1,220	1,976	(1,355–2,598)	
80–84	580	1,302	(664–1,941)		940	1,952	(1,214–2,689)	
85–89	200	865	(232–1,498)		680	2,589	(1,313–3,866)	
90–94	100	1,266	(0–2,574)		60	741	(0–1,822)	
95+	0	0			0	0		
Gender								
Male	2,780	1,542	(1,191–1,894)	1,565	4,100	2,241	(1,834–2,648)	2,252
Female	760	1,035	(553–1,518)	954	1,540	2,091	(1,476–2,706)	2,064
Race/ethnicity								
White	3,380	1,454	(1,146–1,762)	1,454	5,520	2,297	(1,937–2,658)	2,289
Black	40	402	(0–958)	201	80	846	(20–1,672)	1,057
Asian	…	...		…	0	0		0
Hispanic	…	...		…	0	0		0
N. American Native	…	...		…	0	0		0
Region								
Midwest	1,900	3,857	(2,797–4,917)	3,898	3,140	5,747	(4,516–6,977)	5,820
Northeast	240	473	(184–762)	473	380	707	(329–1,086)	782
South	1,120	1,707	(1,044–2,370)	1,646	1,340	1,906	(1,366–2,446)	1,935
West	280	959	(276–1,642)	1,027	780	2,566	(1,456–3,675)	2,237

Continued on next page.

Table 19 (continued). Use of urine cytology in the physician office setting among Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	7,920	3,117	(2,696–3,537)		8,920	3,293	(2,896–3,690)	
Age								
65–69	1,740	4,378	(3,103–5,654)		1,740	4,296	(3,037–5,556)	
70–74	2,000	3,206	(2,251–4,161)		2,060	3,318	(2,516–4,121)	
75–79	1,960	3,112	(2,322–3,902)		2,540	0		
80–84	1,420	2,878	(2,011–3,745)		1,580	2,897	(2,020–3,774)	
85–89	660	2,354	(1,324–3,384)		720	2,351	(1,334–3,369)	
90–94	120	1,263	(0–2,564)		260	2,554	(802–4,306)	
95+	20	1,266	(0–3,747)		20	1,282	(0–3,795)	
Gender								
Male	5,860	3,252	(2,743–3,761)	3,307	6,520	3,346	(2,871–3,821)	3,295
Female	2,060	2,788	(2,045–3,531)	2,625	2,400	3,157	(2,435–3,879)	3,289
Race/ethnicity								
White	7,800	3,293	(2,844–3,742)	3,301	8,540	3,383	(2,965–3,801)	3,375
Black	40	287	(0–948)	199	200	2,000	(652–3,348)	1,800
Asian	0	0		0	60	3,846	(0–9,436)	2,564
Hispanic	20	909	(0–2,691)	0	80	3,333	(0–8,485)	3,333
N. American Native	0	0		0	20	7,692	(0–22,769)	7,692
Region								
Midwest	3,280	5,793	(4,565–7,021)	5,934	2,120	3,563	(2,719–4,407)	3,496
Northeast	1,000	1,940	(1,199–2,682)	2,018	1,200	2,181	(1,418–2,944)	2,290
South	2,820	3,759	(2,894–4,624)	3,626	3,600	4,414	(3,562–5,266)	4,414
West	660	2,170	(1,351–2,988)	2,104	1,920	5,811	(4,375–7,247)	5,751

…data not available.

Based on CPT codes 88104 (cytopathology, non-OB fluids, washing/brushings, except cervical/vaginal smears with interpretation), 88106 (cytopathology, non-OB fluids, washing/brushings, filter only with interpretation), 88107 (cytopathology, non-OB fluids, washing/brushings, smear & filter with interpretation), 88108 (cytopathology, concentration technique, smears & interpretation), 88112 (cytopathology, selective cellular enhancement technique with interpretation (e.g., liquid-based slide method), except cervical or vaginal).

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with a bladder cancer diagnosis on the same claim as the procedure.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 20. Use of cystoscopy in the physician office setting among Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	125,940	48,401 (46,907–49,895)		145,820	55,105 (53,557–56,654)	
Age						
65–69	26,840	52,814 (49,269–56,359)		27,820	59,623 (55,832–63,414)	
70–74	31,800	47,605 (44,712–50,497)		37,820	55,683 (52,605–58,762)	
75–79	31,800	49,922 (46,882–52,961)		35,940	56,634 (53,437–59,831)	
80–84	22,560	49,670 (45,971–53,368)		28,420		
85–89	9,700	41,382 (36,911–45,854)		11,800	44,162 (39,731–48,592)	
90–94	2,860	35,572 (27,882–43,262)		3,400	41,063 (32,878–49,248)	
95–97	300	19,481 (7,442–31,519)		380	25,676 (13,713–37,638)	
98+	80	18,182 (0–39,121)		240	40,000 (17,762–62,238)	
Gender						
Male	86,080	46,610 (44,877–48,344)	47,293	101,700	53,867 (52,057–55,676)	54,492
Female	39,860	52,781 (49,866–55,696)	51,086	44,120	58,190 (55,206–61,174)	56,634
Race/ethnicity						
White	119,040	49,862 (48,286–51,438)	49,820	139,840	56,392 (54,778–58,005)	56,424
Black	2,080	20,635 (15,262–26,008)	19,643	2,800	29,167 (22,898–35,435)	29,375
Asian	…	…	…	320	51,613 (20,296–82,929)	51,613
Hispanic	…	…	…	400	37,736 (19,274–56,198)	37,736
N. American Native	…	…	…	0	0	0
Region						
Midwest	30,380	59,897 (56,261–63,534)	60,055	36,080	64,108 (60,608–67,608)	63,753
Northeast	34,300	65,358 (61,732–68,985)	65,739	37,760	67,573 (63,987–71,159)	66,786
South	40,060	59,190 (56,011–62,369)	59,338	47,540	64,999 (61,889–68,109)	65,819
West	20,620	67,740 (63,030–72,449)	66,294	23,900	75,347 (70,510–80,183)	75,284

Continued on next page

Table 20 (continued). Use of cystoscopy in the physician office setting among Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	151,460	57,541 (55,987–59,095)		177,100	62,815 (61,266–64,364)	
Age						
65–69	25,160	60,539 (56,531–64,547)		27,720	65,132 (61,056–69,207)	
70–74	37,500	57,853 (54,696–61,009)		41,800	64,586 (61,355–67,817)	
75–79	39,600	60,662 (57,435–63,889)		47,920	64,897 (61,836–67,958)	
80–84	30,700	60,172 (56,600–63,745)		35,340	62,527 (59,029–66,024)	
85–89	13,820	48,086 (43,915–52,258)		18,140	57,369 (53,011–61,726)	
90–94	3,940	40,871 (34,030–47,713)		5,200	49,904 (42,111–57,697)	
95–97	540	33,750 (18,179–49,321)		700	44,304 (28,612–59,995)	
98+	200	35,714 (10,584–60,845)		280	41,176 (17,599–64,754)	
Gender						
Male	105,840	56,629 (54,789–58,470)	57,432	126,100	62,167 (60,345–63,990)	62,956
Female	45,620	59,775 (56,877–62,672)	57,809	51,000	64,475 (61,537–67,413)	62,427
Race/ethnicity						
White	145,040	59,041 (57,422–60,660)	59,057	168,440	64,016 (62,405–65,628)	
Black	3,020	29,666 (23,521–35,812)	29,273	4,120	40,392 (33,353–47,431)	
Asian	520	37,143 (20,616–53,670)	31,429	680	43,590 (25,147–62,033)	
Hispanic	820	36,937 (21,901–51,973)	36,937	1,000	40,323 (26,502–54,144)	
N. American Native	20	33,333 (0–98,667)	33,333	200	83,333 (7,679–158,988)	
Region						
Midwest	37,680	63,973 (60,639–67,307)	63,803	42,620	68,411 (65,058–71,764)	68,796
Northeast	36,820	68,515 (64,913–72,117)	68,478	42,100	72,486 (68,979–75,993)	71,109
South	52,380	67,016 (63,985–70,048)	68,270	63,400	74,466 (71,522–77,410)	75,100
West	23,940	75,094 (70,391–79,797)	72,083	28,160	81,340 (76,574–86,106)	81,225

…data not available.

Based on CPT codes 52000 (cystoscopy) and 52001(cystoscopy, removal of clots).

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with a bladder cancer diagnosis on the same claim as the procedure.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 21. Use of retrograde pyelogram in the physician office setting among Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	1,340	528 (378–679)		1,700	663 (498–828)		1,340	528 (375–681)		1,180	436 (289–583)	
Age												
65–69	140	285 (74–497)		340	760 (306–1,214)		260	656 (249–1,062)		240	593 (119–1,067)	
70–74	460	709 (313–1,104)		300	485 (197–718)		300	481 (222–740)		320	517 (170–863)	
75–79	300	483 (223–742)		440	714 (366–1,061)		320	509 (217–801)		320	454 (160–747)	
80–84	300	674 (271–1,076)		320	664 (320–1,008)		380	772 (275–1,268)		180	330 (52–609)	
85–89	100	433 (54–812)		200	762 (166–1,359)		60	214 (0–456)		40	131 (0–312)	
90–94	40	506 (0–1,207)		80	988 (0–2,171)		20	211 (0–623)		80	786 (18–1,554)	
95+	0	0		20	1,370 (0–4,055)		0	0		0	0	
Gender												
Male	700	388 (243–534)	377	1,000	547 (360–733)	558	980	544 (364–725)	555	740	380 (231–530)	370
Female	640	872 (495–1,248)	899	700	950 (611–1,290)	896	360	488 (197–779)	434	440	580 (222–937)	606
Race/ethnicity												
White	1,300	559 (397–722)	568	1,640	683 (509–857)	674	1,260	533 (373–692)	533	1,080	428 (284–572)	428
Black	40	402 (0–958)	201	60	634 (0–1,350)	846	20	199 (0–588)	0	0	0	0
Asian	…	...	…	0	0	0	40	2,985 (0–8,836)	4,478	0	0	0
Hispanic	…	...	…	0	0	0	0	0	0	100	4,202 (0–10,979)	4,202
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	440	894 (459–1,329)	772	580	1,063 (572–1,554)	1,026	300	532 (199–864)	496	220	370 (99–642)	404
Northeast	140	276 (44–507)	315	420	782 (390–1,173)	707	240	466 (144–789)	427	40	73 (0–173.6)	73
South	580	883 (475–1,292)	1,005	600	853 (520–1,187)	882	660	880 (523–1,238)	854	720	885 (507–1,263)	860
West	160	548 (169–927)	479	100	329 (41–617)	329	140	461 (33–888)	592	160	485 (0–1,017)	425

…data not available.

Based on CPT codes 52005 (cystourethroscopy, with ureteral catheterization, with or without irrigation, instillation, or ureteropyelography, exclusive of radiological service) and 74420 (urography, retrograde, with or without KUB (retrograde pyelogram)).

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with a bladder cancer diagnosis on the same claim as the procedure.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 22. Staging evaluation within 4 months prior to cystectomy for Medicare beneficiaries with bladder cancer, count[a,b], rate[c]

	1992		1995		1998		2001	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
				Bone Scan				
Total[d]	620	2,922	880	3,478	960	3,954	1,000	3,928
Age								
65–69	160	1,951	300	4,087	140	2,564	200	3,300
70–74	240	4,743	360	3,797	520	5,169	280	3,955
75–79	80	1,667	180	3,600	220	3,780	240	3,593
80–84	120	5,128	20	800	60	2,564	240	4,898
85–89	0	0	20	2,041	20	5,000	40	5,405
90–94	20	3,571	0	0	0	0	0	0
95–97								
Gender								
Male	460	2,904	680	3,640	740	4,066	800	3,817
Female	160	2,974	200	3,021	220	3,618	200	4,444
Race/ethnicity								
Asian	…	…	0	0	0	0	0	0
Black	0	0	20	3,448	20	3,030	40	3,846
Hispanic	…	…	0	0	40	8,000	0	0
White	500	2,572	860	3,493	900	3,954	960	4,000
Region								
Midwest	40	635	220	2,918	320	5,096	300	3,456
Northeast	260	5,350	160	2,952	220	4,000	240	5,240
South	160	2,640	320	4,360	360	3,782	380	4,051
West	160	4,233	180	3,750	40	1,527	80	2,837
				Computed Tomography Scan				
Total[d]	880	4,147	1,720	6,798	1,740	7,166	2,280	8,955
Age								
65–69	320	3,902	440	5,995	400	7,326	500	8,251
70–74	240	4,743	720	7,595	720	7,157	560	7,910
75–79	140	2,917	360	7,200	400	6,873	660	9,880
80–84	140	5,983	200	8,000	180	7,692	500	10,204
85–89	0	0	0	0	20	5,000	60	8,108
90–94	40	7,143	0	0	20	10,000	0	0
Gender								
Male	740	4,672	1,280	6,852	1,320	7,253	1,800	8,588
Female	140	2,602	440	6,647	420	6,908	480	10,667
Race/ethnicity								
Asian	…	…	0	0	20	9,091	0	0
Black	20	4,000	100	17,241	40	6,061	60	5,769
Hispanic	…	…	0	0	80	16,000	40	33,333
White	780	4,012	1,620	6,580	1,580	6,942	2,080	8,667
Region								
Midwest	160	2,540	420	5,570	480	7,643	740	8,525
Northeast	320	6,584	340	6,273	240	4,364	460	10,044
South	320	5,281	600	8,174	780	8,193	820	8,742
West	80	2,116	360	7,500	180	6,870	260	9,220

Continued on next page

Table 22 (continued). Staging evaluation within 4 months prior to cystectomy for Medicare beneficiaries with bladder cancer, count[a,b], rate[c]

	1992		1995		1998		2001	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
				Intravenous Pyelogram				
Total[d]	280	1,320	460	1,818	240	988	220	864
Age								
65–69	100	1,220	160	2,180	40	733	60	990
70–74	100	1,976	160	1,688	100	994	60	847
75–79	80	1,667	100	2,000	80	1,375	40	599
80–84	0	0	40	1,600	20	855	20	408
85–89	0	0	0	0	0	0	40	5,405
90–94	0	0	0	0	0	0	0	0
Gender								
Male	240	1,515	380	2,034	180	989	200	954
Female	40	743	80	1,208	60	987	20	444
Race/ethnicity								
Asian	…	…	0	0	0	0	0	0
Black	0	0	20	3,448	20	3,030	20	1,923
Hispanic	…	…	0	0	0	0	0	0
White	280	1,440	440	1,787	220	967	200	833
Region								
Midwest	40	635	120	1,592	80	1,274	40	461
Northeast	40	823	80	1,476	40	727	60	1,310
South	140	2,310	160	2,180	120	1,261	100	1,066
West	60	1,587	100	2,083	0	0	20	709
				Magnetic Resonance Imaging				
Total[d]	40	189	100	395	40	165	40	157
Age								
65–69	40	488	0	0	20	366	0	0
70–74	0	0	20	211	0	0	20	282
75–79	0	0	20	400	20	344	0	0
80–84	0	0	0	0	0	0	20	408
85–89	0	0	60	6,122	0	0	0	0
90–94	0	0	0	0	0	0	0	0
Gender								
Male	40	253	100	535	20	110	40	191
Female	0	0	0	0	20	329	0	0
Race/ethnicity								
Asian	…	…	0	0	0	0	0	0
Black	0	0	0	0	0	0	0	0
Hispanic	…	…	0	0	20	4,000	0	0
White	20	103	100	406	20	88	40	167
Region								
Midwest	0	0	20	265	0	0	0	0
Northeast	0	0	20	369	0	0	20	437
South	40	660	60	817	20	210	0	0
West	0	0	0	0	0	0	20	709

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table. Counts were too low to produce reliable CIs.

[b]Includes cystectomies performed in May–December of each year.

[c]Rate per 100,000 person months (persons are Medicare beneficiaries 65+ years with bladder cancer).

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 23. VA users with a diagnosis of transitional cell carcinoma, 1998–2003, count, rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	13,752	460	14,014	431	14,128	404	14,749	378	15,189	351	15,958	345
Age												
40–44	142	55	122	47	137	53	98	38	88	34	84	32
45–54	1,278	149	1,195	140	1,152	135	1,122	131	981	115	965	113
55– 64	2,816	442	2,607	409	2,410	378	2,184	342	2,021	317	1,910	299
65–74	6,563	674	5,973	613	5,299	544	4,751	488	4,317	443	4,219	433
75–84	5,575	794	5,103	727	4,671	665	4,191	597	3,812	543	3,691	526
85+	458	717	461	721	459	719	410	643	368	577	332	520
Gender												
Male	13,629	469	13,883	441	13,994	414	14,601	386	15,048	360	15,820	354
Female	123	140	131	133	134	123	148	120	141	102	138	92
Race/Ethnicity												
White	11,865	584	12,223	546	12,311	502	12,836	463	13,025	430	13,253	428
Black	1,294	307	1,262	287	1,245	275	1,217	263	1,219	259	1,210	259
Hispanic	204	257	185	222	195	225	210	228	240	251	235	248
Other	94	235	106	249	105	235	110	232	127	260	108	224
Unknown	295	70	238	53	272	60	376	71	578	86	1,152	126
Insurance Status												
No insurance/ self-pay	8,183	387	8,162	360	7,566	337	7,044	309	6,947	293	6,805	288
Medicare	1,914	738	2,694	677	4,020	607	5,628	560	6,326	498	7,325	482
Medicaid	9	447	11	427	14	380	23	376	29	334	29	300
Private Insurance/HMO	3,601	597	3,090	548	2,459	442	1,978	339	1,807	282	1,713	248
Other Insurance	45	412	57	333	69	295	72	265	73	236	85	233
Unknown	0	0	0	0	0	0	4	223	7	258	1	61
Region												
Eastern	2,122	478	2,160	447	2,260	426	2,442	372	2,744	363	2,788	357
Central	2,506	482	2,465	428	2,372	391	2,413	348	2,702	312	3,151	308
Southern	5,258	463	5,337	432	5,617	413	6,021	388	6,130	351	6,499	344
Western	3,866	433	4,052	425	3,879	389	3,873	385	3,613	377	3,520	378

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Emergency Room Care

The rate of emergency room care for bladder cancer patients has declined in all regions, for all races, and for both genders. The decline has been steady in those over 65 years of age, but it has not been consistent for those under 65. The rate of emergency room care is higher for individuals over 80 years of age (Table 24).

Treatment of Bladder Cancer and Additional Procedures Accompanying Tumor Resection

The average annualized rate of transurethral surgery in Medicare patients with a diagnosis of bladder cancer is 51% (Table 25). This rate is consistent across genders, geographic regions, and races. It varies between 46% in the youngest age group (65–69 years of age) and 60% in those 90 to 94. The rate was fairly constant over the four years studied. Data from the SEER program indicate that a majority of patients undergo transurethral resection following their initial diagnosis of bladder cancer. This could be a repeat primary resection or resection of recurrent tumors (Table 26). About 20% of patients do not undergo any further surgery, while 8% go on to receive cystectomy. Rates of no further surgery were higher in men, in individuals under 65 years of age, in non-Caucasians, and in those with stage I and stage IV disease.

An annual average of 18,607 per 100,000 Medicare patients with a bladder cancer diagnosis underwent

Table 24. Emergency room visits by Medicare beneficiaries with lower tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	3,860	11 (9–13)	11	2,800	7.9 (7–9)	7.9	2,520	7.5 (6–9)	7.5	1,700	4.8 (4–6)	4.8
Total < 65	80	1.4 (0–2.9)		200	3.3 (1–5)		80	1.3 (0–3)		220	3.1 (1–5)	
Total 65+	3,780	13 (11–15)		2,600	8.9 (7–10)		2,440	8.9 (7–10)		1,480	5.2 (4–6)	
Age												
65–69	1,140	13 (9–16)		660	7.8 (5–10)		480	6.6 (4–9)		360	4.8 (3–7)	
70–74	600	7.9 (5–11)		680	8.8 (6–12)		440	6.3 (4–.9)		300	4.3 (2–7)	
75–79	660	11 (8–15)		540	9.5 (6–13)		520	9.2 (6–13)		300	5.0 (3–8)	
80–84	840	22 (15–29)		480	12 (7–17)		480	12 (8–18)		300	7.4 (4–11)	
85–89	420	20 (12–29)		200	9.2 (4–15)		320	15 (8–22)		160	6.9 (2–12)	
90–94	120	14 (3–26)		40	4.4 (0–11)		160	18 (5–30)		40	4.2 (0–10)	
95–97	0	0		0	0		20	9.9 (0–29)		0	0	
98+	0	0		0	0		20	10 (0–30)		20	9.2 (0–27)	
Gender												
Male	2,660	18 (15–21)	20	1,900	12 (10–15)	12	1,740	12 (10–14)	13	1,320	8.6 (7–11)	8.6
Female	1,200	6.0 (5–8)	4.5	900	4.5 (3–6)	4.5	780	4.1 (3–5)	3.3	380	1.9 (1–3)	1.9
Race/ethnicity												
White	3,520	12 (10–14)	12	2,540	8.4 (7–10)	8.2	2,380	8.4 (7–10)	8.2	1,540	5.1 (4–6)	5.1
Black	300	10 (5–15)	8.8	220	6.8 (3–11)	8.1	100	3.2 (0–6)	3.9	100	2.9 (0–6)	2.9
Asian	…	...	…	20	12 (0–35)	12	0	0	0	0	0	0
Hispanic	…	...	…	0	0	0	20	2.8 (0–8)	5.7	20	2.5 (0–7)	2.5
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	1,400	16 (12–20)	13	660	7.3 (5–10)	6.9	1,060	12 (9–16)	13	560	6.4 (4–9)	6.6
Northeast	600	7.8 (5–11)	8.0	800	10 (7–14)	10	580	8.7 (6–12)	6.6	380	5.5 (3–8)	4.9
South	1,640	13 (11–16)	16	1,080	8.5 (6–11)	9.0	620	5.0 (3–7)	5.3	620	4.7 (3–6)	4.8
West	220	4.0 (2–6)	2.2	260	5.0 (2–8)	5.0	240	4.8 (2–8)	5.2	140	2.6 (1–5)	1.9

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 25. Use of transurethral surgery by Medicare beneficiaries with bladder cancer, 1992–2001 (merged), count[a], rate[b], annualized rate[c], age-adjusted rate[d]

	1992–2001			
	Count	4-Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[e]	408,460	202,589	50,647	
Gender				
Male	292,580	201,197	50,299	204,085
Female	115,880	206,192	51,548	198,683
Age				
65–69	65,800	185,144	46,286	
70–74	98,060	188,504	47,126	
75–79	99,720	210,557	52,639	
80–84	79,020	211,396	52,849	
85–89	45,380	216,095	54,024	
90–94	16,000	240,240	60,060	
95–97	2,740	232,203	58,051	
98+	1,100	229,167	57,292	
Race/ethnicity				
White	376,640	200,960	50,240	200,384
Black	18,440	222,169	55,542	224,096
Asian	1,180	218,519	54,630	218,519
Hispanic	2,200	239,130	59,783	239,130
Region				
Midwest	109,900	271,492	67,873	268,923
Northeast	107,040	266,401	66,600	264,759
South	138,460	263,132	65,783	266,743
West	51,160	245,019	61,255	243,966

Based on CPT codes 52224, 52234, 52235, 52240 (cystourethroscopy, with fulguration (including cryosurgery or laser surgery) or treatment of minor, small, medium or large lesion(s) with or without biopsy and ICD-9 codes 57.4 (transurethral) excision or destruction of bladder cancer, 57.49 (other transurethral excision or destruction of lesion or tissue of bladder.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries with bladder cancer.

[c]Average annualized rate per year.

[d]Age-adjusted to year 1995.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the total.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

intravesical therapy (Table 27). The annualized rates were higher in Caucasians and Asians and lowest among African Americans and Hispanics. Rates of intravesical therapy did not vary greatly by age or region but were lower in the Midwest and Northeast. Over the four years studied, the rate of intravesical therapy ranged from 17,434 to 20,915 per 100,000 Medicare patients with bladder cancer, with the highest rate observed in the most recent year analyzed (2001) (Table 28). Prior reports indicate that several factors influence the use of intravesical therapy, including disease stage and grade, year of physician training, age of patient, lack of comorbidity, and low or intermediate disease risk category (14, 15).

SEER data indicate that the rate of cystectomy in patients with newly diagnosed bladder cancer has not changed significantly over the 10-year period from 1990 to 1999 (Table 29), ranging from 67 to 91 per 1,000 per year. The cystectomy rate is age-sensitive, with the lowest rates consistently being observed in those over 80 years of age. Although the rate of cystectomy in some years is lower among African Americans, the difference is not significant, and the trend is not consistent. The highest rates were observed among patients with stage III and IV disease, but this may be due to the SEER's use of pathologic rather than clinical staging. Many of the individuals with high-stage disease could have undergone a radical cystectomy if they had been at a lower clinical stage and had muscle-invasive disease (stage II). This is often the case in bladder cancer: clinical staging is notorious for underestimation of disease extent. Independent analysis of SEER data suggests that age, stage, and geographic region are the most influential factors dictating whether a patient is a candidate for cystectomy (16).

Historically, radical cystectomy entailed removal of the urethra during the same procedure or in a staged procedure which shortly followed it. However, perhaps in response to data demonstrating low rates of urethral recurrence, urethrectomy is becoming an infrequent procedure in male patients undergoing radical cystectomy. SEER data suggests that urethrectomy is performed in approximately 3% of men who undergo radical cystectomy as a presumed planned procedure (defined as performed within 6 weeks of the date of the radical cystectomy). A further 3% of these men undergo urethrectomy 6 weeks or later, possibly due to detection of recurrence (Table 30).

Types of Urinary Diversion

The frequency of ileal conduit urinary diversion over the 10-year period from 1992 to 2001 averaged 2,433 per 100,000 Medicare patients with bladder cancer per year (Table 31). These data suggest that the rate has not changed greatly, although a slight upturn was observed in the most recent two years studied, when the highest rates were recorded (2,544 and 2,554 per 100,000 in 1998 and 2001) (Table 32). Rates of ileal conduit use did not differ significantly by gender. A decline in ileal conduit usage was also noted in patients 70 to 74 years of age in 2001 compared with prior years and other age groups. While the overall rate of ileal conduit usage per 100,000 patients with bladder cancer has not changed dramatically, there

Table 26. Use of treatments in patients newly diagnosed with bladder cancer within 12 months of diagnosis, 1990–1999, rate[a]

	Cystectomy			Transurethral Surgery			No Surgery		
	Count	Rate		Count	Rate		Count	Rate	
Total	3,051	80	(78–83)	48,305	1,272	(1,262–1,283)	7,577	200	(196–204)
Age									
Under 65	99	89	(72–105)	1,167	1,046	(985–1,106)	352	315	(288–343)
65–69	861	117	(110–124)	9,151	1,242	(1,218–1,267)	1,612	219	(209–228)
70–74	932	101	(95–107)	11,637	1,261	(1,240–1,282)	1,907	207	(198–215)
75–79	767	87	(81–93)	11,339	1,281	(1,260–1,303)	1,758	199	(190–207)
80+	392	34	(31–38)	15,011	1,316	(1,297–1,335)	1,948	171	(164–178)
Gender									
Male	2,291	82	(79–85)	35,451	1,266	(1,254–1,279)	5,789	207	(202–212)
Female	760	76	(71–81)	12,854	1,289	(1,269–1,309)	1,788	179	(172–187)
Race/ethnicity									
White	2,700	80	(77–82)	43,841	1,292	(1,281–1,303)	6,451	190	(186–194)
Black	136	91	(76–106)	1,824	1,222	(1,167–1,277)	363	243	(221–265)
Hispanic	88	75	(60–90)	1,217	1,036	(977–1,094)	362	308	(282–335)
Other	127	93	(77–108)	1,423	1,039	(990–1,089)	401	293	(269–317)
Stage									
Localized	722	24	(22–26)	38,673	1,295	(1,283–1,307)	6,150	206	(201–211)
Regional	2,329	287	(277–297)	9,632	1,188	(1,166–1,209)	1,427	176	(168–184)
AJCC Stage									
Stage 1	722	24	(22–26)	38,673	1,295	(1,283–1,307)	6,150	206	(201–211)
Stage 2	746	194	(181–206)	5,130	1,333	(1,300–1,366)	610	158	(147–170)
Stage 3	857	380	(360–400)	2,424	1,075	(1,040-1,111)	394	175	(193–190)
Stage 4	726	362	(341–383)	2,078	1,035	(995–1,075)	423	211	(193–229)

[a]Rate per 1,000 bladder cancer patients. Rates > 1,000 denote > 1 procedure per patient.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/, 2004.

Table 27. Use of bladder instillation of anticarcinogenic agent in Medicare beneficiaries with bladder cancer, 1992–2001 (merged), count[a], rate[b], annualized rate[c], age-adjusted rate[d]

	1992–2001			
	Count	4-Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[e]	150,060	74,427	18,607	
Gender				
Male	105,220	72,356	18,089	72,810
Female	44,840	79,786	19,947	78,612
Age				
65–69	25,340	71,300	17,825	
70–74	38,420	73,856	18,464	
75–79	39,200	82,770	20,693	
80–84	27,880	74,585	18,646	
85–89	14,120	67,238	16,810	
90–94	4,000	60,060	15,015	
95–97	460	38,983	9,746	
98+	280	58,333	14,583	
Race/ethnicity				
White	141,140	75,307	18,827	74,912
Black	4,920	59,277	14,819	62,410
Asian	460	85,185	21,296	85,185
Hispanic	520	56,522	14,131	54,348
Region				
Midwest	36,040	89,032	22,258	89,081
Northeast	37,220	92,633	23,158	92,982
South	55,240	104,979	26,245	105,929
West	20,940	100,287	25,072	97,126

Based on CPT code 51720 (bladder instillation of anticarcinogenic agent).
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries with bladder cancer.
[c]Average annualized rate per year.
[d]Age-adjusted to year 1995.
[e]Persons of other races, unknown race and ethnicity, and other region are included in the total.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

has been a steady increase in the actual number of ileal conduits used—from 4,520 in 1992 to 5,260 in 2001. This may be an indirect indicator of an increase in the actual number of cystectomies being performed in bladder cancer patients.

The annualized rate of neobladder or continent diversion was 370 per 100,000 Medicare patients with a diagnosis of bladder cancer (Table 33). This is about 85% lower than the usage rate of ileal conduits in this population. To ensure that all types of continent diversions and neobladders were captured in this analysis, an exhaustive set of CPT and ICD codes was used to identify such procedures. While a small increase was observed in the rate of neobladder/continent diversions in 1998, the rate in 2001 had returned to levels comparable to those observed in prior years (Table 34). As expected, the rate is highest among the younger patients in the Medicare population. The rate of neobladder/continent diversions was consistently lowest in the Northeast, and no change was evident in regional variation over the years studied (Table 34). No significant differences by gender or race were observed. A multivariate analysis of SEER data suggested that several factors affect the decision to use diversion, particularly neobladder reconstruction (17). These factors included patient age, geographic region, patient education level, and year of surgery (Table 35). Interestingly, patient comorbidity and race/ethnicity were not predictive of neobladder diversion.

Table 28. Use of bladder instillation of anticarcinogenic agent in Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
Group	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	34,240	17,434 (16,683–18,184)		37,680	18,689 (17,928–19,449)	
Gender						
Male	23,140	16,300 (15,441–17,160)	16,427	25,060	17,233 (16,365–18,101)	17,439
Female	11,100	20,389 (18,876–21,903)	20,022	12,620	22,456 (20,913–23,998)	21,922
Age						
65–69	6,980	18,349 (16,609–20,089)		6,680	18,796 (16,978–20,613)	
70–74	8,660	17,404 (15,914–18,893)		10,700	20,569 (19,016–22,122)	
75–79	8,640	18,023 (16,483–19,562)		9,080	19,172 (17,587–20,758)	
80–84	5,600	16,064 (14,340–17,788)		6,960	18,620 (16,854–20,385)	
85–89	3,100	17,299 (14,821–19,777)		3,220	15,333 (13,152–17,514)	
90–94	980	15,170 (11,254–19,087)		760	11,411 (8,003–14,820)	
95–97	160	14,035 (5,000–23,070)		60	5,085 (0–10,678)	
98+	40	14,286 (0–32,500)		100	20,833 (4,583–37,083)	
Race/ethnicity						
White	32,080	17,900 (17,106–18,694)	17,799	35,500	18,941 (18,148–19,735)	18,867
Black	1,020	12,028 (8,927–15,130)	12,972	1,240	14,940 (11,506–18,373)	16,627
Asian	…	…	…	140	25,926 (9,444–42,407)	25,926
Hispanic	…	…	…	180	19,565 (8,152–30,978)	15,217
N. American Native	…	…	…	0	0	0
Region						
Midwest	8,280	22,785 (20,856–24,714)	23,060	8,720	21,542 (19,750–23,333)	21,196
Northeast	8,640	24,215 (22,228–26,202)	24,215	9,900	24,639 (22,755–26,523)	24,788
South	12,960	27,955 (26,128–29,782)	28,343	13,220	25,124 (23,466–26,781)	25,428
West	4,220	21,865 (19,259–24,472)	20,622	5,760	27,586 (24,875–30,297)	27,011

Continued on next page

Table 28 (continued). Use of bladder instillation of anticarcinogenic agent in Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998			2001		
Group	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	35,060	17,910 (17,150–18,669)		43,080	20,915 (20,129–21,700)	
Gender						
Male	25,380	18,139 (17,236–19,042)	18,096	31,640	21,076 (20,154–21,999)	21,316
Female	9,680	17,335 (15,931–18,739)	17,443	11,440	20,480 (18,983–21,976)	19,835
Age						
65–69	5,360	17,335 (15,450–19,221)		6,320	20,295 (18,298–22,293)	
70–74	8,880	18,309 (16,769–19,849)		10,180	21,378 (19,731–23,024)	
75–79	9,540	19,933 (18,333–21,534)		11,940	22,326 (20,748–23,904)	
80–84	6,760	17,922 (16,190–19,653)		8,560	20,767 (19,015–22,518)	
85–89	3,200	14,815 (12,694–16,935)		4,600	19,726 (17,440–22,011)	
90–94	1,060	14,286 (10,728–17,844)		1,200	16,129 (12,392–19,866)	
95–97	140	10,769 (3,231–18,308)		100	8,475 (1,356–15,593)	
98+	60	13,636 (0–27,954)		80	13,793 (1,207–26,379)	
Race/ethnicity						
White	33,080	18,256 (17,461–19,051)	18,212	40,480	21,178 (20,359–21,997)	21,105
Black	1,360	15,668 (12,247–19,090)	15,899	1,300	15,550 (12,081–19,019)	15,311
Asian	80	6,667 (333–13,000)	6,667	240	21,429 (10,714–32,143)	19,643
Hispanic	140	8,140 (2,384–13,895)	8,140	200	10,638 (4,415–16,862)	11,702
N. American Native	0	0	0	0	0	0
Region						
Midwest	8,300	19,933 (18,216–21,650)	19,741	10,740	24,712 (22,899–26,526)	25,173
Northeast	9,040	23,132 (21,262–25,003)	23,234	9,640	23,861 (22,002–25,720)	23,960
South	12,900	23,696 (22,098–25,294)	23,953	16,160	27,474 (25,860–29,087)	27,236
West	4,700	23,039 (20,456–25,623)	22,745	6,260	28,663 (25,980–31,346)	28,114

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with bladder cancer.

[c]Age-adjusted to year 2001.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 29. Use of cystectomy in patients newly diagnosed with bladder cancer within 12 months of diagnosis, count, rate[a]

	1990			1991			1992			1993			1994		
	Count	Rate		Count	Rate		Count	Rate		Count	Rate		Count	Rate	
Total	206	74	(64–83)	249	84	(74–94)	338	87	(79–96)	336	86	(77–95)	354	91	(82–100)
Age															
Under 65	4	56	(1–111)	10	105	(42–168)	12	109	(50–168)	12	104	(48–161)	14	131	(66–196)
65–69	61	98	(75–122)	73	113	(89–138)	109	132	(109–155)	112	134	(111–157)	103	129	(106–153)
70–74	64	95	(73–117)	81	111	(88–133)	104	108	(88–128)	87	91	(73–110)	112	115	(95–135)
75–79	50	79	(58–100)	61	87	(66–108)	80	89	(70–128)	85	99	(79–119)	80	91	(72–110)
80+	27	34	(21–46)	24	30	(18–42)	33	31	(21–41)	40	35	(25–46)	45	40	(28–51)
Gender															
Male	162	78	(66–89)	183	82	(71–93)	254	89	(79–100)	249	87	(77–98)	266	92	(82–103)
Female	44	61	(44–79)	66	89	(68–109)	84	83	(66–100)	87	84	(67–101)	88	87	(70–105)
Race/ethnicity															
White	190	74	(64–84)	227	82	(72–93)	304	87	(78–96)	294	84	(75–94)	316	91	(81–101)
Black	9	90	(33–147)	9	86	(31–140)	11	83	(36–131)	16	102	(54–150)	12	83	(38–129)
Hispanic	1	16	(0–47)	2	38	(0–93)	8	63	(20–107)	13	103	(49–157)	13	94	(45–143)
Other	6	86	(18–153)	11	164	(73–255)	15	130	(68–193)	13	102	(49–156)	13	96	(46–146)
Stage															
Localized	53	24	(18–30)	65	27	(21–34)	78	26	(20–32)	85	28	(22–34)	71	24	(18–29)
Regional	153	260	(225–296)	184	303	(266–339)	260	304	(273–335)	251	297	(266–328)	283	324	(293–355)
AJCC Stage															
Stage 1	53	24	(18–30)	65	27	(21–34)	78	26	(20–32)	85	28	(22–34)	71	24	(18–29)
Stage 2	41	161	(115–206)	62	210	(163–257)	87	215	(175–256)	86	203	(164–241)	96	229	(189–270)
Stage 3	65	365	(294–437)	57	396	(315–477)	94	387	(325–449)	82	404	(336–472)	105	432	(369–495)
Stage 4	47	303	(230–376)	65	385	(311–459)	79	380	(313–446)	83	381	(316–446)	82	389	(322–455)

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Table 29 (continued). Use of cystectomy in patients newly diagnosed with bladder cancer within 12 months of diagnosis, count, rate[a]

	1995			1996			1997			1998			1999		
	Count	Rate		Count	Rate		Count	Rate		Count	Rate		Count	Rate	
Total	359	89	(81–98)	311	77	(69–86)	324	79	(71–87)	283	67	(60–75)	291	69	(62–77)
Age															
Under 65	12	90	(41–139)	7	61	(17–105)	11	89	(38–141)	7	63	(17–109)	10	74	(29–119)
65–69	113	141	(117–165)	91	116	(94–138)	81	115	(91–138)	58	62	(62–102)	60	93	(71–116)
70–74	113	112	(93–132)	88	94	(75–112)	105	103	(84–121)	96	96	(78–115)	82	85	(67–103)
75–79	75	85	(67–104)	92	97	(78–116)	80	85	(67–103)	76	73	(57–89)	88	82	(65–98)
80+	46	38	(28–49)	33	27	(18–36)	47	36	(26–46)	46	34	(24–43)	51	37	(27–47)
Gender															
Male	274	94	(84–105)	230	78	(68–87)	244	81	(72–91)	216	69	(60–78)	213	69	(60–78)
Female	85	77	(61–92)	81	76	(60–92)	80	73	(58–89)	67	62	(48–76)	78	71	(56–86)
Race/ethnicity															
White	323	90	(81–99)	267	75	(60–83)	286	79	(70–88)	242	65	(57–73)	251	69	(61–77)
Black	12	78	(35–122)	21	128	(76–180)	19	104	(60–149)	16	99	(52–145)	11	57	(24–90)
Hispanic	11	87	(37–137)	11	83	(36–131)	9	66	(24–108)	11	83	(35–130)	9	64	(23–105)
Other	13	86	(41–131)	12	82	(37–127)	10	66	(26–106)	14	74	(36–111)	20	93	(54–132)
Stage															
Localized	86	27	(22–33)	87	27	(21–33)	69	22	(17–27)	69	21	(16–25)	59	18	(13–22)
Regional	273	320	(288–351)	224	282	(251–313)	255	274	(246–303)	214	248	(219–277)	232	257	(299–286)
AJCC Stage															
Stage 1	86	27	(22–33)	87	27	(21–33)	69	22	(17–27)	69	21	(16–25)	59	18	(13–22)
Stage 2	92	215	(176–254)	73	192	(152–232)	91	207	(169–245)	56	146	(110–181)	62	148	(114–182)
Stage 3	97	441	(375–507)	80	376	(310–441)	91	345	(287–402)	88	327	(271–384)	98	354	(297–410)
Stage 4	84	408	(340–475)	71	353	(287–420)	73	324	(263–386)	70	332	(268–396)	72	353	(287–419)

[a]Rate per 1,000 patients with bladder cancer.
SOURCE: SEER, 1990–1999.

Table 30. Frequency and timing of urethrectomy in male SEER registry-identified Medicare beneficiaries undergoing radical cystectomy

Radical Cystectomy only	2,957
Radical Cystectomy and urethrectomy within 6 weeks	103
Radical Cystectomy and late urethrectomy (6 weeks or later)	92

Source: SEER-Medicare database, 1991–2002.

Table 31. Use of ileal conduit in Medicare beneficiaries with bladder cancer, 1992–2001 (merged), count[a], rate[b], annualized rate[c], age-adjusted rate[d]

	1992–2001			
	Count	4-Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[e]	19,620	9,731	2,433	
Age				
65–69	4,600	12,943	3,236	
70–74	6,000	11,534	2,884	
75–79	5,100	10,769	2,692	
80–84	2,980	7,972	1,993	
85–89	740	3,524	881	
90–94	140	2,102	526	
95–97	0	0	0	
98+	0	0	0	
Gender				
Male	13,640	9,380	2,345	9,641
Female	5,980	10,641	2,660	9,929
Race/ethnicity				
White	17,860	9,529	2,382	9,508
Black	920	11,084	2,771	10,843
Asian	120	22,222	5,556	22,222
Hispanic	140	15,217	3,804	13,043
Region				
Midwest	5,720	14,130	3,533	13,933
Northeast	4,540	11,299	2,825	11,000
South	6,560	12,467	3,117	12,923
West	2,700	12,931	3,233	12,548

Based on CPT codes 51590 (Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis), 51595 (Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes), ICD-9 codes 56.5 (cutaneous uretero-ileostomy), and 56.51 (formation of cutaneous uretero-ileostomy).

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries with bladder cancer.

[c]Average annualized rate per year.

[d]Age-adjusted to year 1995.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the total.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 32. Use of ileal conduit in Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	4,520	2,301 (2,005–2,598)		4,860	2,410 (2,111–2,710)	
Age						
65–69	1,260	3,312 (2,508–4,117)		1,240	3,489 (2,636–4,342)	
70–74	1,140	2,291 (1,702–2,880)		1,680	3,230 (2,551–3,908)	
75–79	1,140	2,378 (1,769–2,987)		1,120	2,365 (1,753–2,977)	
80–84	760	2,180 (1,495–2,866)		560	1,498 (947–2,049)	
85–89	140	781 (206–1,356)		220	1,048 (433–1,662)	
90+	60	929 (0–1,981)		20	300 (0–886)	
Gender						
Male	3,060	2,156 (1,817–2,494)	2,226	3,160	2,173 (1,838–2,508)	2,201
Female	1,460	2,682 (2,076–3,288)	2,498	1,700	3,025 (2,391–3,658)	2,918
Race/ethnicity						
White	4,060	2,265 (1,957–2,573)	2,243	4,580	2,444 (2,131–2,756)	2,444
Black	160	1,887 (590–3,184)	1,887	240	2,892 (1,277–4,506)	2,651
Asian	…	…	…	0	0	0
Hispanic	…	…	…	0	0	0
N. American Native	…	…	…	0	0	0
Region						
Midwest	1,200	3,302 (2,479–4,125)	3,247	1,520	3,755 (2,927–4,583)	3,656
Northeast	1,260	3,531 (2,674–4,389)	3,419	1,080	2,688 (1,981–3,395)	2,638
South	1,380	2,977 (2,284–3,669)	3,106	1,440	2,737 (2,113–3,360)	2,775
West	660	3,420 (2,275–4,565)	3,420	800	3,831 (2,668–4,995)	3,831

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	4,980	2,544 (2,232–2,856)		5,260	2,554 (2,249–2,859)	
Age						
65–69	1,020	3,299 (2,409–4,188)		1,080	3,468 (2,559–4,377)	
70–74	1,780	3,670 (2,922–4,419)		1,400	2,940 (2,262–3,618)	
75–79	1,240	2,591 (1,954–3,228)		1,600	2,992 (2,347–3,637)	
80–84	720	1,909 (1,291–2,527)		940	2,280 (1,635–2,926)	
85–89	160	741 (231–1,250)		220	943 (390–1,497)	
90+	40	539 (0–1,280)		20	269 (0–793)	
Gender						
Male	3,460	2,473 (2,109–2,837)	2,544	3,960	2,638 (2,276–3,000)	2,651
Female	1,520	2,722 (2,119–3,326)	2,543	1,300	2,327 (1,769–2,886)	2,220
Race/ethnicity						
White	4,400	2,428 (2,111–2,745)	2,406	4,820	2,522 (2,207–2,836)	2,522
Black	320	3,687 (1,912–5,461)	3,917	200	2,392 (933–3,852)	2,153
Asian	60	5,000 (0–10,500)	5,000	60	5,357 (0–11,250)	5,357
Hispanic	60	3,488 (0–7,384)	3,488	80	4,255 (160–8,351)	3,191
N. American Native	0	0	0	0	0	0
Region						
Midwest	1,440	3,458 (2,673–4,244)	3,410	1,560	3,590 (2,807–4,372)	3,636
Northeast	1,060	2,712 (1,993–3,431)	2,610	1,140	2,822 (2,099–3,545)	2,723
South	1,820	3,343 (2,667–4,019)	3,490	1,920	3,264 (2,622–3,907)	3,332
West	620	3,039 (1,985–4,093)	2,745	620	2,839 (1,854–3,823)	2,747

…data not available.

Based on CPT codes 51590 (Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis), 51595 (Cystectomy, complete, with ureteroileal conduit or sigmoid bladder, including intestine anastomosis; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes), ICD-9 codes 56.5 (cutaneous uretero-ileostomy), and 56.51 (formation of cutaneous uretero-ileostomy).

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with bladder cancer.

[c]Age-adjusted to year 2001.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, and 2001.

Table 33. Use of neobladder/continent diversion in Medicare beneficiaries with bladder cancer, 1992–2001 (merged), count[a], rate[b], annualized rate[c], age-adjusted rate[d]

	1992–2001		
	4-Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[e]	1,478	370	
Age			
65–69	2,589	647	
70–74	1,769	442	
75–79	1,605	401	
80–84	803	201	
85–89	190	48	
90–94	300	75	
Gender			
Male	1,417	354	1,403
Female	1,637	409	1,637
Race/ethnicity			
White	1,441	360	1,451
Black	1,687	422	1,205
Asian	3,704	926	3,704
Hispanic	4,348	1,087	4,348
Region			
Midwest	2,026	507	2,174
Northeast	1,045	261	1,045
South	1,786	447	1,786
West	3,640	910	3,352

Based on CPT code 51596, ICD-9 code 57.87

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries with bladder cancer.

Not required to have bladder cancer diagnosis to be counted except for ICD-9 code 57.87.

[c]Average annualized rate per year.

[d]Age-adjusted to year 1995.

[e]Persons of other races, unknown race and ethnicity, and other region are included in the total.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Chemotherapy

Little data exist regarding the factors affecting the use of systemic chemotherapy for bladder cancer. There are many well-established regimens of combination chemotherapy for the treatment of advanced bladder cancer, but overall survival is still limited in the presence of metastatic disease. Published data suggest that younger individuals are more likely to receive aggressive treatments, including systemic chemotherapy and cystectomy, for advanced bladder cancer than are individuals older than 75 (16) (Table 36).

Complications

The Veterans Affairs (VA) National Surgical Quality Improvement Program (NSQIP) records pre-, intra-, and 30-day post-operative data for all patients undergoing major surgical procedures at VA facilities. The rates of occurrence of bladder cancer as a primary diagnosis among veterans seeking care were from 345 to 460 per 100,000 between 1998 and 2003 (Table 23). These rates have steadily decreased each year during this period, across genders and regions and in both Caucasians and African Americans.

Complications following any bladder cancer surgery occurred in 5.4% to 6.2% of patients over the six years of study (Table 37). The most frequent complications were urinary tract infections (UTIs) or other renal complications, which were observed in 2.4% to 3.4% of patients. The mortality rate was consistently around 1%. The average operative time was 1.3 ± 1.8 hours, and the length of post-operative stay was 5.3 ± 8.5 days.

Data regarding complications following cystectomy and urinary diversion were obtained for 1998 through 2003 by complication type. In the NSQIP dataset, postoperative complications are categorized as wound complications, respiratory complications, urinary tract complications, CNS complications, cardiac complications, or other complications, including excessive bleeding, deep vein thrombosis/thrombophlebitis, sepsis, and graft/prosthesis failure. The data were also stratified by age, race, and geographic region.

One or more complications occurred following cystectomy in 29.1% to 39.1% of patients during the data collection period (Table 38). Complications were consistently maintained below 30% for the latest three years. A majority of the complications occurred in Caucasians and in patients 65 to 74 years of age. There were regional variations in complication rates, with higher rates observed in the South. Wound-related complications were the most frequent, occurring in 10.1% to 15% of patients undergoing cystectomy. Mortality rates were 1.8% to 4.1%, which are in the range of other reported data (18, 19). Re-operation was required in 12% to 20% of patients; no trends were

Table 34. Use of neobladder/continent diversion in Medicare beneficiaries with bladder cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	640	326	(213–438)		660	327	(216–439)	
Age								
65–69	200	526	(200–852)		220	619	(253–985)	
70–74	180	362	(127–597)		240	461	(202–721)	
75–79	180	375	(131–620)		160	338	(103–572)	
80–84	40	115	(0–272)		20	54	(0–158)	
85–89	20	112	(0–329)		0	0		
90+	20	310	(0–913)		0	0		
Gender								
Male	420	296	(170–422)	296	480	330	(198–462)	330
Female	220	404	(165–643)	404	180	320	(112–528)	320
Race/ethnicity								
White	520	290	(179–402)	290	620	331	(214–447)	331
Black	80	943	(24–1,863)	943	20	241	(0–711)	241
Asian	…	...		…	0	0		0
Hispanic	…	...		…	20	2,174	(0–6,413)	2,174
N. American Native	…	...		…	0	0		0
Region								
Midwest	160	440	(135–746)	385	100	247	(30–464)	247
Northeast	120	336	(67–605)	336	60	149	(0–319)	149
South	180	388	(136–641)	431	160	304	(93–515)	304
West	160	829	(259–1,399)	829	320	1,533	(785–2,280)	1,533

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	960	490	(352–629)		720	350	(235–464)	
Age								
65–69	300	970	(482–1,459)		200	642	(244–1,040)	
70–74	320	660	(338–981)		180	378	(132–624)	
75–79	220	460	(188–731)		200	374	(142–606)	
80–84	100	265	(32–498)		140	340	(87–592)	
85–89	20	96	(0–273)		0	0		
90+	0	0			0	0		
Gender								
Male	660	472	(311–633)	457	500	333	(203–464)	333
Female	300	537	(267–808)	573	220	394	(161–627)	394
Race/ethnicity								
White	880	486	(343–629)	475	680	356	(236–475)	356
Black	20	230	(0–680)	230	20	239	(0–706)	239
Asian	20	1,667	(0–4,917)	1,667	0	0		0
Hispanic	0	0		0	20	1,064	(0–3,138)	1,064
N. American Native	0	0		0	0	0		0
Region								
Midwest	300	720	(358–1,083)	768	260	598	(274–923)	644
Northeast	140	358	(92–624)	358	100	248	(30–465)	198
South	320	588	(301–874)	625	280	476	(228–724)	476
West	200	980	(377–1,583)	784	80	366	(9–723)	366

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with bladder cancer.

[c]Age-adjusted to year 2001.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 35. Multivariate analysis of factors associated with continent reconstruction

	OR (95% CI)
Age (vs 65–69)	
70–74	0.68 (0.54–0.87)
75–79	0.43 (0.33–0.55)
	0.19 (0.13–0.27)
Gender (vs female)	
Male	1.45 (1.15–1.84)
Race/ethnicity (vs white)	
African American	0.43 (0.25–.76)
Hispanic	0.92 (0.55–1.53)
Other	1.09 (0.66–1.80)
Marital Status (vs not married)	1.13 (0.90–1.41)
Median Income(vs ≥ $75,000)	
< $20,000	0.70 (0.16–3.07)
$20,000–$50,000	1.22 (0.81–1.84)
$50,000–75,000	1.43 (1.01–2.01)
College Educated (vs less than 25%)	
25–40%	1.14 (0.81–1.61)
At least 40%	1.54 (1.06–2.23)
Charlson Score >(vs 0)	
1–2	0.97 (0.79–1.19)
At least 3	0.71 (0.51–0.97)
SEER Registry (vs. Los Angeles)	
San Francisco	0.38 (0.26–0.56)
Connecticut	0.15 (0.11–0.22)
Detroit	0.16 (0.11–0.24)
Hawaii	0.10 (0.03–0.29)
Iowa	0.11 (0.07–0.17)
New Mexico	0.39 (0.23–0.66
Seattle	1.22 (0.88–1.68)
Utah	0.22 (0.12–0.40)
Atlanta	1.17 (0.74–1.86)
San Jose	0.74 (0.48–1.13)
Year of Surgery (vs 1992–1994)	
1995–1997	1.56 (1.23–1.97)
1998–2000	1.98 (1.53–2.54)
Stage at least III (vs I)	0.85 (0.70–1.03)
Lymph nodes negative	1.04 (0.84–1.28)
Hospital Type	
Acedemic (vs non)	1.43 (1.14–1.81)
NCI Cancer Center (vs non)	5.50 (4.20–7.22)
High Volume Hospital (vs low)	1.49 (1.19–1.86)

SOURCE: Reprinted from Cancer, 107, Gore JL, Saigal CS, Hanley MM, Schonlau M, Litwin MS, and the Urologic Diseases in America Project, Variations in diverstion after radical cystectomy, 729–737, Copyright 2006.

Table 36. Logistic regression analysis of use of systemic chemotherapy or cystectomy for muscle invasive tumors

Characteristic	Unadjusted Weighted (%)	Adjusted Weighted (%)	Adjusted OR (95% CI)
Total	42	…	...
Age			
< 65	43	49	4.3 (1.0–18.3)
65–74	59	61	8.3 (2.3–30.5)
75+	24	23	1.0
Gender			
Male	39	40	0.6 (0.2–2.5)
Female	49	49	1.0
Race/ethnicity			
White Non-Hispanic	43	44	2.3 (0.5–10.9)
Black Non-Hispanic	34	37	1.5 (0.3–7.8)
Hispanic	31	30	1.0
Marital Status			
Married	48	50	2.4 (0.1–4.1)
Other	34	35	1.0
% Residents with high school education			
1st Quartile (18.66–65.63)	32	33	0.7 (0.1–4.1)
2nd Quartile (65.64–78.11)	56	55	2.5 (0.3–19.0)
3rd Quartile (78.12–86.92)	50	49	1.8 (0.3–11.9)
4th Quartile (86.93–98.70)	36	39	1.0
Insurance type			
Private	43	41	0.8 (0.2–2.7)
Public or none	40	46	1.0
Co-morbidities			
None	41	46	1.6 (0.3–8.2)
Any	42	38	1.0

…data not available.

SOURCE: Reprinted from Journal of Urology, 169, Snyder C, Harlan L, Knopf K, Potosky A, Kaplan R. Patterns of care for the treatment of bladder cancer, 1,607–1,701, Copyright 2003, with permission from American Urological Association.

observed over the time period studied. Operative time remained quite stable over the period of analysis at an average of about 6.5 ± 2.1hours. The length of post-operative hospital stay at the VA also remained fairly stable at an average of 12.8 ±12.6 days.

ECONOMIC IMPACT

Analysis of Medicare costs from diagnosis to death reveals that bladder cancer is the most expensive cancer (20). Total expenditures for lower tract TCC in the United States were more than $1 billion in 2000, an increase of more than $160 million since 1994 (Table 39). Annual expenditures for physician office visits accounted for the majority of the increase, growing from $55 million in 1994 to $188 million in 2000, an increase of 239%, substantially outpacing inflation. All other services for treatment of lower tract TCC increased slightly but did so at a rate far less than what would be expected based on inflation, indicating a decrease in real expenditures over the study period. Inpatient services accounted for a progressively smaller proportion of total expenditures over time but were still important, accounting for more than half of total expenditures in 2000. Ambulatory surgery was also an important source of expenditures in 2000, accounting for over 20% of total costs for lower tract TCC.

Lower tract TCC was also an important source of expenditures for Medicare enrollees aged 65 and over. These expenditures totaled $643 million in 2001, an increased of more than 33% since 1992 (Table 40). Similar to those of the general population, Medicare inpatient services accounted for the greatest proportion of expenditures over the study period, but physician office visits were the major driving force behind the increase. Inpatient services and ambulatory surgery also contributed substantially to

Table 37. Complications, by age, race/ethnicity, region, and type, within 30 days following any surgery for lower or upper tract transitional cell carcinoma among VA users

	1998	1999	2000	2001	2002	2003	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Total	1,929	2,275	2,600	2,691	2,672	3,095	
Age							
≤ 39	2 (0.1)	6 (0.3)	5 (0.2)	3 (0.1)	2 (0.1)	4 (0.1)	
40–44	14 (0.7)	15 (0.7)	22 (0.9)	16 (0.6)	5 (0.2)	4 (0.1)	
45–54	148 (7.7)	196 (8.6)	197 (7.6)	201 (7.5)	169 (6.3)	185 (6.0)	
55–64	355 (18)	427 (19)	501 (19.)	503 (19)	564 (21)	717 (23)	
65–74	796 (41)	862 (38)	918 (35)	961 (36)	848 (32)	954 (30)	
75–84	548 (28)	688 (30)	871 (34)	909 (34)	953 (36)	1,059 (34)	
≥ 85	66 (3.4)	81 (3.6)	86 (3.3)	98 (3.6)	131 (4.9)	172 (5.6)	
Race/ethnicity							
White	1,572 (82)	1,863 (82)	2,188 (82)	2,205 (82)	2,116 (79)	2,018 (65)	
Black	170 (8.8)	218 (9.6)	206 (7.9)	180 (6.7)	206 (7.7)	176 (5.6)	
Hispanic	58 (3.0)	55 (2.4)	84 (3.2)	75 (2.8)	77 (2.9)	89 (2.9)	
Asian	4 (0.2)	2 (0.1)	4 (0.2)	6 (0.2)	4 (0.2)	3 (0.1)	
N. American Native	1 (0.1)	6 (0.3)	5 (0.2)	4 (0.2)	4 (0.2)	7 (0.2)	
Unknown	124 (6.4)	131 (5.8)	183 (7.0)	221 (8.2)	265 (9.8)	802 (26)	
Region							
East	481 (25)	558 (25)	571 (22)	576 (21)	636 (24)	689 (22)	
Central	440 (23)	493 (22)	654 (25)	649 (24)	701 (26)	784 (25)	
South	680 (35)	726 (32)	848 (33)	926 (34)	848 (32)	995 (32)	
West	328 (17)	498 (22)	527 (20)	540 (20)	487 (18)	627 (20)	
30-Day Complications (%), age-adjusted to 2000							
1 or More Complications	5.7%	6.2%	6.1%	5.5%	6.2%	5.4%	
Wound Events	1.0%	0.8%	0.9%	1.0%	1.3%	1.3%	
Respiratory Events	1.4%	1.7%	1.0%	1.4%	1.3%	0.9%	
Renal Events	2.4%	2.8%	3.0%	2.7%	3.4%	3.0%	
Urinary Tract Infection	2.1%	2.3%	2.6%	2.5%	2.9%	2.7%	
Central Nervous System Events	0.3%	0.2%	0.2%	0.3%	0.1%	0.1%	
Cardiac Events	0.6%	0.5%	0.3%	0.4%	0.5%	0.5%	
Other Complications	0.9%	0.7%	1.3%	0.5%	0.9%	0.9%	
Deaths within 30 Days	1.0%	1.1%	1.0%	1.1%	1.0%	1.0%	
Returns to the OR	9.4%	10.7%	10.1%	9.5%	9.3%	8.9	**All Years**
Operative Time (hrs), mean ± SD	1.3 ± 1.9	1.3 ± 1.9	1.3 ± 1.8	1.3 ± 1.8	1.3 ± 1.8	1.2 ± 1.8	1.3 ± 1.8
Postoperative Length of Stay (days), mean ± SD	5.3 ± 8.6	6.0 ± 11.1	4.7 ± 6.7	5.5 ± 7.8	5.2 ± 7.6	5.1 ± 8.4	5.3 ± 8.5

SOURCE: VA National Surgical Quality Improvement Program (NSQIP), 1998–2003.

Table 38. Complications, by age, race/ethnicity, region, and type, within 30 days following cystectomy among VA users

	1998	1999	2000	2001	2002	2003	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Total	197	203	230	286	267	272	
Age							
≤39	1 (0.5)	1 (0.5)	1 (0.4)	2 (0.7)	2 (0.8)	1 (0.4)	
40–44	3 (1.5)	2 (1.0)	4 (1.7)	4 (1.4)	1 (0.4)	1 (0.4)	
45–54	27 (14)	29 (14)	31 (14)	50 (18)	26 (10)	25 (9.2)	
55–64	43 (22)	45 (22)	52 (23)	81 (28)	88 (33)	90 (33)	
65–74	75 (38)	79 (39)	84 (37)	94 (33)	95 (36)	97 (36)	
75–84	48 (24)	46 (23)	57 (25)	53 (19)	53 (20)	56 (21)	
≥ 85	0	1 (0.5)	1 (0.4)	2 (0.7)	2 (0.8)	2 (0.7)	
Race/ethnicity							
White	157 (80)	164 (82)	212 (74)	212 (74)	195 (73)	144 (53)	
Black	24 (12)	23 (11)	27 (12)	5,496 (17)	45 (17)	28 (10)	
Asian	1 (0.5)	0	2 (0.9)	0	1 (0.3)	0	
Hispanic	8 (4.1)	5 (2.5)	15 (6.5)	7 (2.5)	7 (2.6)	9 (3.3)	
N. American Native	1 (0.5)	1 (0.5)	1 (0.4)	0	0	0	
Unknown	6 (3.1)	10 (4.0)	15 (6.5)	18 (6.3)	20 (7.5)	91 (34)	
Region							
East	49 (25)	39 (19)	44 (19)	35 (12)	60 (23)	35 (13)	
Central	50 (25)	47 (23)	66 (29)	95 (33)	74 (28)	86 (32)	
South	61 (31)	59 (29)	70 (30)	100 (35)	86 (32)	83 (31)	
West	37 (19)	58 (29)	50 (22)	56 (20)	47 (18)	68 (25)	
30-Day Complications (%), age-adjusted to 2000							
1 or More Complications	35.4%	39.1%	36.1%	29.1%	29.6%	29.1%	
Wound Events	11.6%	10.1%	10.4%	12.3%	11.3%	15.0%	
Respiratory Events	7.1%	12.6%	8.3%	9.4%	7.8%	5.9%	
Renal Events	10.5%	11.2%	10.4%	6.8%	10.0%	9.9%	
Urinary Tract Infections	8.0%	9.8%	8.7%	6.3%	8.9%	7.0%	
Central Nervous System Events	2.1%	0.9%	0.9%	2.3%	0.5%	1.3%	
Cardiac Events	2.1%	1.9%	3.0%	1.8%	1.9%	3.6%	
Other Complications	5.1%	5.2%	9.1%	3.4%	6.2%	6.1%	
Deaths within 30 Days	2.5%	3.4%	3.0%	4.1%	1.8%	3.5%	
Returns to the OR	14.3%	12.0%	20.0%	19.3%	19.6%	17.5%	**All Years**
Operative Time (hrs), mean ± SD	6.8 ± 2.1	6.8 ± 2.0	6.5 ± 2.0	6.2 ± 2.1	6.4 ± 2.1	6.3 ± 2.0	6.5 ± 2.1
Postoperative Length of Stay (days), mean ± SD	13.1 ± 12.1	16.5 ± 18.7	12.4 ± 11.7	11.3 ± 9.7	12.0 ± 10.3	12.6 ± 12.6	12.8 ± 12.6

SOURCE: VA National Surgical Quality Improvement Program (NSQIP), 1998–2003.

Table 39. Expenditures for lower tract transitional cell carcinoma, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$40,041,129	4.4%	$37,564,046	3.9%	$53,019,533	5.1%	$51,105,509	4.8%
Physician Office	$55,430,541	6.1%	$81,277,489	8.5%	$99,639,020	9.6%	$188,128,105	17.5%
Ambulatory Surgery	$220,270,787	24.1%	$262,130,470	27.4%	$279,538,480	26.9%	$226,320,829	21.1%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$596,873,754	65.4%	$576,089,164	60.2%	$607,468,960	58.4%	$608,248,652	56.6%
TOTAL	$912,616,211		$957,061,169		$1,039,665,993		$1,073,803,094	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

the observed expenditure increases over time. Hospital outpatient services and emergency room visits were an insignificant source of costs for treatment of lower tract TCC in the Medicare population over the age of 64.

Expenditures for Medicare enrollees under the age of 65 were substantially lower, amounting to only $44 million in 2001. Nevertheless, increases over time were dramatic, more than doubling since 1995. Inpatient services accounted for more than 80% of these expenditures in 2001 and were responsible for the majority of increases in expenditures over time. While expenditures for physician office visits made up only about 7% of all expenditures in this population in 2001, they more than quadrupled between 1992 and 2001.

Individual-level expenditures for treatment of lower tract TCC were estimated using risk-adjusted regression models controlling for age, sex, work status, income, urban or rural residence, and health plan characteristics (Table 41). Among 18- to 64-year-olds with employer-provided insurance, average annual expenditures for those treated for lower tract TCC were $14,458, compared with $4,873 for similar individuals not treated for this condition, an incremental cost of $9,585. The higher costs associated with diagnosis of lower tract TCC are expected, as the condition is typically treated surgically and is associated with intensive follow up. About 16% of individual-level expenditures went toward pharmaceuticals. Incremental costs associated with lower tract TCC were greatest among individuals 55

Table 40. Expenditures for Medicare beneficiaries for lower tract transitional cell carcinoma, by site of service (% of total)

	Age 65 and over							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$16,832,700	3.5%	$24,037,440	4.6%	$22,842,080	4.1%	$24,617,520	3.8%
Physician Office	$21,156,660	4.4%	$33,381,600	6.3%	$51,158,160	9.2%	$92,023,440	14.3%
Ambulatory Surgery	$75,498,480	15.7%	$116,868,960	22.2%	$125,991,360	22.6%	$114,842,400	17.9%
Emergency Room	$1,459,080	0.3%	$1,599,000	0.3%	$2,247,240	0.4%	$1,139,600	0.2%
Inpatient	$365,577,240	76.1%	$350,875,800	66.6%	$355,359,840	63.7%	$410,143,200	63.8%
TOTAL	$480,524,160		$526,762,800		$557,598,680		$642,766,160	
	Under 65							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$464,000	2.0%	$913,920	4.4%	$1,106,700	3.4%	$816,960	1.8%
Physician Office	$559,420	2.4%	$782,880	3.7%	$1,702,400	5.3%	$2,926,080	6.6%
Ambulatory Surgery	$1,542,240	6.7%	$3,867,420	18.5%	$5,470,920	16.9%	$4,575,680	10.3%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$20,297,140	88.8%	$15,376,240	73.4%	$24,058,440	74.4%	$35,919,240	81.2%
TOTAL	$22,862,800		$20,940,460		$32,338,460		$44,237,960	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 41. Estimated annual expenditures of privately insured employees with and without a medical claim for lower tract transitional cell carcinoma, 2002[a]

	Annual Expenditures (per person)					
	Persons Age 40–64 without Lower Bladder Cancer (N=342,771)			Persons Age 40–64 with Lower Bladder Cancer (N=615)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$3,469	$1,404	$4,873	$12,109	$2,349	$14,458
Age						
50–54	$3,637	$1,482	$5,119	$7,743	$2,258	$10,001
55–59	$3,718	$1,462	$5,180	$9,570	$2,218	$11,788
60–64	$3,569	$1,397	$4,966	$8,268	$2,191	$10,459
Gender						
Male	$3,428	$1,334	$4,762	$10,633	$2,151	$12,784
Female	$3,527	$1,503	$5,030	$14,178	$2,625	$16,803
Region						
Midwest	$3,461	$1,341	$4,802	$12,093	$2,261	$14,354
Northeast	$3,251	$1,493	$4,744	$11,356	$2,499	$13,855
South	$3,646	$1,380	$5,026	$12,737	$2,292	$15,029
West	$3,470	$1,371	$4,841	$12,123	$2,311	$14,434

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 40 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions. Predicted expenditures for persons age 40 to 49 are omitted due to small sample size.

SOURCE: Ingenix, 2002.

to 59 years of age, apparently reflecting differences in medical expenditures rather than pharmaceutical costs, which were similar across age groups. Medical and pharmaceutical costs associated with a diagnosis of lower tract TCC were higher in women ($16,803) than in men ($12,784) but did not vary substantially by region.

Overall 29% of individuals with employer-provided health insurance and a claim for lower tract TCC missed work; almost four days of work, on

Table 42. Average annual work loss of persons treated for bladder cancer, 1999 (95%CI)

			Average Work Absence (hrs)		
	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
Total	92	29%	13.9 (1–27)	18.6 (3–34)	32.4 (12–53)
Age					
30–39	6	50%	54.7 (0–195)	12.3 (0–34)	66.9 (0–202)
40–49	19	47%	10.7 (0–24)	15.8 (3–29)	26.6 (8–45)
50–64	67	22%	11.1 (0–26)	19.9 (0–40)	31 (5–57)
Gender					
Male	70	29%	13.4 (0–28)	23 (3–43)	36.5 (11–62)
Female	22	32%	15.3 (0–46)	4.3 (0–9)	19.6 (0–50)
Region					
Northeast	18	28%	27.6 (0–84)	5 (0–11)	32.6 (0–89)
Midwest	23	35%	9.4 (0–19)	44 (0–94)	53.4 (0–110)
South	32	22%	7.4 (0–16)	15 (0–41)	22.4 (0–49)
West	8	50%	41 (0–138)	9.6 (0–24)	50.6 (0–145)
Unknown	11	27%	0	4.4 (0–11)	4.4 (0–11)

[a]Individuals with an inpatient or outpatient claim for bladder cancer and for whom absence data were collected. Work loss is based on reported absences contiguous to admission and discharge dates of each hospitalization or the date of the outpatient visit.
[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: Marketscan Health and Productivity Management, 1999.

average, were missed per person diagnosed with TCC (Table 42). The proportion was similar for men and women. An average of just under three days of work were missed for outpatient visits, with men appearing to miss more work for such visits than women. Lower tract TCC patients in the Midwest region missed more hours per outpatient visit than did those in the Northeast region.

UPPER TRACT UROTHELIAL CANCER

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Inpatient care for upper tract urothelial cancer has remained stable over the decade of the four index years (1992–2001). While there were no significant differences between age groups or by race, women had a lower rate of inpatient stays than did men, reflecting the demographics of the disease. Rates of inpatient admission varied significantly, being highest in the South most recently and highest in the Northeast and Midwest in previous years (Table 43). HCUP data indicate similar trends, although the overall rate of inpatient admissions for a diagnosis of upper tract TCC declined from 5.8 per 100,000 to 4.5 per 100,000 (Table 44). A majority of the care for upper tract TCC is delivered at urban locations, and this rate is also gradually rising.

Outpatient Care

Ambulatory Surgery

The annualized ambulatory surgery visit rate of occurrence of upper tract TCC is 2.2 per 100,000, according to data from the National Survey of Ambulatory Surgery (Table 45). The rate of visits to ambulatory surgery centers for upper tract TCC increased consistently, from 2.7 per 100,000 in 1992 to 4.8 per 100,000 in 2001 (Table 46). There was significant variation by gender, which can be explained at least in part by the demographics of the disease. Racial and age trends were unclear given the small sample size and the small number of non-Caucasian patients.

Physician Office Visits

Physician office visits have not shown any consistent trends. The highest rate in the most recent data occurred in the Midwest. There were also no specific trends in office visit frequency relating to age and gender (Table 47). Outpatient hospital visits have remained steady over a 10-year period, as have the numbers of visits by gender, except in the Northeast, where they declined.

Table 43. Inpatient stays by Medicare beneficiaries with upper tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	2,240	6.4 (5.2–7.6)	6.4	2,280	6.4 (5.3–7.6)	6.4	1,900	5.7 (4.5–6.8)	5.7	2,180	6.2 (5.0–7.3)	6.2
Total < 65	80	1.4 (0–2.9)		40	0.7 (0–1.5)		40	0.6 (0–1.5)		100	1.4 (0.2–2.7)	
Total 65+	2,160	7.4 (6.0–8.7)		2,240	7.7 (6.2–9.1)		1,860	6.8 (5.4–8.2)		2,080	7.4 (6.0–8.8)	
Age												
65–69	520	5.8 (3.5–8.0)		480	5.7 (3.4–7.9)		180	2.5 (0.8–4.1)		240	3.2 (1.4–5.0)	
70–74	540	7.1 (4.4–9.8)		660	8.5 (5.6–12)		460	6.6 (3.9–9.3)		560	8.1 (5.1–11)	
75–79	380	6.6 (3.6–9.6)		560	9.8 (6.2–14)		520	9.2 (5.7–13)		500	8.4 (5.1–12)	
80–84	320	8.4 (4.3–13)		420	11 (6.1–15)		440	11 (6.7–16)		520	13 (7.9–18)	
85–89	320	16 (7.9–23)		120	5.5 (1.1–9.9)		180	8.2 (2.8–14)		200	8.6 (3.3–14)	
90+	60	7.2 (0–15)		0	0		80	8.8 (0.2–17)		60	6.3 (0–13)	
Gender												
Male	1,320	8.9 (6.7–11)	9.7	1,440	9.5 (7.3–12)	9.9	1,140	7.9 (5.8–9.9)	7.6	1,260	8.2 (6.2–10)	
Female	920	4.6 (3.3–5.9)	3.8	840	4.2 (2.9–5.4)	3.9	760	4.0 (2.7–5.3)	4.2	920	4.6 (3.3–6.0)	
Race/ethnicity												
White	2,060	7.0 (5.6–8.3)	6.8	2,200	7.2 (5.9–8.6)	7.2	1,760	6.2 (4.9–7.5)	6.3	2,000	6.7 (5.4–8.0)	6.5
Black	60	2.0 (0–4.3)	2.7	40	1.2 (0–2.9)	1.2	60	1.9 (0–4.1)	1.9	40	1.2 (0–2.8)	1.2
Asian	…	…	…	0	0	0	20	6.4 (0–19)	6.4	0	0	0
Hispanic	…	…	…	20	5.0 (0–15)	5.0	20	2.8 (0–8.4)	0	40	5.0 (0–12)	2.5
N. American Native	…	…	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	700	8.0 (5.4–11)	7.8	460	5.1 (3.0–7.2)	4.9	620	7.2 (4.7–9.7)	7.6	420	4.8 (2.7–6.8)	5.7
Northeast	400	5.2 (2.9–7.5)	5.5	780	10 (7.0–13)	11	360	5.4 (2.9–7.9)	5.1	460	6.7 (3.9–9.4)	6.1
South	720	5.9 (4.0–7.8)	6.4	760	6.0 (4.1–7.9)	6.1	640	5.2 (3.4–7.0)	5.2	920	6.9 (4.9–8.9)	6.6
West	420	7.7 (4.4–11)	5.8	280	5.4 (2.6–8.2)	3.9	280	5.7 (2.7–8.6)	5.2	340	6.3 (3.3–9.3)	6.3

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 44. Inpatient hospital stays for upper transitional cell carcinoma listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	5,651	5.8 (5.2–6.3)	5.8	6,106	5.8 (5.3–6.4)	5.8	5,402	4.9 (4.5–5.3)	4.9	5,184	4.5 (4.1–4.9)	4.5
Age												
40–54	461	1.0 (0.8–1.2)		508	1.0 (0.7–1.2)		392	0.7 (0.6–0.9)		503	0.8 (0.7–1.0)	
55–64	1,047	5.2 (4.2–6.2)		1,035	4.9 (4.1–5.8)		805	3.6 (3.0–4.3)		917	3.9 (3.3–4.6)	
65–74	2,055	12 (9.9–13)		2,116	12 (10–13)		1,898	11 (9.3–12)		1,694	9.5 (8.3–11)	
75–84	1,704	18 (15–20)		1,955	18 (16–21)		1,921	17 (15–19)		1,595	14 (12–15)	
85+	384	14 (10–17)		492	18 (13–22)		386	13 (10–16)		475	15 (12–19)	
Gender												
Male	3,446	7.6 (6.7–8.4)	8.2	3,678	7.5 (6.7–8.4)	8.2	3,200	6.2 (5.6–6.8)	6.7	3,051	5.7 (5.1–6.2)	6.1
Female	2,205	4.2 (3.6–4.8)	3.9	2,428	4.3 (3.8–4.8)	4.0	2,202	3.8 (3.3–4.2)	3.5	2,133	3.5 (3.1–3.9)	3.3
Region												
Northeast	1,263	6.0 (4.5–7.4)	5.8	1,402	6.5 (5.3–7.8)	6.3	1,174	5.3 (4.2–6.4)	5.2	1,267	5.5 (4.4–6.6)	5.3
Midwest	1,245	5.4 (4.2–6.6)	5.4	1,724	6.9 (5.4–8.4)	6.9	1,359	5.3 (4.5–6.2)	5.2	1,244	4.7 (3.8–5.6)	4.8
South	2,032	6.1 (5.1–7.0)	6.1	1,969	5.3 (4.6–6.1)	5.3	1,873	4.8 (4.2–5.4)	4.8	1,806	4.4 (3.8–4.9)	4.3
West	1,111	5.4 (4.4–6.4)	5.6	1,009	4.7 (4.0–5.4)	4.9	996	4.3 (3.4–5.1)	4.5	868	3.6 (2.9–4.2)	3.7
MSA												
Rural	708	2.7 (2.1–3.2)	2.5	783	3.1 (2.4–3.8)	3.0	723	2.8 (2.2–3.3)	2.6	680	2.5 (2.0–3.0)	2.4
Urban	4,839	6.8 (6.1–7.5)	7.0	5,308	6.7 (6.0–7.3)	6.8	4,660	5.6 (5.1–6.1)	5.7	4,499	5.1 (4.7–5.6)	5.2

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population, 40 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of missing MSA are included in the total.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 45. Ambulatory surgery visits for upper tract transitional cell carcinoma listed as any diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996			
	Count	3-Year Rate	Annualized Rate	3- Year Age-adjusted Rate
Total	6,838	6.7 (2.9–10)	2.2	6.7

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population, 40 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[c]Average annualized rate per year.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Table 46. Visits to ambulatory surgery centers by Medicare beneficiaries with upper tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	940	2.7 (1.9–3.5)	2.7	1,080	3.1 (2.2–3.9)	3.1	1,360	4.1 (3.1–5.0)	4.1	1,700	4.8 (3.8–5.8)	4.8
Total < 65	20	0.4 (0–1.1)		80	1.3 (0–2.6)		40	0.6 (0–1.5)		60	0.9 (0–1.8)	
Total 65+	920	3.1 (2.2–4.0)		1,000	3.4 (2.5–4.4)		1,320	4.8 (3.7–6.0)		1,640	5.8 (4.6–7.1)	
Age												
65–69	160	1.8 (0.5–3.0)		340	4.0 (2.1–5.9)		220	3.0 (1.2–4.8)		180	2.4 (0.8–4.0)	
70–74	180	2.4 (0.8–3.9)		300	3.9 (1.9–5.8)		380	5.4 (3.0–7.9)		480	6.9 (4.1–9.7)	
75–79	200	3.5 (1.3–5.6)		180	3.2 (1.1–5.2)		340	6.0 (3.1–8.9)		560	9.4 (5.9–13)	
80–84	200	5.3 (2.0–8.5)		140	3.5 (0.9–6.2)		180	4.7 (1.6–7.8)		200	4.9 (1.9–8.0)	
85–89	160	7.8 (2.4–13)		20	0.9 (0–2.7)		140	6.4 (1.6–11)		220	9.4 (3.9–15)	
90+	20	2.4 (0–7.1)		0	0		60	6.6 (0–14)		0	0	
Gender												
Male	580	3.9 (2.5–5.3)	4.0	700	4.6 (3.1–6.1)	4.6	820	5.7 (3.9–7.4)	5.4	1,120	7.3 (5.4–9.2)	7.3
Female	360	1.8 (1.0–2.6)	1.7	380	1.9 (1.0–2.7)	1.9	540	2.8 (1.8–3.9)	3.0	580	2.9 (1.9–4.0)	2.9
Race/ethnicity												
White	820	2.8 (1.9–3.6)	2.7	1,020	3.4 (2.4–4.3)	3.4	1,320	4.6 (3.5–5.8)	4.8	1,620	5.4 (4.2–6.6)	5.4
Black	80	2.7 (0.1–5.3)	2.0	40	1.2 (0–2.9)	1.2	20	0.6 (0–1.9)	0	20	0.6 (0–1.7)	0.6
Asian	…	…	…	0	0	0	0	0	0	20	4.2 (0–12)	4.2
Hispanic	…	…	…	0	0	0	20	2.8 (0–8.4)	0	0	0	0
N. American Native	…	…	…	0	0	0	0	0	0	20	30 (0–88)	30
Region												
Midwest	240	2.7 (1.2–4.3)	3.2	240	2.7 (1.2–4.2)	2.7	580	6.7 (4.3–9.2)	7.4	360	4.1 (2.2–6.0)	4.1
Northeast	140	1.8 (0.5–3.2)	2.1	240	3.1 (1.4–4.9)	3.1	180	2.7 (0.9–4.4)	2.7	580	8.4 (5.3–11)	8.4
South	280	2.3 (1.1–3.5)	2.3	460	3.6 (2.1–5.1)	3.5	360	2.9 (1.6–4.2)	2.7	560	4.2 (2.7–5.8)	4.4
West	280	5.1 (2.4–7.8)	3.7	120	2.3 (0.5–4.2)	2.7	240	4.8 (2.1–7.6)	4.0	200	3.7 (1.4–6.0)	3.0

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 47. Physician office visits by Medicare beneficiaries with upper tract transitional cell carcinoma listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	10,640	30 (28–33)	30	15,380	43 (40–47)	43	13,120	39 (36–42)	39	16,380	46 (43–50)	46
Total < 65	300	5.4 (2.7–8.2)		920	15 (11–19)		740	12 (8.1–16)		520	7.4 (4.5–10)	
Total 65+	10,340	35 (32–38)		14,460	49 (46–53)		12,380	45 (42–49)		15,860	56 (52–60)	
Age												
65–69	2,780	31 (26–36)		5,720	68 (60–75)		2,600	35 (29–42)		6,380	85 (75–94)	
70–74	2,340	31 (25–36)		2,680	35 (29–41)		3,220	46 (39–53)		3,800	55 (47–62)	
75–79	3,320	58 (49–67)		3,620	64 (54–73)		3,540	63 (53–72)		2,740	46 (38–54)	
80–84	1,240	33 (25–41)		1,500	38 (29–47)		2,100	55 (44–65)		1,900	47 (37–56)	
85–89	560	27 (17–37)		680	31 (21–42)		760	35 (24–46)		860	37 (26–48)	
90–94	80	9.6 (0.2–19)		100	11 (1.3–21)		140	15 (4.0–27)		120	13 (2.5–23)	
95–97	20	11 (0–31)		80	42 (1.1–83)		20	9.9 (0–29)		40	20 (0–49)	
98+	0	0		80	46 (1.1–90)		0	0		20	9.2 (0–27)	
Gender												
Male	6,520	44 (39–49)	45	8,580	56 (51–62)	58	6,880	48 (42–53)	49	10,980	71 (65–77)	74
Female	4,120	21 (18–23)	20	6,800	34 (30–37)	33	6,240	33 (29–36)	32	5,400	27 (24–30)	25
Race/ethnicity												
White	9,880	33 (31–36)	34	14,140	47 (43–50)	47	12,100	43 (39–46)	43	15,060	50 (47–54)	51
Black	380	13 (7.1–19)	11	460	14 (8.4–20)	16	580	19 (12–26)	21	360	11 (5.7–15)	8.2
Asian	…	…	…	100	60 (7.2–112)	72	160	51 (16–86)	45	100	21 (2.5–40)	21
Hispanic	…	…	…	200	50 (19–81)	65	80	11 (0.3–22)	5.7	140	18 (4.5–31)	18
N. American Native	…	…	…	0	0	0	0	0	0	140	210 (54–366)	240
Region												
Midwest	2,520	29 (24–34)	30	4,120	46 (39–52)	44	3,320	38 (33–44)	38	5,460	62 (55–69)	67
Northeast	3,280	43 (36–49)	39	3,320	43 (37–50)	37	2,420	36 (30–43)	36	2,940	43 (36–49)	38
South	3,660	30 (26–34)	31	5,320	42 (37–47)	45	5,120	41 (36–46)	43	5,500	41 (37–46)	42
West	1,140	21 (15–26)	20	2,620	51 (42–59)	54	2,160	44 (35–52)	40	2,400	44 (36–52)	40

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 48. VA users with a primary diagnosis of upper tract transitional cell carcinoma, 1998–2003, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	754	25	822	25	775	22	723	19	713	16	743	16
Age												
40–44	13	5	18	7	14	5	10	4	4	2	11	4
45–54	103	12	129	15	113	13	100	12	90	11	89	10
55–64	221	35	200	31	179	28	139	22	135	21	114	18
65–74	320	33	311	32	251	26	225	23	192	20	193	20
75–84	239	34	225	32	203	29	149	21	126	18	125	18
85 +	11	17	12	19	15	23	13	20	10	16	8	13
Gender												
Male	744	26	813	26	763	23	714	19	706	17	730	16
Female	10	11	9	9	12	11	9	7	7	5	13	9
Race/ethnicity												
White	569	28	626	28	613	25	565	20	557	18	533	17
Black	130	31	138	31	116	26	109	24	101	21	105	23
Hispanic	18	23	22	26	19	22	17	18	12	13	14	15
Other	10	25	14	33	11	25	7	15	10	20	5	10
Unknown	27	6	22	5	16	4	25	5	33	5	86	9
Insurance Status												
No insurance/self-pay	496	23	521	23	479	21	400	18	368	16	378	16
Medicare	83	32	133	33	172	26	239	24	248	20	293	19
Medicaid	0	0	0	0	1	27	0	0	2	23	5	52
Private Insurance/HMO	174	29	167	30	118	21	82	14	93	15	65	9
Other Insurance	1	9	1	6	5	21	2	7	2	6	2	5
Unknown	0	0	0	0	0	0	0	0	0	0	0	0
Region												
Eastern	103	23	125	26	110	21	104	16	139	18	116	15
Central	119	23	151	26	130	21	121	17	126	15	176	17
Southern	305	27	316	26	320	24	300	19	284	16	287	15
Western	227	25	230	24	215	22	198	20	164	17	164	18

[a]Rate per 100,000 veterans using the VA system.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 49. Expenditures for upper tract transitional cell carcinoma, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Physician Office	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Ambulatory Surgery	$7,058,582	11.3%	$7,687,040	10.5%	$6,639,698	8.7%	$5,304,061	8.2%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$55,396,098	88.7%	$65,185,706	89.5%	$70,112,558	91.3%	$59,005,746	91.8%
TOTAL	$62,454,680		$72,872,746		$76,752,256		$64,309,807	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 50. Expenditures for Medicare beneficiaries for treatment of upper tract transitional cell carcinoma, by site of service (% of total)

	Age 65 and over							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$636,000	2.5%	$366,600	1.4%	$643,080	2.2%	$851,520	2.6%
Physician Office	$785,840	3.1%	$1,286,940	4.8%	$2,154,120	7.3%	$4,107,740	12.7%
Ambulatory Surgery	$1,375,400	5.5%	$2,169,000	8.1%	$2,563,440	8.7%	$2,666,640	8.2%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$22,332,240	88.9%	$23,069,760	85.8%	$24,140,940	81.8%	$24,814,400	76.5%
TOTAL	$25,129,480		$26,892,300		$29,501,580		$32,440,300	
	Under 65							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Physician Office	---	0.0%	$49,680	100.0%	$60,680	100.0%	---	0.0%
Ambulatory Surgery	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$0		$49,680		$60,680		$0	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Outpatient VA Care

Data from the VA system also indicate a gradual decrease in the rate of affected patients in each year up to 2003. A greater number of African Americans sought care in the VA system for upper tract TCC in 1998, and this relationship remained constant through 2003. More males than females with a diagnosis of upper tract TCC were seen at VA facilities; regional differences were not significant (Table 48).

ECONOMIC IMPACT

Total expenditures for upper tract TCC were $64 million in 2000. They peaked in 1998 at $77 million, but no clear trend was observed for total expenditures over time (Table 49). Expenditures related to ambulatory surgery have decreased since 1996 and made up only 8% of total expenditures in year 2000. Inpatient services consistently accounted for about 90% of total expenditures throughout the study period.

Expenditures for upper tract TCC among Medicare enrollees 65 years of age and older increased consistently, from $25 million in 1992 to $32 million in 2001 (Table 50). Increases in expenditures were driven primarily by increases in inpatient services and physician office visits. Expenditures for physician office visits more than quadrupled from 1992 to 2001, and expenditures for ambulatory surgery almost doubled. While inpatient services have accounted for a smaller proportion of total expenditures over time in this population, they still accounted for over 75% of expenditures in year 2001. Expenditures in the Medicare population under the age of 65 were small.

In most years, charges for male patients appeared to be much higher than those for female patients. The largest proportion of the charges was generated by inpatient care, followed by ambulatory surgery care (Tables 49 and 51). Individual-level expenditures associated with a diagnosis of upper tract TCC could not be estimated reliably due to small sample size.

OVERALL BURDEN OF TRANSITIONAL CELL CARCINOMA

The economic impact of TCC in the United States is substantial: expenditures of over $1 billion were attributed to lower tract TCC, and $64 million was attributed to upper tract TCC in year 2000. Bladder cancer was also an important source of healthcare costs among Medicare enrollees, especially those 65 and older. While the impact of upper tract TCC was small relative to that of lower tract disease, it was not insignificant relative to other urologic conditions. Diagnosis of lower tract TCC was associated with enormous personal costs for both men and women. In addition, not only did a substantial proportion of the people with lower tract TCC miss work, an average of almost four days of work were missed per outpatient visit.

Table 51. Visits for individuals with upper tract transitional cell carcinoma having commercial health insurance, primary diagnosis, 1994–2002

	Inpatient		Hospital Outpatient		Ambulatory Surgery		Physician Outpatient		Emergency Room	
	Count	Mean Total Payment	Count	Mean Cost	Count	Mean Cost	Count	Mean Cost	Count	Mean Cost
Total	82	$6,935	13	$143	43	$375	134	$98	1	$170
Year										
1994	8	$4,652	1	$$165	4	$187	12	$71	0	$0
Gender										
Male	6	$5,231	1	$165	4	$187	7	$96	0	$0
Female	2	$2,917	0	$0	0	$0	5	$36	0	$0
1996	12	$5,401	1	$153	2	$145	20	$87	0	$0
Gender										
Male	8	$6,559	1	$153	1	$142	14	$105	0	$0
Female	4	$3,087	0	$0	1	$147	6	$46	0	$0
1998	20	$7,556	2	$74	12	$703	32	$92	0	$0
Gender										
Male	13	$6,901	1	$33	11	$709	21	$73	0	$0
Female	7	$8,773	1	$114	1	$636	11	$128	0	$0
2000	22	$8,363	3	$145	12	$219	41	$96	0	$0
Gender										
Male	14	$8,703	3	$145	9	$237	23	$110	0	$0
Female	8	$7,768	0	$0	3	$164	18	$78	0	$0
2002	20	$6,575	6	$159	13	$309	29	$124	1	$170
Gender										
Male	14	$7,334	4	$205	10	$374	24	$129	1	$170
Female	6	$4,804	2	$67	3	$93	5	$102	0	$0

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

CONCLUSIONS

The available data suggest that bladder cancer is a prevalent disease, with the incidence of new cases holding steady over the past 20 years. The frequency of upper tract tumors is less than that of bladder cancer. The rate of inpatient care is decreasing for both upper and lower tract cancers, while the use of outpatient care venues such as office visits and ambulatory surgery centers is increasing. The use of emergency room care does not appear to be high for this disease and is limited to elderly patients. Office procedures such as urinalysis and cystoscopy are common, but urine cytology seems to be used relatively infrequently. CT scanning is increasingly utilized as a staging modality prior to invasive therapy such as cystectomy. Transurethral resection of the tumor is the most frequently utilized treatment approach, typically followed by no additional surgery in the 12 months after initial diagnosis. Cystectomy for bladder cancer is performed in a few individuals, primarily those with higher-stage disease. Ileal conduit urinary diversion is the most frequent diversion utilized following cystectomy. A course of adjuvant intravesical therapy is not commonly used after transurethral resection of bladder tumors. Mortality following radical cystectomy appears to be low and in keeping with that reported in the literature from several institutional series. Complications following cystectomy are on the order of 30%. The use of additional specialists such as medical oncologists to deliver chemotherapy, particularly in patients with advanced disease, is lower than expected. Almost all of these conclusions hold true for upper tract urothelial malignancies as well as lower tract malignancies.

RECOMMENDATIONS

It would be useful to develop ICD and CPT codes to distinguish upper tract TCC from kidney cancer. This would allow a more clear determination of outcomes specific to upper tract TCC, which is known to be uncommon. Because of its low prevalence, we have to rely on analysis of combined data from multiple sources to yield statistically meaningful outcomes information for patients with the disease.

It may be possible to establish benchmarks for surgical complications, operating room procedure times, and lengths of stay, using data from the VA NSQIP to further quality improvement initiatives.

Data sources such as the NSQIP should be combined with pathologic staging information and pharmacy utilization data to allow interpretation of outcomes after adjustment for disease stage and use of adjuvant therapy.

Further investigation is needed in the following areas.

Risk factors and prevalence

- Evaluate secondhand smoke as a risk factor for urothelial malignancies.
- Evaluate the impact of smoking cessation programs on incidence and prevalence of bladder cancer.
- Identify hereditary and genetic risk factors for urothelial cancers.
- Study the cost-effectiveness of bladder cancer screening.

Diagnosis and staging

- Evaluate costs of various diagnostic and staging algorithms for bladder cancer to identify the least expensive and most efficient approach.
- Evaluate the prevalence of different staging algorithms and their impact on outcomes from urothelial cancers.
- Evaluate the prevalence of various surveillance regimens for follow-up of upper and lower tract TCC; this would help to identify the most cost-effective surveillance regimen.

Treatment

- Evaluate costs and prevalence of use of various first- and second-line intravesical therapy regimens.
- Identify reasons for the observed low utilization of intravesical therapy for bladder cancer, particularly immediate post-resection instillation of chemotherapeutic agents shown to decrease recurrence rates.
- Identify the prevalence of maintenance intravesical therapy and second-line regimens.
- Determine the prevalence of use of bladder-sparing therapy (Chemotherapy and/or radiation therapy) and associated outcomes.

REFERENCES

1. Epstein JI, Amin MB, Reuter VR, Mostofi FK. The World Health Organization/International Society of Urological Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. Bladder Consensus Conference Committee. Am J Surg Pathol 1998;22:1435-48.
2. Nieder A, Soloway M. Eliminate the term "superficial" bladder cancer. J Urol 2006 Feb;175(2):417-8.
3. Messing EM. Urothelial tumors of the urinary tract. In: Campbells Urology 8th edition, Walsh PC, Retik AB, Darracott Vaughan Jr. E, Wein AJ. Saunders, Philadelphia 2002. 2732-84.
4. Porter MP, Voigt LF, Penson DF, Weiss NS. Racial variation in the incidence of squamous cell carcinoma of the bladder in the US. J Urol 2002;168:1960.
5. Leissner J, Ghoneim MA, Abol-Enein H, Thuroff JW, Franzaring L, Fisch M, Shculze H, Managadze G, Allhoff EP, el-Baz MA, Kastendieck H, Buhtz P, Kropf S, Hohenfellner R, Wolf HK. Extended radical lymphadenectomy in patients with urothelial bladder cancer: results of a prospective multicenter study. J Urol 2004;171:139-44
6. O'Donnell MA, Lilli K, Leopold C, National Bacillus Calmette-Guerin/Interferon Phase 2 Investigator Group. Interim results from a national multicenter phase II trial of combination bacillus Calmette-Guerin plus interferon alfa-2b for superficial bladder cancer. J Urol 2004;172:888-93.
7. Herr HW. Urachal carcinoma: the case for extended partial cystectomy. J Urol 1994;151:365-66.
8. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. CA Cancer J Clin. 2006;56(2):106-30.
9. Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds.). SEER Cancer Statistics Review, 1975-2001, National Cancer Institute, Bethesda, MD. Available at http://seer.cancer.gov/csr/1975_2001. 2004.
10. Michaud DS, Clinton SK, Rimm EB, Willet WC, Giovannucci E. Risk of bladder cancer by geographic region in a US cohort of male health professionals. Epidemiology 2001;12:719.
11. Prout GR Jr, Wesley MN, Greenberg RS, Chen VW, Brown CC, Miller AW, Weinstien RS, Robboy SJ, Haynes MA, Blacklow RS, Edwards BK. Bladder cancer: race differences in extent of disease at diagnosis. Cancer 2000;89:1349-58.
12. Hall MC, Womack S, Sagalowsky AI, Carmody T, Erickstad MD, Roehrborn CG. Prognostic factors, recurrence, and survival in transitional cell carcinoma of the upper urinary tract: a 30-year experience in 252 patients. Urology 1998;52:594-601.
13. Schrag D, Hsieh LJ, Rabbani F, Bach PB, Herr H, Begg CB. Adherence to surveillance among patients with superficial bladder cancer. J Natl Cancer Inst 2003;95:588-97.
14. Joudi FN, Smith BR, O'Donnell MA, Konety BR. Contemporary management of superficial bladder cancer in the United States: a pattern of care analysis. Urology 2003;63:1083-88.
15. Snyder C, Harlan L, Knopf K, Potosky A, Kapln R. Patterns of care for the treatment of bladder cancer. J Urol 2003;169: 1607-1701.
16. Konety BR, Joslyn SA. Factors influencing aggressive therapy for bladder cancer: an analysis of data from the SEER program. J Urol 2003;170:1765-71.
17. Gore JL, Saigal CS, Hanley JM, Schonlau M, Litwin MS, and the Urologic Diseases in America Project. Variations in reconstruction after radical cystectomy. Cancer 2006;729-737.
18. Stein JP, Lieskovksy G, Cote R, Groshen S, Feng AC, Boyd S, Skinner E, Bochner B, Thangathurai D, Mikhail M, Raghavan D, Skinner DG. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. J Clin Oncol 2001;19:666-75.
19. Konety BR, Dhawan V, Allareddy V, Joslyn SA. Impact of hospital and surgeon volume on in-hospital mortality from radical cystectomy: data from the health care utilization project. J Urol 2005;173:1695-1700.
20. Riley GF, Potosky AL, Lubitz JD, Kessler LG. Medicare payments from diagnosis to death for elderly cancer patients by stage at diagnosis. Med Care 1995;33:828-41.

CHAPTER 8

Urolithiasis

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Urolithiasis

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INTRODUCTION

It has been estimated that up to 10% of males and 5% of females in the United States will form a kidney stone (i.e., experience urolithiasis) at some time during their lives (1, 2). These figures would be slightly higher if stones that form in other parts of the urinary tract were included. While rarely fatal, urolithiasis causes substantial morbidity. In addition to the pain and suffering of an acute stone event, treatment incurs substantial costs, and additional costs result from time lost from work, as many individuals are affected during their working years.

DEFINITION AND DIAGNOSIS

Urolithiasis denotes stones originating anywhere in the urinary tract, including the kidneys and bladder. However, the pathophysiologic bases for the formation of kidney and bladder stones are entirely different. Kidney stones form as a result of physicochemical or genetic derangements leading to supersaturation of the urine with stone-forming salts or, less commonly, from recurrent urinary tract infection with urease-producing bacteria. Stasis in the upper urinary tract due to local anatomic anomalies may also promote or enhance stone formation in susceptible individuals. In contrast, bladder stones form almost exclusively as a result of urinary stasis and/or recurrent infection due to bladder outlet obstruction or neurogenic bladder. The patient populations at risk for different locations of stones are disparate, with kidney stones occurring most often in otherwise healthy individuals and bladder stones occurring in those with neurologic and/or anatomic abnormalities. For the purposes of this chapter, we have tried to distinguish upper urinary tract stones (kidney and ureteral stones) from lower urinary tract stones (bladder stones), although in some cases the data for the two sites are combined. Table 1 presents diagnosis codes associated with urolithiasis.

Although obstructing urinary tract stones are typically associated with symptoms, a definitive diagnosis of urolithiasis cannot be based on symptoms alone. Because of the embryonic development of the kidneys and genital system, as well as the close nerve and vascular supply, pain due to stones may be referred to the gonads or confused with gastrointestinal pathology such as cholecystitis, appendicitis, gastric ulcer, or diverticulitis. Likewise, cystitis and pyelonephritis may mimic acute renal colic. Musculoskeletal pain, particularly over the flanks, may also be incorrectly attributed to stone pain.

A definitive diagnosis of a stone requires either direct stone retrieval after spontaneous passage or surgical intervention, or identification by radiologic imaging. Although an abdominal x-ray of the kidneys-ureters-bladder (KUB) is simple and requires no preparation, it can fail to reveal small or radiolucent stones. Excretory urography, also known as intravenous pyelography (IVP), is more sensitive than KUB and provides more anatomic information, but IVP can still miss small or radiolucent nonobstructing stones. Ultrasound has the advantage of avoiding exposure to radiation or contrast and can detect

Table 1. Codes used in the diagnosis and management of urolithiasis

Upper Tract	
Individuals with one of the following ICD-9 codes:	
270.0	Disturbance of amino-acid transport
274.11	Uric acid nephrolithiasis
592.0	Calculus of kidney
592.1	Calculus of ureter
592.9	Urinary calculus, unspecified
Individuals with the following ICD-9 disease code and any one of the following procedure codes, or the procedure code alone:	
271.8	Other specified disorders of carbohydrate transport and metabolism
and	
ICD-9 Procedure Code	
55.03	Percutaneous nephrostomy without fragmentation
55.04	Percutaneous nephrostomy with fragmentation
55.92	Percutaneous aspiration of kidney (pelvis)
56.0	Transurethral removal of obstruction from ureter and renal pelvis
56.2	Ureterotomy
59.8	Ureteral catheterization
59.95	Ultrasonic fragmentation of urinary stones
98.51	Extracorporeal shockwave lithotripsy (ESWL) of the kidney, ureter and/or bladder
CPT-4 Procedure Codes	
50060	Nephrolithotomy; removal of calculus
50065	Nephrolithotomy; secondary surgical operation for calculus
50070	Nephrolithotomy; complicated by congenital kidney abnormality
50075	Nephrolithotomy; removal of large staghorn calculus filling renal pelvis and calyces (includes anatrophic pyelolithotomy)
50080	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting, or basket extraction; up to 2 cm
50081	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting, or basket extraction; over 2 cm
50125	Pyelotomy; with drainage, pyelostomy
50590	Lithotripsy, extracorporeal shock wave
50610	Ureterolithotomy; upper one-third of ureter
50620	Ureterolithotomy; middle one-third of ureter
50630	Ureterolithotomy; lower one-third of ureter
52320	Cystourethroscopy (including ureteral catheterization); with removal of ureteral calculus
52325	Cystourethroscopy (including ureteral catheterization); with fragmentation of ureteral calculus (e.g., ultrasonic or electro-hydraulic technique)
52330	Cystourethroscopy (including ureteral catheterization): with manipulation, without removal of ureteral calculus
52351	Cystourethroscopy, with ureteroscopy and/or pyeloscopy; diagnostic (prior to 2001 was 52335)
52352	Cystourethroscopy, with ureteroscopy and/or pyeloscopy; with removal or manipulation of calculus (ureteral catheterization is included (prior to 2001 was 52336)
52353	Cystourethroscopy, with ureteroscopy and/or pyeloscopy; with lithotripsy (ureteral catheterization is included) (prior to 2001 was 52337)
Lower Tract	
Individuals with one of the following ICD-9 codes:	
594.0	Calculus in diverticulum of bladder
594.1	Other calculus in bladder
594.2	Calculus in urethra
594.8	Other lower urinary tract calculus
594. 9	Calculus of lower urinary tract unspecified

most renal calcifications, but it is less sensitive in delineating stone size and number and cannot detect most ureteral stones. Magnetic resonance imaging is not a recommended modality because stones do not generate a signal, although medium to large stones will be seen as signal voids within the collecting system.

The most sensitive imaging modality for the diagnosis of renal, ureteral, and bladder calculi is non-enhanced, thin-cut helical computed tomography (CT), which can detect stones as small as 1 mm in diameter, regardless of composition, with the exception of indinavir stones. In recent years, non-contrast helical CT has emerged as the imaging study of choice for the evaluation of acute flank pain because of its high sensitivity and specificity in detecting renal and ureteral calculi, rapid acquisition time (less than a breath hold), and avoidance of intravenous contrast. Indeed, data derived from the Centers for Medicare and Medicaid Services (CMS) show that although IVP was still used more commonly than CT in 1998, there was a 31% decrease in the use of excretory urography and a threefold increase in the use of non-contrast CT for the diagnosis of urolithiasis between 1992 and 1998 (Table 2).

Individuals with persistent crystalluria may never form a stone, and these individuals are unlikely to be given a diagnosis of urolithiasis unless they form one. There is no clear definition that distinguishes crystalluria (or the passage of *sludge*) from urolithiasis, so the diagnosis depends on the resolution of the imaging method used. Occasionally, calcifications in the renal parenchyma are distinguished from calcifications in the urinary collecting system. Recent work suggests that intrarenal calcifications may be important precursors to stone formation (3), although further studies are needed to clarify this issue. Of the various stone compositions that occur in the urinary tract, each has specific risk factors. Most upper tract stones are composed of calcium oxalate, calcium phosphate, uric acid, struvite, or cystine; most bladder stones are composed of uric acid or calcium phosphate. Less common stones include those made of xanthine, indinavir, ephedrine, and 2,8-dihydroxyadenine.

RISK FACTORS

Risk factors for urolithiasis include age, sex, diet, geographic location, systemic and local medical conditions, genetic predisposition, and urinary composition. Urinary composition determines stone formation based on three factors: exceeding the formation product of stone forming components, the quantity of inhibitors (e.g., citrate, glycosaminoglycans, etc.) and promoters (e.g., sodium, urates, etc.) in the urine. The anatomy of the upper and lower tracts may also influence the likelihood of stone formation by predisposing to urinary tract infection or stasis. The reader is referred to major urology textbooks for additional details.

TREATMENT

The indications for surgical intervention for upper tract stones include recurrent pain, high-grade obstruction, associated infection, growth of stones despite medical therapy, and large size of stones. Treatment options include shock wave lithotripsy (SWL), ureteroscopy, percutaneous nephrostolithotomy (PCNL), and open or laparoscopic stone removal. SWL is the most commonly employed treatment modality for renal and ureteral calculi and for stones associated with some anatomic abnormalities, specifically obstruction (e.g., ureteropelvic junction obstruction, ureteric stricture, etc.) and the only completely non-invasive treatment option. Ureteroscopy is primarily used to treat ureteral stones but is increasingly being used to treat renal calculi for which SWL has failed or is ill-advised. Percutaneous nephrostolithotomy is indicated for large-volume renal calculi and for stones associated with some anatomic abnormalities. Finally, open and laparoscopic surgery are reserved for stones that have not been treatable with less invasive treatment options or are associated with extensive anatomic abnormalities that require simultaneous repair. However, open or laparoscopic therapy for urolithiasis is indicated in fewer than 2% of patients today.

Bladder stones are predominantly treated with endoscopic fragmentation, and less commonly with SWL or open procedures. Rarely, these stones have been approached laparoscopically. Because of the underlying anatomic predisposition to bladder stones,

Table 2. Use of imaging procedures in evaluation of urolithiasis among Medicare beneficiaries, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	131,200	81,466	166,580	91,546	184,320	97,825
Intravenous pyelogram	36,600	22,682	38,820	21,334	31,460	16,697
Ambulatory surgery center	1,720	1,066	1,860	1,022	1,540	817
Inpatient	13,020	8,069	11,820	6,496	7,960	4,225
Hospital outpatient	520	322	620	341	480	255
Physician office	21,340	13,225	24,520	13,475	21,480	11,400
Plain film/KUB	70,760	43,852	93,100	51,165	107,700	57,160
Ambulatory surgery center	13,220	8,193	16,380	9,002	18,220	9,670
Inpatient	15,560	9,643	13,280	7,298	13,640	7,239
Hospital outpatient	1,860	1,153	1,820	1,000	1,940	1,030
Physician office	40,120	24,864	61,620	33,865	73,900	39,221
Ultrasound (renal)	18,320	11,353	27,440	15,080	32,460	17,227
Ambulatory surgery center	520	322	500	275	800	425
Inpatient	6,020	3,731	7,660	4,210	9,800	5,201
Hospital outpatient	240	149	220	121	240	127
Physician office	11,540	7,152	19,060	10,475	21,620	11,474
Magnetic resonance imaging, abdomen	60	37	60	33	100	53
Ambulatory surgery center	0	0	0	0	0	0
Inpatient	40	25	40	22	40	21
Hospital outpatient	0	0	0	0	20	11
Physician office	20	12	20	11	40	21
CT abdomen/pelvis with contrast	1,180	731	1,640	901	2,280	1,210
Ambulatory surgery center	60	37	220	121	160	85
Inpatient	920	570	1,060	583	1,560	828
Hospital outpatient	0	0	0	0	0	0
Physician office	200	124	360	198	560	297
CT abdomen/pelvis without contrast	1,160	719	1,660	912	5,980	3,174
Ambulatory surgery center	60	37	200	110	420	223
Inpatient	640	397	1,020	561	3,320	1,762
Hospital outpatient	20	12	0	0	80	42
Physician office	440	273	440	242	2,160	1,146
CT abdomen/pelvis with and without contrast	1,400	892	2,080	1,143	2,560	1,359
Ambulatory surgery center	200	124	180	99	140	74
Inpatient	720	446	920	506	1,120	594
Hospital outpatient	0	0	60	33	100	53
Physician office	520	322	920	506	1,200	637
CT scan abdomen, unspecified						
Inpatient	1,720	1,200	1,780	978	1,780	945

[a]Unweighted counts were multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 based on number of Medicare beneficiaries with diagnosis of urolithiasis.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

simultaneous treatment of bladder outlet obstruction is commonly performed, combining either open prostatectomy or transurethral prostate resection with stone removal or fragmentation.

Improvements in the instrumentation and technique for endoscopic stone removal and refinements in the indications for SWL treatment have improved success rates and reduced the morbidity associated with stone treatment. As a result, treatment selection has changed over time to accommodate the new technology. These changes, along with changes in prevalence, have altered the economic impact of stone disease. A trend toward less invasive treatment options that require shorter hospital stays and enable quicker convalescence has reduced hospital costs and lessened the burden of lost workdays. Nevertheless, the costs of stone disease—both direct medical expenditures and the costs of missed work and lost wages—are difficult to ascertain. This chapter provides data from a variety of sources to assist in estimating the financial burden of urolithiasis in terms of expenditures by the payor.

While this chapter presents the best available information regarding the financial burden of stone disease, some important limitations should be kept in mind when viewing the tabular data. Although there are clear differences in some rates by age and sex, the rates for many of the factors of interest are age-adjusted only in certain tables, and none of the data were sex-adjusted. This may have an impact on the interpretation of the rates, as indicated later in the chapter. There is no new information available on rates for specific stone types and sizes or for first-time versus recurrent stone formers; nor is there new information on incidence rates in the strict epidemiologic sense (first event). Finally, because of the structure of the databases that were used to collect the information, we cannot draw causal inferences about risk factors.

PREVALENCE AND INCIDENCE

Because stones in the urinary tract may be present but asymptomatic, prevalence estimates based on questionnaires or medical encounters are likely to be underestimates. For clarity of interpretation, it is important to distinguish between *prevalent stones* (stones that are actually in the patient) and *prevalent stone disease* (patients with a history of stone disease but who may not currently have a stone). For this chapter, the term *prevalence* refers to prevalent stone disease unless otherwise noted.

Several factors have hampered our understanding of the prevalence and incidence of urolithiasis. Lack of comprehensive data has led to a variety of beliefs regarding the frequency of stone disease. Because a number of factors, including age and sex, influence prevalence and incidence, care must be taken when interpreting results and comparing studies. Demographic factors that are traditionally believed to

Table 3. Percent prevalence[a] of a history of kidney stones (±SE) in United States adults by gender, age group, and time period (NHANES II, 1976 to 1980; NHANES III, 1988 to 1994)

	Males			Females		
Age	1976 to 1980	1988 to 1994	Difference (95% CI)[b]	1976 to 1980	1988 to 1994	Difference (95% CI)[b]
20–29	0.9 ± 0.31	1.3 ± 0.42	0.4 (–0.6, 1.4)	1.4 ± 0.36	2.0 ± 0.51	0.6 (–0.6, 1.9)
30–39	4.2 ± 0.51	3.6 ± 0.75	–0.6 (–2.4, 1.1)	2.0 ± 0.37	3.0 ± 0.57	1.0 (–0.8, 2.8)
40–49	6.9 ± 0.99	9.5 ± 1.45	2.6 (–0.8, 6.1)	2.2 ± 0.40	4.2 ± 0.70	2.0 (0.4, 3.5)
50–59	7.5 ± 1.26	9.6 ± 1.17	2.1 (–1.3, 5.4)	5.3 ± 0.64	7.0 ± 1.10	1.7 (–0.7, 4.3)
60–69	8.3 ± 0.66	11.1 ± 1.68	2.8 (–0.8, 6.3)	4.2 ± 0.48	5.6 ± 0.88	1.4 (–0.6, 3.3)
70–74	6.7 ± 0.86	13.3 ± 1.81	6.6 (2.7, 10.5)	3.7 ± 0.68	6.9 ± 1.38	3.2 (0.2, 6.3)
All ages[c]	4.9 ± 0.42	6.3 ± 0.56	1.4 (0.05, 2.8)	2.8 ± 0.17	4.1 ± 0.27	1.3 (0.7, 1.5)

[a]Crude unadjusted prevalence.

[b]Difference is prevalence in 1988 to 1994 minus prevalence in 1976 to 1980; 95% CI denotes the lower limit, upper limit of the 95% CI estimate of the difference. Bold type indicates that the difference was statistically significant at P < 0.05.

[c]Persons 20 to 74 years of age.

SOURCE: Reprinted from Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC, Time trends in reported prevalence of kidney stones in the United States: 1976–1994, Kidney International, 63, 1,817–1,823, Copyright 2003, with permission from Blackwell Publishing Ltd.

be associated with risk of upper tract stone disease but are by no means proven include sex (the ratio of male: female incidence is 2:1 to 3:1), age (peak incidence occurs between 20 and 60 years of age), race, and geography (North–South and West–East gradients). The data presented here shed considerable light on the relative importance of these factors.

A recent study based on data from National Health and Nutrition Examination Survey (NHANES) II (1976 to 1980) and NHANES III (1988 to 1994) suggests that kidney stone disease is becoming more common (4) (Table 3 and Figure 1). Prevalence of the disease in US adults increased from 3.8% to 5.2% between the two time periods; it increased across all age groups and in both sexes (Table 4), and in both African Americans and Caucasians in all age groups (Figure 2) (5). Stamatelou et al. also found that a history of kidney stone disease was most common among non-Hispanic Caucasians; prevalence among non-Hispanic African Americans was approximately 70% lower, and among Mexican Americans it was approximately 35% lower. In the 1988–1994 period, the age-adjusted prevalence was highest in the South (6.6%) and lowest in the West (3.3%).

Few studies contain information on true incidence rates for urolithiasis, where incidence is defined as the first stone-related event. Factors that influence incidence rates are sex, age, race, and geographic region. Population-based estimates have ranged from 1 to 3 per 1,000 per year for men and 0.6 to 1.0 per 1,000 per year for women (1, 2, 6, 7). Overall, the age-specific rates for males seem to rise in the early 20s, peak in the 40- to 59-year age group, and then

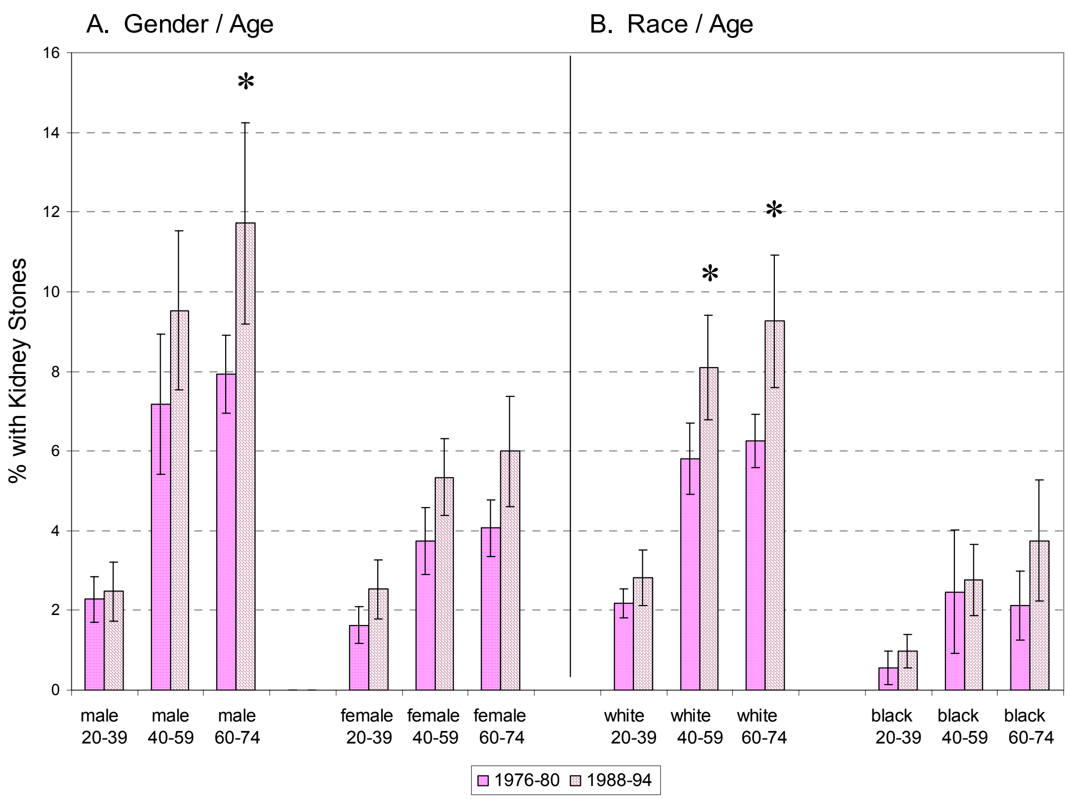

Figure 1. Percent prevalence of history of kidney stones for 1976 to 1980 and 1988 to 1994 in each age group for each gender (A) and each race group (B) . Error bars denote the 95% confidence interval. *Statistically significant time period difference.

SOURCE: Reprinted from Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC, Time trends in reported prevalence of kidney stones in the United States: 1976-1994, Kidney International, 63, 1,817–1,823, Copyright 2003, with permission from Blackwell Publishing Ltd.

Table 4. Age-, race-, and gender-specific prevalence of kidney stones in CPS II and NHANES II

		CPS II								NHANES II	
		White		Black		Hispanic		Asian		White	
Gender	Age	N	Prev.	N	Prev.	N	Prev.	N	Prev.	N	Prev.
Male	30–39	16,920	4.2	1,264	2.0	405	3.0	226	2.2	921	4.7
	40–49	83,914	7.7	3,746	3.2	1,213	6.2	674	4.3	775	7.4
	50–59	178,442	9.2	6,334	4.3	1,672	6.3	1,257	6.4	755	8.3
	60–69	137,643	10.1	4,854	4.6	780	8.6	877	6.6	1,780	8.8
	70+	60,928	9.2	2,583	4.4	328	6.1	320	5.3	608	7.2
	All[a]	477,847	8.9	18,781	4.1	4,398	6.7	3,354	5.7	4,839	7.5
Prevalence ratio[b]		1.0		0.44 (0.41–0.48)		0.70 (0.63–0.79)		0.63 (0.55–0.72)			
Female	30–39	30,661	2.4	2,902	1.2	822	1.8	441	1.1	1,061	2.1
	40–49	136,597	3.0	7,644	1.7	2,081	2.8	1,114	1.6	852	2.5
	50–59	214,096	3.4	10,575	2.3	2,231	3.3	1,692	2.3	883	5.4
	60–69	161,021	3.7	7,644	2.7	1,019	3.6	917	2.1	2,080	4.6
	70+	83,763	3.7	4,408	2.6	537	3.2	316	1.0	829	4.0
	All[a]	626,138	3.4	33,173	2.3	6,690	3.2	4,480	1.7	5,705	4.1
Prevalence ratio[b]		1.0		0.65 (0.60–0.70)		0.88 (0.77–1.01)		0.55 (0.44–0.68)			

CPS, Cancer Prevention Study; NHANES, National Health and Nutrition Examination Survey; Prev, prevalence.
[a] Prevalences are standardized to the age distribution (5-year age groups) of all CPS II participants.
[b] Ratio of the prevalence for race relative to whites (CPS II only).

SOURCE: Reprinted from Soucie JM, Thun MJ, Coates RJ, McClellan W, Austin H, Demographic and geographic variability of kidney stones in the United States, Kidney International, 46, 893–899, Copyright 1994, with permission from Blackwell Publishing Ltd.

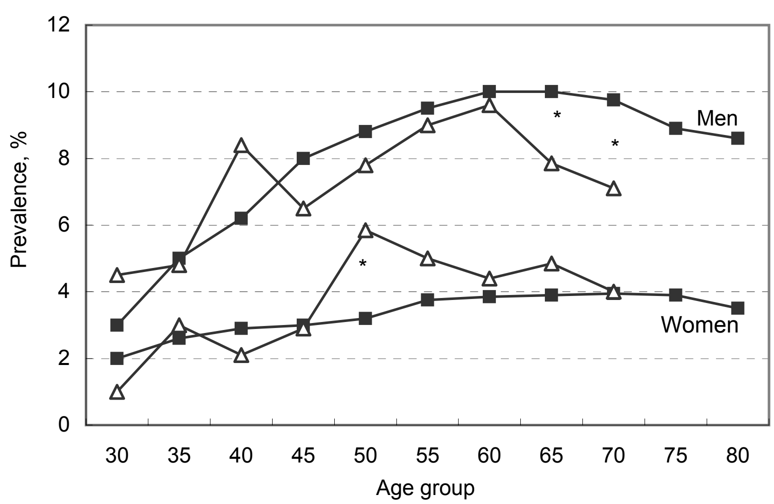

Figure 2. Age-specific prevalence of kidney stones among white men and women in CPS II (■) and NHANES II (∆). No partipants in NHANES II were older than 74 years.

***Prevalence extimates differ significantly between studies (P<0.05).**

SOURCE: Adapted from Soucie JM, Thun MJ, Coates RJ, McClellan W, & Austin H, Demographic and geographic variability of kidney stones in the United States, Kidney International, 46, 893–899, Copyright 1994, with permission from Blackwell Publishing Ltd.

decrease. The rates in women appear to be relatively constant across age groups.

Scant population-based information is available on recurrence rates, which depend on a variety of factors, including how recurrence is defined and how treatments are implemented. New data in this chapter focus on *office* or *hospital outpatient visits* and *procedures*, which cannot be extrapolated to determine the true prevalence of stone disease. In addition, these new data cannot be used to determine incidence or recurrence rates.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Inpatient hospitalizations consist of admissions for surgical treatment of stones and hospitalization for management of acute stone events. Patients admitted for acute management generally receive hydration, analgesics, and antiemetics. Management may also include temporizing procedures prior to definitive stone treatment such as placement of a ureteral stent or percutaneous nephrostomy to relieve obstruction, especially in an infected kidney.

Upper Tract Stones: Hospitalization Rates

According to the Healthcare Cost and Utilization Project (HCUP), the rate of national inpatient hospitalizations for upper tract stones in 2000 was 62 per 100,000 population, with the number of admissions totaling 170,316—a 15% decrease since 1994, when the hospitalization rate was 73 per 100,000 and the total number of admissions was 183,322 (Table 5). The steady decline in the rate of hospitalization for patients with upper tract stones between 1994 and 2000 likely reflects the greater efficiency and reduced morbidity of surgical treatment for upper tract stones that have resulted in more procedures being performed in the outpatient setting, rather than a reduction in admissions for acute stone events; in particular, advances in ureteroscopy and percutaneous nephrostolithotomy have reduced hospital admissions and shortened hospital stays.

According to HCUP, hospitalization rates were highest in the 55- to 64-year age groups in 1994, 1998, and 2000, but were equally high in the 45 to 54, 55 to 64, and 65 to 74 age groups in 1996 (Figure 3). The high rate of inpatient hospitalization for the older age groups likely reflects the lower threshold for admission for an acute stone event or after surgical treatment due to the greater number of comorbidities in these older patients.

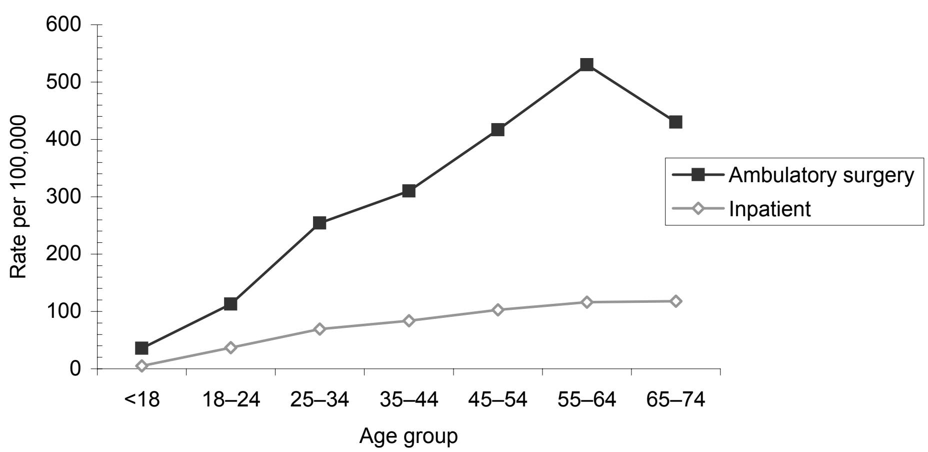

Figure 3. Rates of inpatient and ambulatory surgery visits for urolithiasis by age group, 2000.

SOURCE: Center for Health Care Policy and Evaluation (Ambulatory Surgery); Healthcare Cost and Utilization Project (Inpatient), 2000.

Table 5. Inpatient hospital stays by individuals with upper tract urolithiasis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	183,322	73 (69–76)	170,218	65 (62–67)	165,296	62 (59–64)	170,316	62 (60–65)
Age								
< 18	2,931	4.3 (3.7–4.9)	2,565	3.6 (3.2–4.1)	2,962	4.1 (3.7–4.6)	3,419	4.7 (4.2–5.3)
18–24	10,541	43 (39–46)	9,935	40 (37–43)	9,152	37 (34–39)	9,478	36 (33–39)
25–34	29,608	73 (68–77)	28,370	70 (66–75)	26,402	68 (63–72)	25,511	68 (63–73)
35–44	40,906	102 (96–108)	38,541	90 (84–95)	37,583	85 (80–90)	36,956	83 (78–88)
45–54	37,438	130 (123–138)	35,468	112 (106–118)	34,698	102 (96–107)	36,935	101 (96–107)
55–64	27,009	134 (126–141)	23,513	112 (106–118)	24,283	109 (103–116)	26,138	112 (106–117)
65–74	22,700	128 (121–135)	20,601	113 (107–119)	18,563	104 (98–109)	18,955	107 (101–112)
75–84	10,403	108 (101–115)	9,454	89 (84–94)	9,791	87 (81–92)	10,684	91 (86–96)
85+	1,777	64 (55–73)	1,755	63 (55–71)	1,845	64 (56–71)	2,236	72 (64–79)
Race/ethnicity								
White	122,566	66 (63–69)	111,036	58 (56–61)	106,437	56 (53–58)	107,087	55 (53–58)
Black	6,737	21 (19–23)	6,709	20 (19–22)	6,905	21 (18–23)	6,497	19 (17–21)
Asian/Pacific Islander	1,562	22 (17–27)	1,589	17 (14–19)	1,733	17 (13–21)	1,804	17 (14–20)
Hispanic	8,816	34 (29–39)	9,453	33 (27–39)	9,915	32 (27–37)	11,855	36 (32–40)
Gender								
Male	117,165	95 (90–100)	105,187	82 (78–86)	100,550	77 (73–80)	99,214	74 (71–78)
Female	66,146	51 (49–53)	65,026	48 (46–50)	64,746	47 (45–49)	71,087	51 (49–53)
Region								
Midwest	47,638	79 (72–86)	42,645	69 (63–75)	40,537	65 (60–69)	43,700	69 (64–73)
Northeast	45,722	89 (82–97)	40,272	78 (72–84)	38,591	75 (67–84)	36,159	70 (63–77)
South	67,950	80 (73–86)	66,582	72 (67–78)	64,728	69 (64–73)	66,628	70 (64–75)
West	22,012	39 (36–43)	20,719	36 (32–39)	21,439	36 (32–39)	23,828	38 (35–42)
MSA								
Rural	40,136	63 (58–68)	38,484	65 (60–69)	35,737	59 (55–63)	39,373	65 (61–70)
Urban	142,429	75 (71–79)	131,392	64 (61–68)	128,366	62 (59–65)	130,651	61 (58–64)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of missing age, other races, missing or unavailable race and ethnicity, missing gender, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

When hospitalization rates were stratified by ethnicity, Caucasians had the highest rate. Admission rates for Hispanics were one-half to two-thirds those of Caucasians throughout the periods of observation. Strikingly little regional variation was observed, with the exception of the West, where hospitalization rates were consistently half the rates in the other geographic areas (Northeast, Midwest, and South). Admission rates were similar in urban and rural areas. When rates in HCUP were age-adjusted (Table 6), the geographic variations remained stable; however the ethnic/racial differences were narrower and male-to-female ratios were slightly narrower. In both the age-unadjusted and the age-adjusted data, the male-to-female ratios also fell slightly over time.

Medicare data from the Centers for Medicare and Medicaid Services (CMS) for 1992, 1995, and 1998 (Table 7) indicate that inpatient hospitalization rates for upper tract stones were 2.5 to 3 times higher in this patient population than in the population studied in HCUP. Total admission rates decreased over time, from 194 per 100,000 in 1992 to 188 per 100,000 in 1995 and 184 per 100,000 in 1998, representing an overall 5% reduction in hospitalization rates, compared with a 15% decrease between 1994 and 2000 in the HCUP population (Figure 4). Admission rates of Medicare beneficiaries were consistently higher in the ≥65 age group than in the <65 age group, peaking in the 75- to 84-year group in each year of study. Likewise, the geographic distribution was similar to that seen in the HCUP database, with the highest rates of admission in the Northeast and South and the lowest in the West. In 1995, when CMS racial categories were modified, age-unadjusted admission rates were highest among Caucasians and lowest among Asians; in 1998 the age-unadjusted admission rate was highest in North American Natives, but the relatively small count in this group should lead to caution in interpreting this difference. Age-adjustment did not affect regional differences in admission rates, but it did slightly widen the gender gap. Age-adjustment did not affect admission rates in Caucasians or African Americans, but it did raise the rates in Hispanics and lower the rates in Asians.

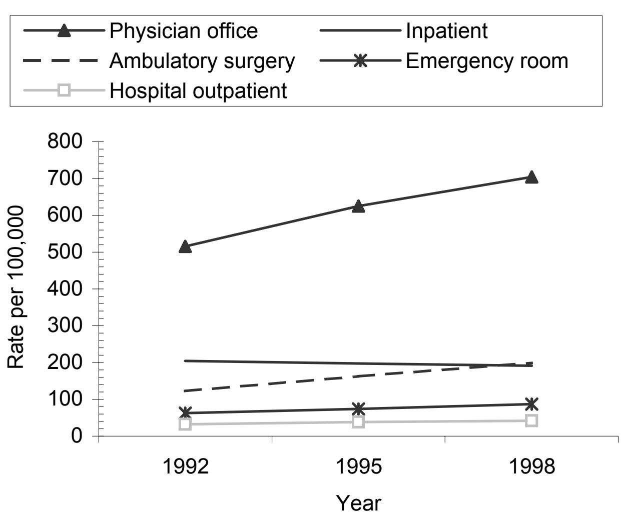

Figure 4. Rates of visits for urolithiasis, by visit setting and year.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

Upper Tract Stones: Length of Stay

According to the HCUP data, the mean hospital length of stay (LOS) associated with admission for upper tract stones as a primary diagnosis declined steadily from 1994 to 2000, dropping from a mean of 2.6 days in 1994 to 2.2 days in 2000 (Table 8). Starting at age 18, there was a steady rise in LOS with age, peaking in the 85+ age group. Indeed, in 2000, the mean LOS in the 18- to 24-year age group was 1.8 days, compared with 4.4 days in the 85+ age group. Although a longer LOS in the elderly population is understandable due to the overall poorer health of this group, reasons for the higher LOS in the pediatric population (<18 years of age) compared with that in the youngest adult group (18 to 24 years) are less clear. However, the disparity in the LOS between these groups narrowed over time, and by 2000 the mean LOS was comparable for the two groups at 1.9 and 1.8 days, respectively.

Using the National Association of Children's Hospitals and Related Institutions (NACHRI) database of pediatric inpatients with a primary diagnosis of urolithiasis (both upper and lower tract stones) (Table 9), during 1999, 2000, and 2001, the mean LOS was nearly twice as high during each of the years of observation for the 0- to 2-year age group as it was in the 3 to 10 or 11 to 17 age group, most likely because stones occurring in infants are often associated with other systemic illnesses, and treatment

Table 6. Inpatient hospital stays by individuals with upper tract urolithiasis listed as primary diagnosis, age-adjusted count, age-adjusted rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	199,638	79 (75–83)	193,325	73 (70–77)	190,129	71 (68–74)	193,699	71 (68–74)
Race/ethnicity								
White	131,957	71 (67–75)	124,173	65 (62–68)	120,284	63 (60–66)	119,745	62 (59–65)
Black	7,772	25 (22–27)	7,957	24 (22–26)	8,272	25 (22–28)	7,643	22 (20–24)
Asian/Pacific Islander	1,818	26 (19–32)	1,831	19 (16–22)	2,038	20 (14–26)	2,068	20 (16–23)
Hispanic	10,205	40 (34–45)	11,366	40 (33–47)	12,153	40 (33–46)	14,724	45 (40–50)
Gender								
Male	123,765	100 (95–106)	116,243	91 (86–95)	112,690	86 (81–91)	108,937	82 (78–86)
Female	75,857	59 (56–61)	77,074	57 (54–60)	77,439	56 (54–59)	84,744	60 (58–63)
Region								
Midwest	51,727	86 (77–94)	48,167	78 (71–85)	46,514	74 (69–80)	49,578	78 (72–84)
Northeast	49,834	97 (88–107)	45,182	88 (81–95)	44,119	86 (76–96)	40,210	78 (69–86)
South	73,657	86 (78–94)	76,193	83 (76–90)	74,548	79 (73–85)	76,661	80 (73–87)
West	24,420	44 (39–48)	23,782	41 (36–45)	24,947	41 (37–46)	27,250	44 (39–48)
MSA								
Rural	43,444	68 (62–74)	43,931	74 (68–80)	41,353	68 (63–74)	45,093	75 (70–80)
Urban	155,363	82 (77–87)	149,002	73 (69–77)	147,378	71 (67–75)	148,257	70 (66–73)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population; age-adjusted to the 2000 US Census.

[b]Persons of missing age, other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 7. Inpatient stays by Medicare beneficiaries with upper tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c] (95% CI)

	1992			1995			1998		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	67,080	194 (193–196)	194	66,460	188 (186–189)	188	61,540	184 (182–185)	184
Total < 65	9,000	164 (161–168)		10,140	165 (162–169)		9,400	151 (148–154)	
Total 65+	58,080	200 (198–201)		56,320	192 (191–194)		52,140	191 (189–192)	
Age									
65–74	34,300	209 (207–211)		30,360	188 (185–190)		25,640	179 (177–181)	
75–84	19,880	211 (208–214)		20,080	208 (205-211)		20,920	220 (217–223)	
85–94	3,660	128 (124–132)		5,520	180 (175–184)		5,280	171 (166–175)	
95+	240	72 (63–80)		360	99 (88–109)		300	75 (67–84)	
Race/ethnicity									
White	58,400	200 (198–202)	199	59,420	196 (194–197)	195	54,560	192 (190–194)	192
Black	4,580	155 (150–159)	158	4,800	149 (145–153)	152	4,320	139 (135–144)	141
Asian	…	…	…	120	72 (59–84)	48	360	115 (103–126)	108
Hispanic	…	…	…	640	160 (148–173)	175	1,180	168 (158–177)	179
N. American Native	…	…	…	60	165 (124–207)	221	120	222 (183–261)	222
Gender									
Male	38,440	261 (258–264)	267	38,200	251 (248–254)	256	33,320	230 (228–233)	234
Female	28,640	145 (143–146)	140	28,260	140 (138–142)	136	28,220	148 (146–150)	145
Region									
Midwest	16,720	192 (189–194)	191	16,120	179 (176–182)	179	15,460	179 (176–182)	176
Northeast	16,980	220 (217–224)	219	17,400	227 (223–230)	225	13,400	200 (197–203)	196
South	26,020	213 (210–215)	216	25,180	198 (196–201)	200	24,600	199 (196–201)	203
West	6,680	131 (128–134)	125	7,280	140 (137–144)	137	7,420	150 (146–153)	149

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[a]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[d]Persons of other races, unkown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

Table 8. Trends in mean inpatient length of stay (days) for individuals hospitalized with upper tract urolithiasis listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	2.6	2.4	2.3	2.2
Age				
< 18	2.5	2.4	2.2	1.9
18–24	2.2	2.0	1.9	1.8
25–34	2.2	2.0	1.9	1.9
35–44	2.3	2.1	2.1	2.0
45–54	2.4	2.3	2.1	2.1
55–64	2.7	2.4	2.3	2.3
65–74	3.4	3.1	2.8	2.6
75–84	4.3	3.7	3.5	3.3
85+	4.7	4.3	4.6	4.4
Race/ethnicity				
White	2.6	2.4	2.2	2.1
Black	3.5	3.4	3.1	3.1
Asian/Pacific Islander	2.8	3.1	2.6	2.7
Hispanic	2.9	2.7	2.6	2.4
Other	3.9	2.4	2.5	2.3
Region				
Midwest	2.4	2.2	2.1	1.9
Northeast	3.1	2.7	2.5	2.4
South	2.6	2.3	2.3	2.3
West	2.4	2.4	2.2	2.3
MSA				
Rural	2.4	2.1	2.0	1.9
Urban	2.7	2.5	2.4	2.3
Primary payor				
Medicare	3.9	3.3	3.1	3.0
Medicaid	3.5	3.2	2.9	2.7
Private insurance/HMO	2.2	2.0	2.0	1.9
Self-pay	2.2	2.1	2.0	2.0
No charge	*	2.3	2.6	2.7
Other	2.6	2.3	2.3	2.3

MSA, metropolitan statistical area; HMO, health maintenance organization.

*Figure does not meet standard for reliability or precision.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

is more challenging than it is in the older pediatric population. As in the adult population, mean LOS of African Americans was consistently longer than that of other racial/ethnic groups.

When stratified by ethnicity, mean LOS in the HCUP database was consistently lowest for Caucasians and highest for African Americans (Table 8). Geographic variation was less pronounced, but mean LOS was marginally highest in the Northeast for all years analyzed and lowest in the Midwest in 1996, 1998, and 2000. Mean LOS was consistently higher in urban than in rural areas.

When LOS was stratified by payor, private insurance/HMO and self-pay groups were associated with the shortest LOS (Table 8). Moreover, these two groups with comparable LOS showed little variation in mean LOS over the years studied. The Medicare group had the highest LOS in each of the years analyzed, likely due to their more advanced age. However, Medicare patients demonstrated the most-pronounced reduction in LOS over time, dropping 23% between 1994 (3.9 days) and 2000 (3.0 days); the Medicaid group likewise showed a similar reduction in LOS, but their overall LOS was shorter than that of the Medicare group.

Lower Tract Stones: Procedures

During hospital admission for urolithiasis, a variety of procedures may be performed, including radiographic studies, drainage procedures for relief of obstruction (i.e., placement of a ureteral stent or percutaneous nephrostomy), or surgical procedures to remove stones. Although most surgical interventions for stone disease are minimally invasive treatments performed on an outpatient basis, some procedures typically used for outpatients may be performed during inpatient admission for an acute stone event to provide definitive treatment after the patient is stabilized. Alternatively, some procedures for stone removal, such as percutaneous nephrostolithotomy, are associated with a short hospital stay. The numbers and rates of procedures performed during inpatient hospitalization on patients with a primary diagnosis of urolithiasis (both upper and lower tract stones) in 1994, 1996, 1998, and 2000, derived from the Center for Health Care Policy and Evaluation, are shown in Table 10. Although the total number of procedures increased from 1994 to 1998, the rate decreased (from

Table 9. Trends in mean inpatient length of stay (days) for children hospitalized with urolithiasis listed as primary diagnosis (95% CI)

	1999			2000			2001		
	Count	Length of Stay		Count	Length of Stay		Count	Length of Stay	
Total	461	3.1	(2.7–3.6)	553	2.8	(2.6–3.1)	619	3.2	(2.7–3.8)
Age									
0–2	43	7.5	(3.8–11.2)	45	4.8	(3.2–6.4)	37	6.2	(4.2–8.2)
3–10	193	2.8	(2.4–3.2)	198	2.6	(2.3–2.9)	225	2.9	(2.4–3.4)
11–17	225	2.6	(2.3–2.9)	310	2.7	(2.3–3.1)	357	3.1	(2.2 - 4.1)
Race/ethnicity									
White	338	3.1	(2.6–3.6)	385	2.7	(2.4–3.0)	447	2.8	(2.5–3.1)
Black	31	3.4	(1.9–5.0)	34	3.7	(2.5–4.8)	38	4.1	(1.8–6.3)
Asian	1	4.0		3	1.3	(0–2.8)	2	1.5	(0–7.8)
Hispanic	36	3.1	(2.4–3.8)	51	2.8	(2.0–3.5)	78	3.4	(2.6–4.1)
N. American Native	0			3	2.7	(0–5.5)	1	2.0	
Other	17	2.4	(1.2–3.5)	21	2.4	(1.5–3.3)	32	8.6	(0–18.6)
Missing	38	3.6	(2.5–4.6)	56	3.6	(2.4–4.7)	21	2.9	(2.1–3.6)
Gender									
Male	261	3.0	(2.5–3.6)	280	2.8	(2.4–3.2)	312	3.0	(2.5–3.4)
Female	200	3.3	(2.6–4.0)	273	2.8	(2.4–3.2)	307	3.5	(2.4–4.5)
Region									
Midwest	160	3.3	(2.4–4.3)	197	2.7	(2.2–3.2)	199	3.2	(1.6–4.8)
Northeast	24	2.5	(1.7–3.2)	39	2.5	(2.0–3.0)	56	2.6	(2.1–3.1)
South	203	3.0	(2.5–3.5)	246	2.8	(2.4–3.2)	287	3.0	(2.6–3.4)
West	61	3.2	(2.4–4.2)	50	3.3	(2.0–4.7)	77	4.4	(3.0–5.7)
Missing	13	3.9	(2.0–5.8)	21	3.9	(2.5–5.3)	0		

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

25 per 100,000 to 22 per 100,000) but then increased in 2000 to the 1994 level. The reasons for these trends in the rates of procedures are not clear from these data; further analysis of the types of procedures performed is required. In all years of study, the rates of procedures increased with age to a maximum in the 55- to 64-year age group. Beyond that age, procedure counts in this database were too small to be reliable. Also, differences in sampling strategies in the datasets analyzed may have contributed to differences in estimates of the burden of stone disease.

Lower Tract Stones: Hospitalization Rates

Inpatient hospitalizations for lower tract stones, primarily bladder stones, demonstrated greater stability over time than did those for upper tract stones. According to data derived from HCUP, the absolute number and the rate of inpatient hospitalizations both remained stable from 1994 to 2000, with rates of 2.5 to 3.3 hospitalizations per 100,000 population (Table 11). For all years of study, hospitalization rates were highest in the 85+ age group, although they increased substantially after age 64—by 2.5 to 5 times—likely reflecting the higher prevalence of bladder stones in the older male population with bladder outlet obstruction. When rates in HCUP were age-adjusted, they remained fairly stable across racial/ethnic, geographic, and rural/urban groups; however, male-to-female ratios dropped from 2:3 to 3:4. (Table 12).

The Medicare population represented in the CMS database experienced a 30% decrease in hospitalization rate for lower tract stones between 1992 and 1998 (from 10 per 100,000 to 7 per 100,000), with a 43% to 60% higher rate of hospitalization in the

Table 10. Inpatient procedures for individuals having commercial health insurance with urolithiasis listed as primary diagnosis, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	272	25	375	24	539	22	682	25
Age								
< 3	1	*	1	*	3	*	4	*
3–10	2	*	0	0	4	*	7	*
11–17	2	*	1	*	7	*	10	*
18–24	7	*	22	*	34	15	46	18
25–34	47	25	69	25	104	25	133	30
35–44	61	28	112	34	144	28	160	29
45–54	93	59	105	43	145	36	175	37
55–64	49	65	54	46	79	39	126	52
65–74	10	*	10	*	17	*	16	*
75–84	0	0	1	*	2	*	5	*
85+	0	0	0	0	0	0	0	0
Gender								
Male	172	33	230	29	323	26	394	29
Female	100	18	145	18	216	18	288	21
Region								
Midwest	177	27	226	25	237	20	325	24
Northeast	31	20	29	*	44	22	42	26
Southeast	53	27	113	26	243	26	305	28
West	11	*	7	*	15	*	10	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for individuals in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

≥65 age group than in the <65 age group (Table 13). Given the higher frequency of bladder stones in men, the rate of hospitalization, not surprisingly, was 6 to 9 times higher in men than in women. Geographic variation was also evident, with rates highest in the Northeast and lowest in the West. Racial/ethnic variation was less consistent, with the highest rates occurring among Hispanics in 1995 and among African Americans in 1998. When the CMS data were age-adjusted, hospitalization rates among Hispanics dropped by 33% in 1995 and rose by 50% in 1998, underscoring the inconsistency in racial/ethnic group differences. Age-adjustment did not affect gender or geographic group comparisons.

Lower Tract Stones: Length of Stay

Similar to the trend observed with upper tract stones, the mean LOS for lower tract stones declined steadily over time, decreasing by 15% from a mean of 3.4 days in 1994 to 2.9 days in 2000 (Table 14). No clear trends with regard to age-specific LOS were discerned except that mean LOS was highest in the 85+ age group. Stratification of LOS by geographic region revealed that the lowest mean LOS occurred in the West. As observed with the upper tract stone data, LOS for lower tract stones was lower in the private pay/HMO and self-pay groups than in the Medicare groups.

Table 11. Inpatient hospital stays by individuals with lower tract urolithiasis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	8,280	3.3 (3.0–3.5)	7,852	3.0 (2.7–3.2)	6,700	2.5 (2.3–2.7)	7,180	2.6 (2.4–2.8)
Age								
< 18	*	*	*	*	*	*	*	*
18–24	166	0.7 (0.4–0.9)	237	1.0 (0.6–1.4)	*	*	164	0.6 (0.4–0.8)
25–34	511	1.3 (1.0–1.6)	325	0.8 (0.6–1.0)	303	0.8 (0.6–1.0)	335	0.9 (0.7–1.1)
35–44	598	1.5 (1.2–1.8)	562	1.3 (1.0–1.6)	460	1.0 (0.8–1.3)	425	1.0 (0.8–1.2)
45–54	798	2.8 (2.2–3.4)	627	2.0 (1.6–2.3)	638	1.9 (1.5–2.3)	598	1.6 (1.4–1.9)
55–64	1,094	5.4 (4.6–6.3)	1,022	5.0 (4.1–5.7)	904	4.1 (3.5–4.7)	950	4.1 (3.4–4.7)
65–74	2,565	14 (13–16)	2,347	13 (11–15)	1,775	9.9 (8.7–11)	1,883	11 (9–12)
75–84	1,767	18 (16–21)	2,015	19 (17–21)	1,851	16 (15–18)	2,055	18 (16–19)
85+	585	21 (17–26)	613	22 (17–27)	507	17 (14–21)	662	21 (17–25)
Race/ethnicity								
White	5,538	3.0 (2.7–3.2)	5,551	2.9 (2.6–3.2)	4,212	2.2 (2.0–2.4)	4,521	2.3 (2.1–2.6)
Black	488	1.5 (1.2–1.9)	473	1.4 (1.1–1.8)	393	1.2 (0.9–1.4)	403	1.2 (0.9–1.5)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	435	1.7 (1.3–2.1)	441	1.6 (1.1–2.0)	443	1.4 (1.1–1.8)	451	1.4 (1.0–1.8)
Gender								
Male	6,784	5.5 (5.0–6.0)	6,735	5.2 (4.7–5.8)	5,700	4.4 (4.0–4.7)	6,151	4.6 (4.2–5.0)
Female	1,495	1.2 (1.0–1.3)	1,110	0.8 (0.7–1.0)	999	0.7 (0.6–0.8)	1,029	0.7 (0.6–0.8)
Region								
Midwest	1,796	3.0 (2.6–3.4)	1,315	2.1 (1.8–2.4)	1,591	2.5 (2.2–2.9)	1,654	2.6 (2.3–2.9)
Northeast	2,259	4.4 (3.6–5.2)	2,332	4.5 (3.7–5.4)	1,727	3.4 (2.9–3.9)	1,928	3.7 (3.1–4.3)
South	3,032	3.6 (3.2–4.0)	2,865	3.1 (2.7–3.6)	2,300	2.4 (2.2–2.7)	2,356	2.5 (2.1–2.8)
West	1,192	2.1 (1.7–2.6)	1,340	2.3 (1.9–2.7)	1,082	1.8 (1.5–2.1)	1,242	2.0 (1.6–2.4)
MSA								
Rural	1,469	2.3 (1.9–2.7)	1,171	2.0 (1.6–2.3)	914	1.5 (1.2–1.8)	1,142	1.9 (1.5–2.3)
Urban	6,803	3.6 (3.3–3.9)	6,673	3.3 (3.0–3.6)	5,763	2.8 (2.6–3.0)	6,038	2.8 (2.6–3.1)

*Figure does not meet standards for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 12. Inpatient hospital stays by individuals with lower tract urolithiasis listed as primary diagnosis, age-adjusted count, age-adjusted rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	5,852	2.3 (2.1–2.5)	5,379	2.0 (1.8–2.2)	4,725	1.8 (1.6–1.9)	4,842	1.8 (1.6–1.9)
Race/ethnicity								
White	3,795	2.0 (1.8–2.2)	3,619	1.9 (1.7–2.1)	2,789	1.5 (1.3–1.6)	2,907	1.5 (1.4–1.7)
Black	390	1.2 (0.9–1.5)	378	1.2 (0.8–1.5)	347	1.0 (0.8–1.3)	297	0.9 (0.6–1.1)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	390	1.5 (1.1–1.9)	409	1.4 (1.0–1.9)	375	1.2 (0.9–1.5)	415	1.3 (0.9–1.6)
Gender								
Male	4371	3.6 (3.2–3.9)	4194	3.3 (2.9–3.5)	3,672	2.8 (2.6–3.0)	3,785	4.6 (4.2–5.0)
Female	1480	1.1 (1.0–1.3)	1181	0.9 (0.7–1.0)	1,053	0.8 (0.6–0.9)	1,058	0.7 (0.6–0.8)
Region								
Midwest	1,287	2.1 (1.8–2.5)	893	1.4 (1.2–1.7)	1,137	1.8 (1.5–2.1)	1,131	1.8 (1.5–2.0)
Northeast	1,538	3.0 (2.4–3.6)	1,513	2.9 (2.4–3.5)	1,192	2.3 (1.9–2.7)	1,176	2.3 (1.9–2.6)
South	2,167	2.5 (2.2–2.9)	2,034	2.2 (1.9–2.6)	1,627	1.7 (1.5–1.9)	1,661	1.7 (1.5–2.0)
West	860	1.5 (1.1–1.9)	938	1.6 (1.3–1.9)	769	1.3 (1.0–1.6)	874	1.4 (1.1–1.7)
MSA								
Rural	1,081	1.7 (1.3–2.0)	812	1.4 (1.0–1.7)	662	1.1 (0.9–1.3)	826	1.4 (1.1–1.7)
Urban	4,761	2.5 (2.3–2.8)	4,556	2.2 (2.0–2.5)	4,046	2.0 (1.8–2.1)	4,017	1.9 (1.7–2.0)

*Figure does not meet standards for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS),CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population; age-adjusted to the 2000 US Census.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

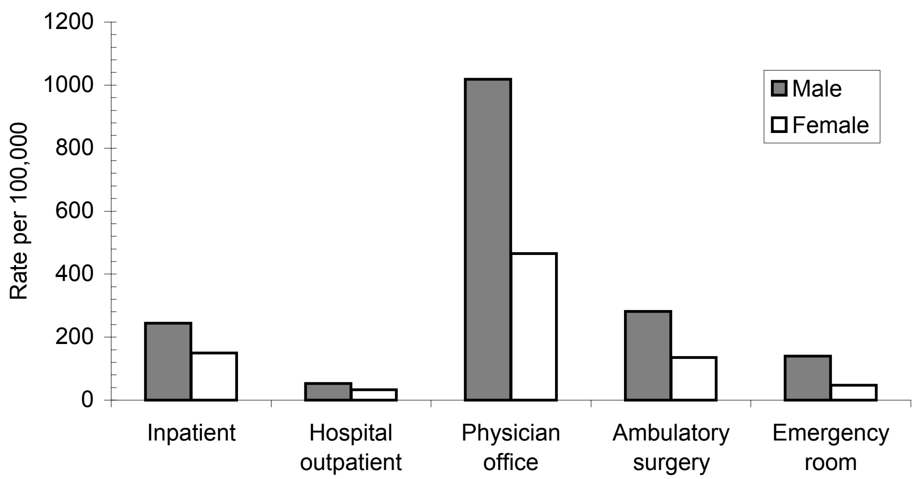

Figure 5. Rates of visits for urolithiasis by gender and site of service, 1998.

SOURCE: Centers for Medicaid and Medicare Services, 1998.

Table 13. Inpatient stays by Medicare beneficiaries with lower tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c] (95% CI)

	1992			1995			1998		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	3,460	10 (9.7–10)	10	3,280	9.3 (8.9–9.6)	9.3	2,360	7.0 (6.8–7.3)	7.0
Total < 65	380	6.9 (6.2–7.6)		400	6.5 (5.9–7.2)		280	4.5 (4.0–5.0)	
Total 65+	3,080	11 (10–11)		2,880	9.8 (9.5–10)		2,080	7.6 (7.3–7.9)	
Age									
65–74	1,760	11 (10–11)		1,280	7.9 (7.5–8.3)		800	5.6 (5.2–6.0)	
75–84	1,080	11 (11–12)		1,220	13 (12–13)		1,080	11 (11–12)	
85–94	240	8.4 (7.3–9.4)		380	12 (11–14)		180	5.8 (5.0–6.7)	
95+	0	0		0	0		20	5.0 (2.8–7.3)	
Race/ethnicity									
White	2,880	9.9 (9.5–10)	10	2,840	9.4 (9.0–9.7)	9.4	2,020	7.1 (6.8–7.4)	7.0
Black	300	10 (9.0–11)	9.5	320	9.9 (8.8–11)	11	280	9.0 (8.0–10.1)	9.7
Asian	…	…	…	20	12 (6.6–17)	12	0	0	0
Hispanic	…	…	…	60	15 (11–19)	10	40	5.7 (4.0–7.4)	8.5
N. American Native	…	…	…	0	0	0	0	0	0
Gender									
Male	2,840	19 (19–20)	20	2,920	19 (18–20)	19	2,020	14 (13–15)	14
Female	620	3.1 (2.9–3.4)	2.8	360	1.8 (1.6–2.0)	1.8	340	1.8 (1.6–2.0)	1.8
Region									
Midwest	620	7.1 (6.5–7.7)	7.3	720	8.0 (7.4–8.6)	7.1	640	7.4 (6.8–8.0)	7.4
Northeast	960	12 (12–13)	12	960	13 (12–13)	12	520	7.8 (7.1–8.4)	7.5
South	1,340	11 (10–12)	12	1,220	9.6 (9.1–10)	10	900	7.3 (6.8–7.7)	7.3
West	500	9.8 (8.9–11)	8.6	300	5.8 (5.1–6.4)	6.2	240	4.8 (4.2–5.4)	4.8

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

Table 14. Trends in mean length of stay (days) for individuals hospitalized with lower tract urolithiasis listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	3.4	3.3	3.2	2.9
Age				
< 18	*	*	*	*
18–24	3.5	2.7	*	2.3
25–34	2.8	2.7	2.5	2.4
35–44	2.4	2.3	2.8	2.6
45–54	2.9	3.6	3.0	2.5
55–64	2.8	2.5	2.7	2.2
65–74	3.5	3.0	3.1	2.8
75–84	3.6	3.6	3.4	3.4
85+	5.3	5.7	4.7	4.0
Race/ethnicity				
White	3.4	3.2	3.1	2.9
Black	3.5	4.2	4.8	4.1
Asian/Pacific Islander	*	*	*	*
Hispanic	3.2	4.3	3.2	3.6
Other	*	*	*	*
Region				
Midwest	3.4	3.2	3.3	2.7
Northeast	4.0	3.7	3.3	3.1
South	3.2	3.2	3.2	3.1
West	2.5	2.9	2.8	2.7
MSA				
Rural	3.2	2.9	3.2	2.9
Urban	3.4	3.4	3.2	3.0
Primary payor				
Medicare	3.8	3.7	3.6	3.2
Medicaid	3.9	3.8	4.3	3.5
Private insurance/HMO	2.7	2.3	2.3	2.2
Self-pay	2.6	2.5	2.6	2.7
No charge	*	…	*	*
Other	3.3	*	*	3.0

… data not available.

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area; HMO, health maintenance organization.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Outpatient Care

An individual may be seen in the outpatient setting as part of the diagnosis of urolithiasis, during urologic treatment (pre- and/or post-procedure), or for medical evaluation and prevention. We have chosen to focus on visits for which urolithiasis (upper and lower tract stones) was the primary diagnosis, except where noted.

Hospital Outpatient Visits: NHAMCS Data

The rates for hospital outpatient visits by patients with urolithiasis as the primary reason for the visit, based on National Hospital Ambulatory Medical Care Survey (NHAMCS) data for the period 1994 to 2000, are presented in Table 15. The estimated rate in 2000 was 40% higher than that in 1994 (63 vs 45 per 100,000); however, the overlapping confidence intervals preclude definitive inferences. The rate for 1996 seems implausibly low. Overall, the absolute number of hospital outpatient visits during this period increased from 114,687 to 171,784.

Information on hospital outpatient visits is also available from Medicare data for 1992, 1995, and 1998 (Table 16). The Medicare data provide more detail than do the NHAMCS data. The visit rate in Medicare patients increased slightly from 1992 to 1998, both for those under 65 and for those 65 years of age and older. For example, in the older group, the rate increased from 28 per 100,000 in 1992 to 36 per 100,000 in 1998. The visit rate decreased with increasing age, and the rates were approximately twice as high in men as in women (Figure 5). Rates were lowest in the South in 1992 and 1995 and in the West in 1998. Rates were

Table 15. Hospital outpatient visits by individuals with urolithiasis, count, rate[a] (95% CI)

	Primary Reason for Visit		Any Reason for Visit	
	Count	Rate	Count	Rate
1994	114,687	45 (29–62)	130,704	52 (34–69)
1996	31,666	12 (6–18)	68,343	26 (13–40)
1998	83,383	31 (14–48)	138,576	52 (30–74)
2000	171,784	63 (34–92)	300,073	110 (69–151)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

SOURCE: National Hospital Ambulatory Medical Care Survey—Outpatient, 1994, 1996, 1998, 2000.

Table 16. Outpatient hostpial visits by Medicare beneficiaries with upper and/or lower tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c] (95% CI)

	1992			1995			1998		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	10,980	32 (31–32)	32	13,320	38 (37–38)	38	13,920	42 (41–42)	42
Total < 65	2,700	49 (47–51)		3,480	57 (55–59)		4,020	65 (63–67)	
Total 65+	8,280	28 (28–29)		9,840	34 (33–34)		9,900	36 (36–37)	
Age									
65–74	5,100	31 (30–32)		5,960	37 (36–38)		6,660	46 (45–48)	
75–84	2,840	30 (29–31)		3,280	34 (33–35)		2,780	29 (28–30)	
85–94	300	10 (9.3–12)		560	18 (17–20)		360	12 (10–13)	
95+	40	12 (8.3–16)		40	11 (7.7–14)		100	25 (20–30)	
Race/ethnicity									
White	8,060	28 (27–28)	28	10,440	34 (34–35)	34	10,560	37 (36–38)	37
Black	1,920	65 (62–68)	65	1,900	59 (56–62)	57	1,820	59 (56–61)	59
Asian	…	…	…	120	72 (59–84)	72	220	70 (61–79)	70
Hispanic	…	…	…	320	80 (71–89)	80	620	88 (81–95)	85
N. American Native	…	…	…	…	…	…	80	148 (115–181)	148
Gender									
Male	5,780	39 (38–40)	41	8,020	53 (52–54)	53	7,620	53 (51–54)	52
Female	5,200	26 (26–27)	25	5,300	26 (26–27)	26	6,300	33 (32–34)	33
Region									
Midwest	3,460	40 (38–41)	39	3,580	40 (38–41)	40	3,800	44 (43–45)	44
Northeast	2,500	32 (31–34)	33	3,860	50 (49–52)	52	3,720	56 (54–57)	53
South	2,560	21 (20–22)	22	3,660	29 (28–30)	28	4,560	37 (36–38)	37
West	2,040	40 (38–42)	39	1,880	36 (35–38)	37	1,720	35 (33–36)	36

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 17. Physician office visits by individuals with urolithiasis, count, rate[a] (95% CI)

	1992		1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
					Primary Reason for Visit					
Total	949,581	379 (234–524)	1,002,487	397 (265–528)	924,895	351 (236–466)	1,289,692	481 (321–641)	1,825,123	668 (464–871)
Age										
< 54	669,280	337 (172–501)	630,282	311 (176–447)	554,821	263 (159–367)	661,079	309 (184–434)	1,184,522	545 (319–771)
55+	*	*	372,205	738 (366–1,111)	*	*	*	*	640,601	1,143 (677–1,610)
					Any Reason for Visit					
Total	1,242,509	496 (334–658)	1,275,273	504 (361–647)	1,374,098	521 (370–673)	1,497,817	558 (391–725)	2,382,217	872 (641–1,102)
Age										
< 54	748,240	376 (203–550)	797,164	394 (247–541)	751,502	356 (223–490)	745,868	349 (217–481)	1,582,354	728 (467–989)
55+	494,269	956 (540–1,371)	478,109	948 (542–1,355)	622,596	1,184 (643–1,725)	751,949	1,385 (743–2,026)	799,863	1,428 (941–1,914)

*Figure does not meet standard for reliaiblity or precision.

[a]Rate per 100,000 based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult civilian non-institutionalized population.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

highest for Hispanics in 1995; in 1998 North American Natives appeared to have a substantially higher rate, but this difference is so dramatic that it must be interpreted with caution. Age-adjustment of the CMS data did not alter the relative differences in racial/ ethnic, gender, or geographic group comparisons.

Physician Office Visits: NAMCS Data

Physician office visit rates for patients with a primary diagnosis of urolithiasis were determined from National Ambulatory Medical Care Survey (NAMCS) data for the even years between 1992 and 2000 (Table 17). The rates were stable between 1992 and 1996, then increased in 1998 and 2000. The visit rate was 43% higher in 2000 than it was in 1992. Small cell sizes preclude interpretation of age-specific rates, and no gender-specific information is available. The total number of visits nearly doubled between 1992 and 2000, increasing from 950,000 to 1,825,000.

Physician Office Visits: Medicare Data

In the Medicare data for 1992, 1995, and 1998, physician office visit rates increased 41% between 1992 to 1998 for those <65 years of age and 25% for those ≥65 (Table 18). The rates peaked in the 65-to 74-year age group and then declined. Rates were highest in the South. In 1995 and 1998, the rates were higher for Hispanics than for Asians and Caucasians, and rates were lowest for African Americans. When the CMS data were age-adjusted, the gender gap in physician office visit rates slightly widened in all three years of study, but the relative differences in geographic and racial/ethnic group comparisons did not change.

Physician Office Visits: VA Data—Adult Outpatients

A few general comments are in order before discussing the Veterans Health Administration (VA) data. Despite the clear differences in rates by age and race indicated by the data, the data have not been age- or race-standardized (see Methods chapter), except where indicated. Although we use the term rate for the VA data, the data represent the number of cases being seen for the specified condition per 100,000 unique VA outpatients; 95% confidence intervals are not available for the VA rates reported here.

The rates for outpatient visits by VA patients with a primary diagnosis of urinary tract stones decreased between 1999 and 2001 (Table 19). This decrease occurred for both upper tract and lower tract stones; the rate for upper tract stones was nearly 10 times that for lower tract stones.

The visit rate was highest in the 55- to 64-year age group for upper tract stones. The rate in the 85+ group is impressive, but it is not simply a reflection of bladder stones being more common (Table 19). The rate for males was 50 percent higher than that for females, and Hispanics as a group had the highest rates. There were also regional differences, with the highest rates occurring in the South.

The VA is one of the few sources that provides information specifically for bladder stones. The visit rate for a primary diagnosis of bladder stones decreased slightly, from 45 per 100,000 in 1999 to 38 per 100,000 in 2001 (Table 20). Two-thirds of the visits for lower tract stones in 2001 were for bladder stones. The visit rate was higher in the 55+ group than in the <55 group, but there was no further increase with age. No regional differences were observed.

Physician Office and Hospital Outpatient Visits Combined

Combined NAMCS and NHAMCS data revealed nearly 2 million visits in 2000 by patients with urolithiasis as the primary reason for the visit. This translates into a rate of 731 per 100,000 population. There were 2.7 million visits by patients with urolithiasis listed as any of the reasons for the visit (982 per 100,000 population). Thus, the vast majority of visits for urolithiasis (74%) are for urolithiasis as the primary diagnosis (Tables 15 and 17).

Ambulatory Surgery Procedures

Visits to an ambulatory surgery center by individuals with commercial insurance who had a primary diagnosis of urolithiasis (upper or lower tract stones) were tabulated for 1994, 1996, 1998, and 2000 from the Center for Health Care Policy and Evaluation Database (Table 21). The total number of visits increased more than fourfold between 1994 and 1998, and the rate of visits increased by 58% (from 117 to 185 per 100,000). These findings reflect the trend of moving outpatient surgical treatment from hospitals to ambulatory care centers to avoid the high overhead cost associated with hospital-based outpatient surgery. However, the data do not represent all outpatient procedures performed in a population, since many

Table 18. Physician office visits by Medicare beneficiaries with upper and/or lower tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c] (95% CI)

	1992			1995			1998		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	178,320	516 (514–519)	516	221,220	625 (622–627)	625	235,920	704 (701–706)	704
Total < 65	20,800	380 (375–385)		34,000	554 (549–560)		39,680	639 (632–645)	
Total 65+	157,520	542 (539–545)		187,220	640 (637–643)		196,240	718 (715–721)	
Age									
65–74	106,340	647 (643–651)		123,640	764 (760–768)		122,760	857 (852–862)	
75–84	44,400	471 (466–475)		55,440	575 (570–580)		63,460	668 (663–673)	
85–94	6,560	229 (223–234)		7,920	258 (252–263)		9,480	307 (301–313)	
95+	220	66 (57–74)		220	60 (52–68)		540	136 (124–147)	
Race/ethnicity									
White	157,460	539 (537–542)	538	200,800	662 (659–664)	661	209,780	738 (735–742)	738
Black	9,660	326 (320–333)	321	10,440	324 (318–330)	316	11,840	382 (375–389)	375
Asian	…	…	…	1,020	610 (573–647)	646	2,560	815 (784–847)	828
Hispanic	…	…	…	3,100	776 (749–803)	821	5,840	830 (809–852)	845
N. American Native	…	…	…	120	331 (273–389)	276	260	481 (422–540)	481
Gender									
Male	109,560	744 (740–748)	756	139,220	915 (910–920)	925	147,360	1,018 (1,013–1,023)	1,031
Female	68,760	347 (344–350)	338	82,000	406 (404–409)	399	88,560	465 (462–468)	454
Region									
Midwest	37,560	430 (426–435)	430	46,920	521 (516–525)	523	51,180	593 (588–598)	594
Northeast	37,700	489 (484–494)	482	47,600	620 (615–626)	612	47,560	710 (704–717)	704
South	72,240	591 (587–595)	596	88,220	694 (689–699)	699	100,020	808 (803–813)	814
West	26,500	520 (514–526)	518	32,580	629 (622–635)	624	30,060	607 (600–614)	597

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis..
[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 19. Frequency of upper and/or lower tract urolithiasis[a] listed as primary diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	Upper Tract Stones						Lower Tract Stones					
	1999		2000		2001		1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	18,584	611	19,246	587	20,717	561	2,051	67	2,113	64	2,107	54
Age												
18–24	66	261	69	293	77	334	5	20	3	13	3	13
25–34	790	524	736	518	774	570	44	29	35	25	50	37
35–44	1,909	578	1,786	572	1,661	554	121	37	119	38	86	29
45–54	5,224	758	5,492	766	5,636	748	355	52	357	50	361	48
55–64	4,080	813	4,406	795	5,167	796	392	78	411	74	438	68
65–74	4,222	556	4,326	524	4,596	483	614	81	625	76	599	63
75–84	2,165	404	2,294	357	2,602	325	474	88	511	79	520	65
85+	128	261	137	235	204	260	46	94	52	89	50	64
Race/ethnicity												
White	11,484	841	11,692	794	12,268	762	1,406	103	1,338	91	1,312	81
Black	1,482	444	1,538	449	1,667	470	205	61	243	71	254	72
Hispanic	1,222	1,068	1,295	1,057	1,183	918	108	94	112	91	127	99
Other	143	739	126	622	151	692	10	52	14	69	9	41
Unknown	4,253	353	4,595	348	5,448	346	322	27	406	31	405	26
Gender												
Male	18,079	624	18,682	598	20,088	570	1,998	69	2,068	66	2,061	58
Female	505	358	564	374	629	381	53	38	45	30	46	28
Region												
Midwest	3,717	541	3,790	509	3,799	459	432	63	505	68	424	51
Northeast	3,890	530	3,934	505	4,251	489	575	78	503	65	533	61
South	7,179	705	7,565	678	8,099	626	654	64	701	63	737	57
West	3,798	632	3,957	623	4,568	653	390	65	401	63	413	59
Insurance status												
No insurance/self-pay	11,434	626	11,574	639	12,186	640	1,108	61	1,085	60	1,063	56
Medicare/Medicare supplemental	4,059	583	4,575	500	5,382	455	650	93	729	80	793	67
Medicaid	41	828	61	772	61	679	6	121	6	76	7	78
Private insurance/ HMO/PPO	2,849	587	2,786	546	2,833	512	275	57	270	53	226	41
Other insurance	186	736	237	824	236	708	10	40	19	66	17	51
Unknown	15	785	13	529	19	210	2	105	4	163	1	11

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for urolithiasis.

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 20. Frequency of bladder stones[a] listed as primary diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	1,188	45	1,282	44	1,255	38
Age						
40–44	26	14	37	21	20	12
45–54	186	28	179	26	174	24
55–64	242	49	258	48	262	41
65–74	387	52	426	52	412	44
75–84	315	61	347	55	352	45
85+	32	70	35	62	35	46
Race/ethnicity						
White	847	68	815	61	792	53
Black	102	36	155	53	152	50
Hispanic	55	53	64	57	82	69
Other	5	29	9	50	7	36
Unknown	179	18	239	21	222	16
Region						
Midwest	274	45	348	52	292	39
Northeast	355	54	331	47	317	40
South	343	39	390	40	414	36
West	216	42	213	39	232	38
Insurance status						
No insurance/self-pay	579	38	625	41	583	36
Medicare/Medicare supplemental	423	62	480	54	533	46
Medicaid	4	93	3	43	4	50
Private insurance/HMO/PPO	172	40	164	36	127	25
Other insurance	8	38	6	25	7	25
Unknown	2	127	4	193	1	13

HMO, health maintenance organization; PPO, preferred provider organization.
[a]Represents diagnosis codes for bladder stones (no coexisting benign prostatic hyperplasia).
[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.
[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.
NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.
SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 21. Visits to ambulatory surgery centers for urolithiasis procedures listed as primary procedure by individuals having commercial health insurance, count, rate[a]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	1,254	117	2,389	150	4,535	185	6,755	246
Age								
<3	1	*	2	*	7	*	8	*
3–10	7	*	7	*	22	*	36	11
11–17	11	*	21	*	49	18	74	25
18–24	56	57	102	72	220	99	291	113
25–34	194	103	410	147	811	195	1,123	254
35–44	363	166	689	211	1,170	230	1,731	310
45–54	380	243	705	286	1,293	321	1,997	417
55–64	190	250	369	316	800	398	1,295	530
65–74	51	323	72	321	141	438	175	430
75–84	1	*	10	*	21	*	21	*
85+	0	0	2	*	1	*	4	*
Gender								
Male	784	149	1,478	187	2,916	236	4,107	298
Female	470	86	911	114	1,619	132	2,648	193
Region								
Midwest	775	119	1,383	153	2,191	182	3,228	237
Northeast	107	71	164	102	253	126	324	197
South	303	155	742	170	1,902	202	2,952	271
West	69	91	100	110	189	174	251	188

*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on member months of enrollment in calendar year for individuals in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

are still done in a hospital setting. Although the ambulatory surgery visits in this dataset were not stratified by upper tract versus lower tract stones, the impact of bladder stone treatment should be minimal, since relatively few procedures for such treatment are performed in ambulatory care centers, and the overall incidence of bladder stones is much lower than that of kidney stones. Bladder stones are usually treated in conjunction with prostate surgeries in an inpatient setting.

During the years studied, the male-to-female ratio varied from 1.5 to 1.8—a bit lower than expected in view of the ratio of incidence rates for stone disease. The peak age for visits was between 65 and 74 for 1994, 1996, and 1998, but it dropped to 55 to 64 in 2000 (Figure 3). Regional differences were apparent: the highest rates were consistently seen in the South; the lowest rates were seen in the Northeast in 1994–1998 and in the West in 2000.

The CMS database revealed that ambulatory surgery visits by Medicare patients with a primary diagnosis of urolithiasis also increased over time, from 42,320 total visits in 1992 to 66,580 in 1998; likewise, the visit rate increased from 123 to 199 per 100,000 (Table 22). The male-to-female ratio remained stable at approximately 2 to 1 (Figure 5).

The available data regarding ambulatory surgery for urolithiasis in children are too scant to provide reliable estimates of utilization.

Table 22. Visits to ambulatory surgery centers by Medicare beneficiaries with upper and/or lower tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	42,320	123 (121–124)	57,580	163 (161–164)	66,580	199 (197–200)
Total < 65	4,480	82 (79–84)	8,040	131 (128–134)	8,480	136 (134–139)
Total 65+	37,840	130 (129–132)	49,540	169 (168–171)	58,100	213 (211–214)
Age						
65–74	23,460	143 (141–145)	30,060	186 (184–188)	33,500	234 (231–236)
75–84	12,600	134 (131–136)	16,800	174 (172–177)	20,580	217 (214–220)
85–94	1,720	60 (57–63)	2,520	82 (79–85)	3,980	129 (125–133)
95+	60	18 (13–22)	160	44 (37–51)	40	10 (7.0–13)
Race/ethnicity						
White	37,820	130 (128–131)	51,840	171 (169–172)	59,760	210 (209–212)
Black	2,500	84 (81–88)	3,600	112 (108–115)	4,380	141 (137–146)
Asian	…	…	200	120 (103–136)	460	146 (133–160)
Hispanic	…	…	500	125 (114–136)	820	117 (109–125)
N. American Native	…	…	40	110 (77–143)	80	148 (115–181)
Gender						
Male	25,900	176 (174–178)	35,880	236 (233–238)	40,860	282 (279–285)
Female	16,420	83 (82–84)	21,700	108 (106–109)	25,720	135 (133–137)
Region						
Midwest	11,800	135 (133–138)	16,840	187 (184–190)	18,920	219 (216–222)
Northeast	7,180	93 (91–95)	10,120	132 (129–134)	13,160	197 (193–200)
South	18,320	150 (148–152)	23,040	181 (179–184)	26,680	215 (213–218)
West	4,980	98 (95–100)	7,380	142 (139–146)	7,480	151 (148–154)

…data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Surgical Trends

A variety of datasets was used to establish trends in the surgical management of upper tract stones. Although no completely new technology for stone treatment has been introduced since extracorporeal shock wave lithotripsy (ESWL) was developed in the 1980s, improvements in endoscopic technique and instrumentation have increased efficacy, reduced morbidity, and increased patient tolerance of the procedures. For example, although ureteroscopy has been used for the treatment of ureteral stones for more than two decades, advances in ureteroscope design and instrumentation have expanded the indications for the procedure to increasingly include lower calyceal renal calculi (8, 9), stones in calyceal diverticuli (10), and large-volume renal stones (11, 12). Likewise, refinements in the indications for ESWL have the potential to improve success rates, but they have also expanded the role of endoscopic management of stones in subgroups of patients who have poor outcomes with ESWL (i.e., those with lower calyceal stones (13).

In Medicare patients with a diagnosis of urolithiasis, rates of ESWL, ureteroscopy, and PCNL treatment of stones remained relatively stable over 1992, 1995, and 1998, with rates of 10,943 to 11,738 per 100,000 population with urolithiasis for ESWL; 8,372 to 8,839 per 100,000 for ureteroscopy; and 665 to 882 per 100,000 for PCNL (Table 23). One of the reasons that the frequency of ESWL has risen slightly may be

Table 23. Procedures for nephrolithiasis among Medicare beneficiaries, count[a], rate[b]

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	46,280	21,496	52,880	21,965	54,080	20,942
PCNL	1,900	882	1,600	665	2,180	844
Ambulatory surgery center	0	0	0	0	0	0
Hospital outpatient	300	139	220	91	520	201
Inpatient	1,580	734	1,340	557	1,660	643
Physician office	20	9.3	40	17	0	0
Other	0	0	0	0	0	0
ESWL	23,560	10,943	28,260	11,738	29,420	11,393
Ambulatory surgery center	1,000	464	1,160	482	1,400	542
Hospital outpatient	15,300	7,106	22,100	9,179	23,680	9,170
Inpatient	5,580	2,592	3,700	1,537	2,960	1,146
Physician office	860	399	840	349	1,000	387
Other	820	381	460	191	380	147
Uteroscopy	18,840	8,751	21,280	8,839	21,620	8,372
Ambulatory surgery center	120	56	640	266	740	287
Hospital outpatient	5,440	2,527	9,080	3,771	12,100	4,686
Inpatient	12,700	5,899	11,120	4,619	8,440	3,268
Physician office	440	204	340	141	280	108
Other	140	65	100	42	60	23
Open stone surgery	1,980	920	1,740	723	860	333
Ambulatory surgery center	0	0	0	0	0	0
Hospital outpatient	60	28	160	66	120	46
Inpatient	1,800	836	1,480	615	720	279
Physician office	60	28	80	33	20	7.7
Other	60	28	20	8.3	0	0
Laparoscopic removal	0	0	0	0	0	0
Ambulatory surgery center	0	0	0	0	0	0
Hospital outpatient	0	0	0	0	0	0
Inpatient	0	0	0	0	0	0
Physician office	0	0	0	0	0	0
Other	0	0	0	0	0	0

ESWL, extracorporeal shock wave lithotripsy; PCNL, percutaneous nephrolithotomy.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries with a diagnosis of nephrolithiasis.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 24. Urolithiasis procedures for individuals having commercial health insurance, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	1,074	100	2,042	128	3,514	143	5,180	188
ESWL								
Ambulatory surgery	515	48	1,069	67	1,853	75	2,765	101
Emergency room	0	0	0	0	0	0	1	*
Inpatient	16	*	25	*	44	1.8	47	1.7
Open stone								
Ambulatory surgery	5	*	7	*	20	*	19	*
Inpatient	17	*	16	*	22	*	29	*
PCNL								
Ambulatory surgery	5	*	21	*	28	*	56	2.0
Inpatient	60	5.6	89	5.6	134	5.5	190	6.9
Uteroscopy								
Ambulatory surgery	258	24	545	34	1068	43	1,627	59
Emergency room	1	*	0	0	1	*	1	*
Inpatient	197	18	270	17	344	14	445	16

ESWL, extracorporeal shock wave lithotripsy; PCNL, percutaneous nephrolithotomy.
*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

the fact that today's lithotriptors are less effective than the original HM3, resulting in multiple retreatments for the same stone. Given the significant advances in the ureteroscopic management of calculi in the very late 1990s and early 2000s, it is not surprising that the improvement in technology is not reflected by an increase in ureteroscopy up to 1998. The introduction of the Holmium laser in 1995 rendered virtually all stones amenable to fragmentation if they could be accessed endoscopically (14); however, this new technology may have not yet reached widespread use by 1998. Only open stone surgery showed a clear-cut trend, decreasing in use from 920 per 100,000 in 1992 to 333 per 100,000 in 1998.

According to Medicare data, the distribution of procedures changed surprisingly little over the years studied. ESWL has traditionally been the most frequently performed procedure, comprising 51% of the procedures in 1992 and 54% in 1998. PCNL remained relatively stable at 3% to 4% of procedures, and ureteroscopy comprised 40% to 41% of the procedures.

The distribution of procedures was remarkably similar between commercially insured individuals (reported in the Center for Health Care Policy and Evaluation database) and Medicare patients (reported in the CMS database). Among the commercially insured population, PCNL comprised 5% to 6% of procedures and remained stable from 1994 to 2000 (Table 24). ESWL comprised 49% of the procedures in 1994, increasing to 54% in 2000. Ureteroscopy remained stable over time and comprised 40% to 42% of the procedures. Open stone surgery made up only 2% of the total procedures in 1994 and dropped to less than 1% in 2000. As numerous studies in the literature have demonstrated, open surgery should be considered a salvage procedure to be used only when endoscopic or shock wave treatment fails, and its use should be indicated in well under 5% of cases (15). Indeed, CMS data revealed a 64% decline in the use of open stone surgery from 1992 to 1998, and in 1998 this modality comprised less than 2% of all stone procedures performed.

Kerbl and colleagues also reviewed the distribution of surgical procedures over time, using data from the Health Care Financing Administration (the federal agency now known as CMS) (16). They found that although ESWL remained relatively stable

Table 25. Emergency room visits by individuals with urolithiasis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	368,667	146 (110–181)	331,758	126 (93–159)	399,403	149 (112–186)	617,647	226 (175–277)
Gender								
Male	246,375	200 (140–260)	189,647	148 (99–196)	268,193	205 (142–267)	406,137	305 (225–385)
Female	122,292	94 (55–134)	142,111	105 (61–149)	131,210	96 (55–136)	211,510	151 (88–214)

[a]Rate per 100,000 based on 1994, 1996, 1998, and 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

SOURCE: National Hospital Ambulatory Medical Care Survey— ER, 1994, 1996, 1998, 2000.

at 70% to 80% of the procedures from 1992 to 2000, ureteroscopy increased from 14% in 1992 to 22% in 2000, still less than half the proportion observed in the Center for Health Care Policy and Evaluation database of commercially insured patients (Table 24). PCNL use remained stable at 4% to 6%, which is comparable to the proportion seen in the Medicare and commercially insured populations. The reason for the differences in the distribution of procedures among the different datasets is unclear.

Emergency Room Care

Between 1994 and 1998, emergency room visits by individuals with a primary diagnosis of urolithiasis remained relatively stable, according to NHAMCS data; however, there was a 50% increase in 2000 (Table 25). Future studies will be needed to determine whether this represented a sharp increase or simply year-to-year variability. In general, the rate for males was twice that for females. It is noted that the confidence intervals for these estimates are wide, and no information is available on geographic variation in rates.

Emergency room visits were less common in the Medicare population (Table 26) than in the NHAMCS population. Among Medicare beneficiaries, the rate increased between 1992 and 1998 for the <65 and ≥65 age groups (53% and 31%, respectively), for both males and females, and in all regions. The visit rate was lower in those 65 and older, and it decreased with increasing age. Males were three times more likely than females to visit an emergency room for urolithiasis. This ratio is higher than that seen in the NHAMCS population (Table 25) and was consistent in age-unadjusted and age-adjusted CMS data; it may be related to different age distributions by sex in the two data sources. There were clear regional variations, with rates highest in the South. The visit rate was higher among Caucasians than African Americans (no data on Hispanics were available for 1992). In both 1995 and 1998, the rates were highest among Hispanics. When the CMS data were age-adjusted, the geographic and racial/ethnic differences did not change.

ECONOMIC IMPACT

The economic impact of urolithiasis includes both the direct medical costs of treating the condition (emergency room visits, office visits, inpatient hospitalizations, ambulatory surgery, and prescription medications) and indirect costs associated with lost work time. Each inpatient or outpatient encounter involves a variety of cost sources, including physician professional fees, radiographic studies, room and board, laboratory, pharmacy, and operating room costs. The distinction between cost, representing the actual cost to the hospital, pharmacy, or laboratory of providing a service, and the charge to the patient or payor, which is related to cost but not necessarily in a predictable manner, is important, although it cannot always be easily arrived at or consistently applied. For the purposes of this chapter, we use the terms *costs* and *expenditures* to reflect total payments made by the patient (co-insurance, co-payments, deductibles, and uncovered expenses) and by all third-party payors (primary and secondary coverage, when available). Using data from the Ingenix dataset for 1999, we estimated that the average annual expenditure for privately insured individuals between the ages of 18 and 64 was $7,656 for those with a medical claim corresponding to a diagnosis of urolithiasis and $3,184 for those without a claim relating to urolithiasis (Table

Table 26. Emergency room visits by Medicare beneficiaries with upper and/or lower tract urolithiasis listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c] (95% CI)

	1992			1995			1998		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	21,840	63 (62–64)	63	26,060	74 (73–75)	74	29,200	87 (86-88)	87
Total < 65	4,900	89 (87–92)		6,700	109 (107–112)		8,460	136 (133-139)	
Total 65+	16,940	58 (57–59)		19,360	66 (65–67)		20,740	76 (75-77)	
Age									
65–74	11,960	73 (71–74)		13,720	85 (83–86)		13,760	96 (94–98)	
75–84	4,200	45 (43–46)		4,920	51 (50–52)		5,980	63 (61–65)	
85–94	720	25 (23–27)		660	21 (20–23)		960	31 (29–33)	
95+	60	18 (13–22)		60	16 (12–21)		40	10 (7.0–13)	
Race/ethnicity									
White	19,200	66 (65–67)	65	23,480	77 (76–78)	78	25,800	91 (90–92)	91
Black	940	32 (30–34)	32	1,460	45 (43–48)	43	1,580	51 (48–54)	51
Asian	…	…	…	100	60 (48–72)	60	260	83 (73–93)	76
Hispanic	…	…	…	360	90 (81–99)	90	720	102 (95–110)	102
N. American Native	…	…	…	0	0	0	20	37 (20–54)	37
Gender									
Male	14,920	101 (100–103)	104	18,160	119 (118–121)	122	20,260	140 (138–142)	141
Female	6,920	35 (34–36)	33	7,900	39 (38–40)	37	8,940	47 (46–48)	46
Region									
Midwest	5,180	59 (58–61)	60	6,880	76 (75–78)	77	7,860	91 (89–93)	92
Northeast	4,040	52 (51–54)	52	3,720	48 (47–50)	47	4,440	66 (64–68)	65
South	8,980	73 (72–75)	73	11,300	89 (87–91)	89	13,000	105 (103–107)	105
West	3,220	63 (61–65)	64	3,800	73 (71–76)	74	3,280	66 (64–68)	66

… data not available.
[a]Unweighted counts were multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis..
[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 27. Estimated annual expenditures of privately insured employees with and without a medical claim for urolithiasis in 1999[a]

	Annual Expenditures (per person)			
	Persons without Urolithiasis (N=276,064)	Persons with Urolithiasis (N=2,886)		
	Total	Total	Medical	Rx Drugs
Total	$3,184	$7,656	$6,498	$1,158
Age				
18–34	$2,776	$7,243	$6,411	$831
35–44	$2,953	$7,506	$6,386	$1,120
45–54	$3,262	$8,379	$7,113	$1,265
55–64	$3,362	$7,172	$6,032	$1,140
Gender				
Male	$2,776	$7,376	$6,263	$1,113
Female	$3,889	$8,619	$7,321	$1,299
Region				
Midwest	$3,066	$8,747	$7,440	$1,306
Northeast	$3,068	$6,918	$5,846	$1,072
South	$3,397	$8,352	$7,132	$1,219
West	$3,221	$7,489	$6,105	$1,384

Rx, prescription.
[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.
SOURCE: Ingenix, 1999.

Table 28. Expenditures for urolithiasis and share of costs, by site of service (% of total)

	Year							
Service Type	1994		1996		1998		2000	
Total[a]	$1,373,900,000		$1,233,900,000		$1,518,500,000		$2,067,400,000	
Inpatient	$785,900,000	(57.2%)	$811,900,000	(65.8%)	$862,500,000	(56.8%)	$971,700,000	(47.0%)
Physician Office	$151,100,000	(11.0%)	$154,200,000	(12.5%)	$236,900,000	(15.6%)	$363,900,000	(17.6%)
Hospital Outpatient	$233,600,000	(17.0%)	$58,000,000	(4.7%)	$135,100,000	(8.9%)	$244,000,000	(11.8%)
Emergency Room	$204,700,000	(14.9%)	$209,800,000	(17.0%)	$285,500,000	(18.8%)	$490,000,000	(23.7%)

[a]Total unadjusted expenditures exclude spending on outpatient prescription drugs for the treatment of urolithiasis. Average drug spending for urolithiasis-related conditions is estimated at $4 million to $14 million annually for the period 1996 to 1998.

SOURCES: National Ambulatory Medical Care Survey, National Hospital Ambulatory Medical Care Survey, Healthcare Cost and Utilization Project, Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

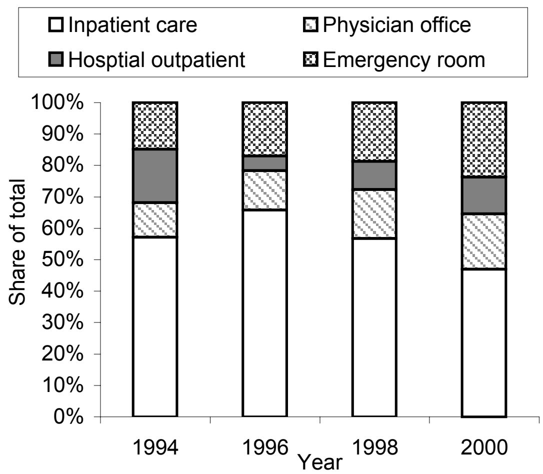

Figure 6. Percent share of costs for urolithiasis by type of service, 1994–2000.

SOURCE: National Ambulatory Medical Care Survey; National Hospital Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

27). Hence, a $4,472 difference per covered individual should be accounted for by expenditures either directly or indirectly related to stone disease (indirect expenditures are those for treatment of systemic illnesses that are associated with stone disease, such as primary hyperparathyroidism, chronic diarrheal syndrome due to bowel disease, etc.). This difference in expenditures may be mitigated by unmeasured differences (such as comorbidities) between those with and without stone disease.

The annual expenditures for those with a medical claim for urolithiasis include the sum of the expenditures for medical care ($6,498) and those for prescription drugs ($1,158). When stratified by age, the expenditures of those without a urolithiasis-related claim rose steadily to a maximum of $3,362 in the 55 to 64 age group. In contrast, the peak total medical expenditure for the group with a urolithiasis-related claim, $8,379, occurred in the 45 to 54 age group, perhaps reflecting the peak incidence of stone disease in this group.

Women have higher medical expenditures than men in both groups, although the difference was slightly larger among those with urolithiasis-related claims. However, given the higher incidence of stone disease in men (a factor of 2 to 3), one might expect a greater impact of gender in the group with stones. It should be noted, however, that the diagnosis of stones may be made incidentally, without necessarily prompting or requiring any intervention. Evaluation of regional differences in medical expenditures suggests that overall higher expenditures for the group without urolithiasis-related claims were found in the South and West, whereas in the urolithiasis group, expenditures were highest in the Midwest and South. As prescription drug costs showed little regional variation, the geographic differences in expenditures are likely related to direct medical expenditures or possibly due to differences in the age distributions of the regions.

National estimates of annual medical expenditures suggest that slightly more than $2 billion was spent on treating urolithiasis in 2000, based solely on inpatient and outpatient claims of individuals with a primary diagnosis of urolithiasis. This estimate includes $971 million for inpatient services, $607 million for physician office and hospital outpatient services, and $490 million for emergency room services (Table 28). That these figures are somewhat lower than the $1.83 billion estimated annual cost of urolithiasis for 1993 reported by Clark and colleagues (17) may be related to our more restrictive definition of hospitalization. Total expenditures (excluding outpatient prescription drug costs) increased by 50% from $1.37 billion to $2.07 billion, between 1994 and 2000. During that time period, non-inpatient services (including physician office visits, emergency room visits, and hospital outpatient services) accounted for an increasing proportion of the total expenditures—43% of the total in 1994 and 53% in 2000 (Figure 6). Interestingly, the relative proportion of total expenditures for emergency room services also increased, from 15% in 1992 to 24% in 2000.

Urolithiasis-related treatment costs for the Medicare population also increased significantly over time. Total expenditures for Medicare beneficiaries 65 and older increased 36% (from $613 million in 1992 to $834 million in 1998), with outpatient services accounting for an increasingly larger share of the total (31% in 1992, 38% in 1998) (Table 29).

According to Medical Expenditure Panel Survey (MEPS) data, annual estimates of spending on outpatient prescription drugs for the treatment of urolithiasis in 1996–1998 ranged from $4 million

Table 29. Expenditures for Medicare beneficiaries age 65 and over for treatment of urolithiasis, by site of service (% of total)

	Year					
	1992		1995		1998	
Total	$613,400,000		$779,400,000		$834,400,000	
Inpatient	$423,700,000	(69.1%)	$513,800,000	(65.9%)	$518,900,000	(62.2%)
Outpatient	$179,200,000	(29.2%)	$250,600,000	(32.2%)	$296,100,000	(35.5%)
Physician Office	$56,700,000	(9.2%)	$81,600,000	(10.5%)	$96,100,000	(11.5%)
Hospital Outpatient	$5,500,000	(0.9%)	$5,100,000	(0.7%)	$4,800,000	(0.6%)
Ambulatory Surgery	$117,000,000	(19.1%)	$163,900,000	(21.0%)	$195,200,000	(23.4%)
Emergency Room	$10,500,000	(1.7%)	$14,900,000	(1.9%)	$19,400,000	(2.3%)

NOTE: Percentages may not add to 100% because of rounding.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

to $14 million (Table 28). Furthermore, MEPS data suggest that 29% of men and 24% of women with urolithiasis filled a prescription for the treatment of the condition, with mean annual expenditures for outpatient prescriptions being $43 for men and $48 for women (Table 30).

In addition to the direct medical costs of treatment, the economic effects of urolithiasis include labor market outcomes such as absenteeism and work limitations. It is estimated that 30% of employed individuals with an inpatient or outpatient claim for upper tract stones missed 19 hours of work time per year in association with their claim (Table 31). Lower tract stones, presumably bladder stones, were also associated with lost workdays for 32% of employees with a medical claim for the condition, but the mean number of hours of lost work was substantially lower (6.1 hours per year).

The medical costs of treating children with urolithiasis are difficult to estimate, largely because of the paucity of data. However, some data are available in the medical and financial records of the National Association of Children's Hospitals and Related Institutions (NACHRI). According to NACHRI data, in 1999–2001, the average inpatient cost per child was $7,355 in 2001, a 32% to 36% increase over the cost in the two previous years (Table 32). Expenditures in 2001 were nearly twice as high among infants (0 to 2 years of age) as they were among children ages 3 to 10 or 11 to 17 and twice as high among African Americans as among Caucasians and Hispanics. However, there were no significant differences in costs across gender.

CONCLUSIONS

Urolithiasis is common in the US population, and its prevalence is increasing. The available data on urolithiasis support the important influences of age, sex, region, and race/ethnicity. The setting for both the acute care and the surgical management of

Table 30. Annual use of outpatient prescription drugs for the treatment of urolithiasis, 1996–1998

	All Persons with Urolithiasis		Conditional on Rx Use	
Gender	Number with Urolithiasis	Percent with Rx Claim for Urolithiasis	Mean Number of Prescriptions	Mean Rx Expenditures
Male	676,144	29.2%	3.6	$43.19
Female	408,948	24.2%	3.9	$47.89
Total	1,085,092	27.3%	3.7	$44.96

Rx, prescription.
SOURCE: Medical Expenditure Panel Survey, 1996–1998.

Table 31. Average annual work loss of persons treated for urolithiasis, 1999 (95% CI)

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs) Inpatient[b]	Outpatient[b]	Total
Upper tract urolithiasis	834	30%	4.4 (2.5–6.3)	14.6 (11.5–17.7)	19.0 (14.5–23.5)
Lower tract urolithiasis	60	32%	0.3 (0–0.8)	5.8 (3.0–8.6)	6.1 (3.2–9.0)

[a]Individuals with an inpatient or outpatient claim for urolithiasis and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.
SOURCE: MarketScan, 1999.

Table 32. Mean inpatient cost per child admitted with urolithiasis listed as primary diagnosis, count, mean cost[a] (95% CI)

	1999		2000		2001	
	Count	Mean Cost	Count	Mean Cost	Count	Mean Cost
Total[b]	461	$5,582 (4,806–6,358)	553	$5,374 (4,790–5,958)	619	$7,355 (5,695–9,015)
Age						
0–2	43	$11,311 (4,717–17,905)	45	$7,811 (5,178 –10,443)	37	$13,875 (7,982–19,767)
3–10	193	$5,253 (4,430–6,076)	198	$5,067 (4,368– 5,766)	225	$7,041 (4,899–9,183)
11–17	225	$4,769 (4,103–5,435)	310	$5,217 (4,354 –6,080)	357	$6,877 (4,405–9,349)
Race/ethnicity						
White	338	$5,925 (4,928–6922)	385	$5,687 (4,947–6,427)	447	$6,252 (5,344–7,160)
Black	31	$4,699 (3,205–6,192)	34	$6,083 (4,806–7,360)	38	$12,627 (1,211–24,042)
Asian	1	$4,222	3	$3,969 (0–12,517)	2	$2,322 (518–4,126)
Hispanic	36	$5,089 (3,799–6,379)	51	$4,561 (3,495–5,628)	78	$5,598 (4,199–6,998)
N.American Native	0	...	3	$4,109 (921–7,297)	1	...
Gender						
Male	261	$5,524 (4,486–6,561)	280	$5,455 (4,500– 6,409)	312	$7,206 (5,418–8,995)
Female	200	$5,658 (4,479–6,836)	273	$5,292 (4,621 –5,963)	307	$7,506 (4,685–10,327)
Region						
Midwest	160	$6,096 (4,280–7,913)	197	$5,568 (4,666 –6,471)	199	$7,895 (3,539–12,250)
Northeast	24	$3,130 (2,239–4,021)	39	$4,685 (3,677– 5,694)	56	$6,321 (5,179–7,462)
South	203	$5,547 (4,737–6,357)	246	$5,788 (4,787 –6,789)	287	$6,221 (5,084–7,357)
West	61	$6,502 (4,445–8,560)	50	$5,369 (3,427–7,312)	77	$10,940 (5,050–16,831)

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.
[b]Persons of other races and missing race and ethnicity are included in the totals.
SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

patients with stones has changed over time: inpatient admissions and length of stay have decreased as outpatient treatment has burgeoned. The trends in distribution of surgical treatment modalities show some inconsistency among various databases; however, shock wave lithotripsy remains the most commonly performed procedure for upper tract stones, followed by ureteroscopy and percutaneous nephrostolithotomy. The one consistent trend identified by all datasets is a dramatic decrease in the use of open surgery, which is now less than 2% of the procedures. The cost of urolithiasis is estimated at nearly $2 billion annually and appears to be increasing over time, despite the shift from inpatient to outpatient procedures and the shorter length of hospital stays, perhaps because the prevalence of stone disease is increasing.

RECOMMENDATIONS

Although the current ICD and CPT codes seem acceptable for the basic diagnostic and therapeutic management of individuals with urolithiasis and the associated procedures, it would be helpful to researchers if ureteroscopy, like ureterolithotomy, were codified as upper, middle, or lower, dependent upon the site of pathology in the ureter. Additional specificity of the ICD coding is unlikely to be useful for research purposes; such detail must be obtained from the medical record.

From a clinical perspective, prevention is essential to reduce costs and morbidity. Primary prevention is not practical at this time, but aggressive prevention of recurrent stone formation is likely to reduce morbidity and costs.

The *Urologic Diseases in America* project expended a great deal of time and effort to obtain the best data available on urolithiasis and identified a number of knowledge gaps that need to be filled. We propose the following topics for investigation to improve the understanding of urolithiasis.

Medical evaluation of patients with upper tract urolithiasis

- How frequently are metabolic evaluations performed for patients with urolithiasis?
- What is the range of evaluations performed?
- Should first-time stone formers undergo a medical evaluation to determine the etiology of stone formation?
- How frequently are preventive measures recommended?
- What is the rate of adherence to medical recommendations, and how does this change over time?
- What are the national recurrence rates, and how are they affected by demographic factors?

Imaging modalities in the diagnosis and follow-up of patients with upper tract urolithiasis

- What is the optimal imaging modality for monitoring patients with a history of urolithiasis?
- Can imaging studies be used to predict stone composition and consequently affect treatment?

Surgical issues in the management of patients with upper tract urolithiasis

- What is the optimal urological management of acute renal colic?
- When should asymptomatic stones be treated?
- How have practice patterns evolved in the balance between ESWL and flexible ureteroscopy as primary management for upper ureteral stones?
- How have practice patterns evolved in the balance between ureteroscopy vs percutaneous nephrostomy in the management of upper ureteral stones?

Miscellaneous

- Is upper tract urolithiasis a risk factor for other conditions (e.g., end-stage renal disease)?

REFERENCES

1. Hiatt RA, Dales LG, Friedman GD, Hunkeler EM. Frequency of urolithiasis in a prepaid medical care program. Am J Epidemiol 1982;115:255-65.
2. Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. Renal stone epidemiology: a 25-year study in Rochester, Minnesota. Kidney Int 1979;16:624-31.
3. Evan AP, Lingeman JE, Coe FL, Parks JH, Bledsoe SB, Shao Y, Sommer AJ, Paterson RF, Kuo RL, Grynpas M. Randall's plaque of patients with nephrolithiasis begins in basement membranes of thin loops of Henle. J Clin Invest 2003;111:607-16.
4. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. Kidney Int 2003;63:1817-23.
5. Soucie JM, Thun MJ, Coates RJ, McClellan W, Austin H. Demographic and geographic variability of kidney stones in the United States. Kidney Int 1994;46:893-9.
6. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med 1993;328:833-8.
7. Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. Ann Intern Med 1997;126:497-504.
8. Schuster TG, Hollenbeck BK, Faerber GJ, Wolf JS, Jr. Ureteroscopic treatment of lower pole calculi: comparison of lithotripsy in situ and after displacement. J Urol 2002;168:43-5.
9. Grasso M, Ficazzola M. Retrograde ureteropyeloscopy for lower pole caliceal calculi. J Urol 1999;162:1904-8.
10. Batter SJ, Dretler SP. Ureterorenoscopic approach to the symptomatic caliceal diverticulum. J Urol 1997;158:709-13.
11. Grasso M, Conlin M, Bagley D. Retrograde ureteropyeloscopic treatment of 2 cm. or greater upper urinary tract and minor Staghorn calculi. J Urol 1998;160:346-51.
12. El-Anany FG, Hammouda HM, Maghraby HA, Elakkad MA. Retrograde ureteropyeloscopic holmium laser lithotripsy for large renal calculi. BJU Int 2001;88:850-3.
13. Albala DM, Assimos DG, Clayman RV, Denstedt JD, Grasso M, Gutierrez-Aceves J, Kahn RI, Leveillee RJ, Lingeman JE, Macaluso JN, Jr., Munch LC, Nakada SY, Newman RC, Pearle MS, Preminger GM, Teichman J, Woods JR. Lower pole I: a prospective randomized trial of extracorporeal shock wave lithotripsy and percutaneous nephrostolithotomy for lower pole nephrolithiasis-initial results. J Urol 2001;166:2072-80.
14. Denstedt JD, Razvi HA, Sales JL, Eberwein PM. Preliminary experience with holmium: YAG laser lithotripsy. J Endourol 1995;9:255-8.
15. Matlaga BR, Assimos DG. Changing indications of open stone surgery. Urology 2002;59:490-3; discussion 493-4.
16. Kerbl K, Rehman J, Landman J, Lee D, Sundaram C, Clayman RV. Current management of urolithiasis: progress or regress? J Endourol 2002;16:281-8.
17. Clark JY, Thompson IM, Optenberg SA. Economic impact of urolithiasis in the United States. J Urol 1995;154:2020-4.

CHAPTER 9

Ureteropelvic Junction Obstruction

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Ureteropelvic Junction Obstruction

Peter G. Schulam, MD, PhD

INTRODUCTION

Ureteropelvic junction (UPJ) obstruction is a condition in which urine is unable to travel from the renal pelvis to the bladder because of a blockage occurring at the UPJ. The etiology of UPJ obstruction includes both congenital and acquired conditions. The majority of cases are congenital. Acquired conditions include stone disease, postoperative or inflammatory strictures, and urothelial neoplasms.

A congenital UPJ obstruction may be due to either an intrinsic or an extrinsic cause, or, in some cases, both. Most common intrinsic obstructions are the result of an adynamic segment. This functional defect may be due to an interruption of the circular musculature of the UPJ (1) or an alteration of the collagen fibers and composition between and around the muscular cells (2). Less common intrinsic causes include valvular mucosal folds, persistent fetal convolutions, and ureteral polyps. The role of aberrant lower pole vessels as an extrinsic cause of UPJ obstruction is less clear in the pathogenesis of the disease. These vessels cross the proximal ureter anteriorly and are thought to be responsible, in part, for functional obstruction. It is unknown whether the vessel alone directly compresses the UPJ or leads to intrinsic narrowing.

DEFINITION AND DIAGNOSIS

In the larger sense, hydroureteronephrosis refers to the dilation of a kidney and its ureter. It may be associated with obstruction or reflux from the bladder. UPJ obstruction typically refers to a blockage at the junction of the renal pelvis and the start of the ureter. The diagnosis of UPJ obstruction is challenging and requires a functional study that confirms the impediment of urine flow out of the renal pelvis. In addition, an anatomic evaluation is necessary to confirm that the sole site of the obstruction is at the UPJ. Therefore, the finding of hydronephrosis alone may result in the overdiagnosis of this anatomic defect. Ultrasonography is the most widely used technique for evaluating the kidney for hydronephrosis. Unfortunately, this modality cannot address the functional significance of the hydronephrosis. Similarly, computed tomography and magnetic resonance urography (MRU) of the abdomen can identify hydronephrosis and suggest a UPJ obstruction when noting a transition in the caliber of the ureter at the UPJ; however, without pyelography, the functional drainage of the kidney cannot be assessed. Historically, intravenous pyelography (IVP) was the functional study most often performed to evaluate obstruction, but radionucleotide renography has now eclipsed IVP as the functional study of choice. Both of these studies can obtain information regarding the differential function and drainage of the kidney. Table 1 presents diagnosis and procedure codes associated with UPJ obstruction.

Hydronephros is secondary to obstruction can lead to progressive renal deterioration. Herein lies the clinical dilemma of UPJ obstruction: when is the obstruction significant enough to warrant repair? Prior to the introduction of routine imaging during the perinatal period, the majority of patients with a UPJ obstruction were symptomatic at the time

Table 1. Codes used in the diagnosis and management of ureteropelvic junction obstruction

Individuals with one or more of the following:	
ICD-9 diagnosis codes	
753.2[a]	Obstructive defects of renal pelvis and ureter
75.20	Unspecified obstructive defect of renal pelvis and ureter
753.21	Congenital obstruction of ureteropelvic junction
CPT procedure codes	
50400	Pyeloplasty (Foley Y-pyeloplasty), plastic operation on renal pelvis, with or without plastic operation on ureter, nephropexy, nephrostomy, pyelostomy, or ureteral splinting; simple
50405	Pyeloplasty (Foley Y-pyeloplasty), plastic operation on renal pelvis, with or without plastic operation on ureter, nephropexy, nephrostomy, pyelostomy, or ureteral splinting; complicated (congenital kidney abnormality, secondary pyeloplasty, solitary kidney, calycoplasty)
50544	Laparoscopy, surgical; pyeloplasty
50575	Renal endoscopy through nephrotomy or pyelotomy, with or without irrigation, instillation, or ureteropyelography, exclusive of radiologic service; with endopyelotomy (includes cystoscopy, ureteroscopy, dilation of ureter and ureteral pelvic junction, incision of ureteral pelvic junction and insertion of endopyelotomy stent)
50740	Ureteropyelostomy, anastomosis of ureter and renal pelvis
50750	Ureterocalycostomy, anastomosis of ureter and renal calyx
52342	Cystourethroscopy; with treatment of ureteropelvic junction stricture (eg, balloon dilation, laser, electrocautery, and incision)
52346	Cystourethroscopy with ureteroscopy; with treatment of intra-renal stricture (eg, balloon dilation, laser, electrocautery, and incision)

[a]Included in definition for datasets prior to 1997.

of presentation. The symptoms include a palpable mass, failure to thrive, feeding difficulties, or sepsis in the infant; in the older child and adult, symptoms include episodic flank pain, nausea, vomiting, urinary tract infections, and hematuria. The introduction of perinatal sonographic screening in the 1980s dramatically changed the presentation and treatment of UPJ obstruction. The majority of congenital UPJ obstructions are now diagnosed prenatally. Historically, there was a trend toward early surgical intervention with the hope of preserving renal function (3). However, since 1988, management of prenatally diagnosed UPJ obstruction in select cases has changed from surgical intervention to observation (4). The indications for intervention include the presence of symptoms associated with obstruction, impairment of overall renal function or progressive impairment of ipsilateral renal function, development of stones or infection, and, rarely, causal hypertension.

Access to healthcare cost and utilization data may help confirm these practice patterns and further elucidate the natural history of asymptomatic UPJ obstruction followed conservatively. Current practice trends suggest that the majority of UPJ obstructions are managed early in life as a result of prenatal screening. Currently, many patients born prior to the era of perinatal sonographic screening are now presenting with UPJ obstruction manifested during a diuretic event, often caused by caffeine or alcohol. If perinatal sonographic screening is successful in detecting congenital UPJ obstruction and those that require intervention are treated during childhood, the number of adult patients admitted for this condition should decline in the future. The exception would be patients with acquired UPJ obstruction. Moreover, the increasing trend toward conservative management of congenital UPJ obstruction may result in these patients becoming susceptible to precipitating events later in life that can convert an asymptomatic UPJ obstruction to a symptomatic one.

TREATMENT

The standard repair for UPJ obstruction has historically been open pyeloplasty. However, over the years, numerous minimally invasive options have become available. Many of these endourological procedures, including percutaneous endopyelotomy (5), "cautery wire balloon" endopyelotomy (6), and ureteroscopic endopyelotomy (7), are associated with reduced length of hospital stay and postoperative recovery. Unfortunately, the success rate for many of them does not approach the rate afforded by open pyeloplasty (8, 9). Laparoscopic pyeloplasty, however, is proving to offer the success rate of an open procedure with the decreased morbidity of an endourological procedure (10). Because of the lack of appropriately-sized instruments, many of the minimally invasive techniques are not available for pediatric patients.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

According to the Healthcare Cost and Utilization Project (HCUP) Kids' Inpatient Database (KID) for 1997 and 2000 (Table 2), the rate of inpatient hospitalizations of patients under the age of 18 has remained unchanged at 2.4 per 100,000 population. KID is based on a sample of pediatric discharges from US community hospitals. Because it samples only pediatric discharges, KID allows a more in-depth analysis of pediatric resource utilization than is available in the all-ages HCUP dataset. KID for 2000 includes 2,784 hospitals from 27 States. KID for 1997 includes 2,521 hospitals from 22 States.

Hospitalization rates were highest in children under 3 years of age from 1997 to 2000, at 8.8 and 9.3 per 100,000. In both 1997 and 2000, the majority of patients were male (71% and 72%, respectively), and hospitalizations occurred almost exclusively at urban centers. These data parallel those recently reported by Nelson et al. in an analysis of HCUP data for patients less than 18 years of age between 1988 and 2000 (11). The study, in which 70.7% of the patients were male, found that fewer neonatal patients were undergoing surgery for UPJ obstruction, but overall, patients tended to be younger at the time of surgery (60.1 vs 69.4 months).

Table 2. Inpatient hospital stays for ureteropelvic junction obstruction listed as primary diagnosis in 1997 and 2000, count, rate[a] (95% CI)

	1997		2000	
	Count	Rate	Count	Rate
Total[b]	1,696	2.4 (2.0–2.7)	1,725	2.4 (1.9–2.8)
Age				
< 3	1,036	8.8 (7.3–10)	1,089	9.3 (7.3–11)
3–10	433	1.3 (1.0–1.6)	432	1.3 (1.0–1.6)
11–17	227	0.8 (0.6–1.0)	204	0.7 (0.5–1.0)
Gender				
Male	1,197	3.3 (2.7–3.8)	1,250	3.4 (2.8–4.0)
Female	498	1.4 (1.2–1.7)	476	1.4 (1.0–1.7)
Region				
Midwest	334	2.0 (1.4–2.6)	322	1.9 (0.8–2.9)
Northeast	399	3.0 (1.8–4.2)	420	3.2 (1.8–4.7)
South	471	1.9 (1.2–2.7)	541	2.2 (1.4–3.0)
West	491	2.9 (2.1–3.8)	443	2.6 (1.6–3.4)
MSA				
Rural	43	*	60	*
Urban	1,653	3.0 (2.6–3.5)	1,650	2.9 (2.4–3.5)

*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area.
[a]Rate per 100,000 is based on 1997 or 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under age 18.
[b]Persons of missing MSA are included in the totals.
NOTES: Counts may not sum to totals due to rounding.
Race/ethnicity breakdown not included because of large percent of missing values.
SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database, 1997 and 2000.

In addition, the percentage of procedures done at urban teaching hospitals increased significantly, from 48.9% to 61.3%. The authors concluded that between 1988 and 2000, the decline in procedures performed in newborns suggested that patients with prenatal hydronephrosis were increasingly being observed instead of undergoing early surgery.

Data from HCUP for patients with a primary diagnosis of UPJ obstruction for the years 1994 to 2000 revealed an overall decrease in the age-adjusted rate of inpatient hospitalization, from 1.1 per 100,000 to 0.8 per 100,000 (Table 3). The data included both adults and children, yet the trend was seen only in patients less than 18 years of age. The overall rate for these patients decreased from 2.8 per 100,000 to 1.7 per 100,000. This may reflect the trend toward conservative management of certain patients with perinatally diagnosed asymptomatic UPJ obstruction. The rates of inpatient hospitalizations for patients 18 years of age and older varied minimally over 1994, 1996, 1998, and 2000 (0.60, 0.60, 0.50, and 0.50 per 100,000, respectively) (Table 3). This finding is not unexpected, since these patients were born before the era of routine sonographic screening. Data for patients born after the initiation of prenatal screening would be expected to have a lower rate of hospitalization for UPJ obstruction. The rate of hospitalization was greater for males than for females in all years reported (60, 66, 65, and 58%, respectively) (calculations based on data in Table 3). The rate appears lower than that reported in male patients less than 18 years of age (Table 3), which would suggest a greater incidence of acquired UPJ obstructions in female patients or an increased likelihood for female patients to become symptomatic from a congenital UPJ obstruction as they become older. The data also indicate that Caucasians had the highest rate of hospitalization and that most hospitalizations took place at urban centers.

Table 3. Inpatient hospital stays for ureteropelvic junction obstruction listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	2,821	1.1 (0.9–1.3)	1.1	2,663	1.0 (0.8–1.2)	1.0	2,304	0.9 (0.7–1.0)	0.9	2,215	0.8 (0.6–1.0)	0.8
Age												
< 18	1,900	2.8 (2.1–3.4)		1,701	2.4 (1.8–3.0)		1,332	1.9 (1.3–2.4)		1,228	1.7 (1.1–2.3)	
> 18		0.6			0.6			0.5			0.5	
18–24	158	0.6 (0.4–0.9)		170	0.7 (0.4–0.9)		225	0.9 (0.6–1.2)		185	0.7 (0.5–1.0)	
25–34	225	0.6 (0.4–0.7)		263	0.6 (0.4–0.8)		173	0.4 (0.3–0.6)		167	0.4 (0.3–0.6)	
35–44	228	0.6 (0.4–0.8)		164	*		175	0.4 (0.3–0.5)		229	0.5 (0.4–0.7)	
45+	295	0.4 (0.3–0.5)		365	0.4 (0.3–0.6)		394	0.4 (0.3–0.6)		406	0.4 (0.3–0.6)	
Gender												
Male	1,690	1.4 (1.1–1.7)	1.3	1,745	1.4 (1.1–1.6)	1.3	1,492	1.1 (0.9–1.4)	1.1	1,288	1.0 (0.7–1.2)	0.9
Female	1,131	0.9 (0.7–1.0)	0.9	918	0.7 (0.5–0.8)	0.7	812	0.6 (0.5–0.7)	0.6	927	0.7 (0.5–0.8)	0.7
Race/ethnicity												
White	1,677	0.9 (0.7–1.1)	1.0	1,563	0.8 (0.6–1.0)	0.9	1,332	0.7 (0.5–0.8)	0.7	1,218	0.6 (0.5–0.8)	0.7
Black	242	0.8 (0.5–1.0)	0.6	185	0.6 (0.3–0.8)	0.5	*	*	*	156	0.4 (0.2–0.7)	0.4
Hispanic	211	*	*	322	1.1 (0.7–1.6)	0.9	*	*	*	169	0.5 (0.2–0.8)	0.4
Region												
Midwest	833	1.4 (1.0–1.7)	1.4	737	1.2 (0.8–1.6)	1.2	623	1.0 (0.7–1.3)	1.0	590	0.9 (0.6–1.2)	0.9
Northeast	516	1.0 (0.6–1.4)	1.0	506	1.0 (0.6–1.4)	1.0	521	*	*	424	0.8 (0.5–1.1)	0.8
South	1,111	1.3 (0.8–1.8)	1.3	950	1.0 (0.7–1.4)	1.0	777	0.8 (0.6–1.1)	0.8	644	0.7 (0.4–0.9)	0.7
West	360	0.6 (0.4–0.8)	0.6	470	0.8 (0.5–1.1)	0.8	383	0.6 (0.3–1.0)	0.6	558	*	*
MSA												
Rural	269	0.4 (0.3–0.6)	0.4	272	0.5 (0.3–0.6)	0.4	235	0.4 (0.2–0.6)	0.4	166	0.3 (0.2–0.4)	0.3
Urban	2,552	1.4 (1.1–1.6)	1.3	2,391	1.2 (0.9–1.4)	1.2	2,055	1.0 (0.8–1.2)	1.0	2,049	1.0 (0.7–1.2)	1.0

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 4. Physician office visits by Medicare beneficiaries with ureteropelvic junction obstruction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	2,320	6.6 (5.4–7.9)		2,200	6.2 (5.1–7.4)		2,360	7.0 (5.8–8.3)		2,260	6.4 (5.2–7.6)	
Total < 65	200	3.6 (1.4–5.9)		200	3.3 (1.2–5.3)		260	4.2 (1.9–6.5)		160	2.3 (0.7–3.8)	
Total 65+	2,120	7.2 (5.8–8.6)	7.6	2,000	6.8 (5.5–8.2)	6.8	2,100	7.7 (6.2–9.2)	7.7	2,100	7.4 (6.0–8.9)	7.3
Age												
65–69	340	3.8 (2.0–5.6)		360	4.3 (2.3–6.2)		400	5.5 (3.1–7.8)		440	5.8 (3.4–8.3)	
70–74	500	6.6 (4.0–9.2)		760	9.8 (6.7–13)		780	11 (7.6–15)		480	6.9 (4.1–9.7)	
75–79	680	12 (7.9–16)		460	8.1 (4.8–11)		400	7.1 (4.0–10)		460	7.7 (4.6–11)	
80–84	520	14 (8.4–19)		220	5.6 (2.3–8.9)		320	8.3 (4.2–12)		420	10 (5.9–15)	
85–89	60	2.9 (0–6.2)		140	6.4 (1.7–11)		160	7.3 (2.2–12)		160	6.9 (2.1–12)	
95+	20	2.4 (0–7.1)		20	2.2 (0–6.6)		20	2.2 (0–6.5)		100	10 (1.3–20)	
Race/ethnicity												
White	1,580	5.3 (4.2–6.5)	5.6	1,640	5.4 (4.2–6.6)	5.2	2,140	7.5 (6.1–9.0)	7.5	2,000	6.7 (5.4–8.0)	6.9
Black	120	4.0 (0.8–7.3)	4.7	160	5.0 (1.5–8.4)	6.2	60	1.9 (0–4.1)	1.9	60	1.8 (0–3.8)	1.2
Asian	…	...	…	0	0	0	120	38 (7.6–69)	38	180	38 (13–63)	25
Hispanic	…	...	…	0	0	0	0	0	0	0	0	0
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Gender												
Male	840	5.6 (3.9–7.3)	6.3	820	5.4 (3.7–7.0)	5.9	540	3.7 (2.3–5.1)	4.1	540	3.5 (2.2–4.8)	3.8
Female	1,480	7.4 (5.7–9.1)	6.9	1,380	6.8 (5.2–8.5)	6.4	1,820	9.6 (7.6–12)	9.1	1,720	8.7 (6.8–10)	8.4
Region												
Midwest	300	3.4 (1.7–5.2)	3.0	180	2.0 (0.7–3.3)	1.8	720	8.3 (5.6–11.1)	8.1	420	4.8 (2.7–6.8)	4.8
Northeast	440	5.7 (3.3–8.1)	6.8	540	7.0 (4.4–9.7)	7.0	300	4.5 (2.2–6.7)	4.5	360	5.2 (2.8–7.6)	4.6
South	1,440	12 (9.1–14)	11	840	6.6 (4.6–8.6)	6.8	840	6.8 (4.7–8.8)	7.1	980	7.4 (5.3–9.5)	8.1
West	100	1.8 (0.2–3.4)	1.8	640	12 (8.1–17)	12	500	10 (6.1–14)	9.7	500	9.3 (5.6–13)	8.1

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 5. Mean inpatient length of stay (LOS) and cost per child admitted with ureteropelvic junction obstruction[a] listed as primary diagnosis, 1999–2003

	Count	Percent	LOS	Mean Cost
Total	3,078		2.9	$7,728
Age				
0–2	1,933	63%	2.9	$7,649
3–10	795	26%	2.8	$7,525
11–17	329	11%	3.0	$8,660
18+	21	1%	3.0	$8,154
Race/ethnicity				
White	2,007	65%	2.7	$7,659
Black	286	9%	3.2	$7,703
Asian	37	1%	3.2	$7,925
Hispanic	333	11%	3.5	$8,542
N. American Native	6	0%	2.5	$8,064
Missing	142	5%	1.9	$5,807
Other	267	9%	3.1	$8,243
Gender				
Female	920	30%	2.7	$7,372
Male	2,158	70%	3.0	$7,880
Region				
Midwest	993	32%	2.7	$7,651
Northeast	489	16%	3.5	$9,581
South	1,065	35%	2.7	$6,930
West	531	17%	2.9	$7,767

[a]Using ICD-9 codes 753.20 (unspecified obstructive defect of renal pelvis and ureter) and 753.21 (Congenital obstruction of ureteropelvic junction).

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2003.

Outpatient Care

Physician Office Visits

The data for physician office visits by Medicare beneficiaries with UPJ obstruction as the primary diagnosis in 1992, 1995, 1998, and 2001 are shown in Table 4. The overall age-adjusted rate for patients over 65 years of age remained relatively unchanged over the reported years. Interestingly, females had the highest rate of physician office visits in this population, and the trend was increasing (64, 63, 77, and 76%, respectively) (calculations based on data in Table 4). These data coincide with data in the HCUP dataset for patients over 18 years of age. As in the other samples, the rate of physician office visits for UPJ obstruction was highest in the Caucasian population.

Length of Stay

The database from the National Association of Children's Hospitals and Related Institutions (NACHRI) for 1999–2003 reported the mean inpatient length of stay (LOS) and cost per child (Table 5). The mean length of stay during this period was 2.9 days. Between 1994 and 2000 (Table 6), LOS dropped further for children than for adults. Nelson et al. observed a decrease from 6.6 days in 1988 to 3.7 days in 1997–2000 (11). These data suggest a further decrease in length of stay between 2000 and 2003. The majority of patients were under the age of 2 (63%) at the time of treatment. This is similar to the trend seen in the HCUP Kids' database for inpatient hospitalizations, where the highest rate was for children less than 3 years of age (Table 2).

ECONOMIC IMPACT

Data on the cost of treating patients with UPJ obstruction are limited. However, NACHRI data suggest that the average cost per hospitalization from 1999 to 2003 was $7,728 (Table 5). While average length of stay associated with the treatment of UPJ obstruction has declined markedly over time,

Table 6. Length of stay (LOS) for patients with a primary diagnosis of ureteropelvic junction obstruction

	1994				1996				1998				2000			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total[a]	2,821	5	4	111	2,663	3.8	3	34	2,304	3.5	3	17	2,215	3.3	3	42
Age																
< 18	1,900	5.3	4	111	1,701	3.9	3	34	1,332	3.3	3	17	1,228	2.8	2	16
18–24	158	4.2	5	9	170	3.1	3	7	225	3.8	4	9	185	3	3	9
25–34	225	4	4	11	263	3.5	3	14	173	3.8	3	8	167	3.3	3	8
35–44	228	3.9	4	9	*	*	*	*	175	3.3	3	7	229	3.4	3	9
45+	295	5.4	5	24	365	4.2	4	17	394	4.1	3	17	406	4.8	4	42
Gender																
Male	1,690	5.1	4	111	1,745	3.8	3	34	1,492	3.4	3	17	1,288	3.3	3	42
Female	1,131	5	4	21	918	3.8	3	19	812	3.8	3	17	927	3.3	3	12
Race/ethnicity																
White	1,677	5	4	111	1,563	3.8	3	17	1,332	3.5	3	17	1,218	3.2	3	16
Black	242	5.6	4	18	185	5.4	4	34	*	*	*	*	156	3.4	3	10
Hispanic	211	5.4	5	16	322	4.2	3	30	*	*	*	*	169	3.3	3	10
Region																
Midwest	833	4.7	4	24	950	3.6	3	17	623	3.5	3	17	590	3.5	3	42
Northeast	516	6.5	4	111	506	4.3	3	34	521	3.7	3	17	424	3.3	3	10
South	1,111	4.9	4	20	950	3.6	3	19	777	3.5	3	12	644	3.6	3	16
West	360	4.1	4	15	470	4	4	30	383	3.5	3	13	558	2.6	2	7
MSA																
Rural	269	3.5	4	8	272	3.4	3	8	235	3.6	3	17	166	4.3	4	12
Urban	2,552	5.2	4	111	2,391	3.9	3	34	2,055	3.5	3	17	2,049	3.2	3	42

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 7. Inpatient expenditures for patients with ureteropelvic junction obstruction

	1994	1996	1998	2000
Total	$12,073,190	$12,274,483	$11,279,536	$11,747,477

SOURCE: National Ambulatory Medical Care Survey; National Hospital Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

there appears to have been no change in aggregate expenditures over this period. Length of stay may have decreased, but there has been at most a small decline in total inpatient spending from $12.1 million to $11.8 million (Table 7). It may be that inpatient services were moved to ambulatory surgery locations, making the overall picture hard to estimate from the data. Additionally, reimbursement for inpatient stays may have gone down in parallel with the decreasing length of stay, but charges may have been artificially inflated, thus masking the decline.

Average length of stay and treatment costs for children remain considerably higher in the Northeast, which may be due to the increased costs associated with minimally invasive procedures. Over the past decade, treatment for UPJ obstruction has shifted from open pyeloplasty to endopyelotomy to laparoscopic pyeloplasty (12, 13).

CONCLUSIONS

The majority of UPJ obstructions are diagnosed in the perinatal period. The practice of surgical intervention during the neonatal period has decreased, while there has been an increasing trend toward conservative management.

RECOMMENDATIONS

The following questions need to be addressed to gain a better understanding of the natural history of UPJ obstruction:

- When (if ever) do patients who are followed conservatively for UPJ obstruction undergo surgical intervention (at what age and how long after diagnosis)?
- What proportion of patients with congenital UPJ obstruction who do not undergo surgical correction during childhood become symptomatic as adults (at what age)?
- Is there an equal propensity of renal failure in males and females with UPJ obstruction?
- Is there an identifiable precipitating event later in the life of untreated patients for whom conservative therapy is not successful?
- How has the increased utilization of prenatal ultrasound impacted the management of pediatric UPJ obstruction?

REFERENCES

1. Murnaghan GF. The dynamics of the renal pelvis and ureter with reference to congenital hydronephrosis. Br J Urol 1958;30:321-24.
2. Hanna JK. Antenatal hydronephrosis and ureteropelvic junction obstruction: the case for early intervention. Urol 2000;55:612-15.
3. Koyle MA, Ehrlich RM. Management of ureteropelvic junction obstruction in the neonate. Urol 1988;31:496.
4. Onen A, Janyanthi VR, Koff SA. Long-term follow-up of prenatally detected severe bilateral newborn hydronephrosis initially managed nonoperatively. J Urol 2002;168:1118.
5. Knudson BE, Cooks AJ, Watterson JD, Beiko DT, Nott L, Razui H, Denstedt JD. Percutaneous antegrade endopyelotomy: long-term results for one institution. Urol 2004;63(2):230-34.
6. Gill HS, Liao JC. Pelviureteric junction obstruction treated with Accucise retrograde endopyelotomy. Br J Urol 1998;82:8-11.
7. Martin SF, Stream SB. Ureteroscopic laser endopyelotomy: a single center experience. J Endourol 2003;17:401-404.
8. Albani JM, Yost AJ, Stream SB. Ureteropelvic junction obstruction: defining durability of endourological intervention. J Urol 2004;171:579-82.
9. Baddwin DD, Dunbar JA, Wells N, McDougall EM. Single center comparison of laparoscopic pyeloplasty, Accucise endopyelotomy and open pyeloplasty. J Endourol 2003;17:155-60.
10. Jarrett TW, Chen DY, Charambura TC, Fugita O, Kavoussi LR. Laparoscopic pyeloplasty: the first 100 cases. J Urol 2002;167:1253-56.
11. Nelson CP, Park JM, Dunn RL, Wei JT. Contemporary trends in surgical correction of pediatric ureteropelvic junction obstruction: data from the nationwide inpatient sample. J Urol 2005;173:232-36.
12. Marcovich R, Jacobson AI, Aldana JPA, Lee BR, Smith AD. Practice trends in contemporary management of adult ureteropelvic junction obstruction. Urol 2003;62:22-25.
13. Tan BJ, Rastinehad AR, Marcovich R, Smith AD, Lee BR. Trends in ureteropelvic junction obstruction management among urologists in the United States. Urol 2005;65:260-64.

CHAPTER 10

Kidney Cancer

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Kidney Cancer

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INTRODUCTION

Kidney cancer, the third most common urologic malignancy and the seventh most common cancer overall, was diagnosed in an estimated 35,000 Americans in 2005, and nearly 13,000 died from it (1). That year, kidney cancer constituted 3% of new cancer cases and 3% of all cancer deaths in men. Kidney cancer occurs about half as often in women and constitutes less than 2% of female cancer cases and deaths (1). When discovered in its early stages, the disease is curable, but metastatic kidney cancer is usually fatal. Fortunately, the recent increase in kidney cancer incidence reflects primarily small tumors discovered incidentally during abdominal imaging. Table 1 lists the diagnosis and procedure codes associated with kidney cancer.

Kidney cancer imposes a significant burden on the US healthcare system, as its diagnosis involves advanced radiologic testing and its treatment often involves surgery, hospitalization, and regular surveillance visits to assess for recurrence. These interventions result in loss of work time and regular activity, not only for the patient but also for family members providing support. Currently, less than 1% of visits to urologists are for the treatment of kidney cancer (Table 2).

DEFINITION AND DIAGNOSIS

The term *kidney cancer* generally refers to any cancer arising in the kidney or renal pelvis, but most of the tumors considered in this analysis are renal cell carcinomas (RCCs), which arise from cells in the tubules of the filtration portion of the kidney. RCC itself includes a variety of distinct biological and disease entities (2). In adults, most kidney cancers are classified as conventional or clear cell RCC and are associated with a defect in the von Hippel-Lindau tumor suppressor gene. This genetic defect can be inherited but usually occurs spontaneously. Each of the other subtypes (papillary RCC, chromophobe RCC, and collecting duct RCC) has a unique genetic abnormality and exhibits different biologic behavior. In children, the most common form of kidney cancer is Wilms' tumor, which also exhibits unique genetic abnormalities and biologic behavior. Wilms' tumors are quite rare and contribute little to the incidence data in current datasets. Transitional cell carcinomas involving the kidney are excluded from the analysis in this chapter whenever possible, because they originate in the urothelial lining of the renal pelvis rather than the filtration component of the kidney. These cancers have various risk factors, exhibit different biologic behavior, and have different treatment options; they are discussed in the bladder and upper tract urothelial cancer chapter of this compendium.

More than 50% of kidney cancers are diagnosed incidentally by abdominal imaging (computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound) performed for unrelated reasons (3). Nonspecific symptoms such as fatigue, weight loss, and peripheral edema may also lead to an evaluation that identifies a kidney cancer. Less commonly, symptoms such as flank pain, hematuria, and/or a flank mass will lead to evaluation that identifies a kidney tumor.

Table 1. Codes used in the diagnosis and management of kidney cancer

Individuals 35 years or older, with one or more of the following:	
ICD-9 diagnosis codes	
189	Malignant neoplasm of kidney and other unspecified organs
189.0	Malignant neoplasm of kidney, except pelvis
189.8	Malignant neoplasm of other specified sites of urinary organs
CPT procedure codes	
50230	Nephrectomy, including partial ureterectomy, any open approach including rib resection; radical, with regional lymphadenectomy and/or vena caval thrombectomy
50240	Nephrectomy, partial
50543	Laparoscopy, surgical; partial nephrectomy
50545	Laparoscopy, surgical; radical nephrectomy (includes removal of Gerota's fascia and surrounding fatty tissue, removal of lymph nodes, and adrenalectomy)

The so-called "classic triad" of symptoms of kidney cancer—hematuria, flank pain, and a mass—occurs rarely (< 10%) and inevitably indicates the presence of advanced disease (4). When such symptoms cause suspicion, X-rays (e.g., intravenous pyelography), CT, MRI, and ultrasound may be utilized to identify tumors and determine their extent. Both CT and MRI are highly sensitive means of identifying the characteristics of kidney cancer, although only removal of the lesion and pathological evaluation are considered diagnostic. Of these, contrast-enhanced CT is the most commonly used modality. Non-excisional biopsy of the tumor is pursued only in rare instances with renal masses of diagnostic uncertainty.

Staging for local extension or metastatic disease is critical in all cases of suspected kidney cancer (Table 3). A chest X-ray (or chest CT) and blood tests are performed to check for lung metastases and paraneoplastic syndromes, respectively. Additionally, if signs or symptoms raise concern for bone metastasis, a bone scan is obtained, and if neurologic symptoms are present, CT or MRI of the brain is obtained. Staging is described by the TNM system that is standard practice in the United States, where the T stage is based on the

Table 2. Physician office visits to urologists, count, percent

Primary diagnosis	1992–2000 Count	Percent
Total	50,191,441	100
Kidney Cancer	383,886	< 1

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 3. TNM staging system for kidney cancer

Primary Tumor (T)	
TX:	Primary tumor cannot be assessed
T0:	No evidence of primary tumor
T1:	Tumor ≤ 7 cm in greatest dimension, limited to the kidney
T1a:	Tumor ≤ 4 cm in greatest dimension, limited to the kidney
T1b:	Tumor > 4 cm but ≤ 7 cm in greatest dimension, limited to the kidney
T2:	Tumor > 7 cm in greatest dimension, limited to the kidney
T3:	Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota's fascia
T3a:	Tumor directly invades adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b:	Tumor grossly extends into the renal vein or its segmental (i.e., muscle-containing) branches, or the vena cava below the diaphragm
T3c:	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4:	Tumor invades beyond Gerota's fascia
Regional lymph nodes (N)	
NX:	Regional lymph nodes cannot be assessed
N0:	No regional lymph node metastasis
N1:	Metastasis in a single regional lymph node
N2:	Metastasis in more than 1 regional lymph node
Distant metastasis (M)	
MX:	Distant metastasis cannot be assessed
M0:	No distant metastasis
M1:	Distant metastasis
Histological grading	
GX:	Grade of differentiation cannot be assessed
G1:	Well differentiated
G2:	Moderately differentiated
G3-4:	Poorly differentiated/undifferentiated

Source: Adapted from Kidney. In: American Joint Committee on Cancer.: AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, 2002, 323–328.

size of the tumor and whether it has extended directly beyond the kidney, N denotes the presence of lymph node involvement, and M denotes metastasis to other parts of the body.

RISK FACTORS

The cause of kidney cancer is not known. Epidemiologic evidence indicates that age beyond 50 years, male gender, and end-stage renal disease are risk factors for developing kidney cancer. Other risk factors include smoking (5), obesity (6), hypertension, and work-related exposures to certain substances, such as leather dyes, cadmium, petroleum products, and asbestos (6). In addition, medications, such as diuretics, and dietary factors, including coffee consumption, high-fat and high-protein (7) diets, and high consumption of red and processed meat (8), have been associated with kidney cancer (9, 10). Interestingly, alcohol consumption is weakly associated with a decreased risk of kidney cancer (11, 12). Despite these associations, no definite causal relationship has been established.

While the specific causes of kidney cancer are unknown, genetic abnormalities are consistently present in each histologic subtype. Patients with a family history of any of these abnormalities have a substantially increased risk of kidney cancer, but hereditary kidney cancer contributes only minimally to the overall incidence of the disease (13). Most likely, kidney cancer is caused by a combination of sporadic genetic events, environmental exposures, and patient factors (14, 15).

TREATMENT

Surgery is the primary treatment for non-metastatic kidney cancer. Surgical removal is the standard of care for tumors confined to the kidney (T1 and T2 cancers), for T3a tumors that have perforated into the fatty tissue around the kidney, and for T3b and T3c tumors that have extended into the venous system.

Several non-surgical alternatives are available for patients who are unsuitable surgical candidates or who are unwilling to have surgery. One alternative is arterial embolization, in which the blood supply to the tumor or to the entire kidney is blocked. In the past decade, less-invasive percutaneous thermal therapies have been developed (e.g., cryotherapy and radiofrequency ablation) that appear in early studies to be effective in selected cases (16). Finally, in very elderly patients who have severe medical comorbidity, kidney tumors may simply be managed expectantly with serial X-rays and clinical follow-up.

Radiation therapy is not effective for kidney cancer except to palliate the pain associated with bone metastases. Chemotherapy also has not been effective in treating this disease, although recent clinical trials show some promise. Over the past several years, intense research has focused on manipulating the immune system to help fight metastatic kidney cancer. As a result, immunotherapy with interleukin-2 or interferon alpha is often used, but with limited success. There appears to be a survival benefit from removal of the kidney tumor (cytoreductive surgery) before immunotherapy for patients with metastatic disease and good functional status (17, 18). In addition, clinical trials for metastatic kidney cancer generally mandate removal of the kidney. Finally, surgical removal of solitary metastatic lesions has shown a survival benefit, particularly in the case of lung lesions (19, 20).

A new agent, sorafenib tosylate (Nexavar™) (21), was approved in 2005 for the treatment of patients with metastatic kidney cancer. In the drug class known as tyrosine kinase inhibitors, it works by inhibiting angiogenesis, the growth of blood vessels, induced by the cancer. In the clinical trial leading to FDA approval, the drug doubled survival time from three to six months. A similar agent, sunitinib malate (Sutent™) (22), was approved in 2006 to treat patients with metastatic kidney cancer. Both of these medications have been shown to extend progression-free survival and continue to be evaluated for their effect on overall survival. In addition, studies are ongoing to evaluate these agents in combination with other agents to further improve the survival of patients with metastatic renal cell carcinoma. It is important to note that both sorafenib and sunitinib do not usually cause disappearance of metastatic lesions as is the traditional goal of chemotherapy, but rather cause stabilization of the disease by arresting further growth and spread. Furthermore, these agents are expensive and cost thousands of dollars per month and treatment duration is indeterminate at this time.

Table 4. Incidence rates of kidney cancer, age-adjusted, by race/ethnicity and gender

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
Year of Diagnosis									
1975	7.1	10.3	4.5	7.3	10.8	4.6	6.2	8.2	4.3
1976	8.0	11.2	5.5	8.1	11.5	5.6	7.8	11.6	4.8
1977	8.1	11.4	5.5	8.1	11.7	5.5	8.5	11.1	6.4
1978	7.8	11.8	4.8	8.0	12.1	4.9	8.0	11.0	5.7
1979	7.6	11.1	5.0	7.8	11.6	5.1	7.3	8.2	6.3
1980	8.1	11.7	5.4	8.4	12.2	5.6	6.0	8.0	4.4
1981	8.5	12.8	5.3	8.6	13.0	5.3	10.0	15.8	5.8
1982	8.3	11.8	5.7	8.5	12.0	5.8	7.6	11.2	4.9
1983	8.9	13.2	5.7	9.2	13.8	5.8	8.8	13.5	5.5
1984	9.2	13.1	6.2	9.5	13.6	6.3	9.0	12.0	6.8
1985	8.9	13.1	6.8	9.2	13.6	5.9	8.6	11.6	6.2
1986	9.7	13.8	6.6	9.8	14.1	6.7	10.1	15.0	6.6
1987	9.9	14.1	6.7	10.1	14.4	6.9	11.1	15.6	7.8
1988	9.9	14.0	7.0	10.1	14.3	7.0	11.5	15.2	8.8
1989	10.3	14.5	7.1	10.6	15.0	7.2	10.8	15.1	7.8
1990	10.4	14.7	7.1	10.7	15.0	7.4	10.6	16.1	6.6
1991	10.6	15.0	7.2	10.8	15.2	7.4	12.2	18.3	7.5
1992	10.7	15.2	7.4	11.1	16.6	7.7	10.9	16.3	7.2
1993	10.7	14.6	7.6	10.8	14.7	7.7	12.7	17.3	9.4
1994	11.3	15.6	7.8	11.5	19.9	8.0	12.7	18.0	8.6
1995	11.1	15.5	7.6	11.1	15.4	7.7	14.4	21.7	9.3
1996	11.3	15.8	7.9	11.4	16.1	7.8	13.5	17.0	10.9
1997	10.9	15.0	7.6	11.0	15.0	7.7	13.4	19.2	9.2
1998	11.8	16.4	8.2	12.1	16.8	8.4	12.6	16.9	9.2
1999	11.4	15.8	7.8	11.6	16.1	8.0	13.5	18.5	9.9
2000	12.3	17.1	8.4	12.5	17.7	8.3	14.6	19.0	11.8
2001	12.0	16.7	8.3	12.2	16.9	8.5	14.5	20.9	9.9
Age at Diagnosis									
All Ages	11.7	16.2	8.1	11.9	16.5	8.2	13.7	18.9	10.0
< 65	6.1	8.2	4.2	6.2	8.2	4.2	7.5	9.8	5.5
> 65	50.0	71.8	34.8	51.2	73.5	35.6	56.9	81.7	41.0
All Ages[a]	8.2	11.2	5.7	8.4	11.4	5.8	9.8	13.3	7.2

In this table, approximately 12% are renal pelvis cancers.

[a]SEER 9 areas. Rates are per 100,000 and are age-adjusted to the International Agency for Research on Cancer (IARC) world standard population.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

These agents will likely have a significant effect on survival from kidney cancer and costs associated with treatment over the next several years, but these are not reflected in the datasets used in this chapter.

Several surgical techniques are used to remove kidney cancers. Radical nephrectomy involves the removal of the entire kidney, its surrounding fatty tissue known as Gerota's fascia, and the nearby adrenal gland. Partial nephrectomy entails removing the entire tumor with a margin of normal kidney but sparing the remainder of the normal kidney and is associated with good long-term results (18). This procedure is technically more challenging than radical nephrectomy and has a higher risk of significant blood loss. Partial nephrectomy, or "nephron-sparing" surgery, is increasingly utilized for T1 tumors and, when technically feasible, for higher-stage tumors in the setting of bilateral disease, solitary kidney, or systemic disease that affects renal function (e.g., diabetes, hypertension).

During the 1990s, the evolution of laparoscopy transformed kidney cancer surgery. This technique involves making several buttonhole-size incisions and inserting a lighted scope and instruments to permit the surgery without making the traditional, larger incision. After the kidney is dissected free, it is usually removed through an incision made lower in the abdomen. Because of the size and location of the incision, pain is decreased and cosmesis is improved. First used for operations such as gallbladder removal, this technique was applied to kidney surgery in the 1990s and has been shown to decrease pain and speed the return to normal activity. Both radical and partial nephrectomy are now performed laparoscopically at many university centers and many non-academic centers as an evolving standard of care. To investigate

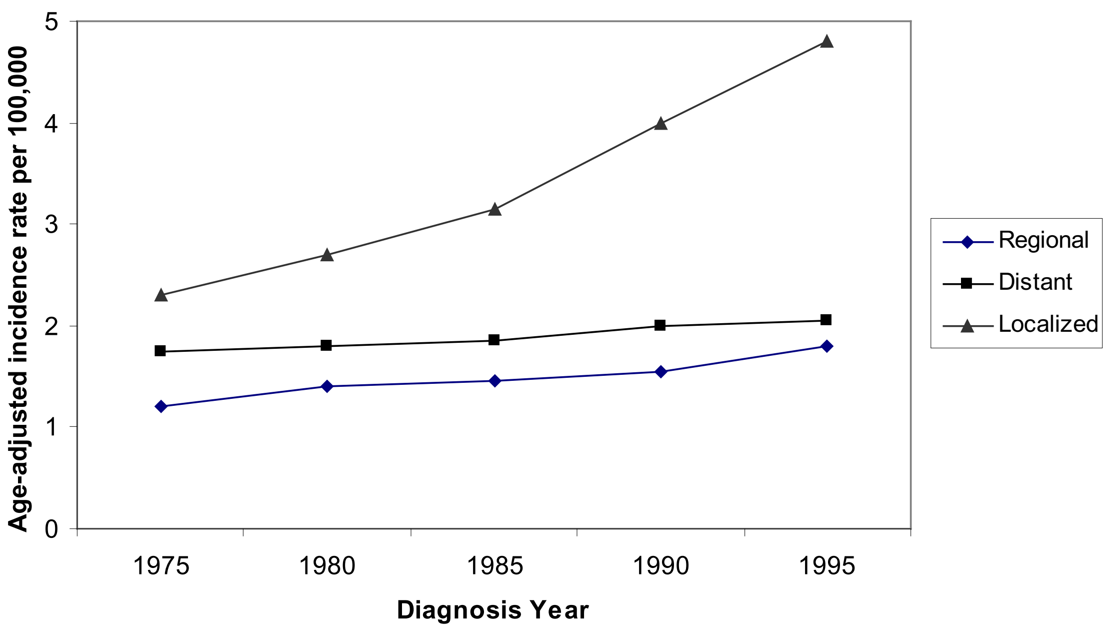

Figure 1. Age-adjusted incidence rates for kidney cancer per 100,000 population, by stage, 1973–1998 (SEER).

In this figure, approximately 12% are renal pelvis cancers. Values over curves indicate annual percent change per 100,000 population. Values in parentheses indicate 95% CI.

SOURCE: Adapted from Journal of Urology, 167, Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data, 57–60, Copyright 2002, with permission from American Urological Association.

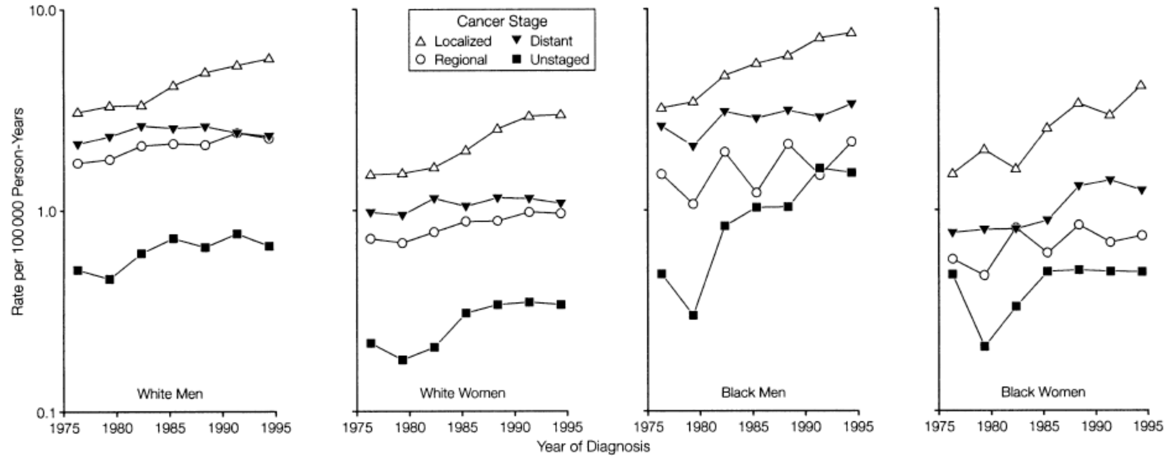

Figure 2. Age-adjusted incidence rates per 100,000 person-years for kidney cancer, by gender, race/ethnicity, and tumor stage at diagnosis, 1975–1977 and 1993–1995 (SEER).

In this figure, approximately 12% are renal pelvis cancers.

SOURCE: Adapted from Journal of the American Medical Association, Chow WH, Devesa SS, Warren JL, Fraumeni JF, Jr. Rising incidence of renal cell cancer in the United States. 1999;281(17):1628–1631, with permission from American Medical Association.

this further, the Urology Residency Review Committee evaluated the surgical database for residents completing training in 2005 (23). CPT codes for laparoscopic nephrectomy, laparoscopic radical nephrectomy, laparoscopic partial nephrectomy, and laparoscopic nephroureterectomy were used. Residents completing four-year urology training programs reported performing an average of 24 of these procedures, with a median of 26.

While the analysis in this chapter is based on the most complete and updated information available regarding the utilization of US healthcare for the treatment of kidney cancer, some important limitations exist. Data are not yet available to describe fully the recent widespread adoption of laparoscopic techniques in kidney cancer surgery, although relevant information is included where possible. Finally, the datasets do not capture non-surgical treatments such as thermal therapy and immunotherapy, because their use is either too recent or uncommon.

INCIDENCE AND PREVALENCE

Incidence

Several excellent resources provide insight into the incidence and prevalence of kidney cancer in the United States. The best sources of information are the Surveillance, Epidemiology, and End Results (SEER) database and the American Cancer Society Surveillance Research Cancer Statistics, both of which show an increasing incidence of kidney cancer over the past three decades. While most of the increased incidence is seen in small, organ-confined disease, there is also a significant increase in the incidence of locally advanced and metastatic disease (Figures 1 and 2).

An important question raised by these data is whether the increased incidence of RCC is due to a real increase in the disease burden or simply to increased detection. The answer appears to be both. In addition, the SEER data reflect an increase in the treatment of RCC. However, the SEER data do not capture cases that are diagnosed radiographically if the tumors are not biopsied or removed; therefore, the incidence is inherently underestimated in this dataset. Certainly, more tumors are diagnosed incidentally through abdominal imaging that is performed for other reasons. A typical scenario is that of a patient who visits the doctor because he is experiencing abdominal pain and subsequently undergoes an abdominal CT for further evaluation. A kidney tumor is identified but is not believed to be the cause of the pain, and the

Table 5. Incidence rates of kidney cancer, age-specific[a], by race/ethnicity and gender

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
Age at Diagnosis									
< 1	1.7	…	…	…	…	…	…	…	…
1–4	2.1	1.9	2.4	2.4	2.2	2.6	…	…	…
5–9	0.6	…	0.7	0.5	…	…	…	…	…
10–14	…	…	…	…	…	…	…	…	…
15–19	…	…	…	…	…	…	…	…	…
20–24	0.3	…	…	…	…	…	…	…	…
25–29	0.5	0.6	…	0.5	…	…	…	…	…
30–34	1.3	1.4	1.2	1.2	1.3	1.1	2.0	…	…
35–39	2.8	3.2	2.4	2.7	3.2	2.3	3.7	…	3.6
40–44	5.7	7.3	4.2	5.7	7.3	4.0	7.6	8.9	6.4
45–49	9.7	13.6	6.0	10.0	14.0	6.1	9.4	14.5	5.0
50–54	15.8	22.0	9.8	15.9	22.0	9.9	21.3	30.3	13.6
55–59	25.8	35.1	17.0	26.3	35.5	17.3	31.7	41.8	23.3
60–64	35.2	48.2	23.4	35.9	48.9	23.7	40.7	54.9	29.4
65–69	45.1	60.9	31.6	46.4	61.8	33.0	52.8	78.6	33.5
70–74	53.2	75.5	35.8	54.7	77.3	36.6	91.9	86.3	45.4
75–79	54.1	77.9	37.3	55.5	80.3	38.2	61.4	84.3	47.0
80–84	54.6	82.7	37.7	55.5	84.3	38.2	61.2	102.2	39.9
> 85	42.0	65.2	32.3	42.1	67.6	31.9	42.8	…	39.8

…data not available.

In this table, approximately 12% are renal pelvis cancers.

[a]SEER 9 areas. Rates are per 100,000 and are age-adjusted to the 2000 US standard population by age groups.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 6. Trends in incidence[a] of kidney cancer, 1975–2001, by race/ethnicity and gender

	Year	APC	Year	APC
Total				
Male and Female	1975–1990	2.4[b]	1990–2001	1.3[b]
Male	1975–1987	2.3[b]	1987–2001	1.2[b]
Female	1975–1992	2.3[b]	1992–2001	1.1[b]
White				
Male and Female	1975–1990	2.4[b]	1990–2001	1.2[b]
Male	1975–1987	1.6[b]		
Female	1975–1992	2.7[b]	1992–2001	0.9[b]
Black				
Male and Female	1975–1990	2.9[b]		
Male	1975–1987	2.8[b]		
Female	1975–1992	3.2[b]		

The APC is the Annual Percent Change based on rates age-adjusted to the 2000 US standard population by 5-year age groups.

In this table, approximately 12% are renal pelvis cancers.

[a]Trends are from the SEER 9 areas.

[b]The annual percent of change is significantly different from zero ($p < 0.05$).

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 7. Estimated annual percent change in incidence rate of kidney cancer, 1975–1998, by stage, age, and race/ethnicity

Stage	Age (yr)	Race	Estimated Annual Percentage of Change
Local	20–59	White	2.87
		Black	4.46
	60+	White	3.06
		Black	4.35
Regional/distant	20-59	White	0.08
		Black	0.12
	60+	White	0.15
		Black	1.82

SOURCE: Reprinted from Urology, 62, Vaishampayan UN, Do H, Hussain M, Schwartz K, Racial disparity in incidence patterns and outcome of kidney cancer, 1,012–1,017, Copyright 2003, with permission from Elsevier.

focus shifts to the treatment of the kidney mass. From the late 1980s into the 1990s, the rate of CT and MRI of the abdomen in Medicare patients nearly doubled, from 2,622 to 4,536 per 100,000 per year (24) and has remained at least as high since that time. Incidentally detected kidney tumors now constitute the majority of the presentations of RCC. Most of these are low-stage tumors, although many of higher stage are also detected incidentally.

With increasing detection of curable, small kidney tumors, one would expect to see a stage migration with a decrease in advanced disease and death rates. This occurred with prostate cancer screening after the advent of the prostate specific antigen blood test in the early 1990s. To date, however, there is limited evidence that it has occurred in kidney cancer (25). The rising rate of obesity (26) and hypertension (27), two known risk factors associated with kidney cancer, may play a role in the increased incidence.

The SEER data show that kidney cancer incidence rises with age—the vast majority of cases are diagnosed in patients over 65 (Table 4). Overall incidence in the United States is greater than that reported by international organizations such as the International

Table 8. Age-adjusted incidence[a] rates of kidney cancer, by race/ethnicity and gender

	Rate per 100,000 persons 1997–2001			Annual Percent Change 1992–2001		
Race/ethnicity	Total	Male	Females	Total	Male	Females
Total	11.3	15.7	7.8	1.4[c]	1.3[c]	1.5[c]
White	11.7	16.2	8.1	1.6[c]	1.4[c]	1.4[c]
White Hispanic[b]	11.5	15.5	8.5	1.9	1.1	2.9[c]
White Non-Hispanic[b]	11.5	16.0	7.8	1.7[c]	1.7[c]	1.4[c]
Black	13.3	18.8	9.4	2.2[c]	1.9	2.8[c]
Asian/Pacific Islander	6.4	8.9	4.3	1.4	0.4	3.1[c]
N. American Native/ Alaska Native	10.0	13.9	7.0	- 5.6[c]	- 5.9[c]	…
Hispanic[b]	11.2	15.1	8.2	2.2[c]	1.4	3.0[c]

…data not available.

In this table, approximately 12% are renal pelvis cancers.

[a]Incidence data are from the 12 SEER areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, and Alaska Native Registry.

[b]Hispanic and Non-Hispanic are not mutually exclusive from Whites, Blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives. Incidence data for Hispanics and Non-Hispanics do not include cases from Detroit, Hawaii, and Alaska Native Registry.

[c]The APC annual percent change is significantly different from zero ($p < 0.05$).

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

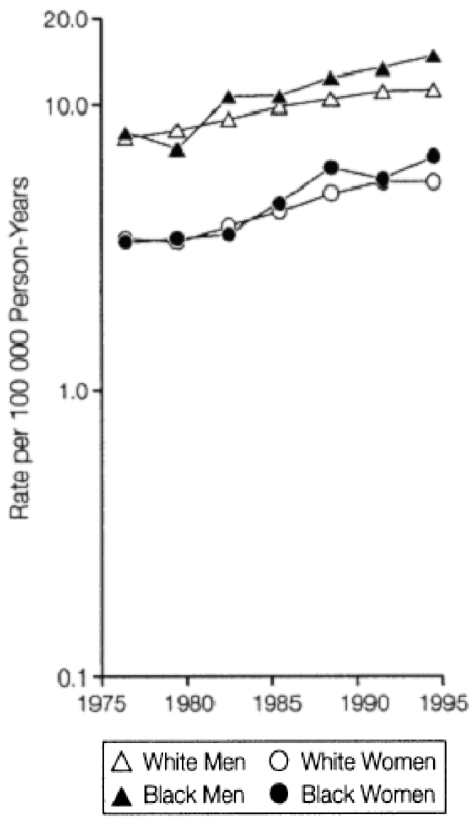

Figure 3. Age-adjusted incidence rates of kidney cancer per 100,000 person-years, by gender and race/ethnicity, 1975–1977 to 1993–1995 (SEER).

In this figure, approximately 12% are renal pelvis cancers.

SOURCE: Adapted from JAMA, Chow WH, Devesa SS, Warren JL, Fraumeni JF, Jr. Rising incidence of renal cell cancer in the United States. 1999;281(17):1,628–1,631, with permission from American Medical Association.

Agency for Research on Cancer (IARC). SEER data also show that among men and women under the age of 65, the incidence is higher in African Americans than in Caucasians. Again, the reasons for this are unclear and may be related to comorbid conditions such as hypertension, which is more common in African Americans, or to genetic variations that have not yet been defined. In all groups, incidence rises with age up to the ninth decade of life (Table 5). As the US population ages, further increases in the incidence of kidney cancer are expected, with a corresponding increase in the burden of disease treatment on the US healthcare system.

Further analysis of the SEER data shows an overall rising trend in the incidence of kidney cancer, but the rates vary among demographic groups. Overall, the incidence of kidney cancer rose 2.4% per year from 1975 to 1990 and 1.3% per year from 1990 to 2001 (Table 6). While kidney cancer occurs approximately twice as often in men as in women, its rate is increasing in women as well (Tables 4 and 5). In addition, incidence is rising more quickly in African Americans than in Caucasians and most rapidly in African American women (Figures 2 and 3). When age and race are considered together, African American men under the age of 60 have the most rapid rise in incidence of RCC (Table 7).

SEER data provide limited information about other demographic groups. From 1997 to 2001, Asian/Pacific Islanders had a lower incidence of kidney cancer than did Caucasians and African Americans, but a rising rate of diagnosis was seen from 1992 to 2001 and is prominent in females. In Native Americans/Alaska Natives, the incidence approaches that of Caucasians, but the rate of cases is not increasing. The incidence of kidney cancer in Hispanics is similar to that in the Caucasian population, but over time, an increasing trend has been seen, particularly in females (Table 8).

Table 9. Prevalence[a] of kidney cancer on Jan 1, 2001

Total	210,994
Males	124,353
Females	86,641
White	185,924
Males	109,937
Females	75,987
Black	21,837
Males	11,106
Females	10,731

In this table, approximately 12% are renal pelvis cancers.

[a]US 2001 cancer prevalence counts are based on 2001 cancer prevalence proportions from the SEER registries and 1/1/2001 US population estimatesbased on the average of 2000 and 2001 population estimates from the US Bureau of the Census.

SOURCE: Ries, LAG., Eisner, MP, Kosary, CL, Hankey, BF, Miller, BA, Clegg, L, Mariotto, A, Feuer, EJ, Edwards, BK. SEER Cancer Statistics Review, 1975–2001, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2001/2004.

Table 10. VA users with a diagnosis of kidney cancer, 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	5,041	147	5,570	152	6,002	154	6,912	162	7,903	169	9,250	186
Age-adjusted Total	6,028	155	6,057	156	6,002	154	6,078	156	6,195	159	6,713	173
Age												
< 25	0	0	3	7	2	5	0	0	1	3	1	3
25–34	20	10	19	9	18	9	22	11	19	9	21	11
35–44	118	29	128	31	134	32	135	33	150	36	150	36
45–54	777	91	848	99	854	100	918	107	918	107	1,021	119
55–64	1,248	196	1,232	193	1,245	195	1,236	194	1,265	198	1,349	211
65–74	2,223	228	2,256	232	2,140	220	2,182	224	2,182	224	2,409	247
75–84	1,537	219	1,456	207	1,495	213	1,479	211	1,555	222	1,648	235
85+	105	164	115	180	114	179	105	165	104	163	114	178
Gender												
Male	4,985	152	5,496	157	5,926	160	6,820	167	7,785	174	9,120	192
Female	56	37	74	45	76	43	92	49	118	59	130	61
Race/ethnicity												
White	3,843	176	4,267	180	4,605	178	5,389	187	6,113	195	6,788	213
Black	806	162	928	183	1,004	196	994	192	1,057	204	1,167	231
Hispanic	149	160	149	154	149	150	176	170	201	188	226	216
Other	52	118	75	163	66	137	73	145	93	180	99	196
Unknown	191	31	151	23	178	28	280	39	439	51	970	86
Insurance Status												
No insurance/ self-pay	3,258	129	3,520	133	3,504	135	3,675	141	3,974	149	4,268	160
Medicare	578	221	885	221	1,432	215	2,194	217	2,794	219	3,709	243
Medicaid	3	130	3	103	5	122	9	136	20	216	23	226
Private Insurance/ HMO	1,184	183	1,129	187	1,023	172	982	158	1,067	157	1,194	163
Other Insurance	18	148	33	174	38	148	47	159	44	131	52	131
Unknown	0	0	0	0	0	0	5	253	4	136	4	222
Region												
Eastern	679	137	777	146	825	143	1,104	157	1,328	165	1,497	181
Central	952	158	1,038	159	1,020	151	1,185	157	1,479	159	1,915	176
Southern	2,078	158	2,221	158	2,543	167	2,949	173	3,345	176	4,012	197
Western	1,332	130	1,534	142	1,614	145	1,674	151	1,751	167	1,826	180

[a]Rates are per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 11. Mortality rates[a] for kidney cancer, age-adjusted, by race/ethnicity and gender

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
Year of diagnosis									
1975	3.6	5.2	2.4	3.7	5.3	2.5	2.8	4.1	1.8
1976	3.6	5.2	2.4	3.7	5.4	2.5	2.9	4.2	1.9
1977	3.7	5.4	2.4	3.8	5.5	2.5	2.9	4.0	2.0
1978	3.7	5.4	2.4	3.8	5.5	2.5	3.2	4.8	1.9
1979	3.6	5.3	2.4	3.7	5.5	2.4	2.9	4.2	2.0
1980	3.7	5.5	2.4	3.8	5.6	2.4	3.0	4.2	2.0
1981	3.7	5.4	2.5	3.8	5.5	2.6	3.2	4.6	2.1
1982	3.9	5.7	2.5	3.9	5.8	2.6	3.4	4.8	2.4
1983	3.8	5.6	2.6	3.9	5.7	2.7	3.3	4.8	2.1
1984	3.9	5.8	2.6	4.0	5.9	2.6	3.5	4.9	2.4
1985	4.0	5.8	2.7	4.0	5.8	2.7	3.8	6.0	2.4
1986	4.0	5.8	2.8	4.1	5.9	2.8	3.7	5.3	2.5
1987	4.1	6.0	2.8	4.2	6.1	2.8	3.7	5.5	2.4
1988	4.0	5.9	2.7	4.1	5.9	2.8	3.8	5.8	2.4
1989	4.2	6.1	2.8	4.2	6.2	2.8	4.0	6.1	2.6
1990	4.2	6.2	2.8	4.2	6.2	2.8	4.2	6.4	2.8
1991	4.3	6.2	2.9	4.3	6.2	3.0	4.3	6.4	3.0
1992	4.3	6.2	2.9	4.4	6.3	2.9	4.0	5.9	2.6
1993	4.2	6.1	2.8	4.2	6.2	2.8	4.1	3.1	2.7
1994	4.3	6.2	2.9	4.3	6.3	2.9	4.2	6.4	2.8
1995	4.3	6.2	3.0	4.4	6.3	3.0	4.4	6.3	3.1
1996	4.3	6.2	2.8	4.3	6.3	2.9	4.1	5.9	2.9
1997	4.3	6.2	2.9	4.3	6.2	2.9	4.3	6.5	2.8
1998	4.3	6.2	2.8	4.3	6.3	2.9	4.0	6.3	2.5
1999	4.1	5.9	2.7	4.1	6.0	2.7	4.2	6.1	2.8
2000	4.2	6.1	2.8	4.3	6.2	2.8	4.1	6.3	2.7
2001	4.3	6.2	2.8	4.3	6.3	2.8	4.3	6.4	2.8
Age at Diagnosis									
All Ages	4.2	6.1	2.8	4.3	6.2	2.8	4.2	6.3	2.7
< 65	1.6	2.3	1.0	1.6	2.3	1.0	1.8	2.7	1.1
> 65	22.1	32.5	15.3	22.5	33.0	15.6	20.7	31.7	14.2
All Ages	2.6	3.8	1.7	2.7	3.8	1.7	2.7	4.1	1.7

In this table, approximately 12% are renal pelvis cancers.

[a]SEER 9 areas. Rates are per 100,000 and are age-adjusted to the International Agency for Research on Cancer (IARC) world standard population.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

A weakness of the SEER dataset is its inclusion of cancer of the renal pelvis in the kidney cancer data. Cancer of the renal pelvis is usually transitional cell carcinoma (TCC), a distinctly different biologic entity than RCC. Transitional cell carcinomas are strongly associated with smoking and are discussed in the bladder and upper tract urothelial cancer chapter in this compendium. The impact of this data contamination is small, however, because of the low incidence of renal pelvis cancers and because renal pelvic tumor incidence has been relatively stable compared with incidence of RCC. In the analyses presented here, approximately 12% of kidney cancers are transitional cell carcinomas, histologically.

Prevalence

According to SEER data, as of January 1, 2001, 210,994 living individuals had ever been diagnosed with kidney cancer. As expected in this dataset, which reflects the racial proportions of the US population,

Table 12. Survival rates for kidney cancer, by race/ethnicity and gender, diagnosis year, and stage

	All			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
5-Yr Survival Rates									
Year of Diagnosis									
1960–1963[a]	…	…	…	37.0	36.0	39.0	38.0	38.0	37.0
1970–1973[a]	…	…	…	46.0	44.0	50.0	44.0	40.0	49.0
1974–1976[b]	51.6	51.0	52.6	51.7	50.9	52.9	49.2	50.2	47.4[d]
1977–1979[b]	51.0	51.2	50.8	51.0	51.5	50.2	51.8	44.7	60.9[d]
1980–1982[b]	51.7	52.1	51.1	51.1	51.9	49.8	56.3	53.8	60.2[d]
1982–1985[b]	55.7	56.5	54.3	55.8	56.8	54.2	55.0	54.1	56.4
1986–1988[b]	57.0	57.4	56.3	57.6	58.2	56.8	53.6	52.2	55.5
1988–1991[b]	60.1	60.7	59.2	60.8	61.9	59.2	58.1	55.1	62.3
1992–1994[b]	62.5	62.1	63.0	63.1	62.9	63.4	60.0	58.3	62.3
1995–2000[b]	63.9[c]	63.9[c]	63.9[c]	63.9[c]	64.1[c]	63.6[c]	63.5[c]	63.5[c]	63.5[c]
1995–2000[b]									
All Stages	63.9	63.9	63.9	63.9	64.1	63.6	63.5	63.5	63.5
Localized	91.1	91.4	90.6	91.7	91.7	91.8	87.7	89.7	85.5
Regional	59.1	60.7	56.4	58.9	60.8	55.8	58.7	61.9[d]	54.3[d]
Distant	9.3	9.3	9.2	3.1	9.2	8.7	9.2	8.4	9.9
Unstaged	32.7	35.0	30.1	33.3	38.3	26.9	21.2[d]	12.8[d]	33.6[e]

…data not available.

In this table, approximately 12% are renal pelvis cancers.

[a]Rates are based on End Results data from a series of hospital registries and one population-based registry.

[b]Rates are from the SEER 9 areas. The are based on data from population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland.

[c]The difference in rates between 1974–1976 and 1995–2000 is statistically significant ($p < 0.05$).

[d]The standard error of the survival rate is between 5 and 10 percentage points.

[e]The standard error of the survival rate is greater than 10 percentage points.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

the majority of the cases were seen in Caucasians (Table 9). Veterans Affairs (VA) data showed 186 cases of RCC per 100,000 VA patients in 2003 (Table 10). The prevalence of kidney cancer is likely to increase significantly over the next several years, partly because more low-stage disease is being detected, and therefore more patients are being cured and are living with the diagnosis of kidney cancer. Another reason, related to the incidence data, is the aging of the US population, which will lead to more diagnoses of kidney cancer with resultant increases in utilization of the healthcare system.

When considering the epidemiologic data, it is important to recognize the difference between mortality, the deaths in the general population due to the specific disease, and survival, which is limited to the patient cohort with the disease. The death rate from kidney cancer has been increasing slowly over the past 30 years, likely due to the increase in the incidence of the disease. In 2001, the overall death rate from kidney cancer was 4.3 per 100,000, compared with 3.6 per 100,000 in 1975 (Table 11). However, five- and ten-year survival rates have steadily increased over the past 25 years (Table 12), suggesting either that treatment is more effective or, more likely, that imaging has led to earlier diagnosis of kidney cancer, where surgical treatment is highly successful. SEER data indicate that advanced and metastatic cases have decreased, and this may account for the improvement seen in survival. However, the increase in mortality rates may be the result of the absolute increase in numbers of cases across all stages. SEER data indicate that most of the increase in incidence reflects the discovery of small, localized tumors (Figure 1). Five-

Table 13. Median survival rates from kidney cancer

	Patients (n)	Median Survival (months)	P-value
Sex			
Male	15,725	51	0
Female	9,268	55	
Stage			
Localized	11,679	142	0
Distant	13,314	13	
Age (yr)			
20–59	9,110	117	0
60+	15,883	36	
Race			
Black	2,024	47	0.03
White	22,969	53	
Localized stage			
Age 20–59			
Black	552	190	< 0.0001
White	4,251	259	
Age 60+			
Black	493	81	< 0.0001
White	6,383	101	
Advanced stage			
Black	450	11	< 0.0001
White	3,857	19	
Age 60+			
Black	529	6	< 0.0001
White	8,478	11	

In this table, approximately 12% are renal pelvis cancers.

SOURCE: Reprinted from Urology, 62, Vaishampayan UN, Do H, Hussain M, Schwartz K, Racial disparity in incidence patterns and outcome of kidney cancer, 1,012–1,017, Copyright 2003, with permission from Elsevier.

year survival increased from approximately 50% in 1980 to approximately 64% in 2000 (Table 12). For patients with localized disease, the five-year survival rate was approximately 90% in 1995–2000. Over the same period, the five-year survival rate for patients with regional disease was approximately 60%, and for those with metastatic disease, it was approximately 9%. Overall, survival rates improved slightly between 1992 and 2001. It appears that increasing survival rates over the past three decades reflect increasing diagnosis of curable tumors, as well as improved survival in Caucasians, who constitute most of the population in the dataset. After remaining flat in the mid 1990s (24) survival in African Americans began to increase at the end of the decade (Table 12).

The SEER incidence data also indicate racial disparity in overall survival. While mortality increased significantly from 1975 to 1990 in both African Americans and Caucasians, the mortality rate of African American men and women increased at more than twice the mortality rate of Caucasians (Table 11). When stratified by age and stage, the median survival for African Americans under 60 years of age with localized disease was 190 months, compared with 259 months for Caucasians in the same age range (Table 13). This difference, nearly six years, may be due to different biologic behavior of the disease between races, or it may be due to comorbid conditions that are more common in African Americans (13). Median survival also is significantly lower for African Americans over age 60 than for similarly aged Caucasians. A similar racial disparity is seen in advanced disease, with median survival of Caucasians being nearly double that of African Americans (Table 13). The survival difference between racial groups with metastatic disease again suggests different biological behavior, because treatments for metastatic disease (such as immunotherapy and chemotherapy) improve survival minimally, and therefore access to advanced medical care probably is not a factor. Again, the greater prevalence of comorbidities in African Americans (12) may play a role (Figure 4). While overall survival from kidney cancer has improved slightly across all racial groups, SEER data showed a modest decrease in survival in African American men and Asian/Pacific Islanders from 1992 to 2001. Because SEER data for RCC indicate overall rather than disease-specific survival, it is difficult to make conclusions about the biology of RCC in different racial groups. Overall survival renders these data susceptible to issues of racial disparities in comorbidities and access to healthcare.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Most adult inpatient hospitalizations for kidney cancer are for surgery. Regardless of the technique used, surgery for kidney cancer always requires hospitalization for at least 24 hours. A small number of admissions are for complications from surgery, biopsy, embolization, immunotherapy, and chemotherapy; and supportive care in the late stages of disease for pain management, blood transfusions, and hydration.

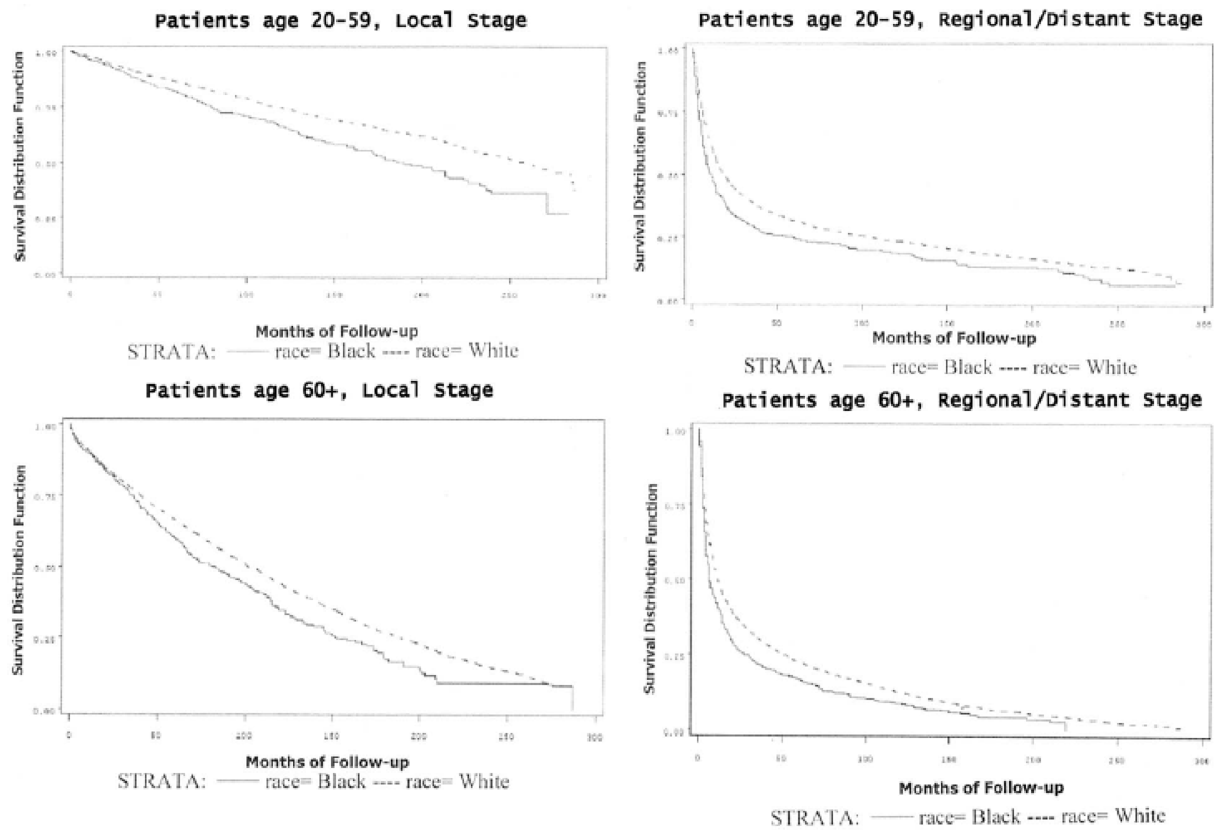

Figure 4. Survival rates from kidney cancer, by race.

SOURCE: Reprinted from Urology, 62, Vaishampayan UN, Do H, Hussain M, Schwartz K, Racial disparity in incidence patterns and outcome of kidney cancer, 1,012–1,017, Copyright 2003, with permission from Elsevier.

Three datasets were used for this analysis of inpatient hospitalizations: Medicare data from Centers for Medicare and Medicaid Services (CMS), the Healthcare Cost and Utilization Project (HCUP), and the National Association of Children's Hospitals and Related Institutions (NACHRI). NACHRI data differ significantly from CMS and HCUP data, because most pediatric kidney cancers are Wilms' tumors, which are frequently treated with inpatient chemotherapy.

CMS data from 1992, 1995, 1998, and 2001 show relatively stable numbers of inpatient hospitalizations for kidney cancer among Medicare beneficiaries, as might be expected from the SEER incidence data (Table 14). As of 2001, the age-adjusted rate of hospitalization for kidney cancer as the primary diagnosis was 25 per 100,000 Medicare beneficiaries. The rate for males was 33 per 100,000, and the rate for females was 18 per 100,000, reflecting the gender distribution of kidney cancer. Admission rates for Medicare beneficiaries were consistently higher in patients over 65 years of age and were highest for patients 65–69 and 75–79. The only age group in which a significant increase was seen over this time period was the 85- to 89-year-olds. This interesting finding raises the question of whether there is truly a higher incidence of RCC in patients aged 85–89, whether there are more healthy octogenarians needing treatment, or whether patients in this age group are being treated too aggressively.

The vast majority of patients in the databases are Caucasian. The numbers of admissions for Asian, Hispanic, and North American Natives are too small to interpret. The Northeast had the highest number of

Table 14. Inpatient stays by Medicare beneficiaries with kidney cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	8,500	24 (22–27)	24	8,520	24 (22–26)	24	8,040	24 (22–26)	24	8,680	25 (22–27)	25
Total < 65	660	12 (7.9–16)		580	9.5 (6.0–13)		660	11 (7.0–14)		660	9.4 (6.2–12)	
Total 65+	7,840	27 (24–29)		7,940	27 (24–30)		7,380	27 (24–30)		8,020	28 (26–31)	
Age												
65–69	2,600	29 (24–34)		2,060	24 (20–29)		1,840	25 (20–30)		2,400	32 (26–38)	
70–74	1,900	25 (20–30)		2,460	32 (26–37)		1,860	27 (21–32)		1,900	27 (22–33)	
75–79	1,920	33 (27–40)		1,920	34 (27–40)		1,800	32 (25–38)		1,900	32 (25–38)	
80–84	1,160	31 (23–38)		1,040	26 (19–33)		1,200	31 (23–39)		1,240	31 (23–38)	
85–89	160	7.8 (2.4–13)		340	16 (8.2–23)		480	22 (13–31)		480	21 (12–29)	
90–94	80	9.6 (0.2–19)		80	8.9 (0.2–18)		200	22 (8.4–36)		60	6.3 (0–13)	
95–97	20	11 (0–31)		20	11 (0–31)		0	0		40	20 (0–49)	
98+	0	0		20	11 (0–34)		0	0		0	0	
Race/ethnicity												
White	7,240	25 (22–27)	25	7,660	25 (23–28)	25	6,880	24 (22–27)	24	7,740	26 (23–28)	26
Black	680	23 (15–31)	22	560	17 (11–24)	19	720	23 (16–31)	22	620	18 (12–25)	18
Asian	…	…	…	20	12 (0–35)	0	20	6.4 (0–19)	6.4	20	4.2 (0–12)	4.2
Hispanic	…	…	…	100	25 (3.0–47)	20	160	23 (7.0–38)	23	20	2.5 (0–7.4)	2.5
N. American Native	…	…	…	0	0	0	0	0	0	20	30 (0–88)	30
Gender												
Male	5,160	35 (30–39)	35	4,980	33 (29–37)	33	5,020	35 (30–39)	36	4,980	32 (28–36)	33
Female	3,340	17 (14–19)	17	3,540	18 (15–20)	17	3,020	16 (13–18)	15	3,700	19 (16–21)	18
Region												
Midwest	1,900	22 (17–26)	22	1,860	21 (16–25)	21	2,040	24 (19–28)	24	2,280	26 (21–31)	26
Northeast	2,280	30 (24–35)	29	1,920	25 (20–30)	25	1,640	24 (19–30)	24	1,940	28 (22–34)	27
South	3,200	26 (22–30)	26	3,840	30 (26–34)	30	3,000	24 (20–28)	24	3,340	25 (21–29)	26
West	1,100	20 (15–25)	19	840	16 (11–21)	15	1,320	27 (20–33)	27	1,040	19 (14–24)	18

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 15. Inpatient hospital stays for kidney cancer listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	23,006	19 (18–20)	19	24,528	19 (18–20)	19	26,069	20 (18–21)	20	30,045	22 (21–23)	22
Age												
35–44	1,445	3.6 (3.1–4.1)		1,630	3.8 (3.3–4.3)		1,823	4.1 (3.5–4.7)		1,986	4.5 (3.9–5.0)	
45–54	3,287	11 (10–13)		3,675	12 (10–13)		4,405	13 (12–14)		5,474	15 (14–16)	
55–64	5,243	26 (24–28)		5,832	28 (26–30)		6,114	28 (25–30)		7,187	31 (28–33)	
65–74	7,368	41 (39–44)		7,342	40 (37–43)		7,724	43 (40–46)		8,428	47 (44–51)	
75–84	4,675	48 (44–52)		5,054	48 (44–51)		5,011	44 (41–48)		5,732	49 (45–53)	
85+	989	36 (29–42)		995	36 (30–41)		991	34 (29–40)		1,239	40 (34–45)	
Race/ethnicity												
White	15,423	16 (15–17)	16	16,356	16 (15–17)	16	16,713	16 (15–18)	16	18,536	18 (17–19)	17
Black	1,561	13 (11–15)	14	1,657	13 (11–14)	14	1,817	13 (11–15)	15	2,002	14 (12–16)	15
Hispanic	710	8.6 (7.0–10)	11	893	9.6 (7.6–11)	12	1,142	11 (8.9–13)	14	1,418	12 (11–14)	15
Gender												
Male	13,872	25 (23–26)	26	14,828	25 (23–26)	26	15,587	25 (23–27)	26	18,217	28 (26–30)	29
Female	9,134	14 (14–15)	14	9,700	14 (13–15)	14	10,483	15 (14–16)	14	11,818	16 (15–17)	16
Region												
Midwest	5,885	21 (19–23)	21	6,277	21 (18–23)	21	6,260	20 (18–22)	20	7,469	24 (21–27)	24
Northeast	5,206	20 (18–23)	20	5,709	22 (19–25)	22	6,256	24 (18–29)	23	6,627	24 (21–28)	24
South	8,273	20 (19–22)	20	8,727	20 (18–21)	19	9,550	20 (19–22)	20	10,758	22 (20–24)	22
West	3,643	14 (13–16)	15	3,814	14 (13–16)	15	4,004	14 (12–16)	15	5,191	18 (15–20)	18
MSA												
Rural	3,318	10 (8.9–12)	9.7	3,048	10 (8.9–11)	9.6	2,807	9.0 (7.6–10)	8.6	3,042	9.6 (8.4–11)	9.0
Urban	19,648	22 (21–24)	23	21,451	22 (21–23)	22	23,170	23 (21–24)	23	26,954	26 (24–27)	26

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population, 35 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 16.Trends in mean inpatient length of stay (LOS) in days and cost per child admitted with malignant neoplasm of kidney[a] listed as primary or any diagnosis, 1999–2003

	Count	Percent	LOS	Mean Cost
Primary diagnosis				
Total	2,011		8.5	$22,890
Age				
0–2	802	40%	8.2	$21,112
3–10	1,070	53%	8.5	$22,986
11–17	120	6%	9.5	$29,888
18+	19	1%	13.6	$48,338
Race/ethnicity				
White	1,240	62%	8.2	$22,106
Black	330	16%	8.4	$23,167
Asian	17	1%	10.2	$22,697
Hispanic	206	10%	10.5	$28,092
N. American Native	13	1%	15.1	$38,981
Missing	82	4%	6.8	$15,951
Other	123	6%	9.0	$24,294
Gender				
Female	1,059	53%	8.3	$22,460
Male	952	47%	8.7	$23,369
Region				
Midwest	618	31%	8.5	$23,064
Northeast	234	12%	7.7	$20,145
South	795	40%	8.5	$23,579
West	364	18%	9.2	$22,853
Any diagnosis				
Total	6,289		5.8	$14,186
Age				
0–2	2,085	33%	5.8	$13,298
3–10	3,591	57%	5.6	$13,456
11–17	530	8%	6.4	$21,068
18+	83	1%	8.6	$24,126
Race/ethnicity				
White	3,848	61%	5.6	$13,675
Black	1,116	18%	5.9	$14,700
Asian	33	1%	6.9	$15,100
Hispanic	789	13%	6.5	$16,230
N. American Native	21	0%	11.6	$28,059
Missing	188	3%	5.4	$11,239
Other	294	5%	6.1	$14,236
Gender				
Female	3,215	51%	5.8	$14,352
Male	3,074	49%	5.8	$14,013
Region				
Midwest	1,696	27%	5.9	$14,522
Northeast	679	11%	5.5	$12,723
South	2,826	45%	5.4	$13,628
West	1,088	17%	6.7	$15,981

[a]Using ICD-9 codes 189.0 (malignant neoplasm of kidney, except pelvis) and 189.8 (malignant neoplasm of other specified sites of urinary organs).

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2003.

admissions, but the age-adjusted rates of admission did not vary significantly between regions over the years examined.

HCUP data from 1994, 1996, 1998, and 2000 indicate that admissions for kidney cancer as the primary diagnosis increased slightly, from 19 per 100,000 in 1994 to 22 per 100,000 in 2000 (Table 15). The highest rate of admissions was in the 75–84 age group. As in the CMS dataset, the gender distribution of kidney cancer is reflected in the HCUP data, with stable rates of admission for men that are nearly double the rates for women. The rate of admission of Caucasians and African Americans was stable, but admissions of Hispanics saw a 1.5-fold increase. It must be noted that these numbers are small and should be viewed with caution. Rates of admission did not change in different geographic regions, but the West had significantly lower rates of admission than did the Northeast, South, and Midwest. Admissions in urban areas were much more common than in non-urban areas, and they increased significantly between 1994 and 2000. While this may indicate a trend in patient migration, it more likely reflects better access to screening and treatment and more resources in urban areas.

The primary kidney cancers in children are Wilms' tumors and neuroblastomas, which are treated with multimodality therapy. Admissions for pediatric kidney cancer may be for many reasons other than surgery, including biopsy for diagnosis and staging, surgery for port placement for chemotherapy, chemotherapy treatments, complications of chemotherapy treatments, and radiation. Pooled NACHRI data from 1999–2003 (Table 16) show a total of 2,011 admissions for kidney cancer as the primary diagnosis, with an average inpatient length of stay of 8.5 days. When the database was queried for kidney cancer as any diagnosis, 6,289 admissions were captured, with an average length of stay of 5.8 days. The majority of children affected were between three and ten years of age, and length of stay increased with increasing age. Admissions for males and females were nearly equal. Over 60% of the admitted patients were Caucasian; nearly 20% were African American; and 10% were Hispanic. The majority of admissions occurred in the South and Midwest.

Outpatient Care

Outpatient care for patients with kidney cancer includes initial visits for symptoms such as flank or abdominal pain or hematuria, subsequent evaluation (which includes radiologic evaluation of the kidneys and ureters and cystoscopic evaluation of the bladder), discussion of the diagnosis, staging, and follow-up after surgery (called *surveillance*).

Physician Office Visits

In the Medicare data, the rate of total physician office visits for kidney cancer as the primary diagnosis increased 29% from 1992 to 2001 (Table 17). Visits for patients under 65 years of age remained stable over this period but peaked in 1995, while visits for patients over 65 increased 35%. This reflects the increased incidence of kidney cancer in the more commonly affected age group. Physician office visit rates varied within regions, but the highest rates were seen in the Northeast in 1998 and 2001. Regional differences in utilization of outpatient resources are difficult to explain because regional incidence data are not available. The disparities may result from differences in practice patterns for the outpatient care delivered for patients with RCC. Visit rates increased significantly for both men and women from 1992 to 2001, but the 2:1 preponderance of disease in men versus women was stable. The rate of visits by Caucasians increased 32% from 1992 to 2001, but rates for African Americans and Hispanics were stable. However, the number of African American and Hispanic patients is small, and the data should be interpreted with caution.

Data from the National Ambulatory Medical Care Survey (NAMCS) for even years from 1992 to 2000 were pooled because of the small numbers of kidney cancer patients and are therefore less informative than the Medicare data (Table 18). NAMCS data indicate more than 1.2 million physician office visits for kidney cancer as the primary diagnosis during these years, an average annualized rate of 195 visits per 100,000 population. The majority of these patients were over 65, Caucasian, and male, and most were seen in urban metropolitan areas. Trends in utilization, as well as age, race, and gender variation, could not be evaluated because of the small number of cases.

Table 17. Physician office visits by Medicare beneficiaries with kidney cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995				1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	89,280	256	(248–263)	256	106,120	300	(292–308)	300	102,540	306	(297–314)	306	115,940	329	(320–337)	329
Total < 65	8,760	158	(143–173)		11,740	191	(176–207)		6,540	105	(94–117)		11,200	159	(146–172)	
Total 65+	80,520	274	(266–283)		94,380	322	(313–332)		96,000	351	(341–361)		104,740	371	(361–381)	
Age																
65–69	26,760	297	(281–313)		33,260	393	(374–412)		25,320	346	(327–365)		26,040	346	(327–365)	
70–74	27,720	36	(346–384)		26,540	343	(325–362)		30,240	432	(410–454)		27,140	390	(369–411)	
75–79	15,960	278	(259–297)		22,460	394	(371–417)		22,540	398	(375–421)		26,260	439	(416–463)	
80–84	7,260	191	(172–211)		9,100	230	(209–252)		13,320	347	(320–373)		16,820	414	(386–442)	
85–89	2,200	107	(87–127)		2,440	112	(92–132)		4,060	186	(160–211)		7,360	316	(284–348)	
90–94	600	72	(46–98)		520	58	(36–80)		520	57	(35–79)		980	103	(74–131)	
95–97	20	11	(0–31)		20	11	(0–31)		0	0			140	72	(18–125)	
98+	0	0			40	23	(0–54)		0	0			0	0		
Race/ethnicity																
White	78,580	266	(258–274)	265	93,300	307	(299–316)	306	91,260	321	(312–331)	323	104,580	349	(340–359)	349
Black	5,620	190	(167–212)	188	8,240	256	(231–280)	276	6,300	203	(181–226)	188	5,880	172	(153–192)	171
Asian	…	...		…	140	84	(22–146)	48	260	83	(38–128)	89	620	131	(85–176)	131
Hispanic	…	...		…	3,000	751	(631–871)	731	2,560	364	(301–427)	350	1,580	199	(155–243)	159
N. American Native	…	...		…	60	165	(0–353)	165	20	37	(0–109)	37	180	270	(94–445)	270
Gender																
Male	56,780	381	(367–395)	389	60,320	396	(382–410)	401	67,200	464	(448–480)	469	74,140	481	(465–496)	476
Female	32,500	162	(154–170)	157	45,800	227	(218–236)	224	35,340	185	(177–194)	181	41,800	211	(202–220)	214
Region																
Midwest	22,600	259	(244–274)	265	31,700	352	(335–369)	360	22,880	265	(250–280)	269	28,020	319	(302–335)	332
Northeast	18,920	246	(230–261)	246	22,140	289	(272–305)	281	24,380	364	(344–384)	358	27,720	401	(380–422)	374
South	33,240	272	(259–285)	271	36,540	287	(274–301)	283	42,340	342	(327–356)	344	45,760	345	(331–359)	357
West	10,260	187	(171–204)	182	12,520	242	(223–261)	249	12,380	250	(230–270)	247	14,020	260	(240–279)	245

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 18. Physician office visits for kidney cancer listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000				
	Count	5- Year Rate		Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	1,236,274	974	(600–1,349)	195	971
Age					
35–64	*	*		*	
65+	670,913	2,134	(1,125–3,143)	427	
Race/ethnicity					
White	922,937	924	(543–1,305)	185	893
Other	*	*		*	*
Gender					
Male	741,161	1,242	(607–1,878)	248	1,293
Female	*	*		*	*
MSA					
MSA	1,028,012	1,078	(638–1,512)	215	1,063
Non-MSA	*	*		*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population, 35 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[c]Average annualized rate per year.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Hospital Outpatient Care

Medicare data from 1992, 1995, 1998, and 2001 showed a significant increase in hospital outpatient visits for kidney cancer as the primary diagnosis from 1992 to 1995; this increase was sustained in 1998 but was followed by a decrease in 2001 (Table 19). As was seen in the Medicare data on physician office visits, the rate of hospital outpatient visits was stable for patients under 65 (a decrease was seen in 2001), while a significant increase was seen in those over 65. However, fewer patients were seen in this setting than in physicians' offices. Again, approximately twice as many visits were made by men than by women. The 75- to 79-year age group had the highest rate of hospital outpatient visits in 1992 and 1995, and the 65- to 69-year age group had the highest rate in 1998 and 2001. The Midwest had high rates of outpatient visits from 1992 to 1998, and in 1995, these rates were three times the rates in other regions. A significant increase in visits occurred in the Northeast from 1992 to 2001.

Ambulatory Surgery

Ambulatory surgery visits for kidney cancer are uncommon, as most surgical interventions require inpatient hospitalization (Tables 20 and 21). Medicare data from 1992, 1995, 1998, and 2001 showed a slight increase in the use of the ambulatory setting, to 4.9 per 100,000 Medicare beneficiaries in 2001 (Table 20). But because the counts are low, meaningful information cannot be gleaned from the data. Similarly, the pooled data from the National Survey of Ambulatory Surgery from 1994 to 1996 do not allow for meaningful interpretation (Table 21). The available data indicate that the ambulatory surgery setting is not an important contributor to the utilization of medical services for kidney cancer.

Emergency Room Care

Emergency room visits for a primary diagnosis of kidney cancer are rare, according to Medicare data (Table 22). Such visits may occur for acute events such as bleeding or surgical complications or for chronic problems such as failure to thrive, but the datasets

Table 19. Hospital outpatient visits by Medicare beneficiaries with kidney cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	11,540	33 (30–36)	33	15,020	42 (39–45)	42	14,100	42 (39–45)	42	13,380	38 (35–41)	38
Total < 65	1,620	29 (23–36)		1,240	20 (15–25)		1,820	29 (23–35)		1,200	17 (13–21)	
Total 65+	9,920	34 (31–37)		13,780	47 (44–51)		12,280	45 (41–49)		12,180	43 (40–47)	
Age												
65–69	3,980	44 (38–50)		4,540	54 (47–61)		4,220	58 (50–65)		4,100	54 (47–62)	
70–74	2,260	30 (24–35)		2,620	34 (28–40)		3,640	52 (44–60)		3,580	51 (44–59)	
75–79	2,700	47 (39–55)		4,980	87 (77–98)		2,180	39 (31–46)		2,640	44 (37–52)	
80–84	420	11 (6.3–16)		1,240	31 (24–39)		1,640	43 (33–52)		1,080	27 (19–34)	
85–89	540	26 (16–36)		300	14 (6.8–21)		560	26 (16–35)		520	22 (14–31)	
90–94	0	0		80	8.9 (0.2–18)		20	2.2 (0–6.5)		240	25 (11–39)	
95–97	0	0		20	11 (0–31)		20	9.9 (0–29)		20	10 (0–30)	
98+	20	13 (0–39)		0	0		0	0		0	0	
Race/ethnicity												
White	9,780	33 (30–36)	33	12,920	43 (39–46)	42	11,340	40 (37–43)	40	10,600	35 (32–38)	35
Black	1,300	44 (33–55)	46	1,700	53 (42–64)	53	1,500	48 (37–59)	47	840	25 (17–32)	24
Asian	…	...	…	0	0	0	140	45 (11–78)	38	220	46 (19–74)	34
Hispanic	…	...	…	200	50 (19–81)	45	260	37 (17–57)	37	140	18 (4.5–31)	15
N. American Native	…	...	…	0	0	0	140	259 (67–452)	222	160	240 (73–406)	210
Gender												
Male	8,520	57 (52–63)	59	9,780	64 (59–70)	62	8,040	56 (50–61)	54	8,660	56 (51–61)	56
Female	3,020	15 (13–17)	14	5,240	26 (23–29)	28	6,060	32 (28–35)	33	4,720	24 (21–27)	24
Region												
Midwest	3,940	45 (39–51)	43	8,220	91 (82–100)	89	5,380	62 (55–70)	61	3,920	45 (38–51)	44
Northeast	2,580	33 (28–39)	29	2,240	29 (24–35)	30	2,820	42 (35–49)	44	3,680	53 (46–61)	52
South	3,760	31 (26–35)	35	2,640	21 (17–24)	21	3,420	28 (23–32)	28	3,240	24 (21–28)	26
West	1,260	23 (17–29)	23	1,900	37 (29–44)	39	2,460	50 (41–58)	48	2,520	47 (39–55)	45

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 20. Ambulatory surgery visits by Medicare beneficiaries with kidney cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995				1998				2001			
	Count	Rate	(95% CI)	Age-Adjusted Rate	Count	Rate	(95% CI)	Age-Adjusted Rate	Count	Rate	(95% CI)	Age-Adjusted Rate	Count	Rate	(95% CI)	Age-Adjusted Rate
Total[d]	1,060	3.0	(2.2–3.9)	3.0	1,100	3.1	(2.3–3.9)	3.1	1,420	4.2	(3.3–5.2)	4.2	1,720	4.9	(3.8–5.9)	4.9
Total < 65	20	0.4	(0–1.1)		120	2.0	(0.4–3.5)		140	2.3	(0.6–3.9)		120	1.7	(0.3–3.1)	
Total 65+	1,040	3.5	(2.6–4.5)		980	3.3	(2.4–4.3)		1,280	2.4	(3.5–5.8)		1,600	5.7	(4.4–6.9)	
Age																
65–69	320	3.5	(1.8–5.3)		240	2.8	(1.2–4.4)		360	4.9	(2.6–7.2)		340	4.5	(2.4–6.7)	
70–74	480	6.3	(3.8–8.9)		380	4.9	(2.7–7.1)		420	6.0	(3.4–8.6)		340	4.9	(2.6–7.2)	
75–79	140	2.4	(0.6–4.3)		240	4.2	(1.8–6.6)		280	4.9	(2.3–7.5)		680	11	(7.5–15.2)	
80–84	100	2.3	(0.3–5.0)		60	1.5	(0–3.2)		140	3.6	(0.9–6.3)		220	5.4	(2.2–8.6)	
85+	0	0			60	2.8	(0–5.9)		60	2.7	(0–5.9)		20	0.9	(0–2.5)	
Race/ethnicity																
White	900	3.0	(2.2–3.9)	2.9	1,060	3.5	(2.6–4.4)	3.5	1,300	4.6	(3.5–5.7)	4.6	1,600	5.3	(4.2–6.5)	5.3
Black	20	0.7	(0–2.0)	0.7	0	0		0	40	1.3	(0–3.1)	1.3	120	3.5	(0.7–6.3)	3.5
Asian	…	...		…	0	0		0	0	0		0	0	0		0
Hispanic	…	...		…	20	5.0	(0–15)	5.0	0	0		0	0	0		0
N. American Native	…	...		…	0	0		0	0	0		0	0	0		0
Gender																
Male	600	4.0	(2.6–5.5)	4.0	700	4.6	(3.1–6.1)	4.7	920	6.4	(4.5–8.2)	6.5	1,180	7.7	(5.7–9.6)	7.9
Female	460	2.3	(1.4–3.2)	2.1	400	2.0	(1.1–2.8)	1.9	500	2.6	(1.6–3.7)	2.5	540	2.7	(1.7–3.7)	2.4
Region																
Midwest	180	2.1	(0.7–3.4)	1.8	400	4.4	(2.5–6.4)	4.2	580	6.7	(4.3–9.2)	7.2	480	5.5	(3.3–7.6)	5.2
Northeast	240	3.1	(1.4–4.9)	3.1	260	3.4	(1.6–5.2)	3.4	180	2.7	(0.9–4.4)	2.1	380	5.5	(3.0–8.0)	5.5
South	500	4.1	(2.5–5.7)	4.3	360	2.8	(1.5–4.1)	2.8	500	4.0	(2.5–5.6)	4.0	760	5.7	(3.9–7.6)	5.7
West	100	1.8	(0.2–3.4)	1.8	80	1.5	(0–3.0)	1.9	140	2.8	(0.7–4.9)	2.0	80	1.5	(0–2.9)	1.5

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 21. Ambulatory surgery visits for kidney cancer listed as any diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), age-adjusted rate[b]

	1994–1996		
	Count	3-Year Rate	3-Year Age-Adjusted Rate
Total	12,897	10 (5.2–16)	10

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population, 35 years and older.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

may not capture these events because the primary diagnosis may not be listed as renal cell carcinoma. Nearly all the counts of emergency room visits for kidney cancer in the Medicare dataset are below 600, which limits definitive interpretation. Regardless, utilization of the emergency room does not contribute substantially to the burden of treatment of kidney cancer in the United States.

Surgical Trends

Traditionally, the presence of a kidney tumor mandated removal of the entire kidney, but surgical techniques have evolved significantly over the past several years. Introduced more than 50 years ago, partial nephrectomy was initially not widely accepted for the treatment of kidney cancer due to concerns of leaving behind residual tumor or small satellite lesions and because of the technical difficulty of the procedure. With improvements in imaging, however, great detail is now available for the surgical planning of partial nephrectomy, including information about the depth of penetration of the tumor into the kidney and its blood supply. Studies of the oncologic efficacy of the procedure, when feasible, have shown that it is as effective as radical nephrectomy, even with a very small margin of normal kidney around the tumor (28). Currently, partial nephrectomy is indicated for tumors less than 4 cm in size, even when the uninvolved kidney is normal, despite the fact that patients can lead essentially normal lives with a solitary kidney. It is reasonable to consider partial nephrectomy to preserve as much functioning kidney as possible in patients who have the potential to develop other diseases that impair renal function later in life, such as diabetes and hypertension. The incidence of chronic renal insufficiency is somewhat higher after radical than after partial nephrectomy (29).

Despite the increasing evidence favoring partial nephrectomy for small tumors, current data do not yet reflect widespread adoption of this practice. However, there has been a small increase in utilization of partial nephrectomy (Table 23). In contrast, CMS (Table 24) data do not show a significant increase in this trend, perhaps because of the smaller number of cases captured in the CMS datasets or because of patient characteristics, advanced age and increased comorbidities, favoring radical nephrectomy in the CMS populations. As expected, the increasing use of partial nephrectomy closely parallels the increase in the rate of diagnosis of kidney cancer, since most of the new incident cases are small tumors that are amenable to partial nephrectomy. Open radical nephrectomy remains the most common surgical approach in the management of kidney cancer (Table 25); however, its use has declined significantly since 1992.

Laparoscopic surgery for kidney cancer has been increasingly adopted since initial reports on the technique in the mid 1990s (30). The major advantages of this technique over traditional open surgery are shorter hospitalization, decreased pain, and earlier return to work and normal activity. The increasing utilization of laparoscopy is difficult to assess in current datasets, because data from the recent past are not publically available yet. However, this trend is becoming apparent with the appearance of both laparoscopic radical nephrectomy and laparoscopic partial nephrectomy in the VA dataset in the early 2000s. Laparoscopic partial nephrectomy first appear in 2001 data; no cases were captured before then (Table 26). In both academic (31) and community (32) settings, laparoscopic techniques are increasingly viewed as the standard of care in the treatment of patients with kidney cancer.

Even more recently, the use of laparoscopic partial nephrectomy is increasing as urologists attempt to replicate the oncologic principles employed in traditional surgery, wherein partial nephrectomy should be performed for small tumors whenever feasible. Advances in instrumentation and materials used for control of bleeding have facilitated the

Table 22. Emergency room visits by Medicare beneficiaries with kidney cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	660	1.9 (1.2–2.5)	1.9	340	1.0 (0.5–1.4)	1.0	720	2.1 (1.4–2.8)	2.1	240	0.7 (0.3–1.1)	0.7
Total < 65	40	0.7 (0–1.7)		80	1.3 (0–2.6)		40	0.6 (0–1.5)		20	0.3 (0–0.8)	
Total 65+	620	2.1 (1.4–2.9)		260	0.9 (0.4–1.4)		680	2.5 (1.7–3.3)		220	0.8 (0.3–1.2)	
Age												
65–69	260	2.9 (1.3–4.4)		60	0.7 (0–1.5)		260	3.5 (1.6–5.5)		60	0.8 (0–1.7)	
70–74	160	2.1 (0.6–3.6)		100	1.3 (0.2–2.4)		240	3.4 (1.5–5.4)		100	1.4 (0.2–2.7)	
75–79	100	1.7 (0.2–3.3)		40	0.7 (0–1.7)		160	2.8 (0.9–4.8)		40	0.7 (0–1.6)	
80–84	60	1.6 (0–3.4)		40	1.0 (0–2.4)		20	0.5 (0–1.5)		0	0	
85+	40	1.9 (0–4.6)		20	2.2 (0–6.6)		0	0		20	0.9 (0–2.5)	
Race/ethnicity												
White	420	1.4 (0.8–2.0)	1.3	260	0.9 (0.4–1.3)	0.9	620	2.2 (1.4–3.0)	2.2	160	0.5 (0.2–0.9)	0.5
Black	220	7.4 (3.0–12)	9.4	80	2.5 (0.1–4.9)	1.9	80	2.6 (0.1–5.1)	2.6	60	1.8 (0–3.8)	1.8
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	0	0	0	20	2.8 (0–8.4)	2.8	20	2.5 (0–7.4)	0
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Gender												
Male	480	3.2 (1.9–4.5)	3.2	140	0.9 (0.2–1.6)	0.9	400	2.8 (1.6–4.0)	2.9	200	1.3 (0.5–2.1)	1.2
Female	180	0.9 (0.3–1.5)	0.8	200	1.0 (0.4–1.6)	1.0	320	1.7 (0.9–2.5)	1.6	40	0.2 (0–0.5)	0.2
Region												
Midwest	160	1.8 (0.6–3.1)	1.4	120	1.3 (0.3–2.4)	1.1	300	3.5 (1.7–5.2)	3.7	60	0.7 (0–1.5)	0.7
Northeast	120	1.6 (0.3–2.8)	1.3	80	1.0 (0–2.1)	1.0	40	0.6 (0–1.4)	0.6	40	0.6 (0–1.4)	0.6
South	140	1.1 (0.3–2.0)	1.0	60	0.5 (0–1.0)	0.5	220	1.8 (0.7–2.8)	1.8	100	0.8 (0.1–1.4)	0.6
West	240	4.4 (1.9–6.9)	5.1	80	1.5 (0–3.0)	1.5	160	3.2 (1.0–5.5)	2.8	40	0.7 (0–1.8)	0.7

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 23. Inpatient hospital stays for kidney cancer listed as primary diagnosis with partial nephrectomy performed, count, rate[a] (95% CI), rate per visits[b] (95% CI)

	1994				1996			
	Count	Rate per 100,000 population[a]	Rate per 100,000 visits for primary diagnosis of Kidney Cancer[b]		Count	Rate per 100,000 population[a]	Rate per 100,000 visits for primary diagnosis of Kidney Cancer[b]	
Total[c]	1,063	0.9 (0.8–1.0)	4,621	(4,169–5,073)	1,446	1.1 (1.0–1.2)	5,895	(5,398–6,393)
Age								
35–44	*	*	*		*	*	*	
45–54	*	*	*		199	0.6 (0.4–0.8)	811	(583–1,044)
55–64	238	1.2 (1.0–1.4)	1,035	(848–1,217)	403	1.9 (1.7–2.2)	1,643	(1,419–1,867)
65–74	406	2.3 (2.0–2.6)	1,765	(1,543–1,982)	418	2.3 (2.0–2.6)	1,704	(1,500–1,908)
75–84	215	2.2 (1.9–2.6)	935	(800–1,074)	280	2.6 (2.3–3.0)	1,142	(995–1,288)
85+	*	*	*		*	*	*	
Gender								
Male	742	1.3 (1.2–1.5)	3,225	(2,908–3,543)	938	1.6 (1.4–1.7)	3,824	(3,547–4,101)
Female	322	0.5 (0.4–0.6)	1,400	(1,134–1,660)	508	0.8 (0.6–0.9)	2,071	(1,700–2,442)
Race/ethnicity								
White	722	0.8 (0.7–0.8)	3,138	(2,804–3,477)	962	1.0 (0.9–1.0)	3,922	(3,543–4,305)
Black	*	*	*		*	*	*	
Hispanic	*	*	*		*	*	*	
Region								
Midwest	219	0.8 (0.6–1.0)	952	(682–1,226)	390	1.3 (1.0–1.6)	1,590	(1,239–1,937)
Northeast	255	1.0 (0.8–1.2)	1,108	(882–1,334)	311	1.2 (1.0–1.4)	1,268	(1,076–1,460)
South	443	1.1 (1.0–1.2)	1,926	(1,708–2,139)	586	1.3 (1.2–1.4)	2,389	(2,149–2,630)
West	*	*	*		160	0.6 (0.5–0.7)	652	(510–795)
MSA								
Rural	*	*	*		*	*	*	
Urban	929	1.1 (0.9–1.2)	4,038	(3,595–4,477)	1,378	1.4 (1.3–1.5)	5,618	(5,141–6,095)

Continued on next page

Table 23 (continued). Inpatient hospital stays for kidney cancer listed as primary diagnosis with partial nephrectomy performed, count, rate[a] (95% CI), rate per visits[b] (95% CI)

	1998				2000			
	Count	Rate per 100,000 population[a]	Rate per 100,000 visits for primary diagnosis of Kidney Cancer[b]		Count	Rate per 100,000 population[a]	Rate per 100,000 visits for primary diagnosis of Kidney Cancer[b]	
Total[c]	1,585	1.2 (1.1–1.3)	6,080	(5,585–6,579)	2,421	1.8 (1.7–1.9)	8,058	(7,625–8,494)
Age								
35–44	158	0.4 (0.3–0.5)	606	(437–771)	162	0.4 (0.3–0.4)	539	(409–669)
45–54	306	0.9 (0.7–1.1)	1,174	(963–1,385)	456	1.2 (1.1–1.4)	1,518	(1,311–1,727)
55–64	419	1.9 (1.6–2.2)	1,607	(1,346–1,868)	658	2.8 (2.5–3.1)	2,190	(1,954–2,426)
65–74	485	2.7 (2.4–3.0)	1,860	(1,638–2,087)	790	4.4 (4.1–4.8)	2,629	(2,406–2,849)
75–84	202	1.8 (1.5–2.1)	775	(637–917)	312	2.7 (2.3–3.1)	1,038	(882–1,195)
85+	*	*	*		*	*	*	
Gender								
Male	1,072	1.7 (1.6–1.8)	4,112	(3,775–4,450)	1,564	2.4 (2.3–2.6)	5,206	(4,883–5,528)
Female	513	0.7 (0.6–0.8)	1,968	(1,661–2,279)	857	1.2 (1.1–1.3)	2,852	(2,566–3,139)
Race/ethnicity								
White	1,033	1.0 (0.9–1.1)	3,963	(3,541–4,388)	1,443	1.4 (1.3–1.5)	4,803	(4,437–5,169)
Black	*	*	*		175	1.2 (1.0–1.4)	582	(476–689)
Hispanic	*	*	*		*	*	*	
Region								
Midwest	349	1.1 (1.0–1.3)	1,339	(1,158–1,519)	593	1.9 (1.7–2.1	1,974	1,771–2,180)
Northeast	516	2.0 (1.6–2.2)	1,979	(1,669–2,290)	608	2.2 (2.0–2.5)	2,024	(1,801–2,250)
South	489	1.0 (0.9–1.2)	1,876	(1,573–2,175)	773	1.6 (1.4–1.7)	2,573	(2,327–2,822)
West	232	0.8 (0.7–1.0)	890	(729–1,051)	446	1.5 (1.3–1.7)	1,484	(1,278–1,691)
MSA								
Rural	*	*	*		*	*	*	
Urban	1,478	1.5 (1.3–1.6)	5,670	(5,194–6,149)	2,310	2.2 (2.1–2.3)	7,688	(7,276–8,101)

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporatiion, for relevant demographic

[b]Rate per 100,000 adults 35+ visits with partial nephrectomy performed is based on estimated number of visits for renal cell carcinoma in HCUP_NIS 1994–2000.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 24. Inpatient procedures for open partial nephrectomy in Medicare beneficiaries with kidney cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	360	2,507 (1,361–3,653)		320	2,228 (1,146–3,311)	
Age						
0–64	20	2,083 (0–6,274)		0	0	
65–69	140	3,448 (917–5,980)		100	2,717 (346–5,089)	
70–74	60	1,676 (0–3,575)		120	2,871 (588–5,153)	
75–79	120	3,797 (784–6,810)		100	3,247 (416–6,078)	
80+	20	1,020 (0–3,046)		0	0	
Race/ethnicity						
White	300	2,443 (1,218–3,668)	1,890	280	2,194 (1,055–3,334)	1,648
Black	20	1,789 (0–5,364)	1,700	40	3,636 (0–8,744)	3,237
Asian	…	...	…	0	0	0
Hispanic	…	...	…	0	0	0
N. American Native	…	...	…	0	0	0
Gender						
Male	300	3,580 (1,794–5,366)	3,084	160	2,010 (625–3,395)	1,566
Female	60	1,003 (0–2,140)	748	160	2,500 (780–4,220)	1,864
Region						
Midwest	60	1,987 (0–4,238)	1,425	120	3,681 (760–6,602)	2,652
Northeast	100	3,268 (419–6,117)	2,263	60	2,256 (0–4,812)	1,663
South	160	3,587 (1,128–6,047)	2,938	100	2,304 (292–4,316)	1,795
West	40	3,077 (0–7,389)	4,644	40	2,899 (0–6,958)	2,250

	1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	400	2,985 (1,693–4,277)		460	2,934 (1,750–4,117)	
Age						
0–64	60	4,478 (0–9,560)		40	2,299 (0–5,511)	
65–69	60	1,875 (0–4,000)		140	3,271 (869–5,673)	
70–74	80	2,454 (54–4,854)		80	2,286 (50–4,522)	
75–79	100	3,497 (449–6,544)		160	4,819 (1,527–8,111)	
80+	100	5,556 (731–10,380)		40	2,105 (0–5,045)	
Race/ethnicity						
White	320	2,817 (1,452–4,182)	2,293	440	3,240 (1,905–4,575)	3,115
Black	60	4,110 (0–8,773)	4,288	20	1,351 (0–4,045)	1,425
Asian	0	0	0	0	0	0
Hispanic	0	0	0	0	0	0
N. American Native	0	0	0	0	0	0
Gender						
Male	300	3,807 (1,909–5,705)	4,001	200	2,227 (857–3,597)	2,242
Female	100	1,812 (228–3,395)	1,396	260	3,881 (1,802–5,959)	3,138
Region						
Midwest	140	5,147 (1,386–8,908)	4,236	120	3,333 (686–5,981)	2,750
Northeast	60	3,000 (0–6,402)	1,928	180	6,923 (2,501–11,345)	5,901
South	80	1,732 (37–3426)	1,718	160	3,030 (949–5,112)	3,068
West	120	8,451 (1,820–15,081)	11,585	0	0	0

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in table.

[b]Rate per 100,000 Medicare beneficiaries with renal cell carcinoma.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the total.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 25. Inpatient procedures for open radical nephrectomy in Medicare beneficiaries with kidney cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	5,520	38,440	(34,873–42,007)		5,200	36,212	(32,688–39,736)	
Age								
0–64	300	31,250	(17,649–44,851)		380	30,645	(18,842–42,448)	
65–69	1,800	44,335	(37,443–51,227)		1,340	36,413	(29,395–43,431)	
70–74	1,260	35,196	(28,132–42,259)		1,420	33,971	(27,497–40,445)	
75–79	1,340	42,405	(34,615–50,195)		1,160	37,662	(29,923–45,401)	
80–84	700	35,714	(26,058–45,370)		660	43,421	(32,020–54,822)	
85–89	100	20,000	(3,148–36,852)		220	44,000	(23,088–64,912)	
90–94	20	16,667	(0–59,510)		20	16,667	(0–59,510)	
95+	0	0			0	0		
Race/ethnicity								
White	4,740	38,599	(34,738–42,461)	36,966	4,820	37,774	(34,002–41,546)	36,879
Black	460	41,071	(27,777–54,366)	37,114	200	18,182	(7,659–28,705)	17,059
Asian	…	...		…	0	0		0
Hispanic	…	...		…	40	22,222	(0–56,117)	31,365
N. American Native	…	...		…	0	0		0
Gender								
Male	3,280	39,141	(34,448–43,833)	36,726	3,020	37,940	(33,152–42,727)	37,418
Female	2,240	37,458	(31,940–42,976)	35,103	2,180	34,063	(28,842–39,283)	33,384
Region								
Midwest	1,320	43,709	(35,706–51,711)	33,865	1,380	42,331	(34,666–49,997)	39,359
Northeast	1,320	43,137	(35,201–51,074)	43,416	1,120	42,105	(33,605–50,606)	39,296
South	2,180	48,879	(42,267–55,491)	45,682	2,140	49,309	(42,604–56,014)	51,216
West	680	52,308	(39,835–64,780)	51,480	560	40,580	(28,697–52,462)	44,555

Continued on next page

Table 25 (continued). Inpatient procedures for open radical nephrectomy in Medicare beneficiaries with kidney cancer, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	4,640	34,627	(31,015–38,239)		4,580	29,209	(26,019–32,399)	
Age								
0–64	340	25,373	(14,679–36,067)		300	17,241	(9,144–25,339)	
65–69	1,080	33,750	(26,344–41,156)		1,340	31,308	(25,045–37,572)	
70–74	1,140	34,969	(27,571–42,368)		920	26,286	(19,699–32,872)	
75–79	1,000	34,965	(27,054–42,876)		1,260	37,952	(30,493–45,411)	
80–84	660	36,667	(26,517–46,816)		660	34,737	(24,986–44,488)	
85–89	340	50,000	(32,292–67,708)		100	13,158	(1,898–24,418)	
90–94	80	30,769	(1,740–59,799)		0	0		
95+					0	0		
Race/ethnicity								
White	4,000	35,211	(31,271–39,151)	33,633	4,100	30,191	(26,730–33,653)	26,801
Black	380	26,027	(15,719–36,336)	29,203	280	18,919	(9,783–28,055)	19,636
Asian	20	50,000	(0–685,310)	17,000	20	50,000	(0–685,310)	17,000
Hispanic	120	46,154	(14,799–77,509)	37,910	20	14,286	(0–49,242)	11,571
N. American Native	0	0		0	0	0		0
Gender								
Male	2,820	35,787	(31,033–40,541)	34,839	2,880	32,071	(27,737–36,405)	29,330
Female	1,820	32,971	(27,390–38,552)	30,721	1,700		(20,689–30,057)	23,368
Region								
Midwest	1,000	36,765	(28,558–44,972)	34,805	1,380	38,333	(31,162–45,504)	34,843
Northeast	860	43,000	(33,127–52,873)	38,096	760	29,231	(21,308–37,154)	24,153
South	1,940	41,991	(35,579–48,403)	42,577	1,880	35,606	(29,792–41,420)	33,661
West	800	56,338	(44,515–68,161)	46,732	540	36,486	(25,257–47,716)	34,044

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in table.

[b]Rate per 100,000 Medicare beneficiaries with renal cell carcinoma.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 26. VA users with laparoscopic partial nephrectomy for kidney cancer, 1998–2003 (merged), count, age-adjusted rate[a]

	1998–2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	0	*	4	*	12	*	6	*
Age-adjusted Total	0	*	4	*	9	*	4	*
Age								
< 25	0	*	0	*	0	*	0	*
25–34	0	*	0	*	0	*	0	*
35–44	0	*	0	*	1	*	0	*
45–54	0	*	4	*	3	*	1	*
55–64	0	*	0	*	4	*	2	*
65–74	0	*	0	*	2	*	1	*
75–84	0	*	0	*	0	*	0	*
85+	0	*	0	*	1	*	0	*
Gender		*		*		*		*
Male	0	*	4	*	12	*	6	*
Female	0	*	0	*	0	*	0	*
Race/ethnicity		*		*		*		*
White	0	*	2	*	10	*	3	*
Black	0	*	0	*	0	*	1	*
Hispanic	0	*	1	*	0	*	0	*
Other	0	*	0	*	0	*	1	*
Unknown	0	*	1	*	2	*	1	*
Insurance Status		*		*		*		*
No insurance/self-pay	0	*	4	*	10	*	5	*
Medicare	0	*	0	*	2	*	0	*
Medicaid	0	*	0	*	0	*	0	*
Private Insurance/HMO	0	*	0	*	0	*	1	*
Other Insurance	0	*	0	*	0	*	0	*
Unknown	0	*	0	*	0	*	0	*
Region		*		*		*		*
Eastern	0	*	2	*	0	*	2	*
Central	0	*	0	*	0	*	1	*
Southern	0	*	2	*	10	*	3	*
Western	0	*	0	*	2	*	0	*

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

development of techniques for laparoscopic partial nephrectomy and its widespread adoption (33). Of the datasets used in this analysis, only the VA dataset captures this trend.

Improvements in perioperative care have led to shorter hospitalizations for surgery patients in general and have impacted length of stay for patients undergoing surgery for kidney cancer as well. These include improvements in anesthesia, postoperative pain management, dietary management, and early mobilization. Inpatient care accounts for a large proportion of the cost of treating RCC, and decreases in the length of hospital stays are important for decreasing the overall costs associated with such treatment. HCUP data from 1994, 1996, 1998, and 2000 show a steady decrease in the inpatient length of stay for a primary diagnosis of RCC; mean length of hospitalization decreased by 25% from 1994 to 2000 (Table 27). The reduced length of stay is seen consistently across genders, age groups, races, and regions. In 2000, the mean length of stay was 6.4 days, and the median length of stay was 5 days. With the wider adoption of laparoscopy, the length of stay will decrease significantly further, as length

Table 27. Length of stay (LOS) for primary diagnosis of kidney cancer

	1994				1996			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total	23,006	8.1	7	97	24,528	7.2	6	154
Age								
35–44	1,445	7.1	6	29	1,630	6.2	5	42
45–54	3,287	7.2	6	41	3,675	6.2	5	42
55–64	5,243	7.7	6	68	5,832	6.8	5	154
65–74	7,368	8.3	7	72	7,342	7.4	6	78
75–84	4,675	9	7	97	5,054	8.5	6	111
85+	989	9.8	8	87	995	8.3	6	62
Gender								
Male	13,872	7.8	6	73	14,828	7.0	5	154
Female	9,134	8.6	7	97	9,700	7.7	6	111
Race/ethnicity								
White	15,423	8.0	7	97	16,356	7.2	6	111
Black	1,561	9.8	7	68	1,657	8.2	6	78
Hispanic	710	8.9	7	34	893	8.0	5	154
Region								
Northeast	5,206	9.2	7	97	5,709	8.2	6	78
Midwest	5,885	8.1	7	67	6,277	7.2	6	111
South	8,273	7.9	7	67	8,727	7.1	6	154
West	3,643	7.0	6	72	3,814	6.3	5	53
MSA								
Rural	3,318	7.6	6	64	3,048	6.4	5	111
Urban	19,648	8.2	7	97	21,451	7.4	6	154

	1998				2000			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total	26,069	6.7	5	255	30,045	6.4	5	117
Age								
35–44	1,823	5.6	5	43	1,986	5.5	4	50
45–54	4,405	5.8	5	44	5,474	5.9	5	116
55–64	6,114	6.3	5	83	7,187	5.9	5	84
65–74	7,724	6.8	5	76	8,428	6.5	5	103
75–84	5,011	7.8	6	255	5,732	7.2	6	64
85+	991	8.1	7	66	1,239	8.4	6	117
Gender								
Male	15,587	6.5	5	75	18,217	6.2	5	87
Female	10,483	6.9	5	255	11,818	6.8	5	117
Race/ethnicity								
White	16,713	6.5	5	255	18,536	6.2	5	117
Black	1,817	7.5	5	70	2,002	8.1	6	116
Hispanic	1,142	7.5	5	75	1,418	6.8	5	58
Region								
Northeast	6,256	7.1	5	136	6,627	6.8	5	117
Midwest	6,260	7.1	6	255	7,469	6.2	5	40
South	9,550	6.3	5	83	10,758	6.4	5	103
West	4,004	6.2	5	71	5,191	6.0	5	116
MSA								
Rural	2,807	6.2	5	83	3,042	6.1	5	55
Urban	23,170	6.7	5	255	26,954	6.4	5	117

MSA, metropolitan statistical area.

Adults 35+ of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 28. Mortality rates and length of stay (LOS), by type of nephrectomy, 1993–1997, 95% CI

		Annual Hospital Nephrectomy Volume			
	Total	Low-Volume Hospitals (< 15 cases/yr)	Medium-Volume Hospitals (15–33 cases/yr)	High-Volume Hospitals (> 33 cases/yr)	P-value
Mortality (%)					
All types of nephrectomy	1.39	1.60	1.49	1.04	0.02
Partial nephrectomy	0.85	2.25	0.57	0.36	0.02
Radical nephrectomy	1.38	1.46	1.52	1.10	0.14
Nephroureterectomy	1.68	2.05	1.66	1.08	0.31
Length of stay (days)					
All types of nephrectomy	7.80 (7.71–7.89)	7.85 (7.71–7.99)	7.83 (7.67–7.99)	7.70 (7.54–7.86)	0.35
Partial nephrectomy	7.34 (7.05–7.63)	7.97 (7.32–8.62)	7.43 (6.90–7.96)	7.06 (6.65–7.47)	0.00
Radical nephrectomy	7.77 (7.67–7.87)	7.76 (7.60–7.92)	7.78 (7.60–7.96)	7.73 (7.55–7.91)	0.84
Nephroureterectomy	8.21 (7.98–8.44)	8.31 (7.92–8.70)	8.24 (7.87–8.61)	7.99 (7.60–8.38)	0.57

SOURCE: Reprinted from Urology, 63, Taub DA, Miller DC, Cowan JA, Dimick JB, Montie JE, Wei JT. Impact of surgical volume on mortality and length of stay after nephrectomy, 862–867, Copyright 2004, with permission from Elsevier.

of stay after laparoscopic surgery for kidney cancer is approximately half that after open surgery. Length-of-stay data for laparoscopic surgery are not available in the datasets used in this analysis.

Recent investigations have brought attention to the concept of quality of care delivered by hospitals and by individual surgeons in an attempt to analyze and improve surgical outcomes. Leaders in this field, including RAND, the Veterans Affairs Outcomes Group, and the Leapfrog Group, have demonstrated that mortality rates are lower at hospitals where high volumes of major surgery are performed (34). In addition, individual surgeon volume has an inverse relationship with complication rates (35). One of the findings of this research is that mortality rates for certain types of surgery could be reduced if patients

Table 29. Characteristics of patients undergoing nephrectomy for kidney cancer, 1993–1997

		Annual Hospital Nephrectomy Volume			
Factor	Total	Low-Volume Hospitals (< 15 cases/yr)	Medium-Volume Hospitals (15-33 cases/yr)	High-Volume Hospitals (> 33 cases/yr)	P-value
Number of hospitals, n(%)	962 (100%)	717 (74.5)	165 (17.2)	80 (8.3)	…
Number of patients, n(%)	20,765 (100%)	7,552 (36.3)	7,104 (34.2)	6,109 (29.4)	…
Mean age (SD) in yrs	62.8 (15.4)	64.6 (13.9)	63.2 (15.1)	60.2 (17.1)	< 0.001
Sex (% male)	60.0	60.0	60.0	62.0	0.08
Race (% white)	68.4	68.6	68.6	67.8	0.47
Urgent admission (%)	22.5	28.3	19.2	19.3	< 0.001
Mortality (%)	1.4	1.6	1.5	1.0	0.02
Length of stay (days)	7.8	7.9	7.9	7.7	0.35
Comorbid conditions (%)					
Chronic obstructive pulmonary disease	8.1	10.3	7.6	5.9	< 0.001
Diabetes mellitus	10.6	10.7	10.9	10.2	0.39
Solid tumor metastasis	11.4	10.7	11.0	12.8	< 0.001
Myocardial infarction	3.1	2.4	3.3	3.6	< 0.001
Liver disease	0.7	0.7	0.7	0.7	0.86
Peripheral vascular disease	2.5	2.8	2.6	2.2	0.09
Chronic renal disease	0.3	0.2	0.2	0.7	< 0.001

…data not available.

SOURCE: Reprinted from Urology, 63, Taub DA, Miller DC, Cowan JA, Dimick JB, Montie JE, Wei JT. Impact of surgical volume on mortality and length of stay after nephrectomy, 862–867, Copyright 2004, with permission from Elsevier.

Table 30. Expenditures for kidney cancer, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$13,315,994	4.9%	$14,501,579	4.6%	$20,096,354	5.4%	$17,570,762	4.4%
Physician Office	$17,650,817	6.4%	$19,222,351	6.1%	$31,895,869	8.6%	$30,903,303	7.7%
Ambulatory Surgery	$8,138,812	3.0%	$8,863,449	2.8%	$9,131,076	2.5%	$6,650,790	1.7%
Emergency Room	$0	0.0%	$0	0.0%	$0	0.0%	$0	0.0%
Inpatient	$235,335,352	85.8%	$273,243,539	86.5%	$309,230,478	83.5%	$346,165,817	86.3%
TOTAL	$274,440,974		$315,830,918		$370,353,777		$401,290,672	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

chose a hospital where more of those surgeries are performed. A strong case is being made for transparent exchange of standard measures of outcomes, which would recognize hospitals for superior outcomes and would improve the overall quality of the healthcare system.

Surgery for kidney cancer has been evaluated in this fashion (36). Not surprisingly, hospitals where high volumes of kidney surgery are performed were found to have lower mortality rates (Table 28). This was the case despite the higher rate of risk factors for surgical complications such as emphysema, history of heart attack, metastatic disease, and chronic renal disease (Table 29) present in patients undergoing surgery at high-volume hospitals. While laparoscopic kidney surgery has not yet been analyzed for outcomes based on surgical volume, this will likely be pursued in the near future.

ECONOMIC IMPACT

Total expenditures in the United States for RCC were $401 million in 2000, a 46% increase since 1994 (Table 30). This increase is largely attributable to rising expenditures for inpatient services, although hospital outpatient services and physician office visits have also increased, albeit inconsistently, since 1994. Inpatient services accounted for about 85% of total RCC expenditures throughout the study period.

Expenditures for RCC by Medicare enrollees age 65 and over amounted to $119 million in 2001, an increase of about $26 million since 1992 (Table 31). Inpatient services and physician office visits

Table 31. Expenditures for Medicare beneficiaries for treatment of kidney cancer, by site of service (% of total)

	Age 65 and over							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$4,692,160	5.0%	$5,966,740	6.0%	$7,638,160	7.0%	$6,976,800	5.8%
Physician Office	$5,153,280	5.5%	$7,078,500	7.1%	$12,384,000	11.3%	$13,720,940	11.5%
Ambulatory Surgery	$1,092,000	1.2%	$1,299,480	1.3%	$1,812,480	1.7%	$1,751,220	1.5%
Emergency Room	$269,700	0.3%	---	0.0%	$455,600	0.4%	---	0.0%
Inpatient	$82,586,560	88.1%	$85,331,180	85.6%	$87,541,560	79.7%	$96,849,520	81.2%
TOTAL	$93,793,700		$99,675,900		$109,831,800		$119,298,480	

	Under 65							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$597,780	9.6%	$802,280	36.3%	$598,780	6.3%	$376,800	3.8%
Physician Office	$604,440	9.7%	$1,408,800	63.7%	$588,600	6.2%	$1,523,200	15.4%
Ambulatory Surgery	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$5,032,500	80.7%	---	0.0%	$8,351,640	87.6%	$8,020,320	80.8%
TOTAL	$6,234,720		$2,211,080		$9,539,020		$9,920,320	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 32. Estimated annual expenditures of privately insured employees with and without a medical claim for kidney cancer in 2002[a]

	Annual Expenditures (per person)					
	Persons without Kidney Cancer (N=394,175)			Persons with Kidney Cancer (N=386)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$3,196	$1,317	$4,513	$13,418	$3,250	$16,668
Age						
35–49	$2,922	$1,215	$4,137	$13,340	$3,499	$16,839
50–54	$3,469	$1,431	$4,900	$15,670	$5,434	$21,104
55–59	$3,441	$1,403	$4,844	$20,014	$2,353	$22,367
Region						
Midwest	$3,062	$1,256	$4,318	$12,843	$3,124	$15,967
Northeast	$3,283	$1,403	$4,686	$13,771	$3,462	$17,233
South	$3,317	$1,292	$4,609	$13,916	$3,157	$17,073
West	$2,826	$1,294	$4,120	$11,854	$3,223	$15,077

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 35 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions. Predicted expenditures for persons age 60 to 64 are omitted due to small sample size.

SOURCE: Ingenix, 2002.

accounted for the majority of this increase, with expenditures for office visits increasing 166% since 1992. Inpatient services accounted for more than 80% of RCC expenditures in 2001, similar to the proportion in the general population. Expenditures by Medicare enrollees under the age of 65 were $10 million in 2001, an increase of $4 million over the level in 1992.

Individual-level expenditures for RCC were estimated using risk-adjusted regression models controlling for age, sex, work status, income, urban or rural residence, and health plan characteristics (Table 32). Average annual expenditures for 35- to 59-year-olds with employer-provided insurance who were treated for RCC were $16,668, compared with $4,513 for similar individuals not treated for the condition; an incremental cost of $12,155 was thus associated with a diagnosis of RCC. The reasons for the substantial difference are not entirely clear, but the excess expenditures may be for major surgery associated with RCC and also for end-of-life care. Individual-level costs varied little by region.

Overall, 48% of men and women with a diagnosis of RCC missed an average of more than 12 days of work per diagnosis. This substantial work loss is probably attributable to recovery time associated with surgical management of RCC (Table 33). An annual average of about 7 days were missed for outpatient visits, while 5 days were missed for inpatient stays. Men and women did not appear to differ with respect to the average number of days missed as a result of inpatient stays for RCC. Each inpatient stay resulted in more than 13 days of work loss (it must be noted that this finding is based on only 20 stays). About 11 hours of work were missed for each outpatient visit. There was some variation by region, with more work missed per visit in the South and West than in the Northeast and Midwest regions.

Healthcare expenditures for RCC were substantial in both the general population and among Medicare enrollees age 65 and over. Treatment and management of individuals with RCC was far more expensive than that of individuals without RCC, primarily because of the enormous excess costs associated with RCC in men. Nearly half of the individuals diagnosed with RCC missed work, and each inpatient stay and outpatient visit resulted in a large amount of work loss.

CONCLUSIONS

The incidence of kidney cancer has increased over the past decade and will likely accelerate in the future because of the aging of the US population and the increase in comorbid diseases associated with kidney cancer. African Americans have an increased risk of

Table 33. Average annual work loss of persons treated for kidney cancer, 1999 (95%CI)

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs)					
			Inpatient[b]		Outpatient[b]		Total	
Total	52	48%	40.3	(15.6-65.1)	56.3	(0–116.1)	96.6	(24.4–168.8)
Age								
18–29	1	100%	181	…	181	…	362	…
30–39	2	50%	48.0	(0–657.9)	52.0	(0–712.7)	100	(0–1370.6)
40–49	9	78%	26.8	(0–73.5)	101.7	(0–301.6)	129	(0–374.0)
50–64	40	40%	39.5	(9.3–69.6)	43.1	(0–111.2)	82.6	(1.5–163.6)
Gender								
Male	42	48%	40.5	(11.5–69.5)	60.9	(0–134.7)	101.3	(13.8–188.9)
Female	10	50%	39.7	(0–91.7)	36.9	(0–188.9)	76.6	(0–179.9)
Region								
Midwest	12	42%	56.4	(0–119.2)	26.4	(0–62.9)	82.8	(0–165.9)
Northeast	7	29%	73.1	(0–239.4)	3.4	(0–11.80)	76.6	(0–251.2)
South	21	52%	24.9	(2.2–47.5)	78.3	(0–211.2)	103	(0–252.9)
West	5	40%	37.1	(0–14.0)	164	(0-600.9)	201	(0–740.9)
Unknown	7	71%	28.6	(0–61.1)	17.1	(0–53.0)	45.7	(0–110.6)

…data not available.

[a]Individuals with an inpatient or outpatient claim for renal cell carcinoma and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

Table 34. Average work loss[a] associated with a hospital stay or an ambulatory care visit for kidney cancer (95% CI)

	Number of Inpatient Stays	Average Hours Missed for Inpatient Stays		Number of Outpatient Visits	Average Hours Missed for Outpatient Visits	
Total	20	105	(50–160)	273	10.6	(8–13)
Age						
18–29	1	181	...	...	45.2	(0–136)
30–39	1	96	...	3	34.7	(0–184)
40–49	3	80	(0–306)	70	13.1	(8–18)
50–64	15	105	(32–178)	200	8.6	(6–12)
Gender						
Male	17	100	(35–165)	252	10.1	(8–13)
Female	3	132	(0–314)	21	14.8	(1–29)
Region						
Midwest	5	135	(0–280)	60	5.0	(0–10)
Northeast	2	256	(0–3102)	35	0.7	(0–2)
South	8	65	(12–118)	95	17.3	(12–23)
West	1	185	…	55	14.9	(9–21)
Unknown	4	50	(0–101)	28	4.3	(0–12)

…data not available.

[a]Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of outpatient visit.

Source: Marketscan Health and Productivity Management, 1999.

kidney cancer and a worse prognosis, particularly in men younger than 60. Trends in incidence, survival, and treatment of kidney cancer in other minorities are poorly characterized. Costs associated with the diagnosis and treatment of kidney cancer totaled approximately $400 million in 2000 and places a considerable burden on the US healthcare system. Inpatient stays, recovery from surgery, and outpatient care keep patients away from other productive activity for substantial amounts of time. However, inpatient stays have decreased over the past decade, and the widespread adoption of laparoscopic techniques will further decrease this costly component of treatment.

RECOMMENDATIONS

Opportunities abound for improving our understanding of the burden of kidney cancer in the United States. Tumor registry data, such as those from SEER, are critically important to the appreciation of racial variations in incidence and survival. Data on minority patients are relatively scant, and greater efforts should be made to capture these numbers and to screen populations at risk. A national cancer registry, based on the SEER model, could further the understanding of kidney cancer by capturing more cases. The SEER data could and should be improved by the separation of upper-tract transitional cell carcinoma from RCC, since these diseases behave very differently. Current ICD-9 codes already make this distinction, but they could be modified to separate pediatric kidney tumors as well, since these tumors also have different treatment and prognosis.

Further investigation into the SEER database with linked SEER and Medicare data could help improve the understanding of the role of end-stage renal disease in the increased incidence of kidney cancer. Prior studies indicate that patients on dialysis clearly have an increased risk of kidney cancer (37), but these analyses do not account for the possibility that patients are living longer on dialysis and after kidney transplant and hence are exposed to the attendant age-related risk of developing kidney cancer.

From the clinical perspective, major efforts should be made in the prevention of diseases that are associated with the development of kidney cancer, including hypertension and obesity. It would also be valuable to ascertain why these diseases are associated with development of RCC. From the research perspective, basic science inquiries into the genetic alterations seen in kidney cancer should receive increased support, as this understanding could lead to more effective treatments for metastatic disease, which is rapidly fatal. Research should also focus on features of the increasingly diagnosed, small, incidental RCCs, some of which may behave in indolent fashion and may not require treatment.

The datasets used in this analysis do not capture standard immunotherapeutic care or the new targeted therapies (tyrosine kinase inhibitors) for patients with metastatic disease. These treatments are quite costly and until recently have had a relatively small impact on survival. The high costs of metastatic disease and end-of-life care probably contribute significantly to the burden of this disease in the United States. Understanding these costs might help garner support for clinical trials rather than utilization of standard immunotherapeutic therapies with marginal survival benefit. In addition, the datasets used in this analysis do not capture newer, less-invasive therapies for localized disease, such as radiofrequency ablation and cryotherapy. It would be useful to understand the degree of adoption of these thermal therapies, along with their costs and effectiveness.

The evolution of surgical techniques has understandably engendered controversy in the surgical management of kidney cancer, and the field is currently in flux. While it appears clear that laparoscopic techniques will ultimately replace traditional surgery in the most common cases of kidney cancer, more data are necessary to support this transformation. In a few years, the datasets used in this analysis for length of stay will begin to reflect the trend toward laparoscopic techniques. Currently the equipment costs for laparoscopic surgery somewhat offset the benefits of shorter hospitalization, but over time these costs will likely decrease.

The compelling case for laparoscopic techniques in the treatment of kidney cancer could best be addressed, however, by looking at disability times and costs in datasets of large disability insurance carriers. As shorter hospitalization times and earlier return to work are increasingly recognized, payors should reimburse these procedures at a higher rate. Third-party payors will probably support laparoscopic (or “minimally invasive”) techniques for retired as well as employed patients when the overall cost of treatment is shown to be less. There is recent precedent for this in the increased reimbursement for less-invasive forms of treatment for benign prostatic hyperplasia (see the benign prostatic hyperplasia chapter in this compendium).

Outcomes research in quality of care is a growing field that will play an increasingly powerful role in healthcare delivery in the future. More effort should be made and more support should be offered for outcomes studies in the treatment of kidney cancer aimed at improving outcomes for patients and providing high-quality care in all regions of the country. One potential issue that could arise from such studies is increased regionalization of care, with patients having to travel long distances from their homes for treatment.

REFERENCES

1. Data from American Cancer Society, http://www.cancer.org.
2. Pavlovich CP, Schmidt LS, Phillips JL. The genetic basis of renal cell carcinoma. Urol Clin North Am 2003;30:437-54, vii.
3. Russo P. Localized renal cell carcinoma. Curr Treat Options Oncol 2001;2:447-55.
4. Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. Urology 1998;51:203-5.
5. Hu J, Ugnat AM. Active and passive smoking and risk of renal cell carcinoma in Canada. Eur J Cancer 2005;41:770-8.
6. Mattioli S, Truffelli D, Baldasseroni A, Risi A, Marchesini B, Giacomini C, Bacchini P, Violante FS, Buiatti E. Occupational risk factors for renal cell cancer: a case--control study in northern Italy. J Occup Environ Med 2002;44:1028-36.
7. Handa K, Kreiger N. Diet patterns and the risk of renal cell carcinoma. Public Health Nutr 2002;5:757-67.
8. Hu J, Mao Y, White K. Diet and vitamin or mineral supplements and risk of renal cell carcinoma in Canada. Cancer Causes Control 2003;14:705-14.
9. Moore LE, Wilson RT, Campleman SL. Lifestyle factors, exposures, genetic susceptibility, and renal cell cancer risk: a review. Cancer Invest 2005;23:240-55.
10. Dhote R, Thiounn N, Debre B, Vidal-Trecan G. Risk factors for adult renal cell carcinoma. Urol Clin North Am 2004;31:237-47.
11. Rashidkhani B, Akesson A, Lindblad P, Wolk A. Major dietary patterns and risk of renal cell carcinoma in a prospective cohort of Swedish women. J Nutr 2005;135:1757-62.
12. Nicodemus KK, Sweeney C, Folsom AR. Evaluation of dietary, medical and lifestyle risk factors for incident kidney cancer in postmenopausal women. Int J Cancer 2004;108:115-21.
13. Vaishampayan UN, Do H, Hussain M, Schwartz K. Racial disparity in incidence patterns and outcome of kidney cancer. Urology 2003;62:1012-7.
14. Washio M, Mori M, Sakauchi F, Watanabe Y, Ozasa K, Hayashi K, Miki T, Nakao M, Mikami K, Ito Y, Wakai K, Tamakoshi A. Risk factors for kidney cancer in a Japanese population: findings from the JACC Study. J Epidemiol 2005;15 Suppl 2:S203-11.
15. Genetics, risk factors, diagnosis, staging, and treatment of renal cell carcinoma. Campbell's Urology. 8th ed. ed: Ch. 75.
16. McDougal WS, Gervais DA, McGovern FJ, Mueller PR. Long-term followup of patients with renal cell carcinoma treated with radio frequency ablation with curative intent. J Urol 2005;174:61-3.
17. Flanigan RC, Mickisch G, Sylvester R, Tangen C, Van Poppel H, Crawford ED. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol 2004;171:1071-6.
18. Novick AC, Gephardt G, Guz B, Steinmuller D, Tubbs RR. Long-term follow-up after partial removal of a solitary kidney. N Engl J Med 1991;325:1058-62.
19. Stener B, Henriksson C, Johansson S, Gunterberg B, Pettersson S. Surgical removal of bone and muscle metastases of renal cancer. Acta Orthop Scand 1984;55:491-500.
20. Dernevik L, Berggren H, Larsson S, Roberts D. Surgical removal of pulmonary metastases from renal cell carcinoma. Scand J Urol Nephrol 1985;19:133-7.
21. Ratain MJ, Eisen T, Stadler WM, Flaherty KT, Kaye SB, Rosner GL, Gore M, Desai AA, Patnaik A, Xiong HQ, Rowinsky E, Abbruzzese JL, Xia C, Simantov R, Schwartz B, O'Dwyer PJ. Phase II placebo-controlled randomized discontinuation trial of sorafenib in patients with metastatic renal cell carcinoma. J Clin Oncol 2006;24:2505-12.
22. Motzer RJ, Rini BI, Bukowski RM, Curti BD, George DJ, Hudes GR, Redman BG, Margolin KA, Merchan JR, Wilding G, Ginsberg MS, Bacik J, Kim ST, Baum CM, Michaelson MD. Sunitinib in patients with metastatic renal cell carcinoma. Jama 2006;295:2516-24.
23. Doris Stoll, Executive Director, Urology Residency Review Committee, personal communication, November 29, 2005.
24. Chow WH, Devesa SS, Warren JL, Fraumeni JF, Jr. Rising incidence of renal cell cancer in the United States. Jama 1999;281:1628-31.
25. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data. J Urol 2002;167:57-60.
26. Centers for Disease Control and Prevention NCfHS, National Health and Nutrition Examination Survey, Hispanic Health and Nutrition Examination Survey (1982-84), and National Health Examination Survey (1960-1962). Overweight, obesity, and healthy weight among persons 20 years of age and over, according to sex, age, race, and Hispanic origin: United States, 1960-62, 1971-74, 1976-80, 1988-94, and 1999-2002.
27. Hypertension among persons 20 years of age and over, according to sex, age, race, and Hispanic origin: United States, 1988-94 and 1999-2002.
28. Permpongkosol S, Chan DY, Link RE, Jarrett TW, Kavoussi LR. Laparoscopic radical nephrectomy: long-term outcomes. J Endourol 2005;19:628-33.
29. McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. Urology 2002;59:816-20.
30. Miller DC, Wei JT, Dunn RL, Hollenbeck BK. Trends in the diffusion of laparoscopic nephrectomy. JAMA 2006;295(21):2480-2.

31. Scherr DS, Ng C, Munver R, Sosa RE, Vaughan ED, Jr., Del Pizzo J. Practice patterns among urologic surgeons treating localized renal cell carcinoma in the laparoscopic age: technology versus oncology. Urology 2003;62:1007-11.
32. Huynh PN, Hollander JB. Trends toward laparoscopic nephrectomy at a community hospital. J Urol 2005;173:547-51.
33. Gerber GS, Stockton BR. Laparoscopic partial nephrectomy. J Endourol 2005;19:21-4.
34. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, Welch HG, Wennberg DE. Hospital volume and surgical mortality in the United States. N Engl J Med 2002;346:1128-37.
35. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med 2003;349:2117-27.
36. Taub DA, Miller DC, Cowan JA, Dimick JB, Montie JE, Wei JT. Impact of surgical volume on mortality and length of stay after nephrectomy. Urology 2004;63:862-7.
37. Stewart JH, Buccianti G, Agodoa L, Gellert R, McCredie MR, Lowenfels AB, Disney AP, Wolfe RA, Boyle P, Maisonneuve P. Cancers of the kidney and urinary tract in patients on dialysis for end-stage renal disease: analysis of data from the United States, Europe, and Australia and New Zealand. J Am Soc Nephrol 2003;14:197-207.

CHAPTER 11

Pediatric Urologic Disorders

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Pediatric Urologic Disorders

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VESICOURETERAL REFLUX

DEFINITION AND DIAGNOSIS

Vesicoureteral reflux (VUR), often referred to simply as reflux, is the retrograde flow of urine from the bladder to the upper urinary tract. Reflux is termed *primary* when it exists as a congenital anomaly that is not associated with any other anatomical or functional abnormality of the urinary tract. *Secondary* VUR is reflux that may be caused by the elevated pressures associated with bladder obstruction. The most common anatomic cause of secondary VUR is posterior urethral valves, which are associated with reflux in approximately 50% of affected boys (1). Common functional causes of secondary VUR may alter bladder dynamics; the ensuing voiding discoordination causes high bladder pressures like those that occur in neurologically normal children with dysfunctional voiding states or the neurogenic bladder seen in children with spina bifida. Analyses for this section are based on the ICD-9 and CPT codes for VUR listed in Table 1.

Reflux severity is usually categorized according to a five-point grading system devised by the International Reflux Study Committee in 1981 (Table 2) to describe VUR by voiding cystourethrography (VCUG). Radionuclide cystography (RNC) does not offer the same level of detail as VCUG, and thus a three-point grading system is employed for VUR described by RNC.

When VUR is suspected, radiographic assessment of the lower urinary tract is warranted. Traditionally, VCUG has been performed as the initial modality to diagnose VUR in infants with prenatally detected hydronephrosis, children under five years of age with a documented urinary tract infection (UTI), and children with a febrile UTI, regardless of age. An RNC is usually employed to follow the progression of VUR once it has been diagnosed and to screen the newborn siblings and offspring of patients with VUR.

Since most cystography is performed to evaluate UTI and 29% to 50% of the children evaluated for UTI have VUR, an alternative strategy has been offered for the evaluation of initial UTI that could reduce the number of children requiring cystography by almost half. This approach is predicated on referring for cystography only those children in whom renal inflammation is identified. It has been shown that an early nuclear renal scan following the first UTI will allow detection of most patients with intermediate-grade VUR and all patients with high-grade VUR (2, 3).

RISK FACTORS

Primary VUR appears to have a multifactorial etiology in addition to an established genetic component. VUR is the most commonly inherited abnormality of the urinary tract. Its incidence in siblings of children with known VUR has been reported to be as high as 45% (4). The incidence is slightly higher among sisters of girls with VUR; however, the association is not strong enough to confirm X-

Table 1. Codes used in the diagnosis and management of pediatric urologic disorders

Vesicoureteral reflux	
Individuals with one or more of the following:	
ICD-9 diagnosis codes	
593.7	Vesicoureteral reflux
593.70	Vesicoureteral reflux, unspecified or without reflux nephropathy
593.71	Vesicoureteral reflux with reflux nephropathy, unilateral
593.72	Vesicoureteral reflux with reflux nephropathy, bilateral
593.73	Other vesicoureteral reflux with reflux nephropathy NOS
CPT procedure codes	
50660[a]	Ureterectomy, total, ectopic ureter, combination abdominal, vaginal and/or perineal approach
50780[a]	Ureteroneocystostomy; anastomosis of single ureter to bladder
50781[a]	Ureteroneocystostomy (pre-1996)
50782	Ureteroneocystostomy; anastomosis of duplicated ureter to bladder
50783	Ureteroneocystostomy; with extensive ureteral tailoring
50785	Ureteroneocystostomy; with vesico-psoas hitch or bladder flap
50947[a]	Laparoscopy, surgical; ureteroneocystostomy with cystoscopy and ureteral stent placement
50948[a]	Laparoscopy, surgical; ureteroneocystostomy without cystoscopy and ureteral stent placement
52327	Cystourethroscopy (including ureteral catheterization); with subureteric injection of implant material
Undescended testes	
Males with one or more of the following:	
ICD-9 diagnosis codes	
752.5	Undescended and retractile testis
752.51	Undescended testis
752.52	Retractile testis
ICD-9 procedure codes	
62.5[b]	Orchiopexy
63.53[b]	Transplantation of spermatic cord
CPT procedure codes	
54550	Exploration for undescended testis (inguinal or scrotal area)
54560	Exploration for undescended testis with abdominal exploration
54640	Orchiopexy, inguinal approach, with or without hernia repair
54650	Orchiopexy, abdominal approach, for intra-abdominal testis (eg, Fowler-Stephens)
54690	Laparoscopy, surgical; orchiectomy
54692	Laparoscopy, surgical; orchiopexy for intra-abdominal testis
54699	Unlisted laparoscopy procedure, testis
Hypospadias	
Males with one or more of the following:	
ICD-9 diagnosis codes	
752.6	Hypospadias and epispadias and other penile anomalies
752.61	Hypospadias
ICD-9 procedure codes	
58.45[c]	Repair of hypospadias and epispadias
CPT procedure codes	
54300	Plastic operation of penis for straightening of chordee (eg, hypospadias), with or without mobilization of urethra
54304	Plastic operation on penis for correction of chordee or for first stage hypospadias repair with or without transplantation of prepuce and/or skin flaps
54308	Urethroplasty for second stage hypospadias repair (including urinary diversion); less than 3 cm
54312	Urethroplasty for second stage hypospadias repair (including urinary diversion); greater than 3 cm
54316	Urethroplasty for second stage hypospadias repair (including urinary diversion) with free skin graft obtained from site other than genitalia
54318	Urethroplasty for third stage hypospadias repair to release penis from scrotum (eg, third stage Cecil repair)

Continued on next page

Table 1 (continued). Codes used in the diagnosis and management of pediatric urologic disorders

54322	One stage distal hypospadias repair (with or without chordee or circumcision); with simple meatal advancement (eg, Magpi, V-flap)
54324	One stage distal hypospadias repair (with or without chordee or circumcision); with urethroplasty by local skin flaps (eg, flip-flap, prepucial flap)
54326	One stage distal hypospadias repair (with or without chordee or circumcision); with urethroplasty by local skin flaps and mobilization of urethra
54328	One stage distal hypospadias repair (with or without chordee or circumcision); with extensive dissection to correct chordee and urethroplasty with local skin flaps, skin graft patch, and/or island flap
54332	One stage proximal penile or penoscrotal hypospadias repair requiring extensive dissection to correct chordee and urethroplasty by use of skin graft tube and/or island flap
54336	One stage perineal hypospadias repair requiring extensive dissection to correct chordee and urethroplasty by use of skin graft tube and/or island flap
54340	Repair of hypospadias complications (ie, fistula, stricture, diverticula); by closure, incision, or excision, simple
54344	Repair of hypospadias complications (ie, fistula, stricture, diverticula); requiring mobilization of skin flaps and urethroplasty with flap or patch graft
54348	Repair of hypospadias complications (ie, fistula, stricture, diverticula); requiring extensive dissection and urethroplasty with, flap, patch or tubed graft (includes urinary diversion)
54352	Repair of hypospadias cripple requiring extensive dissection and excision of previously constructed structures including re-release of chordee and reconstruction of urethra and penis by use of local skin as grafts and island flaps and skin brought in as flaps or grafts
54360	Plastic operation on penis to correct angulation
Ureterocele	
Individuals with one or more of the following:	
ICD-9 diagnosis codes	
593.89	Other specified disorders of kidney and ureter
753.23	Congenital ureterocele
CPT procedure codes	
50660	Ureterectomy, total, ectopic ureter, combination abdominal, vaginal and/or perineal approach
51535	Cystotomy for excision, incision, or repair of ureterocele
52300	Cystourethroscopy; with resection or fulguration of orthotopic ureterocele(s), unilateral or bilateral
52301	Cystourethroscopy; with resection or fulguration of ectopic ureterocele(s), unilateral or bilateral
Posterior urethral valves	
Males with one or more of the following:	
ICD-9 diagnosis codes	
753.6	Congential atresia and stenosis of urethra and bladder neck
CPT procedure codes	
52340	Cystourethroscopy with incision, fulguration, or resection of congenital posterior urethral valves, or congenital obstructive hypertrophic mucosal folds
52400	Cystourethroscopy with incision, fulguration, or resection of congenital posterior urethral valves, or congenital obstructive hypertrophic mucosal folds (2003 and later)

[a]Include only if patient under 30 years old.

[b]Must occur with diagnosis of 550.XX or 752.XX.

[c]Include only if under 18 years old.

Table 2. Grades of vesicoureteral reflux

Grade	Description
I	Into the nondilated ureter
II	Into the pelvis and calyces without dilatation
III	Mild to moderate dilatation of the ureter, renal, pelvis, and calyces with minimal blunting of the fornices
IV	Moderate ureteral tortuosity and dilatation of the pelvis and calyces
V	Gross dilatation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity

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linked inheritance (5). There is a high parent-to-child transmission of VUR that further supports autosomal dominant transmission (5).

TREATMENT

Treatment for VUR has been predicated on the concept that the condition usually resolves spontaneously, although various factors modify the rate of resolution, including the initial grade, age at presentation, and the presence of abnormal toileting habits or bladder obstruction. In 1997, the American Urological Association Pediatric Vesicoureteral Reflux Guidelines Panel published resolution rates based on grade, age, and whether VUR is present in one ureter or both (Figures 1a and 1b). A favorable resolution rate can be predicted for children who are younger at presentation, have lower-grade VUR (grade III or less), and have unilateral VUR. Most VUR resolves within four years, but some cases resolve after five or more years of follow-up, even in the absence of interval improvement (6).

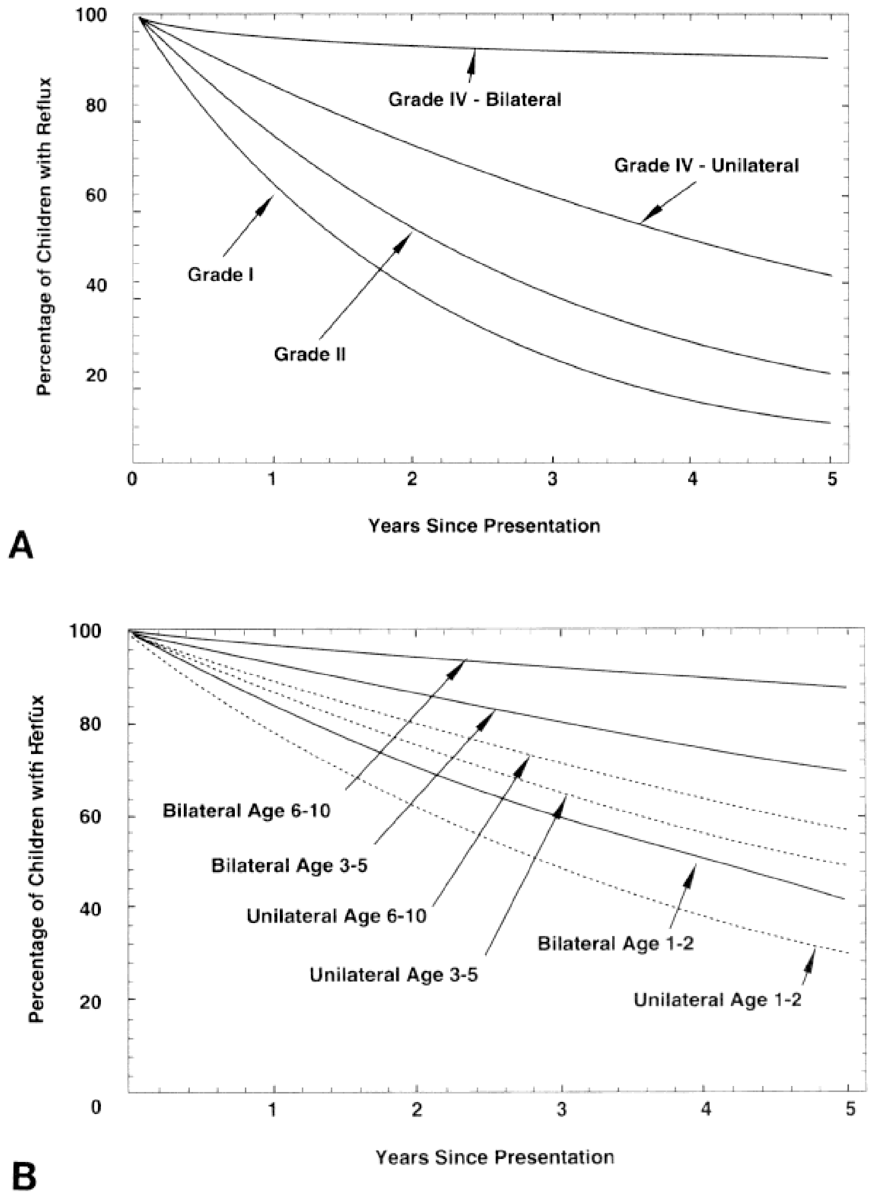
Given the natural history of VUR, initial management in the majority of cases relies on prevention of UTI, the etiology of acquired renal scars in VUR, by the daily administration of low doses of antibiotic. Extended prophylactic antibiotic therapy is generally well-tolerated in children and rarely needs to be discontinued. Breakthrough UTIs occasionally warrant surgical correction of VUR.

Differences of opinion exist regarding the indications for surgical correction of VUR, particularly since the advent of minimally invasive options. Classical indications include grade V reflux that has not resolved after a year of surveillance and acute pyelonephritis with fever and a positive urine culture. Some clinicians contend that VUR should be corrected if there is evidence of renal inflammation on renal scan. Open surgical correction of uncomplicated VUR requires general anesthesia, an abdominal incision, and a one- to three-day hospitalization. Endoscopic treatment of VUR, while also performed under general anesthesia, is an incisionless outpatient procedure in which a dextranomer/hyaluronic acid paste (Deflux™) is injected cystoscopically under the ureteral opening. The success rate for a single open-surgery procedure typically exceeds 95%. The aggregate success rate for one or more endoscopic treatments is 85% but varies by grade and upper tract abnormalities (7)

PREVALENCE AND INCIDENCE

The overall incidence of reflux in all children is estimated at approximately 10%; however, many children with VUR of low severity remain asymptomatic. Sargent performed the most comprehensive review of the prevalence of VUR in children undergoing cystography for various suspected urological indications (Table 3) (6). The data from this review demonstrate that prevalence is largely determined by the mode of presentation and whether there are any coexisting anatomical abnormalities of the urinary tract (8). Sargent found that the prevalence of VUR in children without a history of a UTI was 17.2%; others have found that up to 70% of infants who present with UTIs have VUR (8–12). The advent of high-resolution prenatal ultrasound has facilitated the identification of VUR in fetuses with hydronephrosis, where the prevalence is 37% (13).

A preponderance of the patients with VUR is male when evaluation is performed in infancy in response to prenatal hydronephrosis; in contrast, females predominate when VUR is diagnosed in the evaluation of UTIs later in development (14). Affected infant boys also often arrive with more severe degrees



Figures 1a and 1b. Persistence of vesicoureteral reflux, grades I, II, and IV (panel A) and III (panel B) 1 to 5 years after presentation.

SOURCE: Reprinted from Walsh: Campbell's Urology, 8th ed., Saunders, Copyright 2002.

Table 3. Prevalence of vesicoureteral reflux in children, by clinical indication for cystogram

Indication for cystogram	Prevalence of VUR (95% CI)	Subjects[a]	Prevalence compared with all UTI (P-value)
Normal children	9.0% (6.0–12.0)	31/344	< 0.001
All urinary tract infections	31.1% (29.8–32.4)	1,527/4914	…
Clinical pyelonephritis	31.5% (29.8–32.4)	114/362	…
Symptomatic/febrile UTI	29.0% (25.3–32.6)	170/587	…
Non-specified UTI	31.1% (29.9–32.8)	1,243/,3965	…
UTI < 1 year	31.0% (26.6–35.4)	133/429	…
UTI < 5 years	31.6% (28.9–34.3)	371/1,174	…
UTI > 5 years	30.3% (26.5–34.2)	165/544	…
Male UTI	30.0% (26.2–33.8)	166/553	…
Female UTI	33.1% (30.9–35.3)	600/1,813	…
Asymptomatic bacteriuria	29.8% (25.3–34.4)	114/382	…
All family screening	33.5% (31.3–35.6)	601/1,796	NS
Sibling with VUR	33.4% (31.1–35.7)	547/1,637	NS
Anorectal malformation	30.6% (24.4–36.7)	66/216	NS
Cloaca	60.0% (48.6–73.4)	39/65	< 0.001
Posterior urethral valve	59.6% (53.1–66.1)	130/218	< 0.001
Hypospadias	9.4% (7.9–11.0)	128/1356	< 0.001
Undescended testis	3.3% (1.6–5.0)	14/426	< 0.001
Renal anomaly	23.7% (21.3–26.9)	215/909	< 0.001
UPJO	16.1% (12.6–19.6)	69/428	< 0.001
Multicystic dysplastic	23.3% (17.5–29.1)	48/206	< 0.001
Solitary kidney	40.7% (27.6–55.0)	22/54	NS
Ectopic kidney	14.6% (7.8–24.2)	12/82	< 0.001
Duplex kidney	46.0% (37.8–54.3)	64/139	< 0.001
All prenatal hydronephrosis	20.5% (18.6–22.4)	349/1,702	< 0.001
Prenatal hydronephrosis, persistent postnatal	25.1% (21.7–28.5)	158/630	< 0.001
Prenatal hydronephrosis, normal postnatal	23.8% (14.0–36.2)	15/63	NS
Neonatal hydronephrosis on screening	18.3% (12.4–24.2)	30/164	< 0.001
Neurogenic bladder (MMC etc.)	33.3% (28.9–37.7)	146/438	NS
Voiding dysfunction	12.4% (10.6–14.2)	157/1,268	< 0.001
"Normal kidneys"	17.2% (14.4–20.1)	115/668	< 0.001
Contralateral to prenatal hydronephrosis	24.7% (15.3–36.1)	18/73	NS
Contralateral to neonatal hydronephrosis	11.8% (6.0–17.6)	14/119	< 0.001
Contralateral to UPJO	11.3% (6.4–16.1)	18/160	< 0.001
Contralateral to MCDK	19.6% (15.0–24.1)	57/291	< 0.001
Contralateral to agenesis	32.0% (15.0–53.5)	8/25	NS
Meatal stenosis	14.3% (1.8–42.8)	2/14	NS
Other organ anomalies	25.7% (12.5–43.3)	9/35	NS
Miscellaneous	54.8% (36.0–72.7)	17/31	< 0.001

…data not available.

UTI, urinary tract infection; VUR, vesicoureteral reflux; UPJO, Ureteropelvic junction obstruction; MCDK, multicystic dysplastic kidney; MMC, myelomeningocele.

[a]Subjects: number of children with vesicoureteral reflux/number of children undergoing cystogram.

Source: Reprinted from Pediatric Radiology, 30, Sargent MA, What is the normal prevalence of vesicoureteral reflux?, 587–593 Copyright 2000, with permission from Springer Science and Business Media.

Table 4. Incidence of vesicoureteral reflux severity in females, by race and age

Race and Age (yr)	Count	Incidence (95% CI)
Grades 1–2		
Black		
< 2	40	0.91 (0.82–0.99)
2–6	28	0.82 (0.70–0.95)
White		
< 2	797	0.73 (0.70–0.75)
2-6	908	0.76 (0.74–0.79)
Grade 3		
Black		
< 2	4	0.09 (0.01–0.18)
2–6	6	0.18 (0.05–0.30)
White		
< 2	239	0.22 (0.19–0.24)
2–6	247	0.21 (0.18–0.23)
Grades 4–5		
Black		
< 2	0	0
2–6	0	0
White		
< 2	58	0.05 (0.04–0.07)
2–6	38	0.03 (0.02–0.04)

Source: Reprinted from Journal of Urology, 170, Chand DH, Rhoades T, Poe SA, Kraus S, and Strife CF, Incidence and severity of vesicoureteral reflux in children related to age, gender, race and diagnosis, 1,548–1,550 Copyright 2003, with permission from American Urological Association.

of VUR, especially if diagnosed in infancy or during the postnatal workup of antenatal hydronephrosis (15). Although 85% of VUR diagnosed in older children occurs in girls, boys who present with UTIs have a higher likelihood of having the anomaly (16). Since circumcision status influences the predisposition to infection (17), this same propensity toward UTI affects the detection of VUR as well. In the International Reflux Study in Children, 10% of the VUR patients from the United States were boys, compared with 24% of those from Europe. Notably, circumcision had been performed in 62% of the American boys, but in only 5% of the European boys ($p < 0.001$) (18).

The prevalence of VUR in African American children with UTI is less than that in Caucasian children up to age ten (Table 4) (19, 20). However, once reflux is discovered, its grade and chance of spontaneous resolution are similar for female children of both races (21). Reflux is a concern because of its association with renal scarring. The associated sequelae of renal scarring include high blood pressure and renal insufficiency, the severity of both being related to the proportion of kidney tissue that is scarred. Once the association was established in the 1970s, VUR was identified as the underlying cause in up to 50% of children with high blood pressure and was reported to be present in up to 40% of children in renal failure clinics (22–25). A more contemporary series has estimated that only 6% of children with high blood pressure and renal insufficiency have VUR as the underlying cause. It is unclear whether improved recognition of VUR as a cause of renal scarring and improved treatment algorithms has influenced this rate, or whether the apparent decrease in scarring reflects changes in disease coding (26).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Data from the Healthcare Cost and Utilization Project (HCUP) reveal that for children under 18 years of age, the annual rate of inpatient hospitalizations for VUR increased slightly between 1994 and 2000, from 6.4 per 100,000 children to 7.0 per 100,000 children (Table 5), although this trend did not reach statistical significance. This increasing trend was noted in both girls and boys, with the ratio of girls to boys remaining relatively constant at 3:1. The ratio of Caucasian to Hispanic children hospitalized for VUR has also remained constant at 3:2. Data from the HCUP Kids' Inpatient Database (KID) (1997 and 2000) provide insight into the inpatient visits for each age group (< 3 years, 3 to 10 years, and 11 to 17 years) (Table 6). KID is based on a sample of pediatric discharges from US community hospitals. Because it samples only pediatric discharges, KID allows a more in-depth analysis of pediatric resource utilization than is available in the all-ages HCUP dataset. KID for 2000 includes 2,784 hospitals from 27 States. KID for 1997 includes 2,521 hospitals from 22 States. These data confirm the general trend toward more inpatient visits across all age groups, although the trend does not reach statistical significance. Regionally, the rates have been relatively constant.

Table 5. Inpatient hospital stays for vesicoureteral reflux listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	4,913	1.9 (1.5–2.4)	1.9	5,105	1.9 (1.4–2.4)	1.9	6,469	2.4 (1.3–3.6)	2.4	5,675	2.1 (1.5–2.7)	2.1
Age												
< 18	4,328	6.4 (4.8–7.8)		4,442	6.2 (4.5–8.0)		5,907	8.2 (4.2–12)		5,047	7.0 (4.9–9.1)	
18–24	173	0.7 (0.5–0.9)		155	0.6 (0.4–0.8)		165	0.7 (0.4–0.9)		203	0.8 (0.5–1.0)	
25–34	153	0.4 (0.2–0.5)		167	0.4 (0.2–0.6)		*	*		186	0.5 (0.3–0.7)	
35–54	*	*		193	0.3 (0.2–0.4)		*	*		*	*	
55+	*	*		*	*		*	*		*	*	
Gender												
Male	1,335	1.1 (0.8–1.4)	1.0	1,163	0.9 (0.7–1.1)	0.9	1,574	1.2 (0.6–1.8)	1.2	1,454	1.1 (0.8–1.4)	1.0
Female	3,578	2.8 (2.1–3.4)	2.9	3,942	2.9 (2.1–3.7)	3.0	4,895	3.6 (1.8–5.3)	3.7	4,222	3.0 (2.1–3.9)	3.2
Race/ethnicity												
White	3,279	1.8 (1.3–2.2)	1.9	2,892	1.5 (1.1–1.9)	1.7	4,075	2.1 (0.9–3.4)	2.4	3,488	1.8 (1.2–2.4)	2.0
Hispanic	402	*	1.2	483	*	1.3	574	*	1.5	520	1.6 (0.8–2.4)	1.3
Region												
Midwest	1,369	2.3 (1.5–3.0)	2.2	1,319	2.1 (1.2–3.1)	2.1	1,037	1.7 (1.1–2.2)	1.6	1,375	2.2 (1.3–3.0)	2.1
Northeast	1,070	2.1 (1.1–3.1)	2.2	988	1.9 (0.8–3.0)	2.0	2,426	*	*	877	1.7 (0.9–2.5)	1.8
South	1,751	2.0 (1.1–3.0)	2.1	2,068	2.2 (1.1–3.4)	2.3	2,316	2.5 (1.1–3.8)	2.5	1,584	1.6 (0.8–2.6)	1.7
West	722	1.3 (0.8–1.8)	1.2	730	1.2 (0.8–1.7)	1.2	691	1.2 (0.6–1.7)	1.1	1,839	*	2.8
MSA												
Rural	236	0.4 (0.2–0.6)	0.4	300	0.5 (0.3–0.7)	0.5	227	0.4 (0.2–0.5)	0.4	184	0.3 (0.2–0.4)	0.3
Urban	4,676	2.5 (1.9–3.1)	2.5	4,798	2.4 (1.7–3.0)	2.4	6,233	3.0 (1.5–4.5)	3.0	5,491	2.6 (1.8–3.4)	2.6

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 6. Inpatient hospital stays for vesicoureteral reflux listed as primary diagnosis in 2000, count, rate[a] (95% CI), percent of all hospitalizations

	1997			2000		
	Count	Rate	Percent of all hospitalizations	Count	Rate	Percent of all hospitalizations
Total[b]	6,290	8.8 (7.4–10)	0.10%	7,210	10 (8.3–12)	0.11%
Age						
0–2	2,029	17 (13–21)	0.04%	2,236	19 (15–23)	0.05%
3–10	3,698	11 (9.8–13)	0.56%	4,250	13 (11–15)	0.75%
11–17	564	2.1 (1.7–2.4)	0.06%	723	2.6 (2.0–3.1)	0.08%
Race/ethnicity						
White	…	...	…	4,678	10 (8.2–12)	0.16%
Black	…	...	…	132	1.2 (0.8–1.6)	0.02%
Hispanic	…	...	…	811	6.9 (4.7–9.2)	0.08%
Gender						
Male	1,747	4.8 (3.8–5.7)	0.05%	1,815	4.9 (4.0–5.8)	0.06%
Female	4,544	13 (11–15)	0.14%	5,395	15 (13–18)	0.17%
Region						
Midwest	1,065	6.3 (4.2–8.4)	0.07%	1,117	6.4 (3.9–9.0)	0.08%
Northeast	1,691	13 (6.0–20)	0.14%	1,694	13 (5.7–20)	0.14%
South	1,790	7.3 (4.6–10)	0.08%	2,511	10 (7.2–13)	0.11%
West	1,744	10 (7.4–13)	0.12%	1,888	11 (7.5–14)	0.13%
MSA						
Rural	189	1.2 (0.7–1.6)	0.02%	182	1.2 (0.6–1.8)	0.02%
Urban	6,101	11 (9.2–13)	0.11%	6,996	12 (10–14)	0.13%

…data not available.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian noninstitutional population under age 18.

[b]Persons of other races, missing race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database, 2000.

Table 7. Physician office visits for vesicoureteral reflux, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000			
	Count	5-Year Rate	Annualized Rate	5-Year Age-Adjusted Rate
Primary diagnosis	418,954	160 (73–247)	32	159
Any diagnosis	700,489	268 (139–396)	54	266

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 8. Visits for vesicoureteral reflux listed as primary diagnosis among children having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
					Physician Office					
Total	123	12	239	15	536	22	655	24	617	26
Age										
0–2	33	*	83	143	182	207	232	243	228	305
3–10	59	41	119	58	268	88	333	103	321	124
11–17	11	*	13	*	53	20	48	16	32	13
Gender										
Male	29	*	65	8.3	122	10	150	11	145	12
Female	94	17	174	22	414	34	505	37	472	41
Region										
Midwest	95	15	147	17	250	21	287	21	287	23
Northeast	6	*	16	*	56	28	46	28	22	*
Southeast	9	*	60	14	207	22	300	28	294	32
West	13	*	16	*	23	*	22	*	14	*
					Emergency Room					
Total	0	*	1	*	2	*	0	*	0	*
Age										
0–2	0	*	0	*	1	*	0	*	0	*
3–10	0	*	0	*	0	*	0	*	0	*
11–17	0	*	0	*	0	*	0	*	0	*
Gender										
Male	0	*	1	*	0	*	0	*	0	*
Female	0	*	0	*	2	*	0	*	0	*
Region										
Midwest	0	*	0	*	1	*	0	*	0	*
Northeast	0	*	0	*	1	*	0	*	0	*
Southeast	0	*	0	*	0	*	0	*	0	*
West	0	*	1	*	0	*	0	*	0	*
					Inpatient					
Total	32	3.0	66	4.2	74	3.0	100	3.7	66	2.8
Age										
0–2	7	*	14	*	12	*	21	*	16	*
3–10	17	*	35	17	48	16	66	20	42	16
11–17	3	*	5	*	9	*	8	*	4	*
Gender										
Male	4	*	12	*	11	*	20	*	17	*
Female	28	*	54	6.8	63	5.2	80	5.9	49	4.2
Region										
Midwest	21	*	39	4.4	33	2.8	52	3.8	35	2.8
Northeast	4	*	4	*	10	*	7	*	4	*
Southeast	1	*	19	*	28	*	36	3.3	23	*
West	6	*	4	*	3	*	5	*	4	*

Continued on next page

Table 8 (continued). Visits for vesicoureteral reflux listed as primary diagnosis among children having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	Hospital Outpatient									
Total	15	*	28	*	52	2.1	36	1.3	49	2.1
Age										
0–2	4	*	8	*	16	*	12	*	18	*
3–10	9	*	16	*	28	*	16	*	26	*
11–17	2	*	2	*	5	*	5	*	1	*
Gender										
Male	2	*	9	*	9	*	9	*	13	*
Female	13	*	19	*	43	3.5	27	*	36	3.1
Region										
Midwest	14	*	25	*	47	3.9	26	*	27	*
Northeast	0	0	0	0	2	*	2	*	1	*
Southeast	0	0	2	*	2	*	8	*	21	*
West	1	*	1	*	1	*	0	0	0	0
	Ambulatory Surgery									
Total	14	*	22	*	82	3.4	117	4.3	113	4.8
Age										
0–2	1	*	2	*	17	*	36	38	33	44
3–10	9	*	14	*	42	14	56	17	68	26
11–17	1	*	0	*	11	*	7	*	7	*
Gender										
Male	4	*	3	*	21	*	28	*	21	*
Female	10	*	19	*	61	5.0	89	6.5	92	7.9
Region										
Midwest	9	*	17	*	32	2.7	46	3.4	36	2.9
Northeast	0	*	1	*	23	*	28	*	5	*
Southeast	5	*	3	*	21	*	42	3.9	57	6.2
West	0	*	1	*	6	*	1	*	15	*

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 9. Visits for vesicoureteral reflux listed as primary diagnosis among children having Medicaid health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Physician Office	7	*	39	43	59	103	58	85	32	60
Age										
0–2	4	*	20	*	28	*	30	306	10	*
3–10	3	*	17	*	26	*	27	*	19	*
11–17	0	*	1	*	5	*	1	*	2	*
Gender										
Female	5	*	20	*	29	*	38	92	25	*
Male	2	*	19	*	30	136	20	*	7	*
Region										
Midwest	6	*	10	*	2	*	1	*	0	*
Northeast	0	*	27	*	39	110	36	88	28	*
Southeast	0	*	0	0	0	*	0	*	0	*
West	1	*	2	*	18	*	21	*	4	*
Emergency Room	0	*	0	*	0	*	2	*	0	*
Inpatient	4	*	6	*	4	*	9	*	5	*
Hospital Outpatient	0	0	2	*	2	*	1	*	18	*
Ambulatory Surgery	1	*	3	*	16	*	28	*	18	*

*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Outpatient Care

Physician Office Visits

Data from the National Ambulatory Medical Care Survey (NAMCS) indicate that during five years sampled between 1992 and 2000, 418,954 office visits (32 per 100,000 in each year) were associated with VUR as the primary diagnosis (Table 7). Tables 8 and 9 and Figures 2 and 3 present data from the Center for Healthcare Policy and Evaluation (CHCPE) on visits by children insured commercially or through Medicaid for whom VUR was listed as the primary diagnosis. The rates of visits to physicians' offices doubled during the 1990s for both commercially insured children (12 per 100,000 in 1994, 26 per 100,000 in 2002) and children covered by Medicaid (43 per 100,000 in 1996, 60 per 100,000 in 2002) (Tables 8 and 9). During this period, visit rates for children with Medicaid were higher than for those with commercial insurance. This difference is probably not explained by a greater severity of VUR among Medicaid participants. Rather, socioeconomic factors may have influenced compliance with treatment, leading to more frequent office visits for the management of complications of VUR. Among commercially insured children, the ratio of outpatient visits by girls to visits by boys was constant at 3:1 (Figure 4). This trend could not be analyzed for children with Medicaid, because Medicaid data did not meet the criteria for reliability or precision. Regional data on commercially insured children showed relatively constant rates during the years that could be evaluated (Figure 2).

Ambulatory Surgery

CHCPE data on ambulatory surgery visits by children with VUR as the primary diagnosis demonstrate a trend toward increasing outpatient surgical procedures. Overall, the rate of ambulatory surgery visits by commercially insured children rose from 3.4 per 100,000 in 1998 to 4.8 per 100,000 in 2002 (Table 8). Similar estimates are not available for children covered by Medicaid (Table 9). The increase in ambulatory surgery for VUR may represent more patients opting for Deflux™ implantation in lieu of open surgical correction and/or more repeat Deflux™ procedures. Data from the National Survey

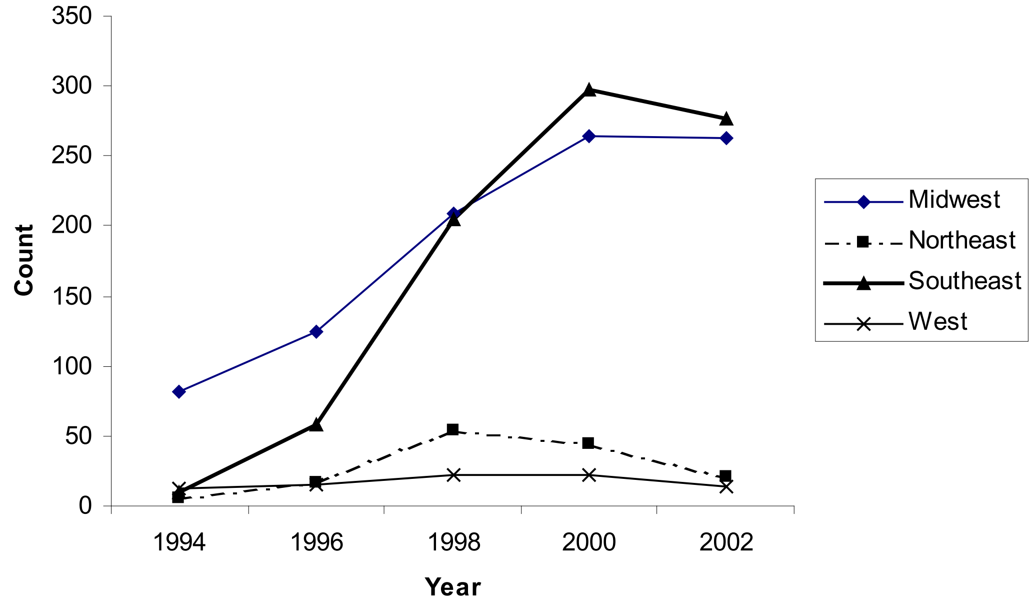


Figure 2. Physician office visits for children with vesicoureteral reflux having commercial health insurance, by region.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

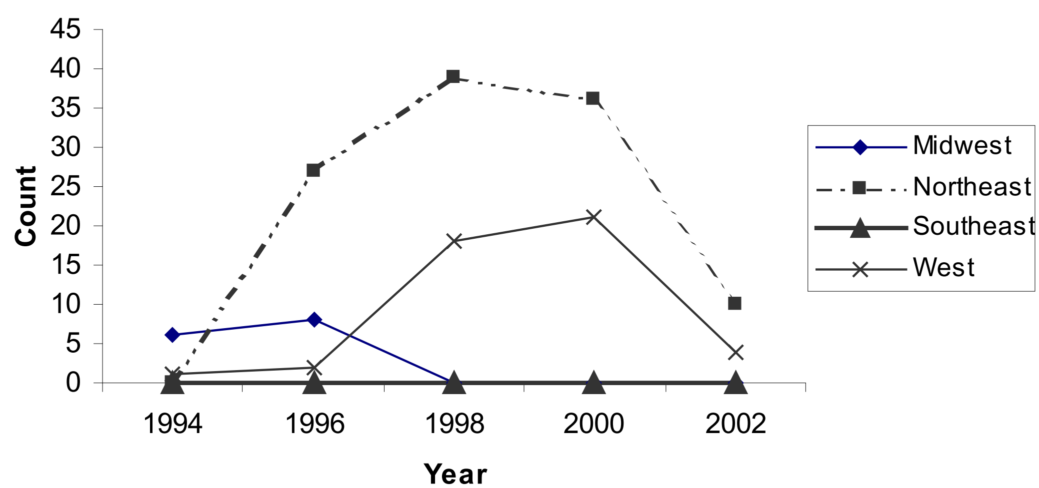


Figure 3. Physician office visits for children with vesicoureteral reflux having Medicaid health insurance, by region.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

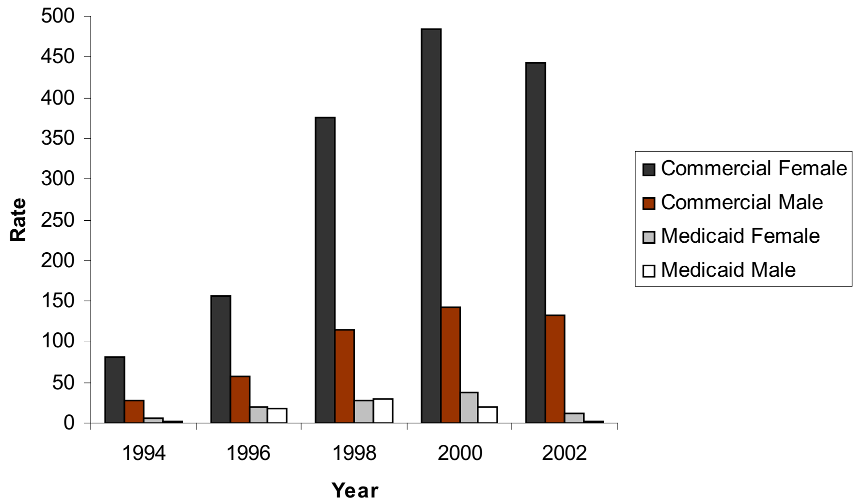


Figure 4. Physician outpatient visits for children with vesicoureteral reflux having commercial or Medicaid health insurance, by gender.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

of Ambulatory Surgery in 1994, 1995, and 1996, reflect an annualized rate of implantation of 0.6 per 100,000 children (Table 10). Approximately two-thirds of these cases were associated with procedure codes for cystoscopy, most of which predated the FDA approval of Deflux™. Few diagnostic cystoscopies are performed on children with VUR, but the authors' anecdotal review of current utilization suggests increased use of therapeutic cystoscopic procedures.

Emergency Room Care

Emergency room utilization by children with a primary diagnosis of VUR is rare, reflecting the trend toward delivery of care in physicians' offices, ambulatory surgery centers, and inpatient hospitals.

ECONOMIC IMPACT

The economic burden of VUR was estimated by combining data from several sources. The National Association of Children's Hospitals and Related Institutions (NACHRI) provided data on the mean cost of treating a child with a primary diagnosis of VUR in 1999–2003, and the HCUP Kids' Inpatient Database provided information on the number of pediatric inpatient hospitalizations for VUR in 1997 and 2000 (Table 11). The average cost per hospitalization derived from NACHRI was applied to case counts reported in KID to calculate annual national estimates for inpatient pediatric VUR expenditures by sex, age, and region. NACHRI data represent practices at specific children hospitals and thus may differ from practices at community hospitals.

In 2000, total expenditures for inpatient pediatric VUR amounted to $47 million, an increase of over $10 million since 1997 (Table 11). Expenditures increased between 1997 and 2000 for all ages and regions and for both sexes. The increase between 1997 and 2000 was particularly large in the South, where expenditures grew by 56%. Inpatient pediatric VUR costs were greatest among three- to ten-year-olds, primarily because of the large number of cases in this group. Inpatient cases of VUR were most costly among 11- to 17-year-olds, totaling $7,699 in 2000. The cost of an inpatient VUR case was slightly higher for males than for females, but there were almost three times as many female cases, leading to higher overall costs for female patients. High spending in the South was the result of a moderate cost per case but a high number of cases, while expenditures in the Northeast reflected a high cost per case and only a moderate number of

Table 10. Ambulatory surgery visits for vesicoureteral reflux listed as primary diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), annualized rate[b], rate per 100,000 visit[c] (95% CI)

	1994–1996			
	Count	3-Year Rate	Annualized Rate	3-YearRate per 100,000 visits
Total	4,928	1.9 (1.1–2.7)	0.6	100,000 (57,082–142,918)
with associated cystoscopy (ICD-9 57.32)	3,387	1.3 (0.6–2.0)	0.4	66,730 (33,868–103,592)

[a]Rate per 100,000 is based on 1994–1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Rate per 100,000 is based on estimated number of visits for vesicoureteral reflux in NSAS 1994–1996.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

cases. Costs were low in the Midwest because of the relatively small number of cases there.

The economic impact of inpatient treatment of pediatric VUR is considerable (Tables 11 and 12). If other service types, such as pharmaceuticals and outpatient and ambulatory services, were taken into account, the observed impact of this condition would certainly be greater. Importantly, the costs of prophylactic medical therapy and emerging therapies such as Deflux™ are not accounted for in this estimate. Furthermore, indirect economic costs such as work loss to parents of pediatric VUR cases were not taken into account, causing an even greater underestimation of the true costs associated with the condition.

RECOMMENDATIONS

- The paucity of data on Medicaid-insured children with VUR should stimulate further research into identifying potential inequities in care of children with VUR who are of lower socioeconomic status.
- Studies should be performed on cost-effective strategies for evaluation of children of various ages who present with UTI.
- Future studies should include cost analysis of various treatment strategies as an outcome, in addition to therapy-related success and complication rates.

Table 11. Cost per child admitted with vesicoureteral reflux[a] listed as primary diagnosis, total number of cases, estimated total costs

	1997			2000		
	Cost per Child	Number of Cases	Estimated Total Cost	Cost per Child	Number of Cases	Estimated Total Cost
Total	$5,892	6,291	$37,061,475	$6,551	7,210	$47,230,671
Age						
0–2	$6,008	2,029	$12,188,151	$6,680	2,236	$14,937,974
3–10	$5,700	3,698	$21,081,036	$6,338	4,250	$26,938,748
11–17	$6,925	564	$3,902,218	$7,699	723	$5,568,983
Gender						
Female	$5,617	4,544	$25,523,411	$6,246	5,395	$33,694,918
Male	$6,726	1,747	$11,749,518	$7,479	1,815	$13,574,641
Region						
Midwest	$6,046	1,065	$6,438,820	$6,722	1,117	$7,510,553
Northeast	$7,607	1,691	$12,864,860	$8,458	1,694	$14,324,996
South	$5,451	1,790	$9,757,451	$6,060	2,511	$15,218,755
West	$5,141	1,744	$8,965,905	$5,716	1,888	$10,790,123

[a]Using ICD-9 codes 593.70 (vesicoureteral reflux, unspecified or without reflux nephropathy), 593.71 (vesicoureteral reflux with reflux nephropathy unilateral), 593.72 (vesicoureteral reflux with reflux nephropathy bilateral), and 593.73 (other vesicoureteral reflux with reflux nephropathy NOS).

SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database, 2000 and National Association of Children's Hospitals and Related Institutions, 1999–2003.

Table 12. Trends in mean inpatient length of stay (LOS) and cost per child (in $) admitted with vesicoureteral reflux[a], 1999–2003

	Count	Percent	LOS	Mean Cost
Primary diagnosis				
Total	14,629		2.7	$6,852
Age				
0–2	4,424	30%	2.9	$6,987
3–10	9,058	62%	2.6	$6,629
11–17	1,090	7%	3.1	$8,053
18+	57	0%	3.3	$8,768
Race/ethnicity				
White	10,744	73%	2.6	$6,792
Black	313	2%	3.5	$8,395
Asian	161	1%	2.9	$7,682
Hispanic	1,338	9%	3.0	$6,741
N. American Native	28	0%	2.8	$6,968
Missing	797	5%	2.6	$6,567
Other	1,248	9%	2.7	$7,170
Gender*				
Female	11,012	75%	2.6	$6,533
Male	3,616	25%	3.1	$7,823
Region				
Midwest	4,403	30%	2.7	$7,031
Northeast	2,132	15%	3.3	$8,847
South	5,628	38%	2.6	$6,339
West	2,466	17%	2.4	$5,979
Any diagnosis				
Total	28,777		5.5	$12,230
Age				
0–2	13,931	48%	7.7	$16,476
3–10	12,641	44%	3.2	$7,654
11–17	2,061	7%	4.7	$11,579
18+	144	1%	5.0	$12,479
Race/ethnicity				
White	19,664	68%	5.1	$11,541
Black	1,411	5%	9.0	$17,896
Asian	389	1%	6.2	$13,021
Hispanic	3,610	13%	5.9	$12,263
N. American Native	69	0%	10.6	$22,731
Missing	1,406	5%	5.7	$12,208
Other	2,228	8%	6.1	$14,213
Gender*				
Female	19,075	66%	4.6	$10,139
Male	9,700	34%	7.3	$16,341
Region				
Midwest	9,062	31%	5.6	$12,534
Northeast	3,285	11%	4.8	$11,717
South	11,757	41%	5.7	$12,113
West	4,673	16%	5.3	$12,293

*Three cases, (1 primary, 2 any) not coded for gender.

[a]Using ICD-9 codes 593.70 (vesicoureteral reflux, unspecified or without reflux nephropathy), 593.71 (vesicoureteral reflux with reflux nephropathy unilateral), 593.72 (vesicoureteral reflux with reflux nephropathy bilateral), and 593.73 (other vesicoureteral reflux with reflux nephropathy NOS).

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2003.

UNDESCENDED TESTIS

INTRODUCTION

Cryptorchidism is derived from two Greek words: *kryptos*, meaning hidden, and *orchis*, meaning testis. Any testis that is not within the scrotum is referred to as cryptorchid, even if it is palpable within the inguinal canal. A cryptorchid testis is also commonly referred to as an *undescended testis* (UDT). The ectopic, absent, and ascending testis are all part of a spectrum representing maldescent of the testis into the normal scrotal position. Analyses for this section are based on the ICD-9 and CPT codes for undescended testes listed in Table 1.

DEFINITION AND DIAGNOSIS

There is no uniform or standard classification of cryptorchidism. In broad terms, the undescended testis can be thought of as either congenital or acquired. The congenitally undescended testis is usually diagnosed at an earlier age and is often located proximal to the external inguinal ring, in association with an open processus vaginalis and epididymal deformities.

The congenital undescended testis can be further classified as palpable or impalpable. The palpable testis is typically either intracanicular (palpable between the internal and the external inguinal rings) or extracanicular (palpable beyond the external inguinal ring). An impalpable testis may be intra-abdominal, absent, or atrophic. A so-called vanishing testis refers to the condition of no identifiable testicular tissue but the intraoperative finding of blind-ending testicular vessels and vas deferens.

The acquired undescended testis refers to testicular ascent wherein a previously-scrotal testis ascends to an extrascrotal position during normal growth and development. The acquired undescended testis usually presents later in childhood and is often identified distal to the external ring and associated with a small hernia sac.

The diagnosis of cryptorchidism is established by physical examination that determines whether the testis is palpable or impalpable. No imaging is necessary for the palpable undescended testis. Some have advocated using ultrasonography or magnetic resonance imaging (MRI) to locate an impalpable testis. MRI is considered the single best imaging method and has an accuracy of 94% in locating UDT (27). However, diagnostic laparoscopy is the most reliable and accurate means for evaluating patients with impalpable testes.

Table 13. Prevalence of cryptorchidism, by birth weight

Weight	%
≤ 2000 gm	7.7%
2000–2499 gm	2.5%
≥ 2500 gm	1.4%

SOURCE: Adapted from Journal of Urology, 170, Barthold JS, Gonzalez R, The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy, 2,396–2,401, Copyright 2003, with permission from American Urological Association.

RISK FACTORS

Gestational age, closely associated with birth weight, has been strongly associated with the likelihood of identifying cryptorchidism (Table 13 and Figure 5) (28). Race does not appear to be a factor, although there does appear to be a genetic component to UDT. Approximately 14% of boys with UDT have some family history in which other males are affected (29). Male siblings of boys with UDT have a 7% to 10% chance of cryptorchidism (30).

TREATMENT

The standard therapy for cryptorchidism is surgical orchiopexy to move the testis into the scrotum. The recommended age for this surgery is at one year, but this has changed dramatically over the years (28).

Hormonal therapy, though not FDA-approved, has also been used, but this approach is based on evidence from a few trials with small sample sizes and risks of bias (31). Medical therapies include exogenous hCG-intramuscular and exogenous gonadotropin releasing hormone (GnRH) or intranasal luteinizing hormone-releasing hormone (LHRH). The mechanism of action is to increase serum testosterone by stimulation of the hypothalamic-pituitary-gonadal axis.

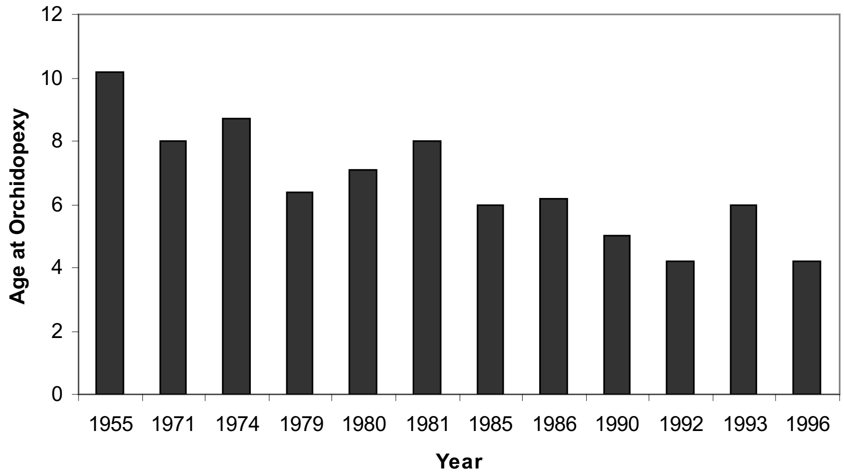


Figure 5. Mean or median age at orchiopexy in selected large cryptorchidism series.

SOURCE: Adapted from Journal of Urology, 170, Barthold JS, Gonzalez R, The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy, 2,396–2,401, Copyright 2003, with permission from American Urological Association.

PREVALENCE AND INCIDENCE

Cryptorchidism affects 3% of full-term male newborns. It is the most common genital anomaly identified at birth in males, and it has not increased in the past few decades. Between 70% and 77% of undescended testes will descend spontaneously by three months of age. By one year of age, the incidence of cryptorchidism declines to about 1% and remains constant. Recent data indicate that spontaneous descent beyond six months of age is rare (32).

Table 14. Physician office visits for undescended testes listed as primary diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000				
	Count	5-Year Rate		Annualized Rate	5-Year Age-Adjusted Rate
Total[c]	611,647	480	(288–671)	96	476
Age					
< 18	534,144	1,492	(838–2,146)	298	
18+	*	*		*	
Race/ethnicity					
White	*	*		*	*
Other	*	*		*	*
MSA					
MSA	583,235	599	(351–847)	120	589
Non-MSA	*	*		*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[c]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

According to NAMCS data, between 1992 and 2000, there were 611,647 physician office visits (96 per 100,000 in each year) for UDT listed as the primary diagnosis (Table 14). The overwhelming majority of the patients were under 18 years of age.

Data from the National Survey of Ambulatory Surgery indicate an annualized rate of 18 cases per 100,000 in 1994–1996 (Table 15); the rate remained relatively constant during these three years. Although orchiopexy rates are highest in children 0–2 years old, as recommended, a substantial minority of these procedures were done in children 3–10 years old. Geographic variation was noted, with higher ambulatory surgery rates in the Northeast and Midwest than in the South and West.

ECONOMIC IMPACT

The consequences of cryptorchidism include neoplasia and infertility. There is a 15- to 40-fold increased risk for testicular malignancy (usually seminoma) among men with a history of cryptorchidism. From 3% to 10% of testicular tumors arise from UDT. The incidence of germ cell tumor in men with formerly cryptorchid is one in 2,550, whereas in the general population it is one in 100,000.

Infertility is also a possible consequence of cryptorchidism, because spermatogenesis is impaired at core body temperature, which is four to five degrees warmer than the temperature in the scrotum. Early surgical relocation of the testis into the scrotum is sometimes undertaken to reduce the risk of infertility.

NACHRI and KID data on cryptorchidism are too sparse to provide insights into its downstream economic costs.

CONCLUSIONS

Cryptorchidism affects 3% of full-term male infants. However 50% to 77% of the undescended testes will spontaneously descend, leaving an incidence of 1% at six months of age. Those that do not descend require surgical intervention. Virtually all orchiopexies are outpatient surgical procedures with high success rates. Long-term consequences include increased risk of neoplasia and infertility.

RECOMMENDATIONS

Longitudinal studies are needed to determine whether earlier intervention, such as orchiopexy, reduces the risk of infertility or alters that of neoplasia and to quantify the economic burden associated with these conditions.

Table 15. Ambulatory surgery visits for undescended testes listed as primary diagnosis, 1994–1996 (merged and by year), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996				1994			1995			1996		
	Count	3-Year Rate	Annualized Rate	3-Year Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total	69,731	55 (47–63)	18	55	24,247	20 (15–25)	20	18,781	15 (11–18)	15	26,703	21 (16–26)	21
Age													
0–2	25,907	422 (329–515)	141		8,622	141 (89–192)		8,581	139 (78–201)		8,704	142 (96–189)	
3–10	31,853	196 (153–239)	65		11,842	74 (45–104)		6,668	41 (28–54)		13,343	81 (53–109)	
11–17	5,782	43 (26–60)	14		*	*		*	*		*	*	
18+	*	*	*		*	*		*	*		*	*	
Region													
Northeast	17,172	69 (46–92)	23	72	7,325	*	31	4,500	*	19	5,347	22 (13–30)	22
Midwest	17,806	60 (44–76)	20	59	5,910	20 (10–30)	20	5,899	20 (10–29)	20	5,997	20 (12–28)	20
South	21,593	50 (37–62)	17	49	5,974	14 (9.4–20)	15	4,656	11 (6.9–14)	11	10,963	25 (14–35)	25
West	13,160	46 (31–61)	15	45	5,038	18 (8.6–28)	17	3,726	13 (5.5–21)	12	4,396	15 (6.7–24)	15

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

HYPOSPADIAS

DEFINITION AND DIAGNOSIS

Hypospadias is an abnormally located opening of the urethral meatus anywhere along the ventral aspect of the penis from the glans to the perineum (Figure 6). It may be associated with an abnormal distribution of foreskin and an abnormal ventral curvature of the penis (chordee). Distal defects (glanular, coronal, and subcoronal) constitute 50% to 75% of hypospadias. In the majority of cases, diagnosis is easily made on visual inspection; however, in milder forms, the abnormal opening may be missed. Various classification systems have been created to describe the severity of hypospadias. Moreover, in many of the datasets analyzed for this compendium, children are subdivided into infants (less than 3 years of age), older children (3 to 10 years of age), and adolescents (11 to 17 years of age). Analyses for this chapter are based on the ICD-9 and CPT codes defining hypospadias and hypospadias-related procedures listed in Table 1.

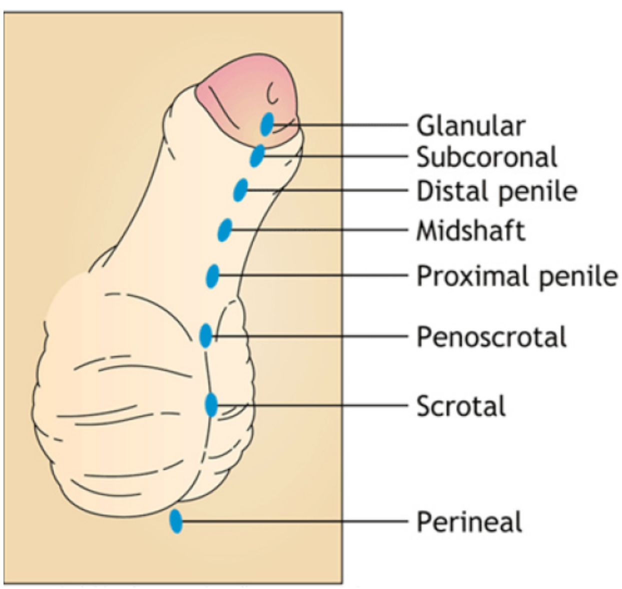


Figure 6. Types of hypospadias.

SOURCE: Reprinted from Walsh: Campbell's Urology, 8th ed., Saunders, Copyright 2002.

RISK FACTORS

Hypospadias is thought to result from incomplete closure of the tissue on the undersurface of the penis that embryologically is destined to become the urethra (33). An inherent endocrine, enzymatic, or tissue defect, environmental endocrine disruptors, and developmental arrest have all been implicated as causes of hypospadias. Inherent defects include impaired testosterone biosynthesis (34), 5-alpha-reductase type 2 gene mutations (35), and androgen receptor mutations (36).

Other risk factors for hypospadias include advanced maternal age (36); paternal risk factors, such as a history of undescended testes and varicoceles (37); prematurity (37, 38); low birth weight (38); and monozygotic-twin gestation (33).

Racial/ethnic risk factors have been proposed to explain an increased incidence of hypospadias in Caucasians. For example, maternal serum testosterone values during early pregnancy have been shown to be 48% greater in African American women than in Caucasian women (39). Additional support for ethnic differences in androgenic exposure during early gestation comes from similar analysis of serum testosterone levels in Hispanic women, whose infants have an incidence of hypospadias between that of Caucasians and that of African Americans.

TREATMENT

At least 200 surgical procedures have been used to correct hypospadias of varying severity. However, the universal concerns of hypospadias repair have always included correction of penile curvature, placement of the urethral opening at the tip of the penis, creation of a cosmetically pleasing glans penis, and complete coverage of the surgical repair with local skin. For hypospadias of low to moderate complexity, correction can be performed at the age of six months in a single outpatient procedure under general anesthesia, with excellent results. More-severe cases may require a two-stage repair at six and twelve months of age. After urethral reconstruction, the infant is discharged with a temporary urinary catheter and may be prescribed oral antibiotics and anticholinergics. Follow-up care is provided in the office setting, where the dressing and urinary catheter are removed. Complications, such

Table 16. Incidence of hypospadias, by race/ethnicity

Race/ethnicity	Male Live Births	Hypospadias	Incidence
White	68,444	520	0.8%
Black	18,984	120	0.6%
Asian	1,761	9	0.5%
N. American Native	175	1	0.6%
Unknown	9,846	59	0.6%
Total	99,210	709	0.7%

SOURCE: Reprinted from Urology, 57, Gallentine ML, Morey AF, and Thompson, IM, Hypospadias: A contemporary epidemiologic assessment, 788–790, Copyright 2001, with permission from Elsevier.

as bleeding, narrowing of the urethra (i.e., meatal stenosis, stricture), formation of urethrocutaneous fistula, infection, and urethral diverticula, may occur but generally do not require emergent reoperation.

PREVALENCE AND INCIDENCE

The classically reported incidence of hypospadias is 0.3% (40), but recent evidence suggests that worldwide incidence is increasing and may have risen to 0.8% (36) of Caucasian newborn males and 0.4% (41–44) of non-Caucasians. These reports are principally from industrialized Western countries, so environmental toxins may play an etiologic role (41, 43–49). Paulozzi, Erickson, and Jackson reported data from two surveillance systems in the United States that demonstrated a near doubling of the rate of hypospadias between 1968 and 1993, with an overall annual rate of increase of 1.4% (41). Analyzed by race, the overall rate of increase was 2.9% per year among Caucasians and 5.7% per year among non-Caucasians (41). Additionally, the rate of severe hypospadias increased three to fivefold (41). Gallantine, Morey, and Thompson reported a contemporary incidence of hypospadias of 0.7% among 99,210 live male births (Table 16) (50). Although no statistically significant racial difference in the incidence of hypospadias was noted, there was a trend toward a greater incidence in Caucasians (50). The authors surmised that the incidence of hypospadias was too low to detect racial group differences. Taken together, these findings strongly indicate an increasing incidence of hypospadias in the United States affecting all racial groups, although non-Caucasians have experienced both greater incidence and greater severity. More-recent data indicate that the rate of increase may be leveling off (51).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

According to HCUP data, annual inpatient hospitalizations for hypospadias decreased by 75% between 1994 and 2000, from 2,669 (2.2 per 100,000 children) to 849 (0.6 per 100,000 children) (Table 17). This declining trend was noted across all racial/ethnic groups from which data were collected. Age-adjusted rates of inpatient hospitalization did not meet the standard for reliability for African Americans and Hispanics, which limited the analysis of utilization trends in recent years for these two groups.

Additional data from the HCUP Kids' Inpatient Database in 1997 and 2000 demonstrate that the majority of inpatient hospitalizations for hypospadias occur in children under three years of age (Table 18). In fact, inpatient hospitalizations were ten times more likely to occur in these children than in those aged three to ten years. This is consistent with the common surgical practice of performing correction in younger children, ideally within the first year of life. Despite the trend toward referring infants less than one year of age for hypospadias repair, some of the children hospitalized for hypospadias in 1997 were as old as 17. Many of the admissions of older children may have been to treat complications of earlier hypospadias repairs or may have been late referrals of children who should have undergone correction earlier. The proportion of visits for children hospitalized in 2000 for hypospadias repair who were older than three rose to 28% (391 of 1,385), which may reflect an overall trend toward performing more infant hypospadias procedures as outpatient surgery. Interestingly, there was a small trend towards an increase in the rate of inpatient stays for hypospadias repair in children aged

Table 17. Inpatient hospital stays for hypospadias listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	2,669	2.2 (1.4–3.0)	2.2	1,955	1.5 (0.8–2.2)	1.5	1,600	1.2 (0.6–1.9)	1.2	849	0.6 (0.4–0.9)	0.6
Age												
< 18	2,558	7.3 (4.6–10)		1,846	5.1 (2.7–7.4)		1,472	4.0 (1.8–6.2)		686	1.8 (1.0–2.7)	
18+	*	*		*	*		129	*		*	*	
Race/ethnicity												
White	1,402	1.5 (0.8–2.3)	1.7	1,064	1.1 (0.5–1.8)	1.3	821	*	1.0	371	0.4 (0.2–0.5)	0.4
Black	424	2.9 (1.6–4.1)	2.2	308	2.0 (0.8–3.2)	1.5	197	*	1.0	*	*	*
Hispanic	231	1.8 (0.8–2.7)	1.4	245	*	1.4	*	*	*	*	*	*
Region												
Midwest	516	1.8 (0.8–2.7)	1.7	164	*	*	*	*	*	*	*	*
Northeast	684	*	*	667	*	*	913	*	*	177	*	*
South	958	*	*	711	*	*	207	0.4 (0.2–0.7)	0.5	187	*	*
West	511	*	*	413	*	*	324	*	*	367	*	*
MSA												
Rural	*	*	*	*	*	*	*	*	*	*	*	*
Urban	2,602	2.8 1.8–3.9)	2.8	1,898	1.9 (1.0–2.8)	1.9	1,572	1.6 (0.7–2.4)	1.6	817	0.8 (0.4–1.1)	0.8

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 18. Inpatient hospital stays for hypospadias listed as primary diagnosis in 1997 and 2000, count, rate[a] (95% CI), age-adjusted rate[b], percent of all hospitalizations

	1997					2000			
	Count	Rate		Age-Adjusted Rate	Percent of all hospitalizations	Count	Rate		Percent of all hospitalizations
Total[c]	1,889	5.2	(3.6–6.7)	5.1	0.06%	1,385	3.7	(2.5–5.0)	0.04%
Age									
0–2	1,421	24	(16–31)		0.06%	993	17	(11–22)	0.04%
3–10	385	2.3	(1.6–3.1)		0.10%	277	1.6	(0.9–2.4)	0.09%
11–17	82	0.6	(0.3–0.9)		0.02%	114	0.8	(0.4–1.1)	0.03%
Race/ethnicity									
White	954	4.0	(2.7–5.4)	4.1	0.07%	643	2.8	(1.8–3.7)	0.04%
Black	169	3.0	(1.5–4.5)	3.1	0.04%	132	2.3	(1.4–3.3)	0.03%
Hispanic	274	*		4.2	0.07%	200	*		0.04%
Region									
Midwest	149	1.7	(0.9–2.6)	1.6	0.02%	140	*		0.02%
Northeast	706	10	(5.6–15)	11.0	0.11%	463	7.0	(3.5–10)	0.08%
South	388	*		3.1	0.03%	282	2.2	(1.0–3.5)	0.02%
West	646	*		7.2	0.08%	499	*		0.06%
MSA									
Rural	44	*		*	0.01%	25	*		0.01%
Urban	1,845	6.6	(4.6–8.5)	6.3	0.07%	1,357	4.7	(3.1–6.2)	0.05%

*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area.
[a]Rate per 100,000 is based on 1997 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian noninstitutional population under age 18.
[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[c]Persons of other races, missing race and ethnicity, and missing MSA are included in the totals.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database, 1997 and 2000.

11 to 17, from 0.6 per 100,000 in 1997 to 0.8 per 100,000 in 2000, which although not statististically significant raises the question of whether more complications are being managed in older children.

Data on inpatient hospital stays for children insured commercially or through Medicaid were insufficient to generate reliable estimates of utilization by insurer type.

Outpatient Care

Tables 19 and 20 present CHCPE data regarding outpatient care of children with commercial and Medicaid insurance, respectively.

Physician Office Visits

In both commercially- and Medicaid-insured boys, the most common site of care was physicians' offices (Tables 19 and 20). The rate of physician office visits for hypospadias by commercially insured boys under three years of age increased, from 429 per 100,000 in 1994 to 655 per 100,000 in 2002. Data from Medicaid for 1994 and 2002 were less reliable; however, they suggest stable utilization of physician office visits at 161 per 100,000 throughout the mid to late 1990s, decreasing to 118 per 100,000 in subsequent years.

Ambulatory Surgery

Since hypospadias is a disease that must be treated surgically in most cases, it is not surprising that almost as many visits occurred in ambulatory surgery centers as in the office setting. Data from commercially-insured boys under three years of age revealed a 1.5-fold overall increase in the rate of hypospadias surgery, from 321 per 100,000 in 1994 to 468 per 100,000 in 2002, reflecting the known increase in hypospadias incidence in the United States during the late 1990s (Tables 19 and 20). Similar estimates could not be obtained for Medicaid-insured boys. Data from

Table 19. Visits for hyspospadias listed as primary diagnosis among children having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Physician Office	124	24	215	27	329	27	387	28	335	28
Age										
0–2	88	429	143	483	224	497	280	583	252	655
3–10	19	*	43	41	70	45	73	44	57	43
11–17	7	*	14	*	13	*	13	*	15	*
Region										
Midwest	84	27	123	28	147	25	168	25	173	27
Northeast	11	*	17	*	41	41	20	*	11	*
Southeast	14	*	56	26	112	24	173	32	141	31
West	15	*	19	*	29	*	26	*	10	*
Emergency Room	0	*	1	*	1	*	4	*	1	*
Inpatient	3	*	6	*	2	*	7	*	6	*
Hospital Outpatient	1	*	15	*	19	*	18	*	21	*
Ambulatory Surgery	86	17	127	16	187	15	262	19	256	22
Age										
< 3	66	321	82	277	134	297	189	387	180	468
3–10	10	*	33	31	36	23	48	29	50	38
11–17	4	*	5	*	8	*	11	*	12	*
Region										
Midwest	55	18	71	16	89	15	126	19	123	19
Northeast	14	*	13	*	18	*	11	*	9	*
Southeast	9	*	28	*	63	13	106	19	112	24
West	8	*	15	*	17	*	19	*	12	*

*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 20. Visits for hypospadias listed as primary diagnosis among children having Medicaid health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Physician Office	19	*	52	161	36	163	32	118	21	*
Age										
0–2	15	*	37	537	29	*	21	*	15	*
3–10	4	*	12	*	5	*	10	*	4	*
11–17	0	*	3	*	2	*	1	*	2	*
Region										
Midwest	18	*	18	*	0	*	0	*	0	*
Northeast	0	*	21	*	19	*	16	*	14	*
Southeast	0	*	0	*	0	*	0	*	0	*
West	1	*	13	*	17	*	16	*	7	*
Emergency Room	0	*	0	*	0	*	0	*	1	*
Inpatient	1	*	1	*	1	*	0	*	0	*
Hospital Outpatient	0	0	0	0	0	0	0	0	6	*
Ambulatory Surgery	10	*	27	*	21	*	21	*	18	*

*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 21. Ambulatory surgery visits for hypospadias listed as any diagnosis, 1994–1996 (merged and by year), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996		
	Count	3- Year Rate	Annualized Rate
Total	39,631	31 (25–38)	10
Age			
0–2	26,381	430 (333–527)	143
3–10	7,296	45 (22–68)	15
11–17	*	*	*
18+	*	*	*
Region			
Midwest	13,480	45 (28–62)	15
Northeast	9,706	39 (19–59)	13
South	8,345	19 (13–25)	6.3
West	8,100	28 (16–40)	9.3

	1994			1995			1996		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total	16,171	13 (8.2–18)	13	10,465	8.2 (5.0–11)	8.2	12,995	10 (7.2–13)	10
Age									
0–2	9,032	147 (84–211)		7,700	125 (75–176)		9,649	158 (104–211)	
3–10	*	*		*	*		*	*	
11–17	*	*		*	*		*	*	
18+	*	*		*	*		*	*	
Region									
Midwest	*	*		*	*		*	*	
Northeast	*	*		*	*		*	*	
South	*	*		*	*		*	*	
West	*	*		*	*		*	*	

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Table 22. Hospital outpatient visits for hypospadias listed as any diagnosis, 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000			
	Count	4- Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total	69,457	54 (30–77)	14	54

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

the National Survey of Ambulatory Surgery showed that during 1994, 1995, and 1996, more than 39,000 visits to ambulatory surgery centers were associated with hypospadias repair, 67% in infants and the remainder in children from three to ten years of age (Table 21). Age-adjusted rates of visits were highest in the Northeast and Midwest—on average, 1.5 to 2.2 times the rates on the West and South, respectively.

Hospital Outpatient Visits

Data from the National Hospital Ambulatory Medical Care Survey indicate an average annualized rate of hospital outpatient visits for hypospadias of 14 per 100,000 children (Table 22). CHCPE data on visits by children insured commercially or through Medicaid for whom hypospadias was listed as a primary diagnosis were inconclusive, since the majority of hypospadias is evaluated on a non-emergent basis (Tables 19 and 20).

Table 23. Mean inpatient cost per child[a] admitted with hypospadias listed as primary diagnosis, 1999–2001 (95% CI)

	Count	Mean Cost
Total	765	\$5,389 (5,170–5,609)
Age		
0–2	551	\$5,194 (4,925–5,463)
3–10	154	\$5,858 (5,414–6,303)
11–17	47	\$5,716 (5,136–6,296)
18–29	13	\$6,914 (4,546–9,282)
Race/ethnicity		
White	453	\$5,366 (5,090–5,642)
Black	83	\$5,802 (4,925–6,679)
Asian	25	\$4,871 (3,889–5,852)
Hispanic	92	\$5,416 (4,822-6,011)
Missing	31	\$6,420 (5,425–7,415)
Other	81	\$4,832 (4,138–5,526)
N. American Native	0	
Region		
Midwest	126	\$5,330 (4,802–5,858)
Northeast	155	\$5,834 (5,309–6,360)
South	233	\$5,582 (5,168–5,996)
West	251	\$4,966 (4,610–5,321)

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

ECONOMIC IMPACT

The average cost per hospitalization for hypospadias exceeded \$5,389, with costs per case being higher in children three years of age and older, although there were more cases for children under three years of age (Table 23). The cost per case of hypospadias was higher in the Northeast and the South than in other regions. A total of 1,385 cases of hypospadias were observed in 2000 in the HCUP Kids' Inpatient Database data (Table 18), incurring an estimated \$8 million in national inpatient expenditures.

RECOMMENDATIONS

The management of patients with hypospadias is primarily surgical, with most pediatric urologists employing a limited number of surgical techniques. Surgical outcomes and the cost of hypospadias management are likely to be only nominally improved by cost-reduction strategies. Significant effort should be placed on identification of environmental risk factors, since prevention of hypospadias by mitigating exposure to endocrine disruptors is the best approach to reducing medical care expenditures for hypospadias treatment in the United States.

URETEROCELE

DEFINITION AND DIAGNOSIS

Ureteroceles are cyst-like dilatations of the terminal ureter. Several classification systems have been used in an effort to reflect the position of the ureterocele and the ureteric opening, the presence of obstruction and renal parenchymal abnormalities, and distortion of the bladder outlet. Each of these features poses management dilemmas and may affect renal function and urinary continence. In routine clinical practice, ureteroceles are described as *intravesical* (within the bladder) or *extravesical* (outside the bladder), with additional comment made as to the presence or absence of obstruction to urine flow. Ureteroceles may be associated with a kidney that is drained by either one ureter (*single system*) or two ureters (*duplex system*). When ureteroceles are associated with duplex systems, they always emanate from the ureter that drains the upper portion (*pole*) of the kidney. The ureter from the lower pole of the affected kidney may be normal or associated with vesicoureteral reflux.

The advent of routine prenatal screening ultrasonography has facilitated the detection of many causes of upper urinary tract dilatation (*hydronephrosis*). Ureteroceles are among the most prevalent diagnoses associated with this condition. The postnatal evaluation includes confirmatory renal and bladder ultrasonography, contrast VCUG, and at times, nuclear renal scintigraphy. Each component of the evaluation paradigm affords the clinician key information with which to direct therapy. While prenatal screening ultrasonography may suggest the presence of a ureterocele by demonstrating a duplication abnormality with isolated hydronephrosis, postnatal ultrasonography is indicated to confirm the anatomical abnormality and to provide a baseline assessment from which to monitor the natural history of the disease and the outcome of any intervention. VCUG is performed to determine whether vesicoureteral reflux is associated with the ureter draining the lower pole of a duplicated collecting system. Finally, renal scintigraphy provides useful information for surgical decision making regarding the renal function.

Postnatal diagnosis is made in the context of UTI, which stimulates evaluation of the infant or child for an underlying urinary tract abnormality, or in the context of bladder outlet obstruction. Analyses in this section are based ICD-9 and CPT codes defining ureteroceles and related procedures listed in Table 1.

RISK FACTORS

Various theories have been proposed to account for ureterocele formation, although the exact etiology remains unclear. These theories include failure of the normal dissolution of a membrane covering the ureteric opening (52), abnormal development of the smooth muscle layer of the terminal ureter (53–55), and abnormal widening of the terminal portion of the ureter during bladder development (56). No genetic or environmental risk factors for ureteroceles have been identified.

TREATMENT

The treatment of ureteroceles is predicated on preservation of renal function. The evaluation paradigm should provide information on whether the ureterocele is associated with a single or double system, the presence of associated vesicoureteral reflux, the presence of renal obstruction, and the degree of renal dysfunction, if any. The management of ureteroceles has become somewhat controversial. An extensive discussion of the indications for various surgical approaches can be found in a general pediatric urology text (57). Non-obstructing, simple ureteroceles in adults may be managed expectantly. Endoscopic and open surgical approaches are available for the management of ureteroceles. Endoscopic puncture of the ureterocele is generally considered a temporizing measure to relieve obstruction, thus preventing loss of renal function. Endoscopic puncture may be the definitive procedure if obstruction is relieved and if any associated vesocioureteral reflux resolves. Open surgical approaches include relief of obstruction by "bypassing" the upper pole collecting system to that of the lower pole, removal of poorly functioning upper-pole segments, and reconstruction at the level of the bladder to remove the ureterocele and treat the vesicoureteral reflux.

Table 24. Inpatient hospital stays for ureterocele listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	2,786	1.1 (1.0–1.2)	1.1	2,848	1.1 (1.0–1.2)	1.1	3,018	1.1 (1.0–1.2)	1.1	2,818	1.0 (0.9–1.2)	1.0
Age												
< 18	257	0.4 (0.2–0.5)		376	0.5 (0.4–0.7)		525	0.7 (0.5–0.9)		494	0.7 (0.4–1.0)	
18–24	*	*		167	0.7 (0.4–0.9)		*	*		169	0.6 (0.4–0.9)	
25–34	320	0.8 (0.6–1.0)		350	0.9 (0.7–1.1)		359	0.9 (0.7–1.2)		224	0.6 (0.4–0.8)	
35–44	504	1.2 (1.0–1.5)		467	1.1 (0.8–1.3)		437	1.0 (0.8–1.2)		373	0.8 (0.6–1.0)	
45–54	413	1.4 (1.0–1.8)		377	1.2 (0.9–1.5)		376	1.1 (0.8–1.4)		424	1.2 (0.9–1.4)	
55–64	316	1.6 (1.1–2.0)		330	1.6 (1.2–2.0)		322	1.4 (1.0–1.9)		290	1.2 (0.9–1.6)	
65–74	475	2.7 (2.1–3.3)		386	2.1 (1.6–2.6)		426	2.4 (1.8–3.0)		398	2.2 (1.8–2.7)	
75+	354	2.8 (2.1–3.6)		393	2.9 (2.2–3.7)		416	2.3 (2.2–3.6)		448	3.0 (2.3–3.7)	
Race/ethnicity												
White	1,692	0.9 (0.8–1.0)	0.9	1,738	0.9 (0.8–1.0)	0.9	1,657	0.9 (0.8–1.0)	0.8	1,578	0.8 (0.7–0.9)	0.8
Black	279	0.9 (0.6–1.1)	1.0	238	0.7 (0.5–0.9)	0.8	256	0.8 (0.6–1.0)	0.8	220	0.6 (0.4–0.9)	0.8
Hispanic	204	0.8 (0.5–1.1)	1.1	252	0.9 (0.6–1.1)	1.2	219	0.7 (0.5–0.9)	1.1	248	0.8 (0.5–1.0)	0.9
Gender												
Male	1,423	1.2 (1.0–1.3)	1.2	1,359	1.1 (0.9–1.2)	1.1	1,546	1.2 (1.0–1.4)	1.2	1,308	1.0 (0.8–1.1)	1.0
Female	1,363	1.0 (0.9–1.2)	1.0	1,489	1.1 (0.9–1.3)	1.1	1,473	1.1 (0.9–1.2)	1.0	1,510	1.1 (0.9–1.2)	1.1
Region												
Midwest	638	1.1 (0.8–1.3)	1.1	714	1.2 (0.9–1.4)	1.2	773	1.2 (1.0–1.5)	1.2	598	0.9 (0.8–1.1)	1.0
Northeast	610	1.2 (0.9–1.5)	1.1	637	1.2 (0.9–1.5)	1.2	596	1.2 (0.8–1.5)	1.1	516	1.0 (0.8–1.2)	1.0
South	1,129	1.3 (1.1–1.6)	1.3	1,066	1.2 (1.0–1.3)	1.2	1,169	1.2 (1.0–1.4)	1.2	1,095	1.1 (1.0–1.3)	1.1
West	409	0.7 (0.5–0.9)	0.8	430	0.7 (0.5–1.0)	0.8	480	0.8 (0.6–1.0)	0.8	610	1.0 (0.7–1.3)	1.0
MSA												
Rural	540	0.8 (0.6–1.1)	0.8	439	0.7 (0.6–0.9)	0.7	571	1.0 (0.7–1.2)	0.9	451	0.8 (0.6–0.9)	0.7
Urban	2,230	1.2 (1.0–1.3)	1.2	2,402	1.2 (1.0–1.3)	1.2	2,434	1.2 (1.0–1.3)	1.2	2,367	1.1 (1.0–1.2)	1.1

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 25. Trends in mean inpatient length of stay (LOS) in days and cost per child admitted with ureterocele[a], listed as primary diagnosis, 1999–2003

	Count	Percent	LOS	Mean Cost
Total	473		3.3	$7,669
Age				
0–2	433	92%	3.3	$7,576
3–10	37	8%	3.5	$8,716
11–17	3	1%	4.3	$8,219
Race/ethnicity				
White	301	64%	3.4	$7,928
Black	25	5%	3.1	$7,465
Asian	6	1%	2.4	$5,891
Hispanic	66	14%	3.4	$7,075
Missing	23	5%	3.3	$7,799
Other	52	11%	2.8	$7,171
Gender				
Female	336	71%	3.3	$7,593
Male	137	29%	3.2	$7,858
Region				
Midwest	115	24%	3.2	$7,812
Northeast	75	16%	3.6	$8,834
South	176	37%	3.4	$7,630
West	107	23%	2.9	$6,765

[a]ICD-9 code 753.23 (congenital ureterocele).

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2003.

PREVALENCE AND INCIDENCE

The incidence of ureteroceles may be as high as one in 500. Ureteroceles occur more commonly in girls than in boys by a 4:1 ratio. Ureteroceles occur in association with duplication of the ureters in 80% of cases, with the ureter to the upper pole of the kidney being affected. In 20% of cases, the ureterocele is associated with a single ureter. Bilateral involvement occurs in 15% of cases. Ureteroceles are associated with duplex systems in 95% of cases in girls, while in boys, only 44% of cases involve duplex systems. Ureteroceles occur almost exclusively in Caucasians.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

According to HCUP data, inpatient hospitalization for ureteroceles remained relatively stable between 1994 and 2000, averaging approximately 2,818 cases annually (1.0 to 1.1 per 100,000 children) (Table 24). The rate of inpatient hospitalization was similar for males and females (1.0 to 1.1 per 100,000 children) and varied little between 1994 and 2000. Of the inpatient admissions, 77% were Caucasians. However, there were no significant differences in the rate of hospitalization among racial/ethnic groups, suggesting that although ureteroceles do occur more commonly in Caucasians, the natural history is independent of race. Averaging across the years studied in Table 24, inpatient admissions for ureteroceles were highest in the South (1,115 cases annually), intermediate in the Northeast and Midwest (590 and 681 cases annually, respectively), and lowest in the West (482 cases annually). The age-adjusted rates differed little among the regions or during the years of study.

In the NACHRI data from 1999 to 2001, 92% of admissions were children under three years of age, and 8% were three- to ten-year-olds. The average length of inpatient stay for ureteroceles was independent of age, 3.3 days, which is consistent with uncomplicated postoperative recovery following open surgery for upper or lower urinary tract reconstruction. The average length of stay was not statistically different when stratified by gender, race/ethnicity, or region (Tables 25 and 26).

Table 26. Inpatient hospital stays for ureterocele listed as primary diagnosis in 1997 and 2000, count, rate[a] (95% CI), age-adjusted rate[b], percent of all hospitalizations

	1997				2000		
	Count	Rate	Age-Adjusted Rate	Percent of all hospitalizations	Count	Rate	Percent of all hospitalizations
Total[c]	608	0.8 (0.7–1.0)	0.8	0.01%	604	0.8 (0.7–1.0)	0.01%
Age							
0–2	321	2.7 (2.1–3.4)		0.01%	350	3.0 (2.2–3.7)	0.01%
3–10	173	0.5 (0.4–0.7)		0.03%	157	0.5 (0.4–0.6)	0.03%
11–17	114	0.4 (0.2–0.6)		0.01%	96	0.3 (0.2–0.5)	0.01%
Race/ethnicity							
White	*	*		…	359	0.8 (0.6–1.0)	0.01%
Black	*	*		…	36	*	0%
Hispanic	*	*		…	78	0.7 (0.4–0.9)	0.01%
Gender							
Male	255	0.7 (0.5–0.9)	0.7	0.01%	285	0.8 (0.6–0.9)	0.01%
Female	353	1.0 (0.8–1.2)	1.0	0.01%	319	0.9 (0.7–1.1)	0.01%
Region							
Midwest	136	0.8 (0.4–1.2)	0.8	0.01%	132	1.0 (0.5–1.5)	0.01%
Northeast	144	1.1 (0.6–1.6)	1.2	0.01%	99	*	0.01%
South	189	0.8 (0.5–1.1)	0.8	0.01%	227	0.9 (0.7–1.2)	0.01%
West	139	0.8 (0.6–1.1)	0.8	0.01%	146	0.8 (0.5–1.2)	0.01%
MSA							
Rural	23	*	*	0%	15	*	0%
Urban	586	1.1 (0.9–1.3)	1.0	0.01%	589	1.0 (0.8–1.2)	0.01%

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1997 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Rate Corporation, for relevant demographic categories of US civilian noninstitutional population under age 18.

[b]Age-adjusted to 2000 US Census.

[c]Persons of other races and missing race and ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding. Race/ethnicity breakdown not included because of large percent of missing values in 1997.

SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database, 1997 and 2000.

Outpatient Care

No reliable data could be obtained on outpatient visits or ambulatory surgery for treatment of ureteroceles.

ECONOMIC IMPACT

NACHRI and HCUP KID include limited data on ureteroceles, and thus could not be used to discern reliable cost trends.

The available data indicate that the mean cost per ureterocele case was nearly $8,000; little variation was observed across age, region, or sex (Table 25). For the 604 cases of ureteroceles in 2000 in the HCUP Kids' Inpatient Database (Table 26), national inpatient expenditures amounted to an estimated $4 million.

RECOMMENDATIONS

The paucity of data on ambulatory treatment of children with ureteroceles should be remedied by more comprehensive data collection and reporting.

POSTERIOR URETHRAL VALVES

INTRODUCTION

Normal fetal bladder development requires a repetitive processes of filling and emptying. In the presence of bladder outlet obstruction, such as posterior urethral valves (PUV), this process is altered. The bladder must work harder to empty, leading to detrusor (bladder muscle) hypertrophy. Increased muscle leads to decreased compliance and higher storage pressures, which ultimately may be transmitted to the ureter and renal parenchyma. In some patients, this can eventually lead to renal insufficiency or renal failure. Fortunately, the incidence of PUV is low, and the condition is most often detected shortly after birth. Early diagnosis has been made possible by the use of routine prenatal ultrasonography. Early diagnosis, ablation of PUV, and close follow-up has maximized the long-term outcome of these patients. Analyses for this condition are based on the ICD-9 and CPT codes defining PUV listed in Table 1.

DEFINITION AND DIAGNOSIS

PUV are persistent embryonic membranes located in the posterior urethra at the level of the verumontanum, causing bladder outlet obstruction during voiding. There are several different types and appearances of PUV, but their diagnosis, treatment, and management are identical. The most widely accepted and used classification comes from Hugh Hamptom Young's original description of the condition (58). The prenatal diagnosis may be suggested by oligohydramnios, hydronephrosis, hydroureteronephrosis, thickened bladder, incomplete emptying of the neonatal bladder, or dilated posterior urethra. The diagnosis is confirmed in the postnatal period by VCUG, which may show a thickened bladder wall, bladder trabeculations, bladder diverticulae, dilated and/or elongated posterior urethra, normal-caliber anterior urethra, vesicoureteral reflux, and reflux of contrast into the prostate, utricle, or ejaculatory ducts. Some or all of these findings may be present. Postnatal renal and bladder ultrasound may be used to assess renal characteristics, such as the presence of hydronephrosis or abnormal renal echogenicity (associated with medical renal disease from ongoing obstruction).

RISK FACTORS

Posterior urethral valves are a congenital condition, the etiology of which has remained elusive. No known risk factors are associated with the development of PUV.

TREATMENT

Relief of PUV requires a surgical procedure. However, initial treatment may include urethral catheterization with a small feeding tube while the newborn is stabilized and any electrolyte imbalances are corrected. Prophylactic antibiotics are used to prevent UTI. The diagnosis is confirmed with a VCUG. Once the infant is stable, operative endoscopic ablation of the PUV may be safely and reliably performed. A post-procedure VCUG ensures complete valve ablation and relief of obstruction. Urodynamic testing is helpful in assessing the degree of bladder dysfunction and may help guide the use of anticholinergic medication to reduce high bladder pressures or uninhibited bladder contractions. Vesicostomy is sometimes performed if renal dysfunction persists. Periodic renal and bladder ultrasounds are necessary to assess renal echogenicity, hydroureteronephrosis, and bladder wall thickness. The presence of the corticomedullary junction can be determined by ultrasound to predict good renal function (59). Consultation with a pediatric nephrologist facilitates medical management and optimizes preservation of renal function. Patients with progressive hydronephrosis, rising serum creatinine and blood pressure, or noncompliant bladder may ultimately need bladder augmentation to increase storage capacity and lower pressure. Even when bladder augmentation has achieved those objectives, progressive renal insufficiency and failure may necessitate renal transplantation.

PREVALENCE AND INCIDENCE

Lary and Paulozzi, from the Centers for Disease Control and Prevention (CDC), studied the Metropolitan Atlanta Congenital Disease Program (MACDP) database to determine the full extent of birth

Table 27. Inpatient hospital stays for posterior urethral valves listed as primary diagnosis in 1997 and 2000, count, rate[a] (95% CI), age-adjusted rate[b], percent of all hospitalizations

	1997				2000		
	Count	Rate	Age-Adjusted Rate	Percent of all hospitalizations	Count	Rate	Percent of all hospitalizations
Total[c]	336	0.6 (0.4–0.8)	0.9	0.01%	225	0.6 (0.4–0.8)	0.01%
Age							
0–2	235	2.8 (2.1–3.6)		0.01%	167	2.8 (2.1–3.6)	0.01%
3–10	74	*		0.02%	46	*	0.01%
11–17	27	*		0.01%	11	*	0%
Race/ethnicity							
White	*	*		*	85	0.4 (0.2–0.5)	0.01%
Black	*	*		*	53	*	0.01%
Hispanic	*	*		*	27	*	0.01%
Region							
Midwest	56	*	*	0.01%	20	*	0.01%
Northeast	75	*	1.2	0.01%	49	*	0.01%
South	136	0.8 (0.5–1.2)	1.1	0.01%	107	0.8 (0.5–1.2)	0.01%
West	69	*	0.8	0.01%	49	*	0.01%
MSA							
Rural	336	0.7 (0.6–0.9)	1.2	0.01%	4	*	0%
Urban		*			215	0.7 (0.6–0.9)	0.01%

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1997 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian noninstitutional population under age 18.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding. Race/ethnicity breakdown not included because of large percent of missing values in 1997.

SOURCE: Healthcare Cost and Utilization Project Kids' Inpatient Database,1997 and 2000.

defects in the population. The MACDP is the oldest continuously operating birth-defects surveillance program in the country. These authors determined the incidence rate of posterior urethral valves to be 2.24 per 10,000 births (60). Casale estimated incidence of posterior urethral valves to be one in 8,000 to 25,000 live male births (61). Atwall suggested a frequency of one in 5,000 to 8,000 live births (62).

At a rate of 2.24 per 10,000 births, 451 male babies will be born with posterior urethral valves in the United States each year.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

PUV was the primary diagnosis in 0.6 cases per 100,000 children in 2000 (Table 27). The vast majority of inpatient hospitalization was for children under three years of age.

Additional HCUP data from 1994 thru 2000 demonstrated a slightly higher incidence, 0.9 cases per 100,000. There were significant racial differences, possibly reflecting differences in prenatal care: Caucasians had an inpatient hospitalization rate of 0.5 per 100,000, while African Americans had a rate of 2.1 per 100,000. There was no difference in occurrence across geographic regions. Nearly all cases occurred in urban centers (Table 28).

Outpatient Care

Insufficient data were available regarding ambulatory surgery visits, hospital outpatient visits, or physicians' office visits by children with PUV to generate reliable estimates of utilization. The national databases surveyed provided no data that would

Table 28. Inpatient hospital stays for posterior urethral valves listed as primary diagnosis, 1994–2000 (merged and by year), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000				
	Count	4-Year Rate		Annualized Rate	4-Year Age-Adjusted Rate
Total[d]	1,173	0.9	0.9 (0.7–1.2)	0.23	0.9
Age					
< 18	1,083	3.0	3.0 (2.2–3.8)	0.75	
18+	*	*	*	*	
Race/ethnicity					
White	499	0.5	0.5 (0.4–0.7)	0.13	0.6
Black	328	2.1	2.1 (1.2–3.1)	0.53	1.7
Region					
Northeast	293	1.2	1.2 (0.6–1.8)	0.3	1.2
Midwest	252	0.8	0.8 (0.4–1.3)	0.2	0.8
South	519	1.2	1.2 (0.6–1.7)	0.3	1.2
West	*	*	*	*	*
MSA					
Rural	*	*	*	*	*
Urban	1,152	1.2	1.2 (0.8–1.5)	0.3	1.2
	1-Year Rate				
1994	340	0.3	0.3 (0.2–0.4)		
1996	320	0.2	0.2 (0.1–0.4)		
1998	366	0.3	0.3 (0.1–0.4)		
2000	148	0.1	0.1 (0–0.2)		

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

enable meaningful conclusions regarding emergency room care for patients with PUV.

ECONOMIC IMPACT

Data on costs per case and on the number of cases occurring each year were too sparse to permit cost estimates to be made. However, the economic impact in absolute dollars is probably smaller than that of more prevalent medical conditions. Nevertheless, because severe PUV can lead to renal insufficiency and renal failure, potentially requiring dialysis or renal transplantation, this condition may have a significant economic impact.

CONCLUSIONS

Posterior urethral valves, a potentially devastating condition, have a low incidence. While treatment of the valve is straightforward, the long-term clinical sequellae are often severe. The degree of bladder dysfunction and renal impairment varies, depending primarily on the severity of obstruction but also on the timing of surgical intervention and long-term medical management. Some patients may ultimately require bladder augmentation because of high bladder storage pressure and small-capacity, noncompliant bladders. Additionally, some patients may require renal transplantation because of progressive renal failure. Most patients will require neither; however, long-term follow-up is essential. Fortunately, PUV is most often detected shortly after birth. Early diagnosis has been made possible with the advent of routine prenatal ultrasonography; and early diagnosis, ablation of PUV, and close follow-up have maximized the long-term prognosis of these patients.

RECOMMENDATIONS

There are approximately 265 independent children's hospitals in the United States, which presumably care for the majority of PUV patients. More active participation and more vigilant data collection would enable more meaningful analysis of the impact of PUV on the US healthcare system. Delayed, long-term costs of PUV sequellae should also be studied.

OVERALL BURDEN OF PEDIATRIC UROLOGIC DISORDERS

Despite limitations of the available data, direct costs related to pediatric urologic hospitalizations appear to be substantial and would be even higher if all service types were accounted for. Further exploration of indirect costs (e.g., parental loss of work time) related to these conditions is warranted and would likely demonstrate that pediatric urologic conditions have an even greater economic burden than that observed in this analysis.

REFERENCES

1. Henneberry MO, Stevens FD. Renal hypoplasia and dysplasia in infants with posterior urethral valves. J Urol 1980;123:912.
2. Hansson S, Dhamey M, Sigström, O, et al. Dimercapto-succinic acid scintigraphy instead of voiding cystourethrography for infants with urinary tract infection. J Urol 2004;172(3):1071-74
3. Gonzalez E, Papazyan JP, Girardin, E. Impact of vesicoureteral reflux on the size of renal lesions after an episode of acute pyelonephritis. J Urol 2005:173(2);571-75.
4. Van den Abbeele AD, Treves ST, Lebowitz RL, et al. Vesicoureteral reflux in asymptomatic siblings of patients with known reflux: Radionuclide cystography. Pediatrics 1987;79:147.
5. Noe HN. The long-term result of prospective sibling reflux screening. J Urol 1992;148:1739.
6. Sargent MA. What is the normal prevalence of vesicoureteral reflux? Pediatr Radiol 2000; 587.
7. J. Elder, M. Diaz, A. Caldamone, et al. Endoscopic therapy for vesicoureteral reflux: a meta-analysis. I. Reflux resolution and urinary tract infection. J Urol 2006 Feb;175(2):716-22
8. Baker R, Maxted W, Maylath J, et al. Relation of age, sex, and infection to reflux: data indicating high spontaneous cure rate in pediatric patients. J Urol 1966;95:27.
9. Smellie JM, Normand ICS. The clinical features and significance of urinary infection in childhood. Proc R Soc Lond 1966;59:415.
10. Scott JES, Stansfeld JM. Ureteric reflux and kidney scarring in children. Arch Dis Child 1968;43:468.
11. Walker RD, Duckett JW, Bartone F, et al. Screening school children for urologic disease. Pediatrics 1977;60:239.
12. Zerin JM, Ritchey ML, Chang AC. Incidental vesicoureteral reflux in neonates with antenatally detected hydronephrosis and other renal abnormalities. Radiology 1993;187:157.
13. Ring E, Petritsch P, Riccabona M, et al. Primary vesicoureteral reflux in infants with a dilated fetal urinary tract. Eur J Pediatr 1993;152:523.
14. Yeung CK, Godley ML, Dhillon HK, et al. The characteristics of primary vesico-ureteral reflux in male and female infants with pre-natal hydronephrosis. Br J Urol 1997; 80:319.
15. Shopfner CE. Vesicoureteral reflux: five year re-evaluation. Radiology 1970; 95;637.
16. Wiswell TE, Enzenauer RM, Holton ME, et al. Declining frequencies of circumcision: implications for changes in the incidence of male to female sex ratio of upper tract infection in early infancy. Pediatrics 1987;79:338.
17. Weiss R, Tamminen-Mobius T, Koskimies O, on behalf of the International Reflux Study in Children. Characteristics of entry in children with severe primary vesicoureteral reflux recruited for a multicenter international therapeutic trial comparing medical and surgical management. J Urol 1992b;148:1644.
18. Kunin CM. Urinary tract infections in children. Hosp Pract 1976;11:91.
19. Askari A, Belman AB. Vesicoureteral reflux in black girls. J Urol 1982;127:747.
20. Skoog SJ, Belman AB. Primary vesicoureteral reflux in the black child. Pediatrics 1991;87:538.
21. McLorie GA, McKenna PH, Jumper BM, et al. High grade vesicoureteral reflux: Analysis of observational therapy. J Urol 1990;144:537.
22. Still JL, Cottom D. Severe hypertension in children. Arch Dis Child 1967;42:34–39.
23. Gill DG, da Costa BM, Cameron JS, et al. Analysis of 100 children with severe and persistent hypertension. Arch Dis Child 1976;51: 951-56.
24. Wyszynska T, Chichocka E, Wieteska-Klimczak A, et al. A single pediatric center experience with 1025 children with hypertension. Acta Paediatr 1992;81:244-46.
25. Londe S. Causes of hypertension in the young. Pediatr Clin North Am 1978;25:55–65.
26. Vallee JP, Vallee PD, Greenfield SP, et al. Contemporary incidence of morbidity related to vesicoureteral reflux. Urology 1999;53:812-15.
27. Nguyen HT, Coakley F, Hricak H. Cryptorchidism: strategies in detection. Eur Radiol 1999;9(2):336-43.
28. Barthold JS, Gonzalez R. The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy. J Urol 2003 Dec;170(6Pt1):2396-401.

29. Scorer CG, Farrington GH. Congenital Deformities of the Testis and Epididymis. New York: Appleton-Century-Crofts, 1972.
30. Jones IR, Young ID. Familial incidence ofcryptorchidism. J Urol 1982;127:508.
31. Henna MR, Del Nero RG, Sampaio CZ, Atallah AN, Schettini ST, Castro AA, Soares BG. Hormonal cryptorchidism therapy: systematic review with metanalys of randomized clinical trials. Pediatr Surg Int 2004 May;20(5):357-9
32. Wenzler DL, Bloom DA, Park JM. What is the rate of spontaneous testicular descent in infants with cryptorchidism? J Urol 2004 Feb;171(sPt1):849-51
33. Baskin LS. Hypospadias and urethral development. J Urol 2000;163: 951–56.
34. Aaronson IA, Cakmak MA, Key LL. Defects of the testosterone biosynthetic pathway in boys with hypospadias. J Urol 1997;157: 1884-88.
35. Silver RI, Russell DW. 5-alpha-reductase type 2 mutations are present in some boys with isolated hypospadias. J Urol 1999;162: 1142-45.
36. Silver RI. What is the etiology of hypospadias? a review of recent research. Del Med J 2000;72: 343-47.
37. Sweet RA, Schrott HG, Kurland R, et al. Study of the incidence of hypospadias in Rochester, Minnesota, 1940–1970, and a case–control comparison of possible etiologic factors. Mayo Clin Proc 1974;49: 52-57.
38. Leung TJ, Baird PA, McGillivray B. Hypospadias in British Columbia. Am J Med Genet 1985;21: 39–48.
39. Henderson BE, Bernstein L, Ross RK, et al. The early in utero oestrogen and testosterone environment of blacks and Caucasians: potential effects on male offspring. Br J Cancer 1988;57:216-18.
40. Borer JG, Bauer SB, Peters CA, et al. Tubularized, incised plate urethroplasty: expanded use in primary and repeat surgery for hypospadias. J Urol 2001;165:581-85.
41. Paulozzi LJ, Erickson D, Jackson RJ. Hypospadias trends in two US surveillance systems. Pediatrics 1997;100: 831-34.
42. Wallace HM, Baumgartner L, Rich H. Congenital malformations and birth injuries in New York City. Pediatrics 1953;12: 525-35.
43. Chavez GF, Cordero JF, Becerra JE. Leading major congenital malformations among minority groups in the United States, 1981–1986. MMWR 1988;37:17-24.
44. Chung CS, Myrianthopoulos NC. Racial and prenatal factors in major congenital malformations. Am J Hum Genet 1968;20: 44-60.
45. Matlai P, Beral V. Trends in congenital malformations of external genitalia. Lancet 1985;1:108.
46. Bjerkedal T, Bakketeig LS. Surveillance of congenital malformations and other conditions of the newborn. Int J Epidemiol 1975;4:31–36.
47. Kallen B, Winberg J: An epidemiologic study of hypospadias in Sweden. Acta Paediatr Scand Suppl 1982;293: 1-52.
48. Silver RI, Rodriguez R, Chang TSK, et al. In vitro fertilization is associated with an increased risk of hypospadias. J Urol 1999;161:1954-57.
49. Czeizel A. Increasing trends in congenital malformations of male external genitalia. Lancet 1985;1: 462-63.
50. Gallantine ML, Morey AF, Thompson, IM. Hypospadias: a contemporary epidemiologic assessment. Urol 2001;57:788-90.
51. Paulozzi LJ. International trends in rates of hypospadias and cryptorchidism. Envir Health Persp 1999;107(4):297-302.
52. Chwalla R. The process of formation of cystic dilation of the vesical end of the ureter and of diverticula at the ureteral ostium. Urol Cutan Ren 1927;31:499.
53. Stephens FD. Caecoureterocele and concepts on the embryology and etiology of ureteroceles. Aust NZ J Surg 1971;40:239.
54. Stephens FD. Congenital Malformations of the Urinary Tract. New York: Praeger, 1983; 320-22.
55. Tokunaka S, Goth T, Koyanagi T, et al. The morphological study of ureterocele: a possible clue to its embryogenesis as evidenced by a locally arrested myogenesis. J Urol 1981;126:726.
56. Tanagho EA. Embryologic basis for lower ureteral anomalies: a hypothesis. Urol 1976;7:451.
57. Keating M. Ureteral duplication anomalies: ectopic ureters and ureteroceles. Clinical Pediatric Urology, 4th ed., Belman, King and Kramer, eds. London: Duni, 2001.

58. Young HH, Frontz WA, Baldwin JC. Congenital obstruction of the posterior urethra. J Urol 1919;3:298-365.
59. Hulbert WC, Rosenberg HK, Cartwright PC, et al. The predictive value of ultrasonography in evaluation of infants with posterior urethral valves. J Urol 1992;148:122-24.
60. Lary JM, Paulozzi LJ. Sex difference in the prevalence of human birth defects: a population-based study. Tetralogy 2002 Sep;66(3):101-2.
61. Casale AJ. Posterior urethral obstruction and of the obstructions of the urethra. Pediatric Urology Practice, Gonzales ET, Bauer SB, eds. Philadelphia: Lippincott Williams & Wilkins, 1999, 223-43.
62. Atwall JD. Posterior urethral valves in the British Isles: a multicenter BAPS review. J Pediatr Surg 1983;18:70.

CHAPTER 12

Urinary Incontinence in Children

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Urinary Incontinence in Children

Eric A. Jones, MD

INTRODUCTION

Most of the healthcare for pediatric urinary incontinence is delivered in the outpatient setting. During the 1990s, approximately 417,000 visits were made per year to physicians' offices and hospital outpatient departments by children with urinary incontinence listed as any diagnosis. Although the majority of these outpatient visits cannot be classified by underlying disease process, nocturnal enuresis is a listed diagnosis in up to 38% of them.

Of the commercially insured children seen for incontinence in the outpatient setting, 75% were 3- to 10-year-olds, and 15% to 20% were 11- to 17-year-olds. Only 2% to 3% of the outpatient visits were made by children under the age of 3, in whom urinary incontinence seldom has a pathologic basis.

Urinary incontinence is a relatively common reason for children to seek medical care, but it rarely requires hospitalization. When it does require inpatient care, the average length of stay is between 5 and 7 days, and the length of stay appears to be even greater in facilities providing tertiary care. Fewer than 10 of every 100,000 visits for incontinence in children are ambulatory surgical visits.

The economic burden of pediatric urinary incontinence is difficult to quantify. Data are not currently available on aggregate direct costs for inpatient, outpatient, or surgical venues. Costs for inpatient care for pediatric urinary incontinence, like those for other conditions, reflect hospital length of stay. The cost per visit for outpatient surgical procedures has increased steadily during the past decade.

DEFINITION AND DIAGNOSIS

In contrast to the adult population, in which the inability to maintain voiding control is virtually always considered pathological, a child with urinary incontinence must be evaluated within the context of his or her developmental age. The impact on social functioning evolves as the child progresses through the first several years of life and is heavily influenced by social, cultural, and environmental factors.

Development of Voiding Control

In the infant, normal micturition occurs via a spinal-cord-mediated reflex. As the bladder fills, it surpasses an intrinsic volume threshold, which results in a spontaneous bladder contraction. This vesico-vesical reflex coordinates relaxation of the bladder neck and external urethral sphincter. Voiding is complete, occurs at low pressure, and is autonomous. In the infant, the volume threshold for urination is low; the infant voids approximately 20 times per day (1).

As the infant develops and neural pathways in the spinal cord mature, the vesico-vesical reflex is suppressed. A more complex voiding reflex, mediated at the level of the pons and midbrain, assumes coordination of voiding control. During this transitional period, functional bladder capacity increases, and the frequency of urination decreases. By 2 years of age, most children void 10 to 12 times per

Table 1. Codes used in the diagnosis and management of pediatric urinary incontinence

Individuals under 18 with one of the following ICD-9 diagnosis codes, but not a coexisting 952.XX or 953.XX code:	
307.6	Enuresis
596.59	Other functional disorder of bladder
596.52	Low bladder compliance
596.51	Hypertonicity of bladder (overactive bladder specified in 2001)
596.8	Other specified disorders of bladder
596.9	Unspecified disorder of bladder
599.8	Other specified disorders of urethra and urinary tract
599.81	Urethral hypermobility
599.82	Intrinsic urethral sphincter deficiency (ISD)
599.83	Urethral instability
599.84	Other specified disorders of urethra
625.6	Stress incontinence, female
788.3	Urinary incontinence
788.31	Urge incontinence
788.3	Urinary incontinence, unspecified
788.32	Stress incontinence, male
788.33	Mixed incontinence, male, female
788.34	Incontinence without sensory awareness
788.36	Nocturnal enuresis
788.37	Continuous leakage
788.39	Other urinary incontinence

day, are aware of bladder fullness, and can announce their need to urinate (1). Between 2 and 3 years of age, children attain the ability to volitionally postpone voiding and to initiate voiding at bladder volumes less than capacity. During this period, an adult pattern of daytime urinary control emerges, characterized by a stable, quiescent bladder.

As with other developmental milestones, the time course for attaining urinary continence demonstrates individual variability. The majority of children master toileting prior to entrance into school, (i.e., by around 5 years of age). Beyond this age, incontinence becomes an increasing social concern. Brazelton and colleagues studied the development of voiding control and found that 26% of children had attained daytime continence by the age of 24 months, 52.5% by 27 months, 85% by 30 months, and 98% by 3 years of age (2). Bloom and colleagues studied 1,186 normal children and found that the age at which toilet training was achieved ranged from 9 months to 5.25 years, with a mean of 2.4 years. Toilet training occurred slightly earlier in females (3).

Defining pediatric urinary incontinence has historically been complicated by the lack of standardized definitions for pediatric voiding disorders. In 1997, the International Children's Continence Society attempted to ameliorate this problem by generating a report on standardization and definitions for lower urinary tract dysfunction in children (4). In the consensus report, urinary incontinence is defined as *the involuntary loss of urine, objectively demonstrable, and constituting a social or hygienic problem.*

Urethral incontinence occurs via a native or reconstructed urethra and is stratified as follows:

- stress incontinence, the involuntary loss of urine occurring in absence of detrusor contraction, when intravesical pressure exceeds urethral pressure;
- reflex incontinence, the loss of urine due to detrusor hyperreflexia and/or involuntary urethral
- relaxation in the absence of the sensation to void;
- overflow incontinence, any involuntary loss of urine associated with overdistension of the bladder;
- urge incontinence, involuntary loss of urine associated with a strong desire to void.

Extraurethral incontinence is defined as urine loss via a conduit other than the urethra, such as ectopic ureters (in girls) and vesicostomies. *Enuresis* denotes a physiologically coordinated void occurring at an inappropriate or socially unacceptable time or place.

The most recent version of the Diagnostic and Statistical Manual (DSM IV-TR) defines the essential features as repeated voiding of urine into bed or clothes and two occurrences per week for at least three months, causing clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning. The child must have reached an age at which continence is expected (a chronological age of 5 years, or a mental age of 5 years for a developmentally delayed child), and the condition must not be due exclusively to the direct physiological effects of a substance or general medical condition (5).

Etiologic Classification of Pediatric Urinary Incontinence

Childhood urinary incontinence can be classified as organic or functional. Organic incontinence refers to an underlying disease process, which can be either neurogenic or structural in nature. Neurogenic forms of incontinence can be congenital or acquired; they include etiologies such as neurospinal dysraphism, sacral agenesis, cerebral palsy, spinal cord injury, and tethered spinal cord. Structural incontinence refers to developmental, iatrogenic, or traumatic anatomic abnormalities of the lower urinary tract that interfere with the urinary system's ability to hold, store, or evacuate urine. Structural incontinence includes diseases such as exstrophy-epispadias complex, ectopic ureter, and posterior urethral valves.

Functional incontinence is that in which no anatomic or neurologic abnormality can be found. It comprises a heterogeneous group of disorders, including the urge syndrome, dysfunctional voiding, lazy bladder, and enuresis. The prevalence of functional incontinence in the pediatric population merits special focus.

Urge incontinence occurs predominantly in girls and is commonly associated with other medical complaints, such as constipation, recurrent urinary tract infections, and vesicoureteral reflux. It is manifested clinically by urinary frequency, the sudden imperative to void, and holding maneuvers such as squatting on the heel (the so-called Vincent's Curtsy), crossing the legs, and flexing the pelvic floor muscles. This symptom complex is the result of overactivity of the detrusor muscle, which results in sudden bladder contractions at volumes below age-expected capacity. Incontinence occurs in those children who are unable to suppress bladder contraction volitionally.

The inability to maintain detrusor quiescence is common during the transitional phase between infantile and adult patterns of urinary control. Urge incontinence represents recurrence or persistence of this transitional phase.

Dysfunctional voiding includes several patterns of voiding with a single underlying feature: overactivity of the pelvic floor muscles during micturition. It is likely that urge incontinence and dysfunctional voiding represent different time points along the natural history of a single disease process. Children with urgency symptoms learn to abort detrusor contractions by volitional contraction of the external urethral sphincter and pelvic floor muscles. The long-term consequences of pelvic floor overactivity include high-pressure voiding, urinary infections, ureteral reflux, and, ultimately, decompensation of the detrusor muscle. Urinary incontinence can occur at any point along the continuum and results from infection, inefficient holding response, or overflow incontinence.

Enuresis is characterized by synergistic bladder-urethral function and typically occurs while the child is asleep (enuresis nocturna). This disorder is extraordinarily common in young children, with a reported incidence of 15% to 20% in 5-year-olds. It is characterized by spontaneous resolution, with 15% resolving each year after the age of 5. At age 7, the prevalence is approximately 8%. Approximately 2% of 15-year-olds continue to have wet nights (6).

A rare type of enuresis, giggle incontinence (enuresis risoria), occurs only during intense laughter. It is characterized by an abrupt, uncontrollable bladder contraction. Bladder emptying is generally complete. Affected individuals often modify their social interactions to avoid situations that are likely to induce laughter. The term diurnal enuresis (enuresis diurna) is commonly used to describe daytime wetting. A better term for this disorder is diurnal incontinence.

Vaginal voiding refers to a specific form of wetting that is characterized by post-void dribbling. It is seen predominantly in slender females who are unable to adopt an appropriate posture while voiding. This leads to trapping of urine in the vagina. It can also be seen in overweight females who are unable to adequately separate their labia during urination. The treatment of vaginal voiding involves modification of voiding posture to prevent pooling of urine in the vagina.

Evaluation of a child with incontinence typically begins in an office-based setting. A thorough medical history will delineate the pattern of incontinence and may identify underlying neurologic or structural anomalies. Parents are carefully questioned about the child's voiding habits, including straining, urinary frequency, posturing, pain with urination, and infection. A meticulous obstetrical history will reveal evidence of fetal distress, anoxia, birth trauma, hydronephrosis, or oligohydramnios. Developmental delays or impaired upper- or lower-extremity motor skills warrant careful attention. The association of encopresis and wetting in the older child raises the suspicion of occult neuropathy.

The physical examination should include inspection of the abdomen, genitalia, and back, as well as a directed neurologic examination. The lower back is inspected for scoliosis and stigmata of occult spinal dysraphism, such as a sacral dimple, hair patch, hemangioma, or lipoma. The coccyx is examined for evidence of sacral agenesis. The genital exam may disclose labial adhesions or an abnormal urethral position in females, or urethral abnormalities in males.

Most patients brought for evaluation before the age of 5 require no more than a history and physical examination. Additional diagnostic studies in patients younger than 5 are generally reserved for those who have evidence of a structural or neurologic abnormality or associated urinary tract symptoms such as infection or hematuria.

Noninvasive diagnostic studies used to evaluate incontinence include urinalysis, spinal tomography, urine-flow measurement, electromyography, and renal/bladder ultrasonography. Invasive studies, such as voiding cystography, and multichannel urodynamic evaluation are reserved for selected clinical situations. These procedures are generally performed in an outpatient setting.

Patients with functional incontinence are treated on an ambulatory basis with observational, medical, or behavioral therapy. Only rarely does a patient with functional incontinence require surgical intervention, and then only after all nonsurgical interventions have been exhausted. Inpatient treatment is largely reserved for those with neurologic or structural abnormalities who require surgical therapy.

ANALYTIC PERSPECTIVE

Pediatric urinary incontinence is commonly seen in both urologic and general pediatric practice. The contemporary literature is replete with patient-based and specialty department-based investigations of voiding disorders in children. Unfortunately, there is a paucity of population-based investigations of these conditions. Data collected from existing healthcare utilization databases do, however, provide insight into the trends in utilization of services for pediatric incontinence. An important caveat is that undercoding or miscoding may lead to undercounting of many conditions which fall under the umbrella of pediatric incontinence.

Most of the data in this chapter come from five databases. The data include observations derived from both public and proprietary sources and represent patient encounters in many healthcare settings. Both commercially insured and government-insured pediatric populations are included. In all cases, pediatric incontinence has been identified for analysis using the relevant 5-digit ICD-9 codes. Patients meeting criteria for inclusion are stratified where possible by age, gender, geographic region, and race/ethnicity. The disease codes used to define urinary incontinence in each of these databases are listed in Table 1.

The pediatric group is defined as patients 0 to 17 years of age. The youngest age group consists of patients less than 3 years of age and represents a cohort in which the majority are physiologically and developmentally incapable of voiding control. Children between the ages of 3 and 11 constitute the cohort in which incontinence encounters are most common. Adolescents and young adults aged 11 to 17 are included in a separate cohort. More detailed age stratification is impossible because of limited sample sizes in the datasets. These age strata present methodological limitations in analyzing nocturnal enuresis, about which awareness increases at about age 7 when children start school and are exposed to a broader social environment. Eighteen-year-olds are included in the adult analyses.

Results are reported within three venues of healthcare delivery—inpatient, outpatient, and ambulatory surgery—followed by an economic perspective. In general, datasets are analyzed by both primary and any listed diagnoses of incontinence. Trend analyses are available for databases with serial years of data.

Given the heterogeneity of the incontinence population and the limitations of ICD-9 coding, it is impossible to stratify subjects etiologically. Samples

Table 2. Inpatient hospital stays by children with urinary incontinence listed as primary diagnosis, count, rate[a] (95% CI)

	Count	Rate
1994	283	0.4 (0.2–0.6)
1996	208	0.3 (0.1–0.4)
1998	195	0.3 (0.1–0.4)
2000	201	0.3 (0.1–0.4)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under 18 years of age.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 3. Trends in mean inpatient length of stay (days) for children hospitalized with urinary incontinence listed as primary diagnosis

	Length of Stay
1994	4.7
1996	5.1
1998	5.3
2000	5.6

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 4. Mean inpatient length of stay (days) for children hospitalized with urinary incontinence listed as primary diagnosis, 1999–2001 (95% CI)

	Count	Length of Stay	
Total	1,251	6.9	(6.5–7.3)
Age			
0–2	83	4.5	(3.1–5.9)
3–10	672	6.5	(6.1–7.0)
11–17	496	7.8	(7.0–8.5)
Race/ethnicity			
White	873	6.7	(6.3–7.2)
Black	116	7.2	(6.1–8.3)
Asian	11	7.1	(4.7–9.5)
Hispanic	150	6.7	(5.8–7.7)
American Indian	2	5.0	(0–18)
Other	42	9.4	(5.8–13)
Missing	57	7.4	(5.5–9.4)
Gender			
Male	593	6.7	(6.3–7.2)
Female	658	7.0	(6.4–7.6)
Region			
Midwest	451	7.4	(6.8–8.0)
Northeast	79	6.5	(2.7–10)
South	512	6.8	(6.4–7.2)
West	197	6.3	(5.5–7.2)
Missing	12	5.2	(2.8–7.7)

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

in which raw counts are less than 30 have been suppressed and are not presented in this chapter. The analyses reported here are limited by the absence of national data on the use of prescription medications for children with incontinence.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Urinary incontinence is a common reason for care-seeking by the pediatric population, but it requires hospitalization far less frequently than is the case for adults. The rate of annual admissions nationwide for a primary diagnosis of incontinence is less than 1 per 100,000 children (Table 2). There is no indication that these numbers changed substantially between 1994 and 2000. However, over the same time period, the average length of hospital stay increased from 4.7 to 5.6 days. Hospital stays were slightly longer, on average, for patients admitted to urban hospitals than for the total group studied (Table 3).

The National Association of Children's Hospitals and Related Institutions (NACHRI) database provides information on several aspects of inpatient care in the nation's pediatric hospitals, including data on length of hospital stay for calendar years 1999 to 2001 (Table 4). A cohort of 1,251 patients with urinary incontinence listed as the principal diagnosis was identified. The average length of hospitalization for these patients was 6.9 days. The duration was greater for older children, averaging 7.8 days in the 11- to 17-year-old cohort, compared with 4.5 days for patients under 3 years of age. Duration of hospitalization did not vary by gender, race/ethnicity, or geographic region. Unlike the length of stay reported in the Health Cost and Utilization Project (HCUP) data, length of stay in the NACHRI data was stable over the time frame studied (Tables 3 and 5). Because NACHRI collects data primarily from tertiary-care pediatric specialty hospitals, its findings are likely weighted toward patients receiving higher intensity care than is represented in the population-based HCUP.

Outpatient Care

Most of the evaluation and management of incontinence in children is performed in physicians' offices. The National Hospital Ambulatory Medical Care Survey (NHAMCS) provides data on a nationally representative sample of visits to hospital outpatient departments. NHAMCS data for patients with urinary incontinence are shown in Table 6. During four years of data collection (1994, 1996, 1998, and 2000), 243,210 hospital outpatient visits were made by children with urinary incontinence listed as any diagnosis. This represents a rate of 343 visits per 100,000 children. There were 127,586 visits for a primary diagnosis of urinary incontinence, a rate of 180 visits per 100,000 children. According to data from Schmitt (7), about 10% of children 6 years of age wet the bed. Taken together, these data suggest that urinary incontinence is a relatively common diagnosis in the pediatric population.

Analogous data from the National Ambulatory Medical Care Survey (NAMCS) are detailed in Table

Table 5. Trends in mean inpatient length of stay (days) for children hospitalized with urinary incontinence listed as primary diagnosis (95% CI)

	1999			2000			2001		
	Count	Length of Stay		Count	Length of Stay		Count	Length of Stay	
Total[a]	371	6.8	(6.2–7.3)	413	7.3	(6.4–8.1)	467	6.6	(6.1–7.2)
Age									
0–2	30	5.2	(2.0–8.3)	26	3.0	(1.6–4.4)	27	5.3	(2.8–7.7)
3–10	198	6.6	(5.9–7.4)	218	6.7	(6.1–7.2)	256	6.4	(5.6–7.2)
11–17	143	7.3	(6.5–8.1)	169	8.7	(6.7–11)	184	7.3	(6.5–8.0)
Race/ethnicity									
White	265	6.6	(6.0–7.2)	291	7.3	(6.1–8.4)	317	6.4	(5.8–6.9)
Black	33	6.8	(5.3–8.2)	37	7.9	(4.9–11)	46	7.0	(5.8–8.1)
Asian	4	5.5	(2.7–8.3)	2	6.5	(0–51)	5	8.6	(3.4–14)
Hispanic	42	6.5	(4.6–8.4)	41	7.0	(5.1–8.9)	67	6.7	(5.4–8.1)
American Indian	1	4.0	...	0	...		1	6.0	...
Other	9	7.2	(3.9–10)	17	8.2	(5.5–11)	16	11.8	(2.5–21)
Missing	17	10.4	(4.2–16)	25	6.4	(4.7–8.1)	15	5.9	(3.9–7.8)
Gender									
Male	204	6.8	(6.0–7.6)	188	7.1	(6.3–7.9)	201	6.3	(5.7–6.9)
Female	167	6.7	(5.9–7.5)	225	7.4	(6.0–8.8)	266	6.9	(6.0–7.7)
Region									
Midwest	138	8.0	(6.9–9.0)	147	7.2	(6.4–8.1)	166	7.0	(5.8–8.1)
Northeast	23	4.4	(2.1–6.7)	28	9.8	(0–20)	28	5.0	(3.6–6.4)
South	139	6.6	(5.9–7.4)	176	7.0	(6.2–7.8)	197	6.7	(6.1–7.4)
West	63	5.3	(4.2–6.4)	58	7.2	(5.4–9.0)	76	6.4	(5.0–7.9)
Missing	8	5.6	(1.9–9.4)	4	4.5	(0.5–8.5)	0	...	

...data not available.

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

Table 6. Hospital outpatient visits by children with urinary incontinence, 1994–2000 (merged), count (95% CI), number of visits, percentage of visits, rate (95% CI)

Total	4-Year Count (95% CI)	Total No. Visits by Males/ Females < 18, 1994–2000	% of Visits	4-Year Rate[a] (95% CI)
Primary diagnosis	127,586 (77,011–178,161)	72,578,652	0.2	180 (109–252)
Any diagnosis	243,210 (173,678–312,742)	72,578,652	0.3	343 (245–442)

[a]Rate per 100,00 based on the sum of weighted counts in 1994, 1996, 1998, and 2000 over the mean estimated base population across those four years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic
categories of US civilian non-institutionalized population under age 18.

SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

Table 7. Physician office visits by children with urinary incontinence, count (95% CI), number of visits, percentage of visits (%), rate[a] (95% CI)

Total	5-Year Count (95% CI)	Total No. Visits by Males/ Females <18, 1992–2000	Percent of Visits	5-Year Rate (95% CI)
Primary diagnosis	1,126,911 (683,252–1,570,570)	809,286,031	0.1%	1,612 (977–2,247)
Any diagnosis	1,781,506 (1,247,877–2,315,135)	809,286,031	0.2%	2,548 (1,785–3,312)

[a]Rate per 100,00 based on the sum of weighted counts in 1992, 1994, 1996, 1998, and 2000 over the mean estimated base population across those five years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation for relevant demographic categories of US civilian non-institutionalized population under age 18.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

7. In contrast to NHAMCS, these data are collected by physicians in office-based settings. During 1992, 1994, 1996, 1998, and 2000, there were 1,781,506 visits for which urinary incontinence was coded as any diagnosis, a rate of 2,548 per 100,000 children. A total of 1,126,911 office visits were made by children with a primary diagnosis of incontinence, a rate of 1,612 per 100,000 children.

Trends in healthcare utilization for urinary incontinence are available from the Center for Health Care Policy and Evaluation (CHCPE). This dataset contains national data from both traditional, commercially managed health plans and managed Medicaid programs. Data were evaluated for even years between 1994 and 2000. Base populations for the rates presented are children with the same demographic characteristics. Among members of commercial health plans, physician outpatient visits for a primary diagnosis of urinary incontinence ranged from 495 per 100,000 to 533 per 100,000; there was no trend toward an increasing rate over time (Table 8). Rates for visits in which incontinence was listed as any diagnosis ranged from 658 per 100,000 in 1994 to 782 per 100,000 in 2000, with an increasing trend over the years studied (Table 8). In each year studied, visits by boys were more common than visits by girls, the ratio being approximately 1.3:1. More than 75% of the visits were made by 3- to 10-year-olds. Interestingly, more than 2% of physician encounters occurred with patients under the age of 3 (Figure 1).

The findings were similar among enrollees in managed Medicaid plans. During the same time frame, 1994 to 2000, outpatient visits for a primary diagnosis of incontinence ranged from 497 per 100,000 to 682 per 100,000 (Table 9). Visit rates for which incontinence was listed as any diagnosis ranged from 739 per 100,000 to 1,083 per 100,000 (Table 9). Boys and girls were seen in similar proportions.

A detailed assessment of disease states contributing to incontinence is beyond the scope of the databases analyzed, in terms of both sample size constraints and the inherent lack of precision in ICD-9 coding. Nevertheless, the CHCPE data allowed us to parse the relative proportion of visits for selected diagnoses of incontinence (Table 10). The most common single condition in outpatients with a diagnosis of incontinence was nocturnal enuresis. The rate of physician outpatient visits for this condition was similar between commercially insured and managed Medicaid populations, ranging from 102 per 100,000 in 1994 to 283 per 100,000 in 2000. A trend

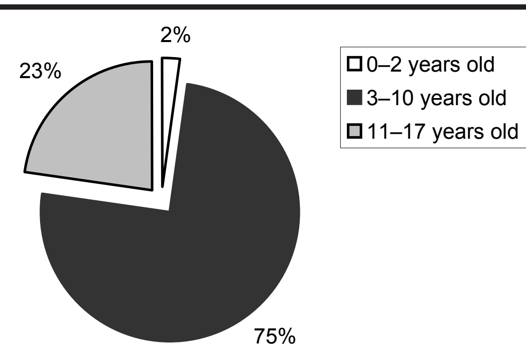

Figure 1. Age distribution of physician outpatient visits for children having commerical health insurance with urinary incontinence listed as primary diagnosis.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 8. Physician outpatient visits for urinary incontinence by children having commercial health insurance, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	As Primary Diagnosis							
Total	1,589	501	2,287	504	3,308	495	3,841	533
Age								
< 3	28	*	65	111	81	91	80	84
3–10	1,166	800	1,714	822	2,501	814	2,882	884
11–17	395	302	508	273	726	266	879	294
Gender								
Male	975	599	1,331	574	1,853	541	2,094	566
Female	614	397	956	432	1,455	447	1,747	498
	As Any Diagnosis							
Total	2,089	658	3,104	685	4,655	697	5,636	782
Age								
< 3	48	118	96	164	123	139	137	144
3–10	1,549	1,063	2,371	1,137	3,565	1,161	4,271	1,310
11–17	492	376	637	342	967	355	1,228	411
Gender								
Male	1,294	795	1,784	769	2,628	767	3,114	842
Female	795	514	1,320	596	2,027	623	2,522	719

*Figure does not meet standard for reliability or precision.

[a]Counts less than 30 should be interpreted with caution.

[b]Rate per 100,000 based on member months of enrollment in calendar year for children in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

toward increased utilization was seen in both groups between 1994 and 2000. The increased utilization of physician outpatient services by children with nocturnal enuresis may be due in part to increased public awareness of the disorder.

Ambulatory Surgery

Because most children with urinary incontinence receive medical or behavioral treatment, their utilization of ambulatory surgical services should be low. In general, those who undergo surgical therapy require inpatient care. CHCPE data support this generalization. Fewer than 9 per 100,000 commercially insured children presenting for ambulatory surgical treatment in 1998 and 2000 had incontinence listed as any diagnosis. As expected, rates were highest among 3- to 10-year-olds (Table 11). Small counts in this dataset preclude reliable estimation of these rates for 1994 and 1996. Stratification by race/ethnicity, gender, and geographic region is also impossible with this dataset.

ECONOMIC IMPACT

Little information is available about the economic burden of pediatric urinary incontinence in the United States. Urinary incontinence encompasses a heterogeneous family of disorders with clinical strategies dictated by the underlying condition. Costs should primarily reflect the nature of that condition. Unfortunately, available data do not allow this type of analysis.

Hospital admissions represent a small fraction of the children seeking care for urinary incontinence. This implies that care delivered in the hospital setting should represent a small proportion of overall costs. NACHRI cost data from its participating children's hospitals indicate that between calendar years 1999

Table 9. Physician outpatient visits for urinary incontinence by children having Medicaid, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	As Primary Diagnosis							
Total	210	656	293	497	246	649	318	682
Age								
< 3	9	*	14	*	3	*	9	*
3–10	178	975	239	735	203	1,049	242	1,039
11–17	23	*	40	311	40	411	67	516
Gender								
Male	96	599	138	467	127	667	160	684
Female	114	713	155	526	119	631	158	680
	As Any Diagnosis							
Total	298	931	436	739	330	871	505	1,083
Age								
< 3	13	*	19	*	5	*	16	*
3–10	252	1,380	348	1,070	277	1,431	392	1,683
11–17	33	568	69	537	48	493	97	747
Gender								
Male	145	904	228	772	181	951	267	1,141
Female	153	957	208	706	149	791	238	1,024

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for children in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 10. Number of plan members per year with a physician outpatient visit for pediatric urinary incontinence, by underlying condition, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	Commercially Insured Population							
Spina bifida-associated	2	0.6	7	1.5	11	1.6	14	1.9
Spinal cord injury-associated	1	0.3	0	0	4	0.6	5	0.7
Neurogenic incontinence NOS	10	3.2	32	7.1	66	9.9	91	13
Nocturnal enuresis	322	102	642	142	1,249	187	1,660	231
Other incontinence	1,224	386	1,687	372	2,380	356	2,642	367
	Medicaid Population							
Spina bifida-associated	0	0	1	1.7	1	2.6	0	0
Spinal cord injury-associated	0	0	0	0	0	0	0	0
Neurogenic incontinence NOS	2	1.1	3	5.1	1	2.6	3	6.4
Nocturnal enuresis	38	119	59	100	61	161	132	283
Other incontinence	182	568	276	468	191	504	233	500

[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 children in the same demographic stratum.
NOTE: Categories are not mutually exclusive. Underlying condition was assigned to the incontinence visit if a diagnosis code for that condition occurred on a claim for that patient that year.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 200.

Table 11. Visits to ambulatory surgery centers for urinary incontinence listed as any diagnosis by children having commercial health insurance, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	20	*	23	*	57	8.5	63	8.8
Age								
< 3	0	0	3	*	3	*	1	*
3–10	15	*	13	*	38	12	44	14
11–17	5	*	7	*	16	*	18	*
Gender								
Male	12	*	9	*	24	*	33	8.9
Female	8	*	14	*	33	10	30	8.6

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for children in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 12. Mean inpatient cost per child[a] admitted with urinary incontinence listed as primary diagnosis, 1999–2001 (95% CI)

	Count	Mean Cost	
Total	1,251	$15,219	(14,158–16,279)
Age			
0–2	83	$8,366	(6,342–10,390)
3–10	672	$14,223	(13,071–15,376)
11–17	496	$17,715	(15,591–19,838)
Race/ethnicity[b]			
White	873	$15,190	(13,911–16,469)
Black	116	$14,157	(11,095–17,220)
Asian	11	$14,291	(9,243–19,340)
Hispanic	150	$14,838	(12,879–16,797)
American Indian	2	$106,191	(0–107,008)
Gender			
Male	593	$14,788	(13,811–15,766)
Female	658	$15,607	(13,791–17,422)
Region[b]			
Midwest	451	$15,472	(13,797–17,147)
Northeast	79	$17,285	(6,081–28,489)
South	512	$15,594	(14,548–16,640)
West	197	$13,763	(11,850–15,675)

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.
[b]Values do not sum to total due to inclusion of children whose region or race/ethnicity is listed as other or missing.
SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

and 2001, the average cost of hospitalization for urinary incontinence was $15,219; it increased from $8,366 in those under age 3 to $14,223 in 3- to 10-year-olds, and to $17,715 in 11- to 17-year-olds (Table 12). This trend appears to reflect a longer average length of hospital stay for the older two groups (Table 4). However, the data are not risk-adjusted and therefore must be interpreted with caution. No variability by gender or race/ethnicity was noted in the costs of hospitalization.

The aggregate costs of delivering outpatient care for incontinence are not available, but CHCPE data provide trends in physician payment over the years from 1994 to 2000. During this period, the total mean payment for physician office visits by commercially insured children with a primary diagnosis of incontinence rose from $45 in 1994 to $60 in 2000, of which $10 to $13 was patient co-payments. Payments did not differ by age group (Table 13). Outpatient physician payments were much lower for children covered by managed Medicaid plans, ranging from $24 in 1994 to $38 in 2000 (Table 14). The differences in payments between commercially insured children and those in managed Medicaid plans were due only in part to the absence of patient co-payments in the latter group.

Although there are no direct measures of the medical coasts associated with pediatric UI, the total probably does not exceed $15 to $20 million. Table 7 shows that there are roughly 225,000 physician

Table 13. Payments by children having commercial health insurance for physician outpatient visits with urinary incontinence listed as primary diagnosis

	Count[a]	Mean Total Payment	Total Amount Paid by Plan	Total Amount Paid by Patient	Count[a]	Mean Total Payment	Total Amount Paid by Plan	Total Amount Paid by Patient
	1994				1996			
Total	1,547	$45	$35	$10	2,245	$50	$40	$10
Age								
<3	27	$38	$28	$9.7	61	$47	$36	$11
3–10	1,137	$46	$36	$10	1,684	$51	$40	$10
11–17	383	$44	$34	$9.5	500	$47	$37	$10
Gender								
Male	953	$43	$34	$9.2	1,313	$49	$38	$10
Female	594	$49	$37	$12	932	$52	$41	$10
	1998				2000			
Total	3,263	$57	$45	$12	3,794	$60	$47	$13
Age								
<3	79	$55	$42	$13	78	$54	$42	$12
3–10	2,466	$57	$45	$12	2,851	$60	$47	$13
11–17	718	$56	$45	$11	865	$57	$45	$12
Gender								
Male	1,835	$54	$43	$11	2,070	$56	$44	$12
Female	1,428	$60	$47	$13	1,724	$63	$50	$13

[a]Counts less than 30 should be interpreted with caution.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 14. Payments by children having Medicaid for physician outpatient visits with urinary incontinence listed as primary diagnosis

	Count[a]	Mean Total Payment	Total Amount Paid by Plan	Total Amount Paid by Patient	Count[a]	Mean Total Payment	Total Amount Paid by Plan	Total Amount Paid by Patient
	1994				1996			
Total	207	$24	$24	$0	290	$36	$36	$0
Age								
<3	9	$28	$28	$0	13	$30	$30	$0
3–10	175	$24	$24	$0	238	$37	$37	$0
11–17	23	$28	$28	$0	39	$31	$31	$0
Gender								
Male	96	$24	$24	$0	136	$33	$33	$0
Female	111	$25	$25	$0	154	$38	$38	$0
	1998				2000			
Total	238	$40	$40	$0	271	$38	$38	$0
Age								
<3	3	$45	$45	$0	6	$34	$34	$0
3–10	197	$40	$40	$0	209	$37	$37	$0
11–17	38	$41	$41	$0	56	$39	$39	$0
Gender								
Male	124	$39	$39	$0	140	$36	$36	$0
Female	114	$41	$41	$0	131	$39	$39	$0

[a]Counts less than 30 should be interpreted with caution.
SOURCE: Center for Health Care Policy and Evalutaion, 1994, 1996, 1998, 2000.

visits for pediatric UI per year. At $50 per visit, this would total $11 million. Similarly, the 200 annual hospitalizations shown in Table 2, at $15,000 per hospitalization would add only another $3 million.

RECOMMENDATIONS

Pediatric urinary incontinence encompasses a vast array of disease states—acute, chronic, congenital, and acquired. As in other patient groups, incontinence in children implies either a symptom or a sign, rather than a specific disease entity. While patterns of care-seeking behavior are often driven by symptoms, resource utilization, management strategies, and costs are generally dictated by the underlying condition. ICD-9 coding currently relegates urinary incontinence to a 4-digit code. Most of the 5-digit ICD-9 codes for incontinence are symptom-based, and while they are illustrative, they do not provide an etiologic context. Future population-based studies should attempt to characterize care-seeking for incontinence by underlying diagnosis.

Unfortunately, it is difficult to obtain reliable epidemiologic data for urinary incontinence in children. Stratification by smaller age cohorts might provide more insight into care-seeking patterns and the natural history of incontinence complaints. A specific finding that warrants further investigation is the demonstrated healthcare utilization by patients under age 3. In most clinical contexts, wetting in this age cohort does not require investigation. It is unclear whether this finding is spurious, reflects the imprecision of ICD-9 coding, or represents changing attitudes toward toilet training in young children. Future analyses could characterize incontinence admissions by specific underlying diagnosis, associated diagnoses, nature of procedures, or distribution of charges. It is likely that patients requiring hospitalization represent a distinct subset of the incontinence population.

Although the majority of pediatric urinary incontinence care is provided in the outpatient setting, several features of such treatment warrant further investigation. The data sources analyzed for this chapter do not allow characterization of pediatric incontinence care by the subspecialty of the treating physician. Likewise, the proportion of costs associated with pharmaceutical usage, behavioral therapy, and diagnostic studies remains obscure. In addition, the available datasets do not allow for meaningful evaluation of long-term trends or regional variation.

The economic burden of urinary incontinence invites further investigation. Direct costs of incontinence could be characterized and stratified in greater detail. The available datasets do not allow evaluation of aggregate costs by treatment venue. An evaluation of indirect costs, including work absenteeism among caretakers and school absences among those treated, is also not available.

Urinary incontinence is a common reason for healthcare visits by children. Despite the prevalence of these complaints in the pediatric age group, relatively little epidemiologic and health services research has been directed at the large information gaps. To estimate the burden of pediatric incontinence care with an accurate picture of contemporary care patterns, this chapter has synthesized data from a broad array of sources, but the sparsity of the data has made the task difficult.

REFERENCES

1. Goellner MH, Ziegler EE, Fomon SJ. Urination during the first three years of life. Nephron 1981;28:174-8.
2. Brazelton TB, Christophersen ER, Frauman AC, Gorski PA, Poole JM, Stadtler AC, Wright CL. Instruction, timeliness, and medical influences affecting toilet training. Pediatrics 1999;103:1353-8.
3. Bloom DA, Seeley WW, Ritchey ML, McGuire EJ. Toilet habits and continence in children: an opportunity sampling in search of normal parameters. J Urol 1993;149:1087-90.
4. Norgaard JP, van Gool JD, Hjalmas K, Djurhuus JC, Hellstrom AL. Standardization and definitions in lower urinary tract dysfunction in children. International Children's Continence Society. Br J Urol 1998;81 Suppl 3:1-16.
5. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. 4th ed. Washington, DC: American Psychiatric Association, 2000.
6. Forsythe WI, Redmond A. Enuresis and spontaneous cure rate. Study of 1129 enuretics. Arch Dis Child 1974;49:259-63.
7. Schmitt BD. Nocturnal enuresis. Pediatr Rev 1997;18:183-90; quiz 91.

CHAPTER 13

Urinary Tract Infection in Children

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Urinary Tract Infection in Children

Andrew L. Freedman, MD

INTRODUCTION

Urinary tract infection (UTI) affects 2.6% to 3.4% of children in the United States annually. Throughout childhood, the risk of UTI is 2% for boys and 8% for girls. UTIs are primarily managed in physicians' offices, where they account for more than 1 million visits (0.7% of all pediatric office visits) per year. The emergency room is also an important site of care, accounting for 5% to 14% of physician encounters for pediatric UTI. Inpatient hospitalization is required in 2% to 3% of cases, with UTI accounting for more than 36,000 admissions in 2000. More care is rendered to girls than to boys, at a ratio of 3–4 to 1. Hospitalization is more frequent for infants, but it is more expensive for adolescents. Overall costs for inpatient hospital care increased during the 1990s despite shorter lengths of stay. The cost of hospitalization for UTI amounts to more than $180 million annually. However, the true financial burden is probably much higher because it includes costs for outpatient services, imaging, other diagnostic evaluations, long-term complications, and management of associated conditions that increase the frequency and morbidity of UTI. The economic impact on the family due to parental work loss is largely unknown. Efforts to lessen the economic burden on patients, payers, and society include decreasing the length and frequency of inpatient hospitalizations, streamlining the post-UTI imaging evaluation, developing new antimicrobials to fight resistant organisms, and generating easy-to-implement nonantimicrobial strategies.

DEFINITION AND DIAGNOSIS

Normally, the urinary tract proximal to the distal urethra is sterile, but it is constantly challenged by infectious pathogens fighting to gain access. A UTI, strictly speaking, occurs when an infectious agent is present within this sterile system; however, a more appropriate clinical definition is that UTI occurs when the infectious agent is not only present, but is also causing illness. This distinction underscores the inherent clinical difficulty of managing patients with UTI. In practice, a diagnosis of UTI is presumed when irritative urinary tract symptoms occur simultaneously with a positive test for infectious agents, such as bacteria, fungi, viruses, or parasites, in the urinary tract. Because other factors can cause similar symptoms, the presence of symptoms in the absence of a positive culture has historically been considered inadequate for diagnosis. Likewise, the presence of leukocytes in the urine is not proof of infection. Asymptomatic bacteriuria may represent colonization or contamination and should be differentiated from UTI. Thus, for clinical purposes, the definition of a UTI requires a combination of symptoms and laboratory findings.

Both the infectious agent and the anatomic location typically define the UTI. The urinary tract is commonly divided into the upper tract (kidneys and ureters) and the lower tract (bladder and urethra). In the male, infections such as prostatitis, epididymitis, and orchitis are frequently included as UTIs but are more accurately considered genital infections; they have a separate epidemiology and natural history.

Table 1. ICD-9 codes used in the diagnosis and management of pediatric urinary tract infection

Individuals under 18 with any one of the following ICD-9 codes:	
Cystitis	
112.2	Candidiasis of other urogenital sites
120.9	Schistosomiasis, unspecified
595.9	Cystitis, unspecified
595.1	Chronic interstitial cystitis
595.0	Acute cystitis
595.3	Trigonitis
595.89	Other specified types of cystitis
595.2	Other chronic cystitis
Pyelonephritis	
590.0	Chronic pyelonephritis
590.00	Chronic pyelonephritis without lesion of renal medullary necrosis
590.01	Chronic pyelonephritis with lesion of renal medullary necrosis
590.1	Acute pyelonephritis
590.10	Acute pyelonephritis without lesion of renal medullary necrosis
590.11	Acute pyelonephritis with lesion of renal medullary necrosis
590.2	Renal and perinephric abscess
590.3	Pyeloureteritis cystica
590.8	Other pyelonephritis or pyonephrosis, not specified as acute or chronic
590.9	Infection of kidney, unspecified
593.89	Other specified disorders of kidney and ureter
Orchitis	
016.5	Tuberculosis of other male genital organs
072.0	Mumps orchitis
603.1	Infected hydrocele
604.0	Orchitis epididymitis and epididymo-orchitis with abscess
604.9	Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess
604.90	Orchitis and epididymitis, unspecified
604.99	Other orchitis epididymitis and epididymo-orchitis without abscess
608.0	Seminal vesiculitis
608.4	Other inflammatory disorders of male genital organs
Other	
597.89	Other urethritis
599.0	Urinary tract infection, site not specified
607.1	Balanoposthitis
607.2	Other inflammatory disorders of penis
646.5	Asymptomatic bacteriuria in pregnancy

In this chapter, genital infections are excluded from the definition of UTI, and non-sexually transmitted orchitis is discussed separately.

UTIs are also categorized as complicated or uncomplicated. Complicated UTIs are infections in which there is a comorbidity that predisposes a child either to infection or to greater morbidity due to the infection. Comorbidities include the presence of stones, neurological impairment affecting urinary tract functioning, and anatomic abnormalities such as obstruction, reflux, or enterovesical fistula.

UTI is a frequent complication of medical care, especially hospitalization. Unfortunately, the datasets analyzed for this chapter preclude distinguishing nosocomial from community-acquired infections.

In this compendium, children are defined as persons less than 18 years of age. Where possible, they are further subdivided into infants (under 3 years of age), older children (3 to 10), and adolescents (11 to 17). Most of the datasets analyzed for this chapter do not distinguish the site of the UTI, with the notable exception of data from the Healthcare Cost and Utilization Project (HCUP) and MarketScan, in which pyelonephritis and orchitis, respectively, are distinguished from UTIs in other sites. The method by which the site of UTI is determined in these datasets is based on diagnostic coding and likely varies across the population.

The vast majority of UTIs are caused by bacterial agents, the most important of which are the Enterobacteriaciae, a family of gram-negative bacilli. *Escherichia coli* accounts for more than 80% of acute UTIs in children. The rest of the cases are distributed primarily among *Proteus mirabilis*, *Klebsiella pneumonia*, and *Pseudomonsa aeruginosa*. Less common infectious agents include gram-positive cocci, such as *Enterococcus* and *Staphylococcus*. Fungal infections, particularly *Candida*, are usually seen in nosocomial infections, complicated UTIs, or catheter-associated UTIs. Viral infections are under-recognized because of difficulties with culture and identification, but they have clearly been associated with infectious bladder symptoms. Cytomegalovirus is frequently seen in immunocompromised patients, particularly following organ transplantation.

Analyses for this chapter are based on the ICD-9 codes defining UTI listed in Table 1.

The clinical diagnosis of UTI is usually based on a combination of symptoms, physical and radiographic findings, and laboratory results. Diagnostic methods vary markedly and depend on presentation, clinical suspicion, medical history, and local practice patterns. Children pose a unique challenge in the diagnosis of UTI, because they often are unable to provide an accurate history or description of symptoms. Obtaining adequate specimens may also be difficult, and clinical signs such as fever and leukocytosis may be unreliable in the very young.

A lower tract infection is typically suspected in the presence of dysuria, urgency, frequency, and, less commonly, suprapubic pain. Upper tract involvement is typically heralded by fever, flank pain, nausea, vomiting, and lethargy. In the young child, there can be significant overlap in the clinical presentations of upper and lower tract infections. Symptoms may not be verbalized, and the diaper may conceal the voiding pattern. Fever is frequently the presenting sign, although lethargy may be the sole indicator of significant infection in infants. Parents' perception of an odor is an unreliable sign of infection (1). Hence, the clinician must have a high index of suspicion to make an accurate diagnosis of UTI.

Diagnosis is further hindered by the difficulty of obtaining adequate samples for laboratory testing. Urinalysis, the standard initial screening test for UTI, ideally requires a midstream, clean catch of urine, but this may be impossible in the very young. Alternatively, urine can be obtained by sterile catheterization or suprapubic needle aspiration. However, both of these techniques are invasive and frequently met with parental disapproval. Urine may be obtained by the adherence of a sterile collection bag to the perineum, but this method has a high rate of contamination, limiting its reliability. Once obtained, urine is examined with a reagent dipstick for the presence of nitrates and leukocyte esterase. A finding that the urine is crystal clear to visual inspection has a 97% negative predictive value for UTI (2). The urine can also be microscopically examined after gram-stain, as well as cultured for the presence of bacteria or fungi. Other adjunctive laboratory tests include serum white blood cell count and C-reactive protein level (3).

Imaging studies can assist in diagnosis, but they play a more prominent role in elucidating underlying comorbid conditions that may increase the risk or morbidity of infection. Ultrasound, the most common imaging study employed in cases of pediatric UTI, is used to evaluate for the presence of obstruction or stones, which can greatly increase the severity and sequelae of infection. The ultrasonographic appearance of the kidney can also be altered by the presence of acute infection. Ultrasound can assist in localizing the site of infection in the presence of renal abscess, parenchymal edema (lobar nephronia), or pyonephrosis. Despite the many advantages of ultrasound (it has no ionizing radiation and is non-invasive, well-tolerated, relatively low-cost, and readily available), its usefulness for identifying acute UTI has recently been questioned, given its relatively low yield in an era of widespread prenatal screening (4). Indeed, significant controversy has arisen over the timing of imaging studies and their implications for therapy recommendations in children with UTIs (4).

The nuclear renal scan with dimercaptosuccinic acid (DMSA) has been proposed as the most sensitive means for documenting renal involvement in UTI (5). It has been reported to be the best method for confirming acute pyelonephritis and later for assessing the presence of scarring. Many advocate basing further evaluation and follow-up care on the results of the DMSA scan (6). Computed tomography (CT) can also be useful for identifying anatomic anomalies, stones, and intrarenal abscess, as well as for documenting renal involvement in UTIs. CT is often used to exclude alternate diagnoses, such as appendicitis, in the presence of fever and abdominal pain or hematuria. Intravenous pyelography (IVP) is rarely used in the evaluation of pediatric UTI, particularly in young children, in whom renal visualization is limited by poor renal concentrating ability and increased small bowel air. Voiding cystourethrography (VCUG) has no role in the diagnosis of acute UTI, although it is nearly universally recommended for identifying vesicoureteral reflux or other anatomic abnormalities that may contribute to future infection risk.

NATURAL HISTORY

The natural history of uncomplicated acute cystitis is generally benign and free of significant long-term morbidity. The course is typically characterized by discomfort and irritative voiding symptoms with rapid resolution following the initiation of appropriate antimicrobials. The primary risk is that of recurrence or persistence. Children with constipation or voiding dysfunction are particularly prone to recurrence; 10% of these children develop a rapid recurrence following the completion of a course of antimicrobials. However, most recurrences do not progress to severe infections in the absence of anatomic abnormalities, and recurrent childhood UTIs tend to disappear in adolescence.

The natural history of pyelonephritis carries greater potential for long-term morbidity. Pyelonephritis can result in irreversible scarring of the renal parenchyma due to interstitial inflammation and virulence factors from the pathogen. Renal scarring is frequently, although not exclusively, associated with the simultaneous presence of reflux and infection. The likelihood of scarring increases with the number of infectious episodes, but significant renal damage can occur after a single infection. Renal scarring can lead to renal insufficiency and subsequent hypertension. The actual incidence of renal insufficiency due to scarring is unknown, in part because of changing definitions of reflux nephropathy and changing clinical presentations that have resulted from the widespread use of prenatal ultrasound. Historically, reflux nephropathy was considered responsible for 3% to 25% of the ESRD cases in children (7).

RISK FACTORS

The urinary tract is challenged by the ubiquitous presence of pathogens in close proximity. Any factors that enhance bacterial virulence or detract from host defense can predispose to UTI. Bacterial virulence factors include adhesins, K-antigen, hemosysins, and colicin. Bacterial colonization of the perineum typically precedes acute infection in the susceptible host. Adhesins are specialized structures that enable the bacteria to adhere to specific receptors on the uroepithelium. Such attachment leads to ascension into the urinary tract and promotes tissue invasion, inflammation, and tissue injury. Adhesins may also help promote intestinal carriage of more virulent bacteria, leading to perineal colonization. K-antigen helps prevent phagocytosis of bacteria; hemosysins damage renal tubular cells; and colocin helps kill competing bacteria near the colocin-producing cell.

Successful host defense depends on the proper functioning of the urinary system. A primary function of the urinary tract is the frequent and complete emptying of urine in a low-pressure environment. This effectively flushes out bacteria prior to their establishment of clinical infection. Any breakdown in this process can tip the balance toward the pathogen and result in UTI. Host risk factors are thought to include vesicoureteral reflux, dysfunctional voiding, constipation, obstruction, and gender-specific anatomy (the short urethra in females and the prepuce in males).

Vesicoureteral reflux is a frequent finding in children presenting with febrile infections. Present in approximately 1% of the asymptomatic population and 35% of those with UTI, reflux increases the risk of infection, in part by increasing post-void residual. Reflux also bypasses one of the host defense mechanisms against upper tract invasion by allowing less virulent strains of bacteria to reach the kidney.

Obstruction at the ureteropelvic junction, ureterovesical junction, or urethra is an infrequent but important host risk factor that can contribute to increased morbidity, persistence, and recurrence. Obstruction is present in fewer than 1% of children with UTI.

Dysfunctional voiding and dysfunctional elimination (constipation or functional fecal retention) are increasingly recognized as important host risk factors for UTI, particularly recurrent infections in anatomically normal children. Dysfunctional voiding refers to a learned pattern of behavior surrounding voiding that frequently begins with voluntary holding. It can present clinically with irritative symptoms such as urgency, frequency, urge incontinence, pelvic pain, and signs of holding such as squatting. Alternatively, it can present as an atonic bladder with infrequent voiding and high post-void residuals. In both patterns, elevated intravesical pressure, infrequent voiding, and poor emptying enhance the risk of UTI. Frequently, dysfunctional voiding can be compounded by chronic constipation. The exact mechanism by which constipation exerts its influence on voiding is unclear, but it frequently coexists in children with recurrent UTIs, and its resolution is often associated with resolution of the UTIs.

The relatively short length of the female urethra has traditionally been blamed for the increased risk of UTIs in girls. In the past, there was concern that a tight ring narrowed the urethra, often prompting urethral dilation in girls with UTI. Current evidence indicates that urethral constriction is not a reproducible finding, nor does it cause infection. Urethral dilation should play no role in the contemporary management of UTI in girls.

In boys, the most widely discussed host risk factor for UTI is the presence of the prepuce. It is clear that male infants with an intact prepuce are at a significantly higher risk of UTI during their first year of life. Colonization of bacteria on the inner preputial mucosa occurs, but it is not clear whether this is the etiology of infection (8). Circumcision is protective against UTI, but it carries its own risks. Uncircumcised boys have an overall 12-fold increased risk of urinary infection during their first 6 months compared with circumcised boys, in addition to a significantly higher probability of hospital admission for UTI (7.02 of 1,000) as compared with circumcised boys (1.88 of 1,000; $P<0.0001$) (9). A fuller discussion of this controversial subject is beyond the scope of this chapter.

INCIDENCE

It is difficult to estimate accurately the incidence of UTI in the pediatric population. Contributing questions include whether the determination of infection is based on symptoms, positive culture, or both; how accurate the method of specimen collection is; how accurate the history is, especially in young children; whether evaluation is focused on a specific age group or gender; whether the data are prospective or retrospective; whether or not the infections are associated with fever; and what the baseline rate of circumcision is in the population.

Frequently quoted estimates place the incidence of UTI in infants at approximately 1% during the first year of life (boys and girls), cumulative incidence at approximately 2% at two years of life (boys and girls), and cumulative childhood risk at 2% for boys and 8% for girls (10). Beyond the age of 2, UTIs in boys are not common enough to alter the childhood incidence through age 17.

Boys are at the greatest risk for UTI in the first months of life, but the risk decreases significantly after age 2. Boys who are uncircumcised have a tenfold higher risk of UTI in the first year of life than do circumcised boys (11, 12).

Girls have an increased risk of febrile infection in the first year of life, then the risk steadily declines throughout childhood. Their risk of nonfebrile infections is higher during childhood than during infancy.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Data from the Healthcare Cost and Utilization Project (HCUP) reveal that annual inpatient hospitalizations for UTI decreased slightly between 1994 and 2000, from 41,204 (60 per 100,000 children) to 36,568 (51 per 100,000 children) (Table 2). This declining trend was noted in both genders but was inconsistent across racial/ethnic groups and geographic regions. In 2000, hospitalization rates for UTI in infants (174 per 100,000) were substantially higher than those for older children (29 per 100,000) or adolescents (24 per 100,000). During the mid to late 1990s, girls were about 2.5 times more likely than boys to be hospitalized for UTI. Although not age-adjusted, the data from HCUP suggest that Hispanics were at much greater risk for UTI-related hospitalization than other racial/ethnic groups and that African Americans were at greater risk than Caucasians.

HCUP data also indicate that between 1994 and 2000, annual inpatient hospitalizations associated with pyelonephritis as a primary diagnosis remained stable at about 13,000 per year (18 to 20 per 100,000) (Table 3). Despite recent support for outpatient treatment of pediatric pyelonephritis (13), these data indicate no trend downward in hospitalization rates for this condition. From 1996 onward, the hospitalization rate was at least 2.5 times higher for infants than it was for older children or adolescents. The female-to-male ratio was at least 5:1 for each year analyzed. Racial/ethnic stratification suggested that African American children had a trend toward somewhat lower hospitalization rates for pyelonephritis, and that rates for Asian children were even lower. While the gender differences are consistent with clinical experience, the reasons for the racial/ethnic differences are not apparent. Hospitalization rates did not appear to vary by geographical region, but urban teaching hospitals had higher rates than did rural hospitals.

Age differences were most prominent among patients requiring hospitalization. The rate of inpatient hospital stays was 6.4 times higher among commercially insured infants than the rate among older children, and 11 times higher than the rate among adolescents (Table 4). This reflects the fact that UTIs in young children are more likely to involve the upper tract or to be complicated by comorbidities such as anatomic abnormalities. It also reflects more aggressive treatment patterns in the very young that tend to include parental antimicrobials.

Outpatient Care

Tables 4 and 5 present data from the Center for Health Care Policy and Evaluation (CHCPE) on visits by children insured commercially or through Medicaid for whom UTI was listed as the primary diagnosis. In both groups, the most common site of care for UTI was physicians' offices. Overall rates of visits to physicians' offices for UTI remained stable throughout the 1990s at approximately 2,400 per 100,000 (2.4%) for children with commercial insurance (Table 4) and 2,800 per 100,000 (2.8%) for children with Medicaid (Table 5). Among other settings—all much less commonly used than physicians' offices—emergency room (ER) visits were three times more common than inpatient hospitalizations. Of all encounters for which UTI was listed as the primary diagnosis, the rates of ER visits were substantially higher for those insured by Medicaid (Table 5) than the rates for those insured commercially (Table 4). Hospital outpatient clinics and ambulatory surgical centers contributed minimally, especially in the Medicaid population. Children with Medicaid visited physicians' offices, ERs, and ambulatory surgery centers more often than did children with commercial insurance.

That children with Medicaid visited emergency rooms for UTI-related care 2.8 times more frequently in 2000 than did those with commercial insurance (422 per 100,000 vs 150 per 100,000) is consistent with well-known patterns of care in socioeconomically disadvantaged populations. The slight decrease in the use of ERs by those insured through Medicaid from 1994 to 2000 may reflect improved access to primary care physicians or increasing dissatisfaction with the availability of ER care.

Table 2. Inpatient hospital stays by children with urinary tract infection listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	41,204	60 (54–67)	40,378	57 (51–63)	39,822	56 (50–61)	36,568	51 (46–55)
Age								
0–2	21,128	177 (150–203)	22,797	191 (163–219)	22,591	194 (166–222)	20,372	174 (153–195)
3–10	11,629	38 (34–41)	10,185	32 (28–35)	9,987	31 (27–34)	9,323	29 (26–31)
11–17	8,447	33 (30–36)	7,396	27 (25–30)	7,245	26 (24–28)	6,874	24 (23–26)
Gender								
Male	12,516	36 (30–42)	12,341	34 (28–40)	11,317	31 (26–36)	10,258	28 (24–31)
Female	28,678	86 (79–94)	28,037	81 (73–89)	28,501	81 (75–88)	26,306	75 (68–81)
Race/ethnicity								
White	18,579	41 (38–44)	17,276	38 (34–41)	16,339	36 (33–39)	14,504	32 (28–35)
Black	5,954	55 (48–62)	5,601	50 (43–57)	4,373	39 (33–46)	3,364	30 (25–36)
Asian/Pacific Islander	549	28 (20–37)	411	14 (8–20)	900	29 (20–39)	851	28 (19–38)
Hispanic	6,872	74 (50–97)	8,452	82 (56–107)	7,159	66 (45–86)	8,032	69 (58–80)
Region								
Midwest	8,394	51 (45–56)	7,393	44 (37–51)	7,443	44 (39–48)	7,666	44 (37–51)
Northeast	7,553	59 (49–68)	7,600	58 (48–67)	8,231	64 (51–76)	6,044	46 (39–54)
South	17,204	75 (61–90)	16,756	69 (57–80)	16,453	66 (55–77)	15,036	61 (52–71)
West	8,053	50 (38–63)	8,630	52 (34–69)	7,695	45 (35–56)	7,822	45 (37–53)
MSA								
Rural	7,946	46 (41–52)	7,738	48 (42–53)	6,780	41 (38–45)	6,938	44 (40–48)
Urban	33,114	65 (57–73)	32,595	59 (51–67)	32,794	59 (53–66)	29,594	52 (47–58)
Hospital type								
Rural	7,946	12 (10–13)	7,738	11 (10–12)	6,780	9 (9–10)	6,938	10 (9–10)
Urban non-teaching	16,230	24 (21–27)	16,764	24 (20–27)	10,929	15 (13–17)	11,435	16 (14–18)
Urban teaching	16,885	25 (20–30)	15,831	22 (17–27)	21,865	31 (26–35)	18,159	25 (21–29)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under age 18.

[b]Persons of missing gender, other races, missing or unavailable race and ethnicity, missing MSA, and missing hospital type are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 3. Inpatient hospital stays by children with pyelonephritis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	13,334	20 (18–21)	13,536	19 (17–21)	13,226	18 (17–20)	12,926	18 (16–20)
Age								
0–2	3,372	28 (23–33)	4,537	38 (31–45)	4,206	36 (29–43)	4,466	38 (32–45)
3–10	5,268	17 (15–19)	4,818	15 (13–17)	4,728	15 (12–17)	4,450	14 (12–15)
11–17	4,695	18 (17–20)	4,181	15 (14–17)	4,292	16 (14–17)	4,010	14 (13–16)
Gender								
Male	2,229	6.4 (5.3–7.4)	2,200	6.0 (4.7–7.4)	2,024	5.5 (4.5–6.6)	2,206	6.0 (4.9–7.0)
Female	11,099	33 (30–36)	11,336	33 (30–36)	11,201	32 (29–35)	10,720	30 (27–33)
Race/ethnicity								
White	7,150	16 (14–17)	6,869	15 (13–16)	6,647	14 (13–16)	5,934	13 (11–15)
Black	1,398	13 (11–15)	1,297	12 (10–14)	928	8.3 (6.5–10.1)	940	8.4 (6.2–10.6)
Asian/Pacific Islander	178	9.2 (5.2–13)	*	*	185	6.0 (3.2–8.8)	171	5.7 (3.2–8.2)
Hispanic	1,390	15 (12–18)	2,170	21 (15–27)	1,443	13 (9–17)	1,942	17 (13–20)
Region								
Midwest	3,032	18 (16–21)	3,036	18 (15–21)	3,066	18 (15–21)	3,263	19 (15–22)
Northeast	2,422	19 (14–23)	2,476	19 (15–22)	2,227	17 (14–20)	1,881	14 (12–17)
South	5,019	22 (19–25)	4,630	19 (16–22)	4,860	20 (17–23)	4,701	19 (15–23)
West	2,861	18 (14–21)	3,394	20 (14–27)	3,073	18 (13–23)	3,080	18 (14–22)
MSA								
Rural	3,314	19 (16–22)	2,903	18 (16–20)	3,104	19 (17–21)	2,846	18 (16–21)
Urban	9,964	20 (17–22)	10,589	19 (17–22)	10,025	18 (16–20)	10,067	18 (16–20)
Hospital type								
Rural	3,314	4.9 (4.1–5.6)	2,903	4.1 (3.6–4.6)	3,104	4.3 (3.8–4.9)	2,846	3.9 (3.4–4.5)
Urban nonteaching	5,450	8.0 (7.1–8.8)	5,552	7.8 (6.8–8.8)	3,933	5.5 (4.8–6.2)	4,169	5.8 (5.0–6.6)
Urban teaching	4,514	6.6 (5.3–8.0)	5,037	7.1 (5.5–8.6)	6,092	8.5 (6.8–10.2)	5,898	8.2 (6.6–9.7)

*Figure does not meet standard of reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under age 18.

[b]Persons of other races, missing or unavailable race and ethnicity, missing MSA, and missing hospital type are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 4. Visits for urinary tract infections listed as primary diagnosis among children having commerical health insurance, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
	Physician Office Visits							
Total	7,600	2,395	10,801	2,382	16,206	2,425	17,101	2,374
Age								
<3	1,234	3,033	1,802	3,078	3,001	3,383	3,033	3,181
3–10	4,105	2,816	5,923	2,841	9,059	2,950	9,338	2,864
11–17	2,261	1,727	3,076	1,651	4,146	1,522	4,730	1,582
Gender								
Male	1,474	906	2,057	887	2,988	872	3,087	835
Female	6,126	3,961	8,744	3,950	13,218	4,059	14,014	3,997
	Emergency Room Visits							
Total	431	136	575	127	958	143	1,079	150
Age								
<3	81	199	97	166	197	222	183	192
3–10	185	127	271	130	422	137	459	141
11–17	165	126	207	111	339	124	437	146
Gender								
Male	85	52	132	57	176	51	218	59
Female	346	224	443	200	782	240	861	246
	Inpatient Visits							
Total	147	46	206	45	370	55	367	51
Age								
<3	68	167	104	178	178	201	202	212
3–10	54	37	67	32	115	37	108	33
11–17	25	*	35	19	77	28	57	19
Gender								
Male	32	20	41	18	56	16	88	24
Female	115	74	165	75	314	96	279	80
	Hospital Outpatient Visits							
Total	27	*	75	17	185	28	153	21
Age								
<3	2	*	16	*	58	65	40	42
3–10	16	*	48	23	94	31	79	24
11–17	9	*	11	*	33	12	34	11
Gender								
Male	3	*	14	*	28	*	28	*
Female	24	*	61	28	157	48	125	36
	Ambulatory Surgery Visits							
Total	49	15	63	14	211	32	139	19
Age								
<3	6	*	13	*	70	79	49	51
3–10	31	21	40	19	105	34	69	21
11–17	12	*	10	*	36	13	21	*
Gender								
Male	19	*	16	*	44	13	32	8.7
Female	30	19	47	21	167	51	107	31

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for children in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

Table 5. Visits for urinary tract infections listed as primary diagnosis among children having Medicaid, count[a], rate[b]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
				Physician Office Visits				
Total	910	2,842	1,428	2,420	1,096	2,893	1,309	2,806
Age								
<3	193	2,427	350	2,569	312	3,551	335	3,232
3–10	554	3,035	838	2,576	572	2,955	733	3,147
11–17	163	2,804	240	1,868	212	2,177	241	1,855
Gender								
Male	214	1,334	337	1,140	271	1,424	305	1,304
Female	696	4,355	1,091	3,704	825	4,378	1,004	4,318
				Emergency Room Visits				
Total	193	603	303	514	155	409	197	422
Age								
<3	52	654	93	683	56	637	80	772
3–10	95	520	125	384	65	336	75	322
11–17	46	791	85	662	34	349	42	323
Gender								
Male	40	249	68	230	33	173	59	252
Female	153	957	235	798	122	647	138	594
				Inpatient Stays				
Total	36	112	59	100	43	114	44	94
Age								
<3	22	*	39	286	31	353	32	309
3–10	12	*	16	*	11	*	7	*
11–17	2	*	4	*	1	*	5	*
Gender								
Male	10	*	17	*	14	*	14	*
Female	26	*	42	143	29	*	30	129
				Hospital Outpatient Visits				
Total	7	*	23	*	13	*	7	*
Age								
<3	1	*	10	*	2	*	6	*
3–10	4	*	11	*	9	*	0	0
11–17	2	*	2	*	2	*	1	*
Gender								
Male	4	*	5	*	2	*	0	0
Female	3	*	18	*	11	*	7	*
				Ambulatory Surgery Visits				
Total	4	*	3	*	59	156	31	66
Age								
<3	0	0	1	*	31	353	15	*
3–10	4	*	1	*	26	*	16	*
11–17	0	0	1	*	2	*	0	0
Gender								
Male	2	*	2	*	15	*	7	*
Female	2	*	1	*	44	233	24	*

*Figure does not meet standard for reliability or precision.
[a]Counts less than 30 should be interpreted with caution.
[b]Rate per 100,000 based on member months of enrollment in calendar year for children in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000.

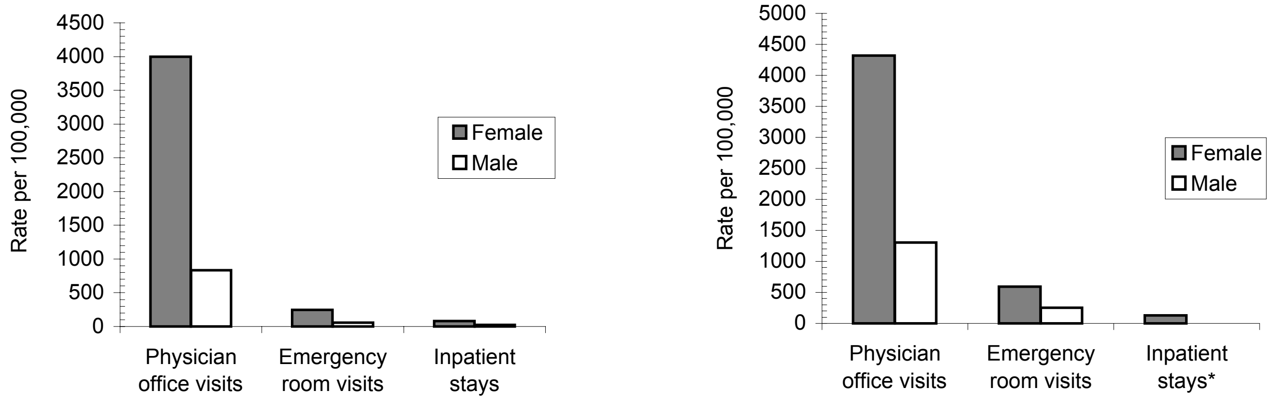

Figure 1. Urinary tract infections listed as primary diagnosis among children having commercial health insurance (left) and Medicaid (right) by visit setting and gender.

***The rate for males in this category was too low to produce a reliable national estimate.**

SOURCE: Center for Health Care Policy and Evaluation, 2000.

As expected, girls had much higher visit rates than boys did (Tables 4 and 5, Figure 1). The female-to-male ratio for physicians' office visits by commercially insured children rose from 4.4:1 in 1994 to 4.8:1 in 2000 (Table 4), but it remained stable at about 3.3:1 for children insured through Medicaid during the same time period (Table 5). The differences in these ratios are difficult to explain, but they may be due in part to the fact that boys covered by Medicaid are less likely to be circumcised. Caucasians are considerably more likely to be circumcised than are African Americans or Hispanics (81% vs 65% or 54%); these differences remain significant when other variables are controlled (14). Circumcision is not a covered service, and families insured through Medicaid may not be able to afford to pay for it out-of-pocket; the cost of circumcision typically ranges from $250 to $750. Families insured through Medicaid may also be more likely to have social norms that do not include routine circumcision. In the office setting, adolescents had lower visit rates than did either infants or older children, regardless of insurance status (Tables 4 and 5).

Data from the National Ambulatory Medical Care Survey showed that during 1992, 1994, 1996, 1998, and 2000, there were there were more than 1.1 million annual physician office visits (1,590 per 100,000 in each year) associated with UTI as the primary diagnosis and 1.4 million annual physician office visits (2,051 per 100,000 in each year) associated with UTI as any listed diagnosis (Table 6). Because counts were low for this diagnosis in children, these counts and rates were derived by first collapsing data from the even years in 1992–2000 and then dividing by 5. As a primary diagnosis, UTI accounted for 0.7 % of all physician office visits by children during those years. Data from the National Hospital Ambulatory Medical Care Survey showed that during 1994, 1996, 1998, and 2000, approximately 94,000 annual hospital outpatient visits (132 per 100,000 in each year) were associated with UTI as a primary diagnosis, representing 0.5% of all hospital outpatient visits by children (Table 7). Because counts were low for this diagnosis in children, these counts and rates were derived by first collapsing data from the even years in 1994–2000 and then dividing by 4.

NON-SEXUALLY TRANSMITTED ORCHITIS

Isolated orchitis is extremely rare in the prepubertal male and in most cases is due to the extension of acute epididymitis into epididymo-orchitis. Most cases occur in adolescents and present with fever, pain, testicular swelling, and scrotal erythema. The primary differential diagnosis is torsion of the testis or appendix testis. Often, there is a simultaneous UTI. Frequently, an associated

Table 6. Physician office visits by children with urinary tract infections, 1992–2000 (merged), count (95% CI), number of visits, percentage of visits, rate[a] (95% CI)

	5-Year Count (95% CI)	Total No. Visits by Male/Females <18, 1992–2000	% of Visits	5-Year Rate (95% CI)
Primary diagnosis	5,556,971 (4,502,468–6,611,474)	809,286,031	0.7	7,949 (6,440–9,457)
Any diagnosis	7,171,390 (5,995,021–8,347,759)	809,286,031	0.9	10,258 (8,575–11,941)

[a]Rate per 100,000 based on the sum of weighted counts in 1992, 1994, 1996, 1998, and 2000 over the mean estimated base population across those five years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under age 18.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 7. Hospital outpatient visits by children with urinary tract infections, 1994–2000 (merged), count (95% CI), number of visits, percentage of visits, rate[a] (95% CI)

	4-Year Count (95% CI)	Total No. Visits by Males/Females <18, 1994–2000	% of Visits	4-Year Rate (95% CI)
Primary diagnosis	374,907 (298,369–451,445)	72,578,652	0.5	529 (421–637)
Any diagnosis	527,424 (430,174–624,674)	72,578,652	0.7	744 (607–882)

[a]Rate per 100,00 based on the sum of weighted counts in 1994, 1996, 1998, and 2000 over the mean estimated base population across those four years. Population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population under age 18.

SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

predisposing factor, such as urethral obstruction, ectopic ureter, neurogenic bladder dysfunction, or recent catheterization, is present. On rare occasions, orchitis may be caused by hematogenous spread of bacteria. Nonbacterial epididymitis can also result from vasal reflux of urine causing an inflammatory response. Rare, nonbacterial cases include viral, tuberculous, and mumps orchitis.

HCUP data indicate that inpatient hospitalization for orchitis is rare, 1.6 per 100,000 in 2000 (Table 8). MarketScan data from 1999 indicate that despite the general recommendation for antimicrobial treatment for orchitis, only 22% of children treated in physicians' offices or hospital outpatient clinics received an antimicrobial within a week of the visit, and only 43% received an antimicrobial within a year of the visit (Table 9). Of those treated in ERs, 56% received an antimicrobial. In the ER, adolescents were twice as likely to receive an antimicrobial as were boys 3 to 10 years of age. The unexpectedly low utilization of antimicrobials may be due in part to incorrect coding, as many children with torsion of the appendix testis are misclassified as having epididymitis despite the absence of infection. The higher rate of antimicrobial usage in adolescents may represent an appropriate understanding that the true infectious form of this disease is more common in this age group. Greater rigor in diagnosis and terminology is necessary to utilize antimicrobials appropriately in the treatment of patients with orchitis.

ECONOMIC IMPACT

Direct Cost

Pediatric UTIs are a significant source of healthcare expenditures. Data analyzed for this chapter are limited to the immediate costs of

Table 8. Inpatient hospital stays for children with orchitis[a], count, rate[b]

Year	Count	Rate
1994	1,036	3.0
1996	777	2.1
1998	576	1.6
2000	612	1.6

[a]Orchitis defined as ICD-9 code 604.xx.

[b]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population under age 18.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 9. Use of antibiotics in the treatment of pediatric orchitis, 1999

	# of boys who had a physician office visit or hospital outpatient visit for orchitis	% of boys w/ office visit who received an antibiotic within a year of the visit	% of boys w/ office visit who received an antibiotic within a week of the visit	# of boys who had an ER visit for orchitis	% of boys w/ ER visit who received an antibiotic within a year of the visit	% of boys w/ ER visit who received an antibiotic within a week of the visit
Total	60	43%	22%	9	56%	56%
Age						
0–2	5	40%	0%	0		
3–10	12	58%	33%	3	33%	33%
11–17	43	40%	21%	6	67%	67%
Region						
Midwest	23	48%	26%	3	33%	33%
Northeast	13	23%	15%	3	33%	33%
South	17	47%	18%	0		
West	4	50%	25%	3	100%	100%
Unknown	3	67%	33%	0		

SOURCE: MarketScan, 1999.

treatment of the acute infection; however, UTI is frequently a manifestation of a larger underlying condition. Hence, much of the economic burden of diagnosing and treating the related conditions is not included here. Costs are not included for follow-up imaging, long-term antimicrobials, or treatment of anatomic abnormalities, dysfunctional elimination, and neurological abnormalities. Also not included in these analyses are long-term costs related to the sequelae of repeated pyelonephritis and scarring, such as hypertension or renal insufficiency.

According to data from the National Association of Children's Hospitals and Related Institutions (NACHRI), the mean cost per child admitted for a UTI from 1999 to 2001 was $4,501 (Table 10). The cost was higher among adolescents ($6,796) than among infants ($4,069) or older children ($4,554). Costs were higher for boys ($5,165) than for girls ($4,094). Costs were highest in the Northeast ($5,518) and lowest in the Midwest ($3,948). No racial/ethnic differences in costs were apparent. Inpatient costs per admission rose from $3,869 in 1999 to $4,444 in 2000 and $5,145 in 2001, although the increase was not caused by significant changes in any particular gender, geographic, or racial/ethnic group (Table 11).

Despite shorter length of stay for all groups analyzed between 1999 and 2001 (Table 12), nominal costs increased in all regions of the country (Table 11) in children hospitalized for UTI. Although hospitalized less often than girls (Tables 4 and 5), boys had higher inpatient costs (Table 10), no doubt related to their longer hospital stays, a finding noted in data from both NACHRI (Table 12) and HCUP (Table 13). Stays were longer in urban teaching hospitals, a finding likely related to differences in case mix between teaching and nonteaching facilities. The general trend toward shorter length of stay for UTI may reflect changing practice patterns in the management of uncomplicated UTI, with a greater reliance on outpatient oral antimicrobials to complete the therapeutic course initiated in the hospital. Nonetheless, the data suggest that inpatient costs have risen, despite efforts to decrease them through shorter hospital stays. Caution should be used in interpreting this trend, because these costs are not adjusted for inflation.

Given an average of 40,000 hospitalizations per year for UTIs (Table 2) and an average cost of $4,500 per inpatient episode (Table 10), a rough estimate of the annual economic burden for inpatient treatment of UTI would be $180 million. However, it is important to remember that while inpatient is by far the most expensive treatment setting, it represents a small fraction of UTI care. Hence, comprehensive estimates of the financial burden of pediatric UTI also need to incorporate the costs of outpatient and ER care, as well as those associated with evaluating and treating associated conditions.

Table 10. Inpatient cost per child admitted with urinary tract infection listed as primary diagnosis, 1999–2001, mean cost[a] (95% CI)

	Count	Mean Cost	
Total[b]	16,024	$4,501	(4,324–4,678)
Age			
0–2	10,383	$4,069	(3,963–4,175)
3–10	3,774	$4,554	(4,177–4,930)
11–17	1,867	$6,796	(5,630–7,963)
Race/ethnicity			
White	7,807	$4,500	(4,263–4,737)
Black	2,862	$4,730	(4,158–5,302)
Asian	300	$4,569	(3,966–5,172)
Hispanic	3,050	$4,778	(4,364–5,192)
American Indian	39	$8,851	(475–17,227)
Gender			
Male	6,092	$5,165	(4,776–5,554)
Female	9,932	$4,094	(3,938–4,249)
Region			
Midwest	4,635	$3,948	(3,812–4,084)
Northeast	850	$5,518	(4,794–6,241)
South	7,900	$4,864	(4,535–5,194)
West	2,363	$4,531	(4,259–4,804)

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.
[b]Children of other races and missing race/ethnicity or region are included in the total.
SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

Indirect Cost

Because children do not contribute direct economic support in most families, the impact of lost productivity or time off from school cannot be determined. However, an ill child usually means work loss for parents and, as such, may generate

Table 11. Inpatient cost per child admitted with urinary tract infection listed as primary diagnosis, count, mean cost[a] (95% CI)

	1999			2000			2001		
	Count	Mean Cost		Count	Mean Cost		Count	Mean Cost	
Total[b]	5,039	$3,869	(3,706–4,033)	5,551	$4,444	(4,182–4,706)	5,434	$5,145	(4,726–5,564)
Age									
0–2	3,248	$3,702	(3,498–3,906)	3,617	$3,954	(3,827–4,081)	3,518	$4,526	(4,315–4,738)
3–10	1,223	$3,611	(3,417–3,805)	1,287	$5,357	(4,314–6,399)	1,264	$4,648	(4,331–4,964)
11–17	568	$5,381	(4,630–6,132)	647	$5,365	(4,867–5,863)	652	$9,450	(6,216–12,684)
Race/ethnicity									
White	2,525	$3,951	(3,769–4,132)	2,600	$4,286	(4,058–4,513)	2,682	$5,226	(4,595–5,857)
Black	867	$4,227	(3,511–4,943)	1,011	$4,386	(3,968–4,804)	984	$5,526	(4,047–7,005)
Asian	87	$4,041	(3,256–4,827)	100	$4,571	(3,416–5,727)	113	$4,973	(3,881–6066)
Hispanic	749	$3,562	(3,376–3,748)	1,087	$5,327	(4,236–6,418)	1,214	$5,036	(4,704–5,369)
American Indian	5	$2,737	(705–4,768)	17	$15,163	(0–35,084)	17	$4,337	(2,879–5,795)
Gender									
Male	1,877	$4,327	(3,946–4,709)	2,114	$4,697	(4,427–4,966)	2,101	$6,384	(5,346–7,423)
Female	3,162	$3,598	(3,468–3,727)	3,437	$4,288	(3,898–4,678)	3,333	$4,364	(4,171–4,557)
Region									
Midwest	1,505	$3,481	(3,277–3,686)	1,596	$3,934	(3,762–4,106)	1,534	$4,420	(4,111–4,730)
Northeast	180	$4,929	(4,062–5,796)	325	$5,034	(3,922–6,145)	345	$6,281	(4,907–7,655)
South	2,399	$4,261	(3,973–4,549)	2,744	$4,799	(4,328–5,270)	2,757	$5,454	(4,673–6,235)
West	800	$3,937	(3,593–4,281)	765	$4,684	(4,050–5,319)	798	$4,981	(4,579–5,382)

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.

[b]Children of other races and missing race/ethnicity or region are included in the totals.

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

substantial indirect costs. Better tools are needed to assess the parental economic impact of pediatric UTI.

PREVENTION

Strategies to prevent UTI primarily revolve around enhancing host defenses. Such practices as proper hygiene, good voiding habits, and relief of constipation are the primary methods for preventing uncomplicated infections. In some patients, prophylactic antimicrobials may be beneficial. For those with complicated UTIs, the correction of underlying anatomic abnormalities or the institution of adaptive approaches, such as intermittent catheterization, can be important. Efforts to reduce nosocomial infections though proper catheter management and to prevent resistance through more selective use of antimicrobials are increasing.

From a public health standpoint, there is continuing debate over the roles of both routine newborn circumcision and sibling screening for reflux once an index case is identified. Prenatal ultrasound screening may decrease the burden of illness by identifying anatomic abnormalities prior to the first infection.

RECOMMENDATIONS

The management of patients with acute uncomplicated UTI is well established, but ongoing efforts are likely to streamline diagnosis and treatment. Further research is needed to optimize the evaluation phase following the diagnosis of UTI in order to improve quality of care and decrease cost. To ensure proper access to care for all children, investigation is needed into who is and who is not receiving appropriate evaluation. In addition, there is a need for greater education among parents and healthcare providers regarding the role of dysfunctional voiding and constipation in UTI risk.

Table 12. Trends in mean inpatient length of stay (days) for children hospitalized with urinary tract infection listed as primary diagnosis (95% CI)

	1999		2000		2001	
	Count	Length of Stay	Count	Length of Stay	Count	Length of Stay
Total	5039	3.7 (3.6–3.8)	5551	3.6 (3.5–3.8)	5434	3.6 (3.6–3.7)
Age						
0–2	3,248	3.8 (3.6–4.0)	3,617	3.5 (3.4–3.6)	3,518	3.7 (3.6–3.8)
3–10	1,223	3.4 (3.2–3.5)	1,287	3.8 (3.3–4.3)	1,264	3.3 (3.1–3.4)
11–17	568	3.9 (3.5–4.2)	647	3.8 (3.5–4.1)	652	4.3 (3.8–4.7)
Race/ethnicity						
White	2,525	3.4 (3.3–3.5)	2,600	3.3 (3.2–3.4)	2,682	3.5 (3.3–3.6)
Black	867	4.2 (3.5–5.0)	1,011	3.8 (3.3–4.4)	984	3.7 (3.5–4.0)
Asian	87	3.3 (2.8–3.8)	100	3.4 (2.8–4.1)	113	3.7 (3.1–4.4)
Hispanic	749	3.7 (3.5–3.8)	1,087	4.0 (3.8–4.3)	1,214	4.0 (3.8–4.2)
American Indian	5	2.2 (0.8–3.6)	17	6.2 (2.9–9.4)	17	3.5 (2.4–5.5)
Other	325	3.9 (3.4–4.3)	345	3.4 (3.1–3.7)	242	3.4 (3.0–3.7)
Missing	481	4.3 (4.0–4.6)	391	3.9 (3.5–4.3)	182	3.3 (3.0–3.6)
Gender						
Male	1,877	4.2 (3.8–4.5)	2,114	3.9 (3.8–4.1)	2,101	4.1 (3.9–4.3)
Female	3,162	3.4 (3.3–3.5)	3,437	3.4 (3.2–3.6)	3,333	3.3 (3.2–3.4)
Region						
Midwest	1,505	3.2 (3.1–3.4)	1,596	3.1 (3.0–3.2)	1,534	3.2 (3.1–3.4)
Northeast	180	3.8 (3.2–4.4)	325	3.4 (3.1–3.8)	345	3.4 (3.0–3.7)
South	2,399	4.1 (3.8–4.4)	2,744	3.9 (3.7–4.2)	2,757	3.9 (3.8–4.1)
West	800	3.2 (3.0–3.4)	765	3.5 (3.2–3.8)	798	3.5 (3.3–3.7)
Missing	155	4.2 (3.6–4.8)	120	5.1 (4.3–5.9)	0	

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

For hospitalized patients, urethral catheterization remains the primary risk factor for nosocomial UTI. Enhanced awareness of the morbidity and cost of this complication should lead to more judicious use of catheters and improved protocols for their management.

Table 13. Trends in mean length of stay (days) for children hospitalized with urinary tract infection listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	4.2	3.6	3.4	3.1
Age				
0–2	4.7	3.9	3.6	3.4
3–10	3.7	3.2	3.1	2.8
11–17	3.5	3.0	3.1	2.7
Gender				
Male	4.9	4.2	4.0	3.7
Female	3.8	3.3	3.1	2.9
Race/ethnicity				
White	3.7	3.3	3.1	2.9
Black	5.1	4.2	4.0	3.6
Asian/Pacific Islander	4.8	4.1	3.6	4.2
Hispanic	4.4	4.2	4.2	3.6
Other	6.8	4.4	3.3	3.6
Region				
Midwest	3.5	3.2	2.9	2.8
Northeast	5.0	4.0	3.5	3.6
South	4.2	3.7	3.5	3.2
West	3.8	3.5	3.6	3.0
MSA				
Rural	3.5	3.0	2.8	2.6
Urban	4.3	3.7	3.5	3.2
Hospital Type				
Rural	3.5	3.0	2.8	2.6
Urban nonteaching	3.7	3.4	3.1	3.1
Urban teaching	4.9	4.1	3.7	3.4

MSA, metropolitan statistical area.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

REFERENCES

1. Struthers S, Scanlon J, Parker K, Goddard J, Hallett R. Parental reporting of smelly urine and urinary tract infection. Arch Dis Child 2003;88:250-2.
2. Bulloch B, Bausher JC, Pomerantz WJ, Connors JM, Mahabee-Gittens M, Dowd MD. Can urine clarity exclude the diagnosis of urinary tract infection? Pediatrics 2000;106:E60.
3. Isaacman DJ, Burke BL. Utility of the serum C-reactive protein for detection of occult bacterial infection in children. Arch Pediatr Adolesc Med 2002;156:905-9.
4. Hoberman A, Charron M, Hickey RW, Baskin M, Kearney DH, Wald ER. Imaging studies after a first febrile urinary tract infection in young children. N Engl J Med 2003;348:195-202.
5. Rushton HG, Majd M. Dimercaptosuccinic acid renal scintigraphy for the evaluation of pyelonephritis and scarring: a review of experimental and clinical studies. J Urol 1992;148:1726-32.
6. Haycock GB. A practical approach to evaluating urinary tract infection in children. Pediatr Nephrol 1991;5:401-2; discussion 403.
7. Puri P, Cascio S, Lakshmandass G, Colhoun E. Urinary tract infection and renal damage in sibling vesicoureteral reflux. J Urol 1998;160:1028-30; discussion 1038.
8. Fussell EN, Kaack MB, Cherry R, Roberts JA. Adherence of bacteria to human foreskins. J Urol 1988;140:997-1001.
9. Shortliffe LM, McCue JD. Urinary tract infection at the age extremes: pediatrics and geriatrics. Am J Med 2002;113 Suppl 1A:55S-66S.
10. Jakobsson B, Esbjorner E, Hansson S. Minimum incidence and diagnostic rate of first urinary tract infection. Pediatrics 1999;104:222-6.
11. Wiswell TE, Hachey WE. Urinary tract infections and the uncircumcised state: an update. Clin Pediatr (Phila) 1993;32:130-4.
12. Schoen EJ, Colby CJ, Ray GT. Newborn circumcision decreases incidence and costs of urinary tract infections during the first year of life. Pediatrics 2000;105:789-93.
13. Hoberman A, Wald ER, Hickey RW, Baskin M, Charron M, Majd M, Kearney DH, Reynolds EA, Ruley J, Janosky JE. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. Pediatrics 1999;104:79-86.
14. Laumann EO, Masi CM, Zuckerman EW. Circumcision in the United States. Prevalence, prophylactic effects, and sexual practice. JAMA 1997;277:1052-7.

CHAPTER 14

Male Infertility

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Male Infertility

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INTRODUCTION

Male infertility presents a particularly vexing clinical problem. While the patient's semen may seem to be the target for diagnostic and therapeutic interventions and analysis, a positive outcome is in fact manifested by another person, a mother, giving birth to a child. And whereas presence of offspring is the ultimate proof of male reproductive health, the manner in which outcomes are expressed in this area are perhaps the most sensitive in medicine to probabilistic statements. For example, outcomes of artificial reproductive techniques are expressed in probabilities, such as the "take-home baby rate," the likelihood per intervention that a particular therapy will result in a live birth. For these reasons, epidemiologic statements regarding male reproductive dysfunction present formidable challenges, and the patients undergoing diagnosis and treatment for infertility are often understandably confused.

DEFINITION AND DIAGNOSIS

Infertility is typically defined as failure to conceive within a certain period of time. For the male, this definition is particularly problematic, as it relies on an outcome for his female partner, who may have reproductive issues of her own. *Fecundability* is the term used for the probability of a woman in a sexually active couple becoming pregnant per menstrual cycle without contraception. The measurement of fecundability is subject to a number of biases, including the prevalence of contraception prior to intended conception and how previous pregnancies are counted in a study design model (1). These biases may skew estimates of fecundability by as much as 30% to 100% (1).

It is customary to define infertility clinically as the inability of a couple trying to conceive to do so within one year. This may make the usual definitions of *prevalence* and *incidence* somewhat confusing in this context. In this chapter, we use *incidence* as it is classically defined—a proportion per unit time. However, many authors use *prevalence* to describe the percentage of couples failing to conceive after one year.

As detailed below in the section on prevalence and incidence, approximately 15% of sexually active couples without contraception do not conceive within one year. The difficulty inherent in defining infertility in this manner is obvious: some couples without reproductive dysfunction who wish to conceive fail to do so by probability, or simple bad luck, while others harbor reproductive-system pathologies that prevent conception. If a good assay were available for male reproductive function, independent of the female, a sensible and practical definition of male infertility would be "the condition of the subset of males with a positive assay within the set of couples that fail to conceive within one year." Such an assay does not currently exist. The most common initial assessment of male reproductive potential, the "bulk semen assay," is notoriously poor. The raw data from MacLeod's seminal 1951 publication indicate that the receiver operating characteristic (ROC) curve area for semen density to predict infertility is 0.59, and for that

Table 1. Codes used in the diagnosis and management of male infertility

Males 18 years or older with one or more of the following:	
ICD-9 diagnosis codes	
456.4	Scrotal varices
606	Male infertility
606.0	Azoospermia
606.1	Oligospermia
606.8	Infertility due to extratesticular causes
606.9	Male infertility, unspecified
CPT procedure codes	
52347	Cystourethroscopy with transurethral resection or incision of ejaculatory ducts
54500	Biopsy of testis, needle (separate procedure)
54505	Biopsy of testis, incisional (separate procedure)
54900	Epididymovasostomy, anastomosis of epididymis to vas deferens; unilateral
54901	Epididymovasostomy, anastomosis of epididymis to vas deferens; bilateral
55200	Vasotomy, cannulization with or without incision of vas, unilateral or bilateral (separate procedure)
55300	Vasotomy for vasograms, seminal vesiculograms, or epididymograms, unilateral or bilateral
55400	Vasovasostomy, vasovasorrhaphy
55530	Excision of varicocele or ligation of spermatic veins for varicocele; (separate procedure)
55535	Excision of varicocele or ligation of spermatic veins for varicocele; abdominal approach
55540	Excision of varicocele or ligation of spermatic veins for varicocele; with hernia repair
55550	Laparoscopy, surgical, with ligation of spermatic veins for varicocele
55870	Electroejaculation
74440	Vasography, vesiculography, or epididymography, radiological supervision and interpretation

of motility, 0.50, literally no better than flipping a coin (2). Fifty years later, in a large study by Guzick et al., the ROC area for semen density was 0.60; for motility, 0.59; and for morphology, 0.66—none of which inspires confidence in the predictive ability of the bulk semen analysis (3). In fact, these investigators, using the findings from a classification and regression tree (CART) analysis, suggest using two thresholds for each bulk seminal parameter to counsel male patients about their reproductive potential (3).

Table 1 presents the diagnosis and treatment codes for the analyses detailed in this chapter. Diagnosis codes referring to laboratory abnormalities (such as oligospermia) are mixed with codes deriving from identifiable physical conditions (such as varicocele) that may result in laboratory abnormalities. Such overlapping diagnosis codes plague any analysis of available data.

Table 2 lists conditions identified in men presenting for evaluation of infertility in studies of distribution of diagnoses from 1978 and 1997 (4, 5). It appears that in the 20 years between these two reports, more diagnoses became available, and more risk factors for infertility were identified. Interestingly, the proportion of men labeled with idiopathic infertility remained similar, at approximately 25% in 1978 and 23% in 1997.

For the clinician and researcher, a sensible method of classifying reproductive dysfunction is to separate problems into medical and surgical, with the latter including anatomic defects. Genetic conditions such as hermaphroditism or congenital absence of the vas deferens may be manifest in either category. Both medical and surgical ailments may or may not be observed in abnormalities in the bulk semen analysis; therefore, the practice of basing a primary diagnosis on bulk seminal anomalies for the purposes of data analysis is discouraged. (We note that clinicians commonly make an initial diagnosis based on seminal parameters before clinical evaluation reveals an underlying condition. For example, a case may initially be identified as "azoospermia," and later as "obstruction." While such practice is understandably unavoidable in clinical conduct, it confounds the analyses presented in this chapter.) Medical diagnoses include immunologic conditions such as antisperm antibodies, infectious diseases (which may result in surgical diagnoses if anatomic obstruction ensues), endocrinopathy, gonadotoxin exposure, and systemic illness (e.g., cancer). Surgical diagnoses include ductal obstruction (*ductal* here refers to the entire reproductive anatomic tract), congenital anatomic anomalies, varicocele, and erectile dysfunction. Medical and surgical diagnoses may coexist in the same condition, such as in the congenital anomaly unilateral cryptorchidism, in which the undescended testis exerts an as yet incompletely understood toxic effect on the contralateral descended testis.

What remains in a binary medical and surgical categorization of male reproductive dysfunction are cases of spermatogenic dysfunction (such as hypospermatogenesis, maturation arrest, and Sertoli-cell only syndrome) and specific sperm anomalies

Table 2: Distribution of male infertility diagnoses, 1978 and 1997

Diagnosis	1978[a] Percent (n=420)	1997[b] Percent (n=1,430)
Varicocele	37.4	42.2
Idiopathic	25.4	22.7
Obstruction	6.1	14.3
Female Factor	...	7.9
Cryptorchidism	6.1	3.4
Immunologic	...	2.6
Volume	4.7	...
Agglutination	3.1	...
Viscosity	1.9	...
Ejaculatory Dysfunction	1.2	1.3
Testicular Failure	9.4	1.3
Drug/Radiation	...	1.1
Endocrinologic	0.9	1.1
Infection	...	0.9
Sexual Dysfunction	2.8	0.3
High Density	0.5	...
Necrospermia	0.5	...
Systemic Disease	...	0.3
Sertoli-Cell Only	...	0.2
Ultrastructural Defect	...	0.2
Genetic	...	0.1
Testis Cancer	...	0.1

...data not available.

[a]SOURCE: Adapted from Journal of Urology, 119, Greenberg SH, Lipshultz LI, Wein AJ. Experience with 425 subfertile male patients, 507–510, Copyright 1978, with permission from American Urological Association.

[b]SOURCE: Adapted from Lipshultz LI, Howards SS. Evaluation of the subfertile male. In: Lipshultz LI, Howards SS, eds. Infertility in the male. St. Louis: Mosby-Year Book, Inc., 1997:173–193.

(such as necrospermia), in which other diagnoses are not obvious. With the Human Genome Project completed and the next step of correlating genes with function under way in earnest, these diagnostic quandaries may be resolved as genetic dysfunctions are correlated with specific testicular and sperm pathologies. For the present, these two outlying categories may be considered medical.

RISK FACTORS

While not as dramatic as the decline in fecundability with increasing maternal age, male fertility, according to recent evidence, also appears to decline with age, due to decreased sperm function and accumulating genomic damage (6, 7). Other risk factors for male reproductive dysfunction include gonadotoxins such as chemotherapeutic agents, radiation exposure, and a variety of pharmaceutical agents that act either as direct spermatotoxins or through a steroidal pathway (5). Common drugs known to impair male fertility include cimetidine, sulfasalazine, nitrofurantoin, ethanol, cannabis, and androgenic steroids (5). Whether nicotine results in impaired male fertility is controversial; however, because of its negative effect on erectile function, nicotine use is discouraged in men attempting to impregnate their partners (8). While prior fatherhood is no guarantee of current reproductive health, having produced biological offspring in the past is expected to increase the probability of successful reproduction in the male. A male who does not have biological offspring and who presents for reproductive evaluation is labeled as having "primary infertility," whereas one who is unable to impregnate his partner but who already has biological children is referred to as having "secondary infertility" (5).

TREATMENT

The treatment of male infertility includes therapies targeted to specific medical and surgical diagnoses, empiric pharmacologic agents intended to improve spermatogenesis, and artificial reproductive techniques employed to bypass reproductive barriers in the female genital tract. Often, two or all three types of therapy are implemented simultaneously. Male reproductive medicine and surgery remains one of the most actively evolving areas in urology, with a variety of therapeutic modalities under investigation. The most commonly applied treatments are described in this chapter. For further information, the reader is directed to one of the standard clinical texts such as Lipshultz and Howards' *Infertility in the Male* or Goldstein's *Surgery of Male Infertility* (9, 10).

If the diagnosis is ductal obstruction, (e.g., epididymal, vasal, or ejaculatory ductal), surgical therapy is employed to bypass or relieve the obstruction. For the microscopic ducts of the epididymis and vas, microsurgical technique or, at a minimum, optical magnification is required for optimal reconstruction. Vasal obstruction may be investigated by incision of the vas, injection of dye in the direction away from the testis, or radiography, and also by injection of saline and intraoperative assessment of whether the fluid flows easily or requires substantial pressure, indicating obstruction farther within the abdominal course of the vas deferens. Sites of obstruction amenable to reconstruction are those between the epididymis and the inguinal canal. At present, the usual therapy for ejaculatory ductal obstruction is resection of the ejaculatory duct itself via the transurethral route. The presence of this form of obstruction is initially assessed by transrectal ultrasonography, although surgeons have also described cannulation of the ductal system and injection of dye. Obstruction between the inguinal canal and the intraprostatic ductal system is not currently amenable to surgical reconstruction, and if sperm are present, reproduction must be addressed by testicular sperm retrieval and specialized techniques of *in vitro* fertilization (IVF) with the female partner.

One common form of surgical therapy for male infertility is based on the recognition that varicose veins within the scrotum impair spermatogenesis (11). If microsurgical techniques are employed, the testicular artery may be spared. As spermatogenesis requires approximately 72 to 74 days for completion, patients must wait approximately three months before improvement is evident from such therapies that aim to improve spermatogenesis.

Other forms of surgical therapy include extraction of sperm for use in artificial reproductive techniques if obstruction is not amenable to reconstruction or if spermatogenesis is impaired. Such cases generally present with azoospermia, and surgeons have classically used testis biopsy to determine whether the etiology is obstructive, where spermatogenesis will appear to be normal on biopsy, or spermatogenic pathology. If sperm are present, surgeons typically use biopsy procedures to obtain sperm for artificial reproductive techniques as well. (12). If the etiology is obstructive, sperm may be obtained by percutaneous aspiration of the testis or epididymis, biopsy-style surgical incision of the testis, or microsurgical aspiration from the epididymis. In the case of spermatogenic dysfunction, aspiration yields insufficient sperm, and incision of the testis is required. Schlegel described a microsurgical approach in which the surgeon bivalves the testis and surveys each lobule, extracting dilated tubules; this approach is highly effective for obtaining sperm in cases of azoospermia due to spermatogenic dysfunction (13).

A special case of obstruction is that in which the nerves controlling seminal emission are impaired, such as in paraplegia. Depending on the severity of the neural impairment, patients with this condition may be treated by vibratory stimulation of the penis or by transrectal electrical stimulation (14).

Medical therapy may be either for specific male reproductive disorders or empiric. Specific disorders amenable to medical therapy include endocrine disorders such as Kallmann's syndrome, where maldevelopment of specific neurons in the brain causes abnormalities of smell and insufficient release of pituitary hormones; these cases are treated by hormonal replacement (15). Other, more subtle forms of insufficient pituitary hormonal release may also be treated by direct pituitary hormonal replacement or, if the pituitary dysfunction is not severe, with agents that increase pituitary hormonal release, such as clomiphene citrate. If the patient's estradiol levels are too high, aromatase inhibitors may be prescribed (16). Other forms of specific medical therapy include antibiotics for the infrequent acute identifiable infection that is the sole cause of infertility, and immunosuppression for antisperm antibodies, using agents such as prednisone, which is often used in conjunction with artificial reproductive techniques. For patients who ejaculate sperm retrograde into the bladder, sympathomimetic agents may be employed to increase bladder neck tone. Retrieval of sperm from the bladder for use in artificial reproductive techniques in the female is often required in such cases.

The common condition of too few sperm and/or poor motility on semen analysis, without a specific identifiable medical or anatomic abnormality, may be treated by empiric therapy with agents such as clomiphene citrate used to increase sperm production. Few studies in the body of literature on such empiric treatment are placebo-controlled and blinded. With spermatogenesis taking nearly three months to complete, and thus the duration of medical therapy similarly long, the statistical effect of regression to the mean plagues studies that are not stringently conducted, as improvement may be an artifact of the selected population of patients rather than due to the therapy under study.

Discussion of artificial reproductive techniques employed in the female is beyond the scope of this chapter. However, if sufficient motile sperm are available (generally numbering in the millions), they may usually be placed directly through the cervix into the uterus. Intrauterine insemination (IUI) thus bypasses the cervical barrier. If fewer sperm are available, IVF may be used. In this technique, ova are aspirated from the female and incubated with sperm. Embryos that form are then replaced into the female reproductive tract. In a substantial technological leap, Palermo et al. described a technique referred to as Intracytoplasmic Sperm Injection (ICSI), in which a single sperm is injected into an ovum (17). ICSI is required when sperm are extracted directly from the testis, because the sperm are immature.

PREVALENCE AND INCIDENCE

Both in the literature and to their patients, clinicians commonly cite a 15% rate of couple infertility at one year, and this number is likely not far off the mark. Simmons referred to the 15% rate in 1956 but cited "information from reliable sources" without specific evidence (18). MacLeod referred to a 15% rate in 1971, candidly attributing the figure to "rather hackneyed, but probably reliable statistics in the United States and in all countries where reliable records are kept" (19). In this landmark paper, MacLeod noted the selection bias inherent in assigning responsibilities to each gender, a difficulty that plagues accurate assessment of the incidence of the male component of couple infertility to this day (19). In one of the earlier attempts to assess the rate of infertility in the

United States, the incidence of female infertility was calculated to be between 11% and 30%, depending on parity and marital status (20). However, the study was hampered by selection bias based on whether the couple was trying to conceive, and it did not assess whether subjects had ever tried to become pregnant (20). Page, one of the first to attempt to determine the prevalence and incidence of infertility in a population, computed that a study of 3,500 would be sufficient to reduce the confidence intervals to acceptable levels (21). In 1991, the World Health Organization published tables based on the then-available data (22). Although the incidence of infertility varied somewhat by location, as MacLeod noted 20 years earlier, 15% was a remarkably reasonable assessment (22).

In the 1990s, investigators reported fertility rates from localized regions around the globe. Gunnell et al. followed Page's recommendations and sent questionnaires to more than 3,000 British women (23). If failure to conceive after one year was used as the definition of infertility, the overall incidence was 16.1%, with a 95% confidence interval of 14.6% to 17.6%, again remarkably similar to the oft-cited 15% figure (23). The incidence of secondary infertility was 15.8%, and 26.5% of women were found to be infertile at some time in their reproductive lifespan (23). Philippov et al. reported an overall incidence of infertility of 16.7% for 2,000 married women 18 to 45 years of age in Tomsk, Western Siberia, interestingly close to the rate reported in Somerset (24). Given the diagnoses available in the study, the gender distribution was 38.7% for both partners, 52.7% for the female partner only, 6.4% for the male partner only, and 2.2% undetermined (24). However, the study was hampered by a small male sample (n = 168) and limited male diagnoses (24). Interestingly, of the males studied, 45.7% had abnormal semen analyses, with a 9.1% rate of azoospermia (24). Ikechebelu et al. reported gender-specific infertility rates in 314 Nigerian couples, defining male infertility on the basis of an abnormal semen analysis alone (25). In contrast to the results reported by Philippov et al., a positive male factor alone was found in 42.4% of the couples in the Nigerian cohort, and in 25.8%, the female alone appeared to be responsible (25). A combination of male and female factors was found in 20.7% of the couples, while the cause of infertility was unexplained in 11.1% (25). In almost a mirror image of these findings, Bayasgalan et al. reported data from 430 infertile couples in Mongolia (26). A female factor alone was identified in 45.8% of the couples, while a male factor alone was found in 25.6% (26). In 9.8% of the couples, no demonstrable cause was found in either partner, and in 18.8%, both appeared to be responsible (26). Given the similarity in overall incidence for couple infertility, the variability in these results is most likely due to study methodology and sampling biases rather than local geographic factors. An elegant description of sources of bias in computing the incidence of male infertility is given in a paper by Tielemans et al. (27). It is tempting to speculate that if all biases were accounted for, about one-third of infertility would be due to the female alone, one-third to the male alone, and one-third to both partners.

In the available data on the incidence of infertility, the delivery of medical care related to male infertility is largely confined to the physician office and outpatient surgical settings, as might be expected. Moreover, the dollar amount spent on the management of male infertility appears to be relatively small compared with healthcare expenditures for other disease states. This may be due, at least in part, to the fact that infertility treatment is not often covered by health insurance and thus may be underrepresented in databases that use information provided by health insurance entities. Given these caveats, male infertility does appear to constitute a relatively small percentage of ambulatory healthcare delivery in the United States. According to data from the National Ambulatory Medical Care Survey, which are systematically derived directly from physician encounter forms rather than from insurance providers, although more than 750,000 physician office visits were made for the management of male infertility (as any listed diagnosis) during a

Table 3. Physician office visits for male infertility, 1992–2000 (merged), count, percent

	1992–2000	
	Count	Percent
Total	1,122,162,099	100
Visits for infertility as primary diagnosis	748,498	0.1
Visits for infertility as any diagnosis	792,063	0.1

NOTE: Count and percent based estimated number of adult male visits in NAMCS 19922000.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 4. Inpatient hospital stays for males with infertility listed as primary diagnosis, 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000			
	Count	4-Year Rate	Annualized Rate	4-Year Age-Adjusted Rate
Total[d]	797	0.9 (0.5–1.2)	0.2	0.8
Age				
18–34	400	1.2 (0.7–1.8)	0.3	
35+	397	0.6 (0.4–0.9)	0.2	
Race/ethnicity				
White	524	0.8 (0.4–1.1)	0.2	0.8
Other	161	0.7 (0.3–1.1)	0.2	0.7
MSA				
Rural	*	*	*	*
Urban	749	1.0 (0.6–1.5)	0.3	1.0

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 5. Inpatient hospital stays for males with infertility listed as primary diagnosis, by diagnosis code, count, percent[a]

		Male Infertility ICD-9 Code 606.X		Varicocele ICD-9 Code 456.4	
	Visits for Male Infertility	Count	Percent	Count	Percent
Total	797	145	18%	438	55%
Age					
18–34	400	*	*	223	56%
35+	397	*	*	215	54%
Race/ethnicity					
White	524	*	*	307	59%
Other	161	*	*	*	*
MSA			*		
Urban	749	145	19%	420	56%
Rural	48	*	*	*	*

*Figure does not meet standard for reliability or precision.

[a]Percent of weighted visits for primary diagnosis of male infertility (within each demographic category) with diagnosis code.

NOTE: Counts were too low to report admissions for ICD-9 codes 606.0 (azoospermia), 606.1 (oligospermia), 606.8 (infertility due to extratesticular causes), and 606.9 (male infertility unspecified).

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample 1994, 1996, 1998, 2000.

Table 6. Ambulatory surgery visits for males with infertility listed as any diagnosis, 1994–1996 (merged and by year), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996			
	Count	3-Year Rate	Annualized Rate	3-Year Age-Adjusted Rate
Total	55,411	61 (50–73)	20	61
Age				
18–24	*	*	*	
25–34	25,356	126 (88–165)	42	
35–44	17,078	83 (59–107)	28	
45+	7,463	20 (11–28)	6.7	
Region				
Midwest	15,250	72 (48–95)	24	72
Northeast	18,680	104 (64–143)	35	107
South	15,580	50 (35–66)	17	50
West	5,901	29 (16–42)	10	29
	1-Year Rate			
1994	20,788	24 (16–31)		
1995	15,858	17 (12–23)		
1996	18,765	20 (14–27)		

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

four-year observation period, they accounted for only 0.1% of all visits during that time period (Table 3)

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient and Emergency Room Care

Data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample, shown in Tables 4 and 5, indicate that during 1994, 1996, 1998, and 2000, there were 797 inpatient hospital stays for a primary diagnosis of male infertility among the US adult male civilian noninstitutional population. This represented an age-adjusted rate of 0.8 admissions per 100,000. The rate for men 18 to 34 years of age was 1.2 per 100,000, while the rate for men over 35 was 0.6 per 100,000. The admission rate per 100,000 was very similar among Caucasians and non-Caucasians (0.80 vs 0.70) but was higher among urban than among rural dwellers (749 of the 797 admissions were urban dwellers). It appears that 55% of the stays involved a diagnosis of varicocele (Table 5), which suggests that during the time of observation, varicocele repair was still sometimes undertaken in an inpatient setting.

Outpatient Care

According to data from the National Survey of Ambulatory Surgery, utilization of ambulatory surgical visits for male infertility is much higher, as shown in Table 6. This would be expected, given that surgical therapy for the management of male infertility is typically performed in an ambulatory setting. In 1994, 1995, and 1996, the cumulative rate of ambulatory surgery visits was 61 per 100,000 (a total of 55,411 visits nationally). Stratified by age, men 25 to 34 years of age appeared to have the highest utilization rate (126 per 100,000), followed by men 35 to 44 (83 per 100,0000), then men 45 and over (20 per 100,000), although overlapping confidence intervals suggest inadequate analytic power. Data were not sufficient to produce estimates for men aged 18 to 24. Men living in the Northeast had a rate of 104 per 100,000 ambulatory surgical visits associated with a diagnosis of male infertility, while those in the Midwest had 72 per 100,000 and those in the South had 50 per

100,000. Men living in the West had the lowest rate of ambulatory surgical visits, 29 per 100,000, which was significantly lower than men living in the Northeast or Midwest (104 and 72 per 100,000, respectively). The reason for this geographic variation is not clear but may relate to regional variations in insurance coverage for the treatment of infertility.

CHCPE data on ambulatory surgery visits also indicate a much higher utilization rate than was seen in the inpatient or ER setting, with the highest use being among individuals 25 to 34 years of age (Table 7).

CHCPE data on physician office visits for male infertility indicate that utilization is highest among men 25 to 34, followed by men 35 to 44 (Table 8). As was seen in the National Survey of Ambulatory Surgery data on ambulatory surgery visits, the utilization rate for physician office visits was far higher in the Northeast than in other parts of the country. It is noteworthy that according to National Ambulatory Medical Care Survey data, the rate of physician office visits for women with a primary diagnosis of infertility was also much higher in the Northeast than in the Midwest or West (Table 9). The concentration of infertility clinics in the Northeast may explain the higher rates of service utilization in that region.

Among 792,063 men seen in physician offices for the diagnosis of male infertility during 1992, 1994, 1996, 1998, and 2000, fully 53% (418,790 visits) were identified as having a diagnosis of varicocele (Table 10). This suggests that the incidence of varicocele among men being treated for infertility is higher than was previously estimated and highlights the importance of this clinical lesion among such patients.

Table 7. Ambulatory surgery visits for males with infertility having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	140	39	175	32	279	32	325	32	253	29
Age										
18–24	17	*	20	*	32	29	42	33	37	35
25–34	61	70	89	66	112	54	139	63	100	54
35–44	52	51	45	29	91	36	91	33	80	34
45–54	9	*	18	*	34	17	39	17	23	*
55+	1	*	3	*	10	*	14	*	13	*
Region										
Midwest	85	39	92	30	123	29	155	32	145	31
Northeast	26	*	26	*	22	*	18	*	8	*
Southeast	21	*	44	28	119	34	132	32	89	25
West	8	*	13	*	15	*	20	*	11	*
As Any Diagnosis										
Total	146	41	187	34	295	33	347	35	275	31
Age										
18–24	19	*	20	*	33	30	44	34	37	35
25–34	63	72	90	66	123	60	144	65	109	59
35–44	54	53	51	33	92	37	101	37	88	37
45–54	9	*	21	*	37	19	43	19	28	*
55+	1	*	5	*	10	*	15	*	13	*
Region										
Midwest	89	41	101	32	130	31	165	34	153	33
Northeast	27	*	27	*	22	*	19	*	10	*
Southeast	21	*	46	30	125	36	142	35	100	28
West	9	*	13	*	18	*	21	*	12	*

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 8. Physician office visits for males with infertility having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	580	162	754	136	1,246	141	1,375	136.8	1,156	131
Age										
18–24	43	91	69	99	97	87	144	112	141	132
25–34	298	342	342	252	564	274	596	270	501	270
35–44	190	187	248	158	445	178	475	172	369	156
45–54	31	41	78	66	111	57	125	54	106	51
55+	18	*	17	*	29	*	35	25	39	31
Region										
Midwest	313	144	414	133	622	146	664	135	608	131
Northeast	163	315	125	223	178	245	134	226	76	202
Southeast	68	102	173	111	392	112.7	516	126.0	444	125
West	36	152	42	142	54	150	61	136	28	*
As Any Diagnosis										
Total	632	176	863	156	1,448	164	1,687	168	1,507	171
Age										
18–24	54	115	79	114	117	105	182	142	169	158
25–34	317	364	376	277	637	309	716	325	622	335
35–44	202	199	286	183	511	205	573	208	492	208
45–54	37	49	96	81	139	71	163	70	150	72
55+	22	*	26	*	44	34	53	37	74	55
Region										
Midwest	350	162	492	158	727	170	817	166	775	167
Northeast	170	329	130	232	191	263	145	245	100	266
Southeast	72	108	193	124	466	134	644	157	602	170
West	40	169	48	163	64	178	81	180	30	129

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 9. Physician office visits by *females* with infertility listed as primary diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000			
	Count	5-Year Rate	Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	4,759,019	4,755 (3,848–5,663)	951	4,741
Age				
18–34	3,013,841	9,170 (7,033–11,308)	1,834	
35+	1,745,178	2,597 (1,741–3,452)	519	
Race/ethnicity				
White	3,919,766	5,227 (4,129–6,325)	1,045	5,455
Other	*		*	*
Region				
Northeast	2,237,450	11,022 (7,459–14,586)	2,204	11,500
Midwest	751,718	3,209 (2,035–4,383)	642	3,243
South	*	*	*	*
West	1,147,913	5,390 (3,600–7,180)	1,078	5,273
MSA				
MSA	4,094,638	5,345 (4,249–6,440)	1,069	5,215
Non-MSA	*	*	*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult female civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 10. Physician office visits by males with any diagnosis of infertility, by diagnosis code, count, percent[a]

		Male Infertility ICD-9 Code 606.X		Varicocele ICD-9 Code 456.4	
	Visits for male infertility	Count	Percent	Count	Percent
Total	792,063	407,569	51%	418,790	53%
Age					
18–34	482,679	*	*	*	*
35+	309,384	*	*	*	*
Race/ethnicity					
White	630,959	*	*	346,647	55%
Other	*	*	*	*	*
MSA					
MSA	629,331	383,038	61%	280,589	45%
Non-MSA	*	*	*	*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Percent of weighted visits for any diagnosis of male infertility (within each demographic category) with diagnosis code.

NOTE: Counts were too low to report admissions for ICD-9 codes 606.0 (azoospermia), 606.1 (oligospermia), 606.8 (infertility due to extratesticular causes), and 606.9 (male infertility, unspecified).

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Varicocele

Varicocele was the most common diagnosis code among males undergoing ambulatory surgical procedures for the management of infertility (Tables 11 and 12). Indeed, according to data from the National Survey of Ambulatory Surgery, 67% of patients undergoing ambulatory surgery for the treatment of male infertility had a diagnosis of varicocele. The highest procedure rate appears to be among men 25 to 34 years of age.

According to CHCPE data, the most common diagnosis code among men seen for infertility in physician office visits was male infertility unspecified, followed by varicocele (Tables 13 and 14).

The Infertile VA Population

The Veterans Affairs (VA) Health System is a major healthcare provider for the male population of the United States. Data from the VA system for 1998 to 2003 show that the heavy users of care for male infertility in this population are once again young men between the ages of 25 and 34 (Table 15). Interestingly, the rate of infertility as a primary diagnosis rose steadily during the observation period among the three youngest age groups, which were also the most heavily represented in all three years. Another interesting finding in the VA data is that Caucasian males did not have the highest frequency of treatment for male infertility.

In civilian populations, Caucasians are typically the most frequent users of infertility resources. This is generally thought to be the result of socioeconomic factors related to the relatively high cost of such treatment, combined with the fact that fertility treatment is often not covered by insurance. In the VA system, where such factors presumably would not play as significant a role, the diagnosis of infertility was most frequent among Hispanics, followed by African Americans and then Caucasians. The VA database thus provides a unique perspective on the management of this disease state.

The VA data also examine the frequency of the diagnosis of male infertility by geographic location. While data on utilization of healthcare resources in the private sector consistently indicate that such resources are most heavily used in the Northeast and least heavily used in the West, this trend is not seen among VA patients. This supports the proposition that such trends may be influenced by geographic variations in health insurance coverage in the private sector.

Male Infertility and Artificial Reproductive Techniques

The treatment of male infertility has been dramatically affected by recent advances in assisted reproductive technology (ART). To assess the relationship between male infertility and the use of ART, we analyzed data from the Society for Assisted Reproductive Technology (SART). The SART database collects assisted reproductive technology procedure-related information from 399 member assisted reproductive medicine clinics. More than 95% of the assisted reproductive medicine clinics in the United States are represented in the SART database. Data are collected regarding age of both partners, the nature of the infertility problem identified in the couple, the technologies used in the infertility procedure, and the success rates of these procedures. SART and the Centers for Disease Control (CDC) jointly maintain a comprehensive database on the outcomes of ART in the United States, and this is the premier source of such information. All of the SART tables and figures pertain to couples for whom ART was utilized in the treatment of male infertility.

One statistic that stands out in the SART data on the use of IVF technologies in the treatment of male factor infertility is that well over 20,000 IVF procedures were performed for the management of this condition during the observation year. An IVF cycle typically costs from $10,000 to $20,000, so the contribution of IVF to the cost of treating male infertility is substantial. Such costs would not typically be captured, however, in analyses of expenditures made for this condition.

According to SART data, the age of the female partner (identified as the patient in this database) plays a very significant role in whether or not couples utilize ICSI in the IVF procedure. As shown in Table 16, the younger the partner, the more likely it is that ICSI would be incorporated in the IVF procedure. While the cost of applying ICSI technology to an IVF procedure varies from program to program, it typically increases the cost of the IVF cycle. Figure 2 details the presence of male factor infertility among couples using ICSI. Figure 3 compares couples with

Table 11. Ambulatory surgery visits for males with infertility due to scrotal varices having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	89	17	111	14	167	14	198	14	167	14
Age										
18–24	15	*	17	*	27	*	36	28	34	32
25–34	44	51	65	48	77	37	82	37	76	41
35–44	28	*	22	*	50	20	51	18	39	17
45–54	2	*	5	*	10	*	24	*	14	*
55+	0	0	2	*	3	*	5	*	4	*
Region										
Midwest	56	18	47	11	65	11	90	13	89	14
Northeast	12	*	19	*	13	*	11	*	4	*
Southeast	14	*	33	15	79	17	81	15	65	14
West	7	*	12	*	10	*	16	*	9	*
As Any Diagnosis										
Total	95	18	119	15	176	14	217	16	186	16
Age										
18–24	17	*	17	*	28	*	38	30	34	32
25–34	46	53	65	48	84	41	86	39	84	45
35–44	30	30	25	*	50	20	60	22	45	19
45–54	2	*	8	*	11	*	27	*	19	*
55+	0	0	4	*	3	*	6	*	4	*
Region										
Midwest	60	19	54	12	69	12	100	15	96	15
Northeast	13	*	20	*	13	*	12	*	6	*
Southeast	14	*	33	15	81	17	88	16	74	16
West	8	*	12	*	13	*	17	*	10	*

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 12. Ambulatory surgery visits by males with any diagnosis of infertility, by diagnosis code, count, percent[a]

		Male infertility ICD-9 Code 606.X		Varicocele ICD-9 Code 456.4	
	Visits for Male Infertility	Count	Percent	Count	Percent
Total	55,411	22,519	41%	37,070	67%
Age					
18–24	5,514	*	*	*	
25–34	25,356	9,885	39%	18,358	72%
35–44	17,078	7,630	45%	10,414	61%
45+	7,463			*	
Region					
Midwest	15,250	*	*	10,297	68%
Northeast	18,680	*	*	13,261	71%
South	15,580	7,213	46%	9,570	61%
West	5,901	*	*	*	

*Figure does not meet standard for reliability or precision.

[a]Percent of weighted visits for any diagnosis of male infertility (within each demographic category) with diagnosis code.

NOTE:Counts were too low to report admissions for ICD-9 codes 606.0 (azospermia), 606.1 (Oligospermia), 606.8 (Infertility due to extratesticular causes), and 606.9 (male infertility unspecified).

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Table 13. Physician office visits for males with unspecified infertility having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	332	64	397	51	632	52	635	46	475	40
Age										
18–24	5	*	15	*	24	*	25	*	13	*
25–34	187	215	204	151	301	146	306	139	233	126
35–44	123	121	136	87	247	99	250	91	187	79
45–54	13	*	37	31	56	29	43	19	35	17
55+	4	*	5	*	4	*	11	*	7	*
Region										
Midwest	165	53	211	48	290	48	295	43	241	38
Northeast	125	169	91	115	141	141	104	130	52	104
Southeast	30	32	85	39	188	40	217	40	172	37
West	12	*	10	*	13	*	19	*	10	*
As Any Diagnosis										
Total	347	67	427	55	700	57	729	53	578	49
Age										
18–24	7	*	15	*	28	*	31	24	14	*
25–34	193	222	218	161	334	162	346	157	280	151
35–44	128	126	147	94	268	107	287	104	229	97
45–54	15	*	42	35	65	33	53	23	44	21
Region										
Midwest	176	56	232	52	328	55	339	50	286	45
Northeast	128	173	92	117	147	147	111	139	60	120
Southeast	31	33	92	43	208	44	255	47	221	48
West	12	*	11	*	17	*	24	*	11	*

*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on member months of enrollment in calendar yearsfor males in the same demographic stratum.
SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 14. Physician office visits for males with infertility due to scrotal varies having commercial health insurance, count, rate[a]

	1994		1996		1998		2000		2002	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
As Primary Diagnosis										
Total	202	39	274	35	426	35	559	41	507	43
Age										
18–24	34	72	51	74	63	56	109	85	127	119
25–34	87	100	102	75	184	89	206	93	186	100
35–44	56	55	80	51	119	48	158	57	115	49
45–54	11	*	31	26	40	21	65	28	52	25
55+	14	*	10	*	20	*	21	*	27	*
Region										
Midwest	124	40	154	35	226	38	270	40	278	44
Northeast	31	42	27	*	27	*	29	*	24	*
Southeast	29	*	69	32	142	30	228	42	190	41
West	18	*	24	*	31	57	32	48	15	*
As Any Diagnosis										
Total	237	46	342	44	542	44	752	55	717	61
Age										
18–24	42	89	60	87	78	70	139	108	153	143
25–34	99	114	119	88	215	104	276	125	244	132
35–44	63	62	101	64	160	64	207	75	185	78
45–54	15	*	43	36	55	28	93	40	83	40
55+	18	*	19	*	34	*	37	26	52	38
Region										
Midwest	150	48	203	46	283	47	365	54	380	60
Northeast	34	46	29	*	34	34	33	41	39	78
Southeast	32	34	81	38	189	40	308	57	282	61
West	21	*	29	*	36	66	46	68	16	*

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on member months of enrollment in calendar years for males in the same demographic stratum.

SOURCE: Center for Health Care Policy and Evaluation, 1994, 1996, 1998, 2000, 2002.

Table 15. Male VA users with a diagnosis of infertility, 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	2,033	62	2,105	60	2,206	59	2,183	53	2,310	52	2,318	49
Age-adjusted Total	2,160	58	2,144	58	2,206	59	2,111	57	2,157	58	2,109	57
Age												
< 25	32	110	47	159	43	147	54	184	63	215	68	230
25–34	262	158	280	169	322	194	341	206	368	222	381	230
35–44	354	97	367	100	412	113	445	122	506	138	485	132
45–54	553	67	606	74	619	76	589	72	563	69	547	67
55–64	341	55	327	52	311	50	310	50	312	50	289	46
65–74	400	41	319	33	324	34	239	25	216	22	213	22
75–84	203	30	181	27	160	23	124	18	125	18	120	18
85+	15	25	17	27	15	24	9	14	4	6	7	11
Race/ethnicity												
White	1,138	54	1,159	51	1,259	51	1,173	42	1,209	40	1,118	36
Black	485	103	463	96	428	88	416	85	403	82	393	82
Hispanic	109	120	96	102	111	115	106	106	101	98	95	94
Other	12	28	22	49	18	39	25	51	17	34	24	49
Unknown	289	50	365	61	390	66	463	70	580	73	688	66
Insurance Status												
No insurance/self-pay	1,589	66	1,661	66	1,691	69	1,614	65	1,675	66	1,607	64
Medicare	104	41	126	32	202	31	257	26	294	24	332	22
Medicaid	3	137	1	37	2	52	6	96	11	127	8	84
Private Insurance/HMO	329	53	308	53	291	51	284	48	307	47	349	50
Other Insurance	8	71	9	52	19	81	20	74	22	72	22	61
Unknown	0	0	0	0	1	115	2	105	1	35	0	0
Region												
Eastern	312	65	328	64	351	63	364	53	418	54	388	49
Central	276	48	306	49	327	51	290	40	363	41	399	38
Southern	907	73	803	60	893	62	938	58	1,002	55	1,024	53
Western	538	55	668	65	635	60	591	56	527	53	507	53

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 16. Use of intracytoplasmic sperm injection (ICSI) in *females* undergoing *in vitro* fertilization, 1999, by age

	Count[a]	Percent
Total	22,426	
Age		
18–29	3,390	89.7%
30–34	7,763	86.7%
35–37	5,028	84.9%
38–40	3,785	83.4%
41–42	1,494	81.7%
42–66	966	80.6%

[a]7,596 were missing information on ICSI status.

SOURCE: Society for Assisted Reproductive Technology (SART)/ American Society of Reproductive Medicine (ASRM) database, 1999.

male factor infertility that used IVF with and without ICSI.

SART data confirm that the age of the female partner plays a critical role in the success of IVF in regard to both pregnancy and live birth rate. There is a direct relationship between the age of the female partner and the likelihood of achieving both pregnancy and live birth via IVF, with younger women being much more likely to become pregnant than their older counterparts (Tables 17). Since couples who are not successful during the first IVF cycle may choose to repeat the process, the cost of IVF is greater among those in whom the female partner is older. Additionally, when couples do not become pregnant during the first IVF cycle, subsequent cycles tend to be less successful.

The data in Table 18 suggest that the likelihood that a couple will become pregnant is also related to the ethnicity of the female partner. Unfortunately, these data were not controlled for age. If there is a correlation between the race and the age of the female partner, these results may be misleading.

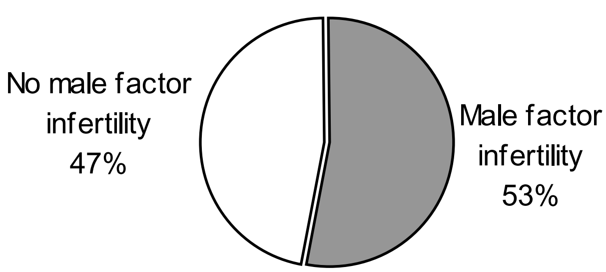

Figure 2. Presence or absence of male factor infertility diagnosis in 50,648 fresh non-donor cycles of ICSI, 2003.

SOURCE: Adapted from Center for Disease Control and Prevention, 2003 Assisted Reproductive Technology (ART) Report.

ECONOMIC IMPACT

Economic calculations based on data available for this analysis substantially underestimate actual costs, as location of care of infertility patients are atypical in the databases, and a substantial portion pay cash for services. In 2000, total expenditures for male infertility were approximately $17 million, a decrease of more than $2.5 million since 1994 (Table 19). This decrease can be attributed to reduced expenditures for ambulatory surgery. Costs for physician office visits remained constant from 1994 to 2000, but after inflation is accounted for, this represents a decrease in real expenditures. Additionally, IVF treatment based on 120,000 ART cycles at a cost of $15,000 per cycle puts the total cost at about $1.8 billion, (possibly dwarfing the rest of the costs in this section).

Individual-level expenditures for male infertility were estimated using risk-adjusted regression models controlling for age, work status, income, urban or rural residence, and health plan characteristics (Table 20). Among 18- to 64-year-old males with employer-provided insurance, average annual expenditures were $3,515 for those treated for male infertility, compared with $3,722 for similar men not treated for the condition. The apparent cost saving associated with male infertility is certainly an artifact and is likely a function of two factors: First, a selection effect may be operating in which men who seek treatment for infertility have generally better health than men of similar age not receiving treatment. Second, infertility costs often are not covered by health insurance, so the true costs resulting from an infertility diagnosis may be missing in claims data. We can only conclude that excess costs associated with diagnosis of male infertility appear to be modest with respect to

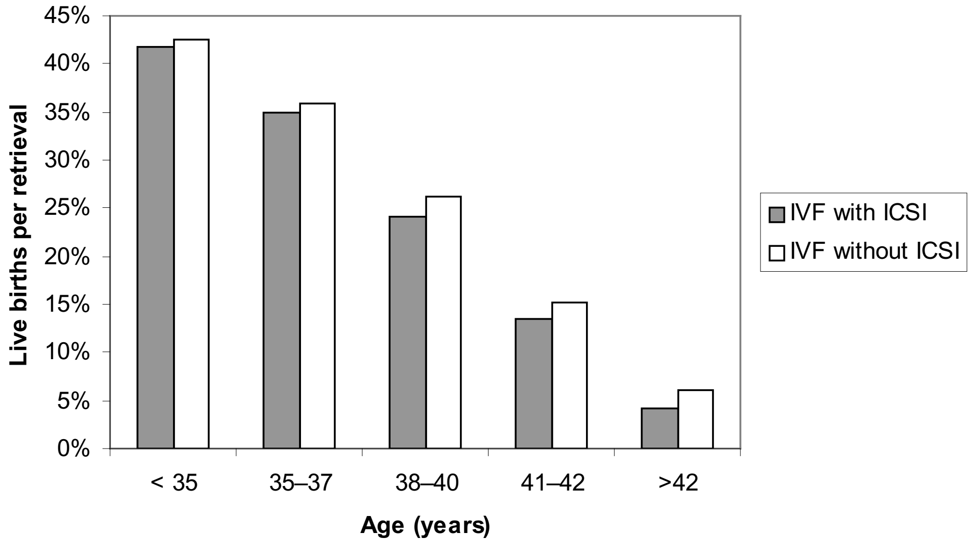

Figure 3. **Live births per retrieval for Assisted Reproductive Technology (ART) cycles using fresh non-donor eggs or embryos among couples diagnosed with male factor infertility who used IVF with or without ICSI, by woman's age[a] , 2003.**

[a]Cycles using donor sperm and cycles using gamete intra-fallopian transfer (GIFT) or zygote intra-fallopian transfer (ZIFT) are excluded. The comparison group of IVF without ICSI includes couples with all diagnoses except male factor infertility.

Source: Adapted from Center for Disease Control and Prevention, 2003 Assisted Reproductive Technology (ART) Report.

Table 17. Likelihood of outcomes in females undergoing *in vitro* fertilization, 1999, by age

	Pregnancy		Live Birth	
	N	Percent	N	Percent
Total	29,995		29,995	
Age				
18–29	4,350	37.5%	4,350	32.8%
30–34	10,298	33.9%	10,298	28.7%
35–37	6,659	30.1%	6,659	24.9%
38–40	5,151	24.9%	5,151	15.6%
41–42	2,084	19.5%	2,084	13.2%
43–66	1,453	22.0%	1,453	16.1%

Source: Society for Assisted Reproductive Technology (SART)/American Society of Reproductive Medicine (ASRM) database, 1999.

Table 18. Likelihood of a pregnancy in females when undergoing *in vitro* fertilization, 1999, by race/ethnicity

	Count	Percent
Total	29,995	
White, non-Hispanic	17,287	30.6%
Black, non-Hispanic	756	25.0%
Asian, non-Hispanic	1,041	27.2%
Hispanic	1,055	30.1%
Other, Unknown, and N. American Native	9,856	30.9%

Source: Society for Assisted Reproductive Technology (SART)/American Society of Reproductive Medicine (ASRM) database, 1999.

Table 19. Expenditures for infertility, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Physician Office	$11,032,826	55.9%	$10,372,643	58.9%	$10,561,761	63.1%	$11,238,832	65.9%
Ambulatory Surgery	$8,707,207	44.1%	$7,226,463	41.1%	$6,168,275	36.9%	$5,807,572	34.1%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$19,740,033		$17,599,105		$16,730,036		$17,046,404	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

insurance but may pose a larger financial burden on patients themselves.

Approximately 8% of privately insured men in treatment for infertility missed some work related to their condition; the average work loss was 2.6 hours, the vast majority of which was for outpatient visits (Table 21). The proportion of men missing some work, as well as the number of hours missed, varied by age, with 14% of 18- to 29-year-olds missing an average of 5.0 hours. Overall, about 2.5 hours of work were missed for each outpatient visit for male infertility.

The relatively small economic impact of male infertility is a function of both low excess costs associated with the diagnosis and the low frequency with which treatment is sought for the condition; less than 0.5% of privately insured 18- to 64-year-old men had a claim for infertility. A majority of the costs related to infertility is likely to have been missed by these data, however, as patients typically pay a substantial amount of money out-of-pocket.

CONCLUSIONS

Approximately one of every seven couples who attempt to conceive will fail to do so within one year. Some form of reproductive pathology may be identified in the majority of couples, but at present, biases in the available surveys make it difficult to determine the proportions of male and female factors. It is likely, however, that approximately one-third of

Table 20. Estimated annual expenditures for privately insured male employees with and without a medical claim for infertility in 2002[a]

	Annual Expenditures (per person)					
	Males without Infertility (N=284,379)			Males with Infertility (N=952)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$2,684	$1,038	$3,722	$2,487	$1,028	$3,515
Age						
18–34	$1,285	$654	$1,939	$2,411	$846	$3,257
35–44	$2,157	$880	$3,037	$1,746	$698	$2,444
45–54	$3,067	$1,217	$4,284	$3,154	$1,011	$4,165
55–64	$3,227	$1,138	$4,365	$2,411	$1,320	$3,731
Region						
Midwest	$2,599	$1,025	$3,624	$2,407	$1,019	$3,426
Northeast	$2,628	$1,122	$3,750	$2,434	$1,112	$3,546
South	$2,736	$974	$3,710	$2,534	$961	$3,495
West	$2,902	$1,067	$3,969	$2,688	$1,067	$3,755

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions.

SOURCE: Ingenix, 2002.

Table 21. Average annual work loss of males treated for infertility, 1999 (95%CI)

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs) Inpatient[b]	Outpatient[b]	Total
Total	278	8%	0.1 (0–0.3)	2.5 (1.1–3.9)	2.6 (1.2–4.1)
Age					
18–29	49	14%	0.7 (0–2)	4.4 (0–9.3)	5.0 (0–10)
30–39	159	7%	0	1.8 (0.4–3.3)	1.8 (0.4–3.3)
40–49	61	5%	0	3.1 (0–7.0)	3.1 (0–7.0)
50–64	9	0%	0	0	0
Region					
Midwest	93	9%	0	1.8 (0.4–3.3)	1.8 (0.4–3.3)
Northeast	16	6%	0	0.3 (0–0.8)	0.3 (0–0.8)
South	94	9%	0.3 (0–1)	2.9 (0.4–5.3)	3.2 (0.7–5.7)
West	44	7%	0	3.1 (0–8.2)	3.1 (0–8.2)
Unknown	31	3%	0	3.6 (0–11)	3.6 (0–11)

…data not available.

[a]Individuals with an inpatient or outpatient claim for infertility and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

couple infertility is due to the male alone, one-third to the female alone, and one-third to both partners. The available data indicate that men with reproductive dysfunction are either paying for their care themselves or are being treated simply as sperm donors for artificial reproductive techniques in the female. A report from the Bertarelli Foundation's second global conference on infertility in the third millennium put it well: "The current treatment of male infertility has become so dominated by the breakthrough technology of ICSI that a kind of nihilism has become widespread in the field." This cynical viewpoint was summed up as follows: "As long as a few motile sperm are present, no further review of the male is needed" (28). In view of the great expense of IVF and the sensible position of directly treating underlying disease in the infertile male, further systematic examination of the causes and treatment of male reproductive dysfunction is highly warranted. A quarter of a century ago, MacLeod noted that "the entire field of human male fertility (definitions, etiology and therapy) remains in a state of groping development that has gathered momentum only in recent years" (19). Oddly, the advent of a great technological breakthrough in reproductive therapy for the female, ICSI, caused that momentum to slip. It is time to regain it.

RECOMMENDATIONS

It is clear that much of the practice of male infertility is not identified in current large-scale databases. The following would further the diagnosis and treatment of male infertility and the understanding of its basis:

- A standardized list of male infertility diagnosis codes that identifies clinical and laboratory abnormalities (including semen analyses) independently.
- A large-scale, well-conducted survey of infertile couples, with the standardized list applied to the male to determine the gender distribution and epidemiology of infertility, as well as the related health resource expenditures.
- A large-scale study to correlate semen analysis parameters and the probability of conceiving, expressing the result in actual time to conceive.
- A new assay of male reproductive function with high sensitivity and specificity.

REFERENCES

1. Sallmen M, Weinberg CR, Baird DD, Lindbohm ML, Wilcox AJ. Has human fertility declined over time?: why we may never know. Epidemiol 2005;16:494-99.
2. MacLeod J. Semen quality in 1000 men of known fertility and in 800 cases of infertile marriage. Fertil Steril 1951;2:115-39.
3. Guzick DS, Overstreet JW, Factor-Litvak P, Brazil CK, Nakajima ST, Coutifaris C, Carson SA, Cisneros P, Steinkampf MP, Hill JA, Xu D, Vogel DL, National Cooperative Reproductive Medicine Network. Sperm morphology, motility, and concentration in fertile and infertile men. N Engl J Med 2001;345:1388-93.
4. Greenberg SH, Lipshultz LI, Wein AJ. Experience with 425 subfertile male patients. J Urol 1978;119:507-10.
5. Sigman M, Lipshultz LI, Howards SS. Evaluation of the subfertile male. In: Lipshultz LI, Howards SS, eds. Infertility in the male. St. Louis: Mosby-Year Book, Inc., 1997:173-93.
6. Ng KK, Donat R, Chan L, Lalak A, Di Pierro I, Handelsman DJ. Sperm output of older men. Hum Reprod 2004;19:1811-15.
7. Sloter E, Nath J, Eskenazi B, Wyrobek AJ. Effects of male age on the frequencies of germinal and heritable chromosomal abnormalities in humans and rodents. Fertil Steril 2004;81:925-43.
8. Elhanbly S, Abdel-Gaber S, Fathy H, El-Bayoumi Y, Wald M, Niederberger CS. Erectile dysfunction in smokers: a penile dynamic and vascular study. J Androl 2004;25:991-95.
9. Lipshultz LI, Howards SS, eds. Infertility in the male. St. Louis: Mosby-Year Book, Inc., 1997.
10. Goldstein M, ed. Surgery of male infertility. Philadelphia: W.B. Saunders Co., 1995.
11. Dubin L, Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. Fertil Steril 1970;21:606-09.
12. Schoor RA, Elhanbly S, Niederberger CS, Ross LS. The role of testicular biopsy in the modern management of male infertility. J Urol 2002;167:197-200.
13. Schlegel PN. Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision. Hum Reprod 1999;14:131-35.
14. Thomas RJ, McLeish G, McDonald IA. Electroejaculation of the paraplegic male followed by pregnancy. Med J Aust 1975;2:789.
15. Franco B, Guioli S, Pragliola A, Incerti B, Bardoni B, Tonlorenzi R, Carrozzo R, Maestrini E, Pieretti M, Taillon-Miller P, Brown CJ, Willard HF, Lawrence C, Persico MG, Camerino G, Ballabio A. A gene deleted in Kallmann's syndrome shares homology with neural cell adhesion and axonal path-finding molecules. Nature 1991;353:529-36.
16. Raman JD, Schlegel PN. Aromatase inhibitors for male infertility. J Urol 2002;167:624-29.
17. Palermo G, Joris H, Devroey P, and Van Steirteghem AC. Pregnancies after intracytoplasmic injection of a single spermatozoon into an oocyte. Lancet 1992;340:17-18.
18. Simmons FA. Human infertility. N Engl J Med 1956;255:1140-92.
19. MacLeod J. Human male infertility. Obstet Gynecol Surv 1971;26:325-51.
20. Mosher WE. Reproductive impairments in the United States, 1965-1982. Demography 1985;22:415-30.
21. Page H. Estimation of the prevalence and incidence of infertility in a population: a pilot study. Fertil Steril 1989;51:571-77.
22. World Health Organization. Infertility: A tabulation of available data on prevalence of primary and secondary infertility. Geneva. WHO Programme on Maternal and Child Health and Family Planning, Division of Family Health, 1991.
23. Gunnell DJ, Ewings P. Infertility prevalence, needs assessment and purchasing. J Public Health Med 1994:16:29-35.
24. Philippov OS, Radionchenko AA, Bolotova VP, Voronovskaya NI, Potemkina TV. Estimation of the prevalence and causes of infertility in western Siberia. Bull World Health Organ 1998;76:183-87.
25. Ikechebelu JI, Adinma JI, Orie EF, Ikegwuonu SO. High prevalence of male infertility in southeastern Nigeria. J Obstet Gynaecol 2003;23:657-59.
26. Bayasgalan G, Naranbat D, Tsedmaa B, Tsogmaa B, Sukhee D, Amarjargal O, Lhagvasuren T, Radnaabazar J, Rowe PJ. Clinical patterns and major causes of infertility in Mongolia. J Obstet Gynaecol Res 2004;30:386-93.
27. Tielemans E, Burdorf A, te Velde E, Weber R, van Kooij R, Heederik D. Sources of bias in studies among infertility clients. Am J Epidemiol 2002;156:86-92.
28. Lunenfeld B, Van Steirteghem A, Bertarelli Foundation. Infertility in the third millennium: implications for the individual, family and society: condensed meeting report from the Bertarelli Foundation's second global conference. Hum Reprod Update 2004;10:317-26.

CHAPTER 15

Erectile Dysfunction and Peyronie's Disease

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Erectile Dysfunction and Peyronie's Disease

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INTRODUCTION

Male sexual health has taken on increased importance as the United States population ages, develops coexisting medical conditions, and undergoes interventions that can affect sexual health. This chapter focuses on two major areas of male sexual health, erectile dysfunction (ED) and Peyronie's disease (PD). Related domains, including sexual desire, vitality, ejaculatory and orgasmic function, partner intimacy, and female sexual health, are also important, but they are beyond the scope of this chapter.

It is estimated that ED affects as many as 30 million men in the United States (1). In 1985, the estimated total direct costs for ED exceeded $146 million (2). Patient interest in and treatment for ED surged with the introduction of oral phosphodiesterase-5 inhibitors (PDE-I) in 1998, and expenditures for office visits and other outpatient treatments increased during that time. The available data likely underestimate current treatment utilization given that in the 22 months after the first PDE-I, sildenafil (Viagra™), was launched, nearly 18 million prescriptions were filled at an approximate cost of $90 per 10-tablet prescription (3). The emergence of effective, convenient, and generally well-tolerated new treatment options (along with educational campaigns initiated by the pharmaceutical industry) has contributed to increased public awareness and a greater acceptability of and attention to the health and socioeconomic impacts of male sexual health. This is an important issue for men considering or having received treatment for prostate cancer, a condition that is increasingly being identified through widespread prostate specific antigen testing. In addition, the use of androgen replacement has increased in recent years, as testosterone is often equated with youth, vitality, strength, and sexual performance (4).

Neither ED nor PD is life-threatening. However, these conditions may result in withdrawal from sexual intimacy, reduced quality of life, decreased working productivity, and increased healthcare utilization (5). Dramatic changes in first-line treatment options for ED are likely to lead more men to seek treatment. Patterns of care may shift away from surgical and device therapies provided by urologists and toward pharmacologic treatments and/or multidisciplinary approaches coordinated by primary care providers. With men increasingly seeking to preserve sexual function and quality of life as they age, it is important to characterize the burden and severity of disease, treatment patterns, and economic consequences of male sexual health.

ERECTILE DYSFUNCTION

DEFINITION AND DIAGNOSIS

ED is defined as the persistent "inability to achieve or maintain an erection sufficient for satisfactory sexual performance" (1). This definition suggests that reports of ED prevalence, severity, treatment effectiveness, and healthcare utilization may vary based on patients' and partners' perceptions and expectations about erectile function and sexual performance. As newer oral and

Table 1. Codes used in the diagnosis and management of erectile dysfunction and Peyronie's disease

Erectile dysfunction	
Males 18 years or older with one or more of the following:	
ICD-9 diagnosis codes	
302.71	Psychosexual dysfunction with inhibited sexual desire
302.72	Psychosexual dysfunction with inhibited sexual excitement
302.74	Psychosexual dysfunction with inhibited male orgasm
607.82	Vascular disorders of penis
607.84	Impotence of organic origin
607.89	Other specified disorders of penis
607.9	Unspecified disorder of penis
ICD-9 procedure codes	
64.94	Fitting of external prosthesis of penis
64.95	Insertion or replacement of non-inflatable penile prosthesis
64.96	Removal of internal prosthesis of penis
64.97	Insertion or replacement of inflatable penile prosthesis
CPT procedure codes	
37788	Penile revascularization, artery, with or without vein graft
37790	Penile venous occlusive procedure
54115	Removal foreign body from deep penile tissue (eg, plastic implant)
54230	Injection procedure for corpora cavernosography
54231	Dynamic cavernosometry, including intracavernosal injection of vasoactive drugs (eg, papaverine, phentolamine)
54235	Injection of corpora cavernosa with pharmacologic agent(s) (eg, papaverine, phentolamine)
54240	Penile plethysmography
54250	Nocturnal penile tumescence and/or rigidity test
54400	Insertion of penile prosthesis; non-inflatable (semi-rigid)
54401	Insertion of penile prosthesis; inflatable (self-contained)
54402	Removal or replacement of non-inflatable or inflatable penile prothesis
54405	Insertion of multi-component, inflatable penile prosthesis, including placement of pump, cylinders, and reservoir
54406	Removal of all components of a multi-component, inflatable penile prosthesis without replacement of prosthesis
54407	Removal, repair, or replacement of inflatable penile prosthesis, including pump and/or reservoir and/or reservoir and/or cylinders
54408	Repair of component(s) of a multi-component, inflatable penile prosthesis
54409	Surgical correction of hydraulic abnormality of inflatable prosthesis, including pump and/or reservoir and/or cylinders
54410	Removal and replacement of all component(s) of a multi-component, inflatable penile prosthesis at the same operative session
54411	Removal and replacement of all components of a multi-component inflatable penile prosthesis through an infected field at the same operative session, including irrigation and debridement of infected tissue
54415	Removal of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis, without replacement of prosthesis
54416	Removal and replacement of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis at the same operative session
54417	Removal and replacement of non-inflatable (semi-rigid) or inflatable (self-contained) penile prosthesis through an infected field at the same operative session, including irrigation and debridement of infected tissue
Peyronie's disease	
Males 18 years or older with one or more of the following:	
ICD-9 diagnosis codes	
607.81	Balanitis xerotica obliterans, induratio penis plastica
ICD-9 procedure codes	
64.4[a]	Repair and plastic operation on penis
64.42[a]	Release of chordee
CPT procedure codes	
54110	Excision of penile plaque (Peyronie's disease)

Continued on next page

Table 1 (continued). Codes used in the diagnosis and management of erectile dysfunction and Peyronie's disease

54111	Excision of penile plaque (Peyronie's disease); with graft to 5 cm in length
54112	Excision of penile plaque (Peyronie's disease); with graft greater than 5 cm in length
54200	Injection procedure for Peyronie's disease
54205	Injection procedure for Peyronie's disease; with surgical exposure of plaque
54360	Plastic operation on penis to correct angulation

[a]Must occur with diagnosis of 607.84 (impotence of organic origin) or 607.89 (other specified disorders of penis).

topical (e.g., testosterone patches and gels) therapies have become available and the public has become more aware of ED, the reported prevalence and severity of this condition have increased, and associated practice patterns have shifted. Comprehensive, validated scales have been developed (e.g., the International Index of Erectile Function (IIEF)) (6) to define ED presence, severity, and response to treatment. Symptom-based definitions are rapidly replacing the routine use of physiologic measures of erectile function such as penile tumescence. Thus the epidemiology of the disease and the methods of defining it are evolving. Table 1 presents diagnosis and procedure codes associated with ED and PD.

The diagnosis of ED requires a detailed sexual and medical history, physical examination, and laboratory tests. Self-administered questionnaires are useful adjuncts to the case history, but they are not sufficient to diagnose ED correctly or treat it safely. The definition of ED provided by the National Institutes of Health does not include the duration of dysfunction; subsequent recommendations by the World Health Organization specify a three-month minimum duration of symptoms to establish that diagnosis (7), except in cases of trauma or surgically induced ED. Objective physiologic testing may be used to support the diagnosis of ED, but it cannot substitute for the patient's self-report in establishing the diagnosis.

Pharmacological, psychophysiological, and radiological tests are used in efforts to determine the cause of ED. Intracavernosal injection, penile duplex Doppler ultrasonography, dynamic infusion cavernosometry and cavernosography, and internal pudendal arteriography all may be used to identify vasculogenic ED. Nocturnal penile tumescence testing can be useful to document an intact neurovascular axis, and the absence of nocturnal erectile activity may imply a neurogenic etiology. However, the sensitivity, specificity, and clinical usefulness of these techniques have been questioned. Furthermore, since the introduction of oral PDE-I therapy and the acceptance of goal-oriented therapy for most cases of ED (8), the rationale for extensive testing has weakened, as reflected in decreasing rates of intracavernosal injection, nocturnal penile tumescence, and penile plethysmography between 1992 and 2001 (8).

Until 1998, rates of specialized diagnostic testing steadily increased for Medicare beneficiaries with a primary diagnosis of ED; in the following years, overall use of such testing declined significantly by 65% from 1995 to 2001 (Table 2, Figure 1). Previously divergent age-related rates of testing converged (Table 3, Figure 2), indicating that variability in utilization based on age may reflect different patient goals. For example, elderly patients may be less willing to undergo invasive testing for the evaluation and treatment of ED.

While urologists performed the majority of ED diagnostic testing prior to 1998, other specialists, especially primary care providers, also contributed to the increasing rates (Table 4). The data from 1998 and 2001 suggest that both primary care providers and urologists have dramatically changed the way they diagnose ED. Moreover, most patients with ED are now being diagnosed, evaluated, and treated by primary care doctors, the majority of whom rely on history and physical examination for diagnosis (9). Nocturnal penile tumescence and Doppler studies are rarely performed (Figure 3).

Only a small subset of men with ED benefit from vascular testing, which can identify specific arterial or venous dysfunction amenable to surgical reconstruction. For the vast majority, such testing is unlikely to change management strategy. Thus, specialized testing is now limited to PDE-I

Table 2. Physician office visits for use of intracavernosal injection, penile plethysmography, or nocturnal penile tumescence testing in Medicare beneficiaries with erectile dysfunction, count[a], rate[b] (95% CI)

	1992			1995			1998			2001		
	Count	Rate		Count	Rate		Count	Rate		Count	Rate	
Intracavernosal Injection	20,640	14,294	(13,486–15,101)	39,880	19,865	(19,084–20,645)	24,520	7,808	(7,389–8,228)	13,440	7,003	(6,492–7,514)
Penile Plethysmography	10,580	7,327	(6,726–7,928)	17,180	8,557	(8,010–9,105)	9,400	2,993	(2,727–3,260)	1,260	657	(495–818)
Nocturnal Penile Tumescence Testing	10,280	7,119	(6,526–7,712)	14,760	7,352	(6,841–7,863)	14,520	4,624	(4,295–4,952)	3,080	1,605	(1,353–1,856)

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with erectile dysfunction.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

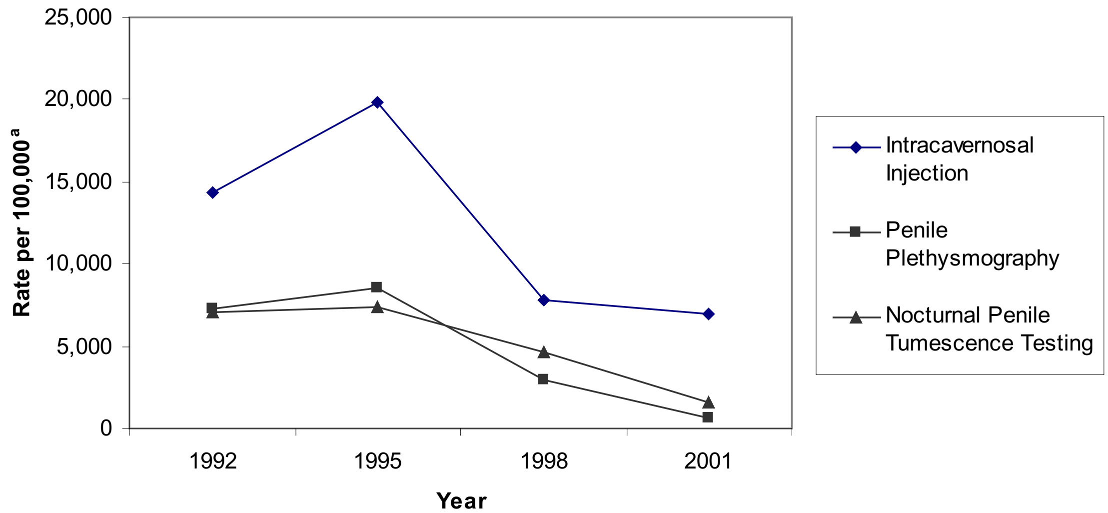

Figure 1. Physician office visits for use of intracavernosal injection, penile plethysmography, or nocturnal penile tumescence testing in Medicare beneficiaries with erectile dysfunction.
[a]Rate per 100,000 Medicare beneficiaries 65 years and older with erectile dysfunction, age-adjusted.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

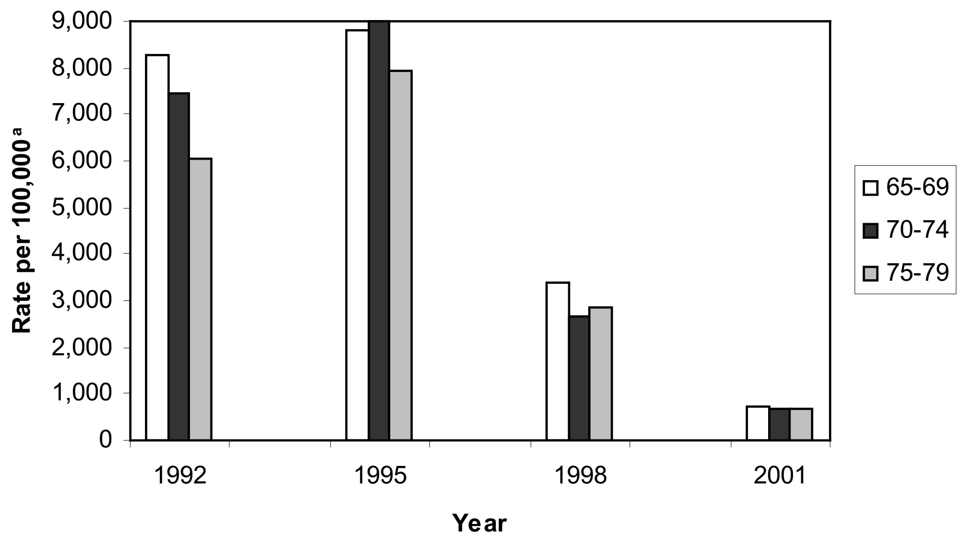

Figure 2. Physician office visits for the use of penile plethysmography among Medicare beneficiaries with erectile dysfunction.
[a]Rate per 100,000 Medicare beneficiaries in the same age group with erectile dysfunction, age-adjusted.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 3. Physician office visits for use of penile plethysmography in Medicare beneficiaries with erectile dysfunction, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	10,580	7,327	(6,726–7,928)	7,327	17,180	8,557	(8,010–9,105)	8,557
Age								
65–69	5,340	8,295	(7,342–9,247)	8,295	7,780	8,807	(7,971–9,643)	8,807
70–74	3,500	7,456	(6,394–8,519)	7,456	5,920	9,022	(8,041–10,002)	9,022
75–79	1,380	6,047	(4,664–7,430)	6,047	2,520	7,935	(6,605–9,264)	7,935
80–84	300	3,916	(1,974–5,859)	3,916	800	6,957	(4,877–9,036)	6,957
85+	60	2,778	(0–5,877)	2,778	140	5,036	(1,400–8,672)	5,036
Region								
Midwest	2,080	6,025	(4,903–7,148)	6,083	3,580	7,553	(6,489–8,617)	7,679
Northeast	1,080	5,384	(3,987–6,781)	5,583	2,400	8,333	(6,906–9,761)	8,472
South	5,460	8,678	(7,694–9,661)	8,551	9,620	10,713	(9,808–11,617)	10,601
West	1,760	6,886	(5,497–8,274)	6,964	1,280	3,926	(2,983–4,869)	3,865
Race/ethnicity								
White	9,000	7,277	(6,629–7,924)	7,245	14,800	8,433	(7,852–9,014)	8,319
Black	880	6,995	(5,002–8,989)	6,995	1,660	9,295	(7,390–11,199)	10,078
Asian	...	...		...	20	3,448	(0–10,089)	3,448
Hispanic	…	...		…	240	10,909	(5,083–16,735)	11,818

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	9,400	2,993	(2,727–3,260)	2,993	1,260	657	(495–818)	657
Age								
65–69	4,140	3,375	(2,923–3,827)	3,375	540	721	(450–992)	721
70–74	2,780	2,671	(2,233–3,108)	2,671	420	700	(402–998)	700
75–79	1,680	2,843	(2,243–3,442)	2,843	240	658	(287–1,029)	658
80–84	640	3,022	(1,991–4,053)	3,022	40	266	(0–635)	266
85+	140	2,448	(657–4,238)	2,448	20	455	(0–1,343)	455
Region								
Midwest	1,900	2,448	(1,994–2,982)	2,461	140	318	(83–553)	363
Northeast	1,040	2,274	(1,663–2,885)	2,230	260	957	(439–1,474)	1,030
South	5,180	3,704	(3,261–4,146)	3,704	560	638	(403–874)	593
West	820	1,685	(1,174–2,197)	1,685	220	730	(300–1,160)	730
Race/ethnicity								
White	8,100	2,936	(2,654–3,218)	2,914	1,000	605	(438–772)	593
Black	880	3,343	(2,372–4,315)	3,419	100	569	(72–1,066)	455
Asian	20	1,099	(0–3,241)	1,099	40	3,333	(0–7,875)	3,333
Hispanic	220	4,151	(1,749–6,553)	4,151	100	2,778	(377–5,179)	2,778

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries 65 years and older with erectile dysfunction.

[c]Age-adjusted to US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 4. Use of various procedures in Medicare beneficiaries with erectile dysfunction, by physician specialty, count[a], percent

Specialty	1992 Count	1992 Percent	1995 Count	1995 Percent	1998 Count	1998 Percent	2001 Count	2001 Percent
Nocturnal Penile Tumescence Testing								
Total	10,280	100	14,760	100	14,520	100	3,080	100
General practice/Family medicine	420	4	2,480	17	4,120	28	100	3
Internal medicine	280	3	1,040	7	2,180	15	720	23
Urology	8,900	87	8,500	58	6,960	48	2,180	71
Other	680	7	2,740	19	1,260	9	80	3
Dynamic Cavernosometry								
Total	0	0	300	100	680	100	260	100
General practice/Family medicine	0	0	0	0	160	24	0	0
Internal medicine	0	0	0	0	40	6	220	85
Urology	0	0	240	80	300	44	40	15
Other	0	0	60	20	180	26	0	0
Intracavernosal Injection								
Total	20,640	100	39,880	100	24,520	100	13,440	100
General practice/Family medicine	140	1	2,020	5	3,200	13	440	3
Internal medicine	40	0	380	1	1,160	5	80	1
Urology	19,820	96	35,740	90	18,840	77	12,320	92
Other	640	3	1,740	4	1,320	5	600	4
Penile Plethysmography								
Total	10,580	100	17,180	100	9,400	100	1,260	100
General practice/Family medicine	460	4	3,140	18	1,700	18	100	8
Internal medicine	560	5	2,240	13	1,060	11	60	5
Urology	7,660	72	7,580	44	5,180	55	1,000	79
Other	1,900	18	4,220	25	1,460	16	100	8

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

nonresponders, young men with posttraumatic or primary ED, and medicolegal investigations.

RISK FACTORS

The prevalence and severity of ED increase with age, even after controlling for age-related conditions such as diabetes, heart disease, hypertension, dyslipidemia, depression, and use of certain medications (10, 11). The prevalence of ED rises with each decade of patient age (12). By the time men reach their seventies, 69.4% will have ED to some extent (Table 5). Other risk factors include hypertension, diabetes, smoking, hyperlipidemia, vascular disease, and poor socioeconomic status or education level (which correlate with the physiological risk factors).

ED can be broadly categorized as psychogenic, organic, or mixed. Psychological factors overlay most cases of ED and are important in planning treatment, but in the majority of cases, the causes are considered to be organic. Organic ED can be further divided into neurogenic, vasculogenic, myogenic, and hormonal etiologies. Neurogenic causes may be central (e.g., spinal cord injury, multiple sclerosis) or peripheral (e.g., radical pelvic surgery, sacral cord and nerve root compression or trauma, diabetic polyneuropathy). Vasculogenic ED encompasses arterial insufficiency related to arteriosclerosis, tobacco abuse, or trauma and venoocclusive insufficiency due to trauma, PD, or congenital anomalies. Dysfunction of the intrinsic smooth muscle cells of the erectile tissues may result from hypertension, radiation injury, benign prostatic hyperplasia, or the metabolic consequences of hyperglycemia and hyperlipidemia. Hormonal influences on both central proerectile pathways and end organ cavernosal tissues can be significant, although hypogonadism is not considered to be a principal cause of ED in the majority of patients. The interaction between neural, vascular, and hormonal signaling pathways in the pathophysiology of ED

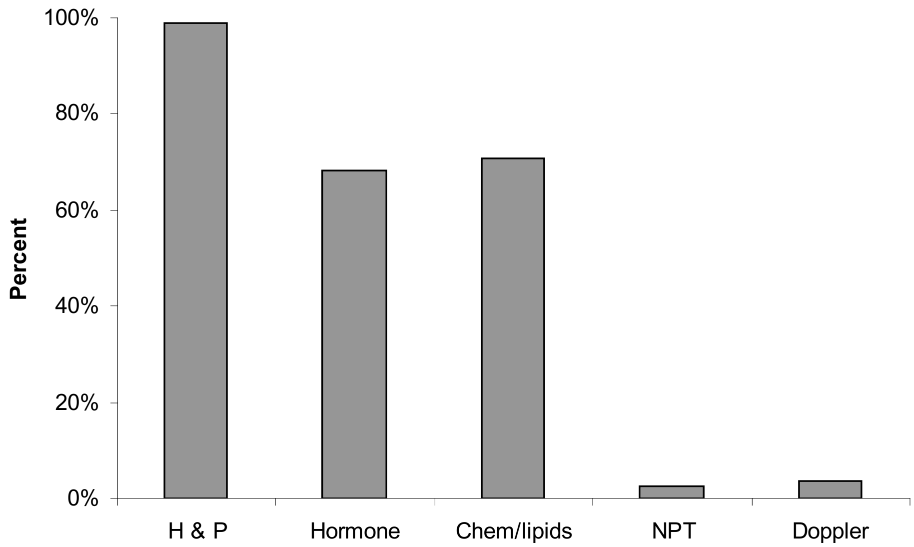

Figure 3. Use of diagnostic evaluations in men with erectile dysfunction in a survey of 85 family paractitioners. H&P, history and physical examination; Hormone, serum hormonal levels; Chem/lipids, serum chemistry and lipid profile; NPT, nocturnal penile tumescence studies; Doppler, arterial Doppler ultrasound.

Source: Adapted from Urology, 57, Rutchik SD, Baudiere M, Wade M, Sullivan G, Rayford W, Goodman J, Practice patterns in the diagnosis and treatment of erectile dysfunction among family practice physicians, 146–150, Copyright 2001, with permission from Elsevier.

remains incompletely understood but is being actively investigated.

TREATMENT

Treatment options for ED have evolved considerably over the past decade to encompass psychological counseling; oral, topical, intraurethral, and intracavernosal vasoactive therapy; oral therapies with other or unknown mechanisms; hormone replacement; vacuum constriction devices; and surgery, including vascular bypass procedures and penile implants. The goal of treatment is to restore satisfactory erections with minimal adverse effects. Men have demonstrated a strong preference for oral treatments even if they have low efficacy (13), suggesting that efforts to optimize treatment of ED should not only target physiologic and clinical measures of improvement but should also address patient/partner satisfaction and preference. The costs associated with oral pharmacotherapy will become significant burdens on the US healthcare system as preferences for new, less-invasive treatments increase the number of men seeking evaluation and treatment of ED.

PREVALENCE AND INCIDENCE

The Massachusetts Male Aging Study, a population-based study conducted prior to the

Table 5. Population prevalence of erectile dysfunction, by age group

	Prevalence
Age	
50–54	26.0%
55–59	34.9%
60–64	46.9%
65–69	57.8%
70–76	69.4%

SOURCE: Adapted from Annals of Epidemiology, 10, Ansong KS, Lewis C, Jenkins P, Bell J, Epidemiology of ED: a community-based study in rural New York state, 293–296, 2000.

Table 6: Frequency of responses to the question, "How would you describe your ability to get and keep an erection adequate for satisfactory intercourse? Would you say that you are..." (95% CI), by age

	Always or almost always able		Usually Able		Sometimes Able		Never Able	
Total	65%	(62–68)	17%	(15–18)	12%	(11–14)	6%	(5–8)
Age								
20–29	81%	(78–84)	12%	(9–16)	5%	(3–7)	2%	(1–3)
30–39	88%	(84–92)	8%	(5–11)	3%	(1–5)	0%	(0–1)
40–49	72%	(67–76)	20%	(15–25)	7%	(4–10)	1%	(0–3)
50–59	56%	(50–63)	20%	(14–26)	20%	(15–25)	4%	(1–7)
60–69	29%	(22–35)	28%	(22–33)	27%	(23–31)	17%	(11–22)
70–74	19%	(11–27)	21%	(14–29)	39%	(29–48)	22%	(14–29)
75+	6%	(1–10)	17%	(12–21)	30%	(24–36)	47%	(40–55)

NOTE: Based on data from the National Health and Nutrition Examination Survey.

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Table 7: Frequency of responses to the question, "How would you describe your ability to get and keep an erection adequate for satisfactory intercourse?", by race/ethnicity

Race/Ethnicity	Response to Erectile Function Question	Mean (95% CI)		Count
Caucasian	Always or almost always able	66%	(61–70)	42,166,116
	Usually able	15%	(12–18)	9,720,185
	Sometimes able	12%	(11–14)	7,719,754
	Never able	7%	(5–9)	4,513,273
Black (non-Hispanic)	Always or almost always able	62%	(57–66)	5,320,404
	Usually able	22%	(20–25)	1,930,336
	Sometimes able	13%	(9–16)	1,092,557
	Never able	4%	(1–6)	307,653
Mexican American	Always or almost always able	64%	(60–69)	4,254,622
	Usually able	20%	(15–25)	1,331,461
	Sometimes able	10%	(7–13)	668,185
	Never able	6%	(4–7)	374,352
Other Hispanic	Always or almost always able	64%	(52–75)	3,019,237
	Usually able	14%	(1–27)	657,696
	Sometimes able	19%	(3–35)	882,115
	Never able	4%	(1–6)	166,660
Other or Multi-Racial	Always or almost always able	63%	(50–76)	1,766,502
	Usually able	26%	(13–39)	727,977
	Sometimes able	10%	(3–17)	289,029
	Never able	1%	(0–3)	23,673

NOTE: Based on data from the National Health and Nutrition Examination Survey.

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introduction of oral medical therapy, documented a prevalence of moderate or complete ED of almost 35% in Caucasian men between the ages of 40 and 70 (14). However, the data failed to address either national variations in race and ethnicity or the prevalence of ED in men over 70. Estimates from the National Health and Social Life Survey suggested a similar prevalence of ED based on a 1992 sample of adult men 59 years of age and younger (15). Recognizing that the prevalence of ED rises with age, Bacon and colleagues recently reported information on sexual function in men older than 50 (16). The age-standardized prevalence of ED was 33% in a cohort of health professionals who disproportionately tended to be Caucasian, healthier, and of higher socioeconomic status than the general population. The National Institutes of Health Consensus Panel on Impotence identified a clear need for national epidemiologic data to provide answers to questions regarding prevalence and risk factors for ED (1).

Table 8. Odds ratios associated with various correlates of erectile dysfunction

	Odds Ratio (95% CI)	
Age (vs 20–29)		
30–39	0.6	(0.3–1.3)
40–49	1.2	(0.7–2.3)
50–59	3.8	(2.4–6.1)
60–69	9.0	(4.8 –17)
> 70	31.0	(16–60)
Race (vs White)		
Hispanic	1.9	(1.2–2.9)
Black	1.0	(0.7–1.4)
Other	0.7	(0.3–1.5)
Comorbid State (vs absence of comorbidity)		
Diabetes	2.7	(1.6–4.5)
Obesity	1.6	(1.1–2.3)
Heart disease	1.4	(0.9–2.4)
Hypertension	1.6	(1.7–2.3)
Currently smoking	1.7	(1.2–2.6)
Former smoker	1.4	(1.0–2.1)

NOTE: Based on data from the National Health and Nutrition Examination Survey.

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To obtain a better understanding of the national estimates of prevalence and risk factors for ED, we examined data from the 2001–2002 release of the National Health and Nutrition Examination Survey (NHANES) (17). This survey has the advantage of being population-based and administered after the introduction of Viagra™; also, it oversamples certain racial and ethnic groups to provide more realistic estimates. Although NHANES used only a single question to identify men with ED, this limitation is shared by most of the other major studies. As shown in Table 6, almost one in five males experienced ED, as defined by respondents' self-reports of being "sometimes or never able to get and keep an erection adequate for satisfactory intercourse." More than 75% of the men over 75 years of age met this criterion. Fewer then 7% of men younger then 60 stated that they were never able to have and maintain an erection satisfactory for intercourse, compared with 47% of men age 75 and older. ED also varied by race (Table 7). Hispanic men were approximately twice as likely to report ED as Caucasians, after controlling for other factors known to be associated with ED, including diabetes, obesity, and hypertension (Table 8). The increased prevalence in Hispanics overall was primarily due to high prevalence in those younger than 50 (17).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Outpatient Care

Recent trends suggest that the greatest increases in utilization and expenditures for ED in the future will be for outpatient evaluation and treatment. The age-adjusted rate of physician office visits by Medicare beneficiaries primarily for ED doubled between 1992 and 1998, from 1,609 per 100,000 to 3,387 per 100,000, before decreasing in 2001 (Table 9). A similar trend was seen for national hospital outpatient visits with ED listed as any diagnosis (Table 10), which more than doubled between 1994–1996 and 1998–2000 (Table 11). These temporal trends were present across all racial, regional, and age categories.

The 1998 peak in rates for physician office visits and hospital outpatient visits (Tables 9 and 10) by Medicare beneficiaries may be associated with the introduction of Viagra™. Many physician offices had

Table 9. Physician office visits by Medicare beneficiaries with erectile dysfunction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	239,720	1,609	(1,581–1,638)	1,609	377,400	2,480	(2,445–2,515)	2,480
Total < 65	41,240	1,320	(1,264–1,377)		65,180	1,892	(1,828–1,956)	
Total 65+	198,480	1,686	(1,653–1,719)		312,220	2,652	(2,611–2,693)	
Age								
65–69	89,420	2,197	(2,133–2,261)		138,880	3,605	(3,522–3,689)	
70–74	67,160	2,066	(1,996–2,135)		103,160	3,094	(3,011–3,177)	
75–79	29,420	1,300	(1,234–1,366)		50,040	2,206	(2,120–2,291)	
80–84	9,540	728	(663–793)		16,300	1,173	(1,093–1,253)	
85–89	2,680	449	(374–525)		3,440	540	(460–621)	
90+	260	128	(59–198)		400	189	(106–272)	
Race/ethnicity								
White	197,120	1,570	(1,539–1,600)	1,557	321,160	2,471	(2,433–2,508)	2,459
Black	26,500	2,077	(1,966–2,187)	2,138	41,760	3,016	(2,888–3,143)	3,095
Asian	…	...		…	1,120	1,537	(1,137–1,936)	1,454
Hispanic	…	...		…	4,420	2,226	(1,936–2,516)	2,246
N. American Native	…	...		…	380	1,889	(1,049–2,729)	1,988
Region								
Midwest	51,420	1,386	(1,333–1,439)	1,401	81,460	2,113	(2,049–2,177)	2,135
Northeast	33,400	1,053	(1,003–1,103)	1,065	55,580	1,748	(1,683–1,812)	1,756
South	109,700	2,094	(2,039–2,149)	2,088	176,020	3,209	(3,143–3,274)	3,203
West	42,740	1,769	(1,695–1,844)	1,743	60,200	2,596	(2,504–2,688)	2,561

	1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	490,380	3,387	(3,345–3,429)	3,387	256,960	1,666	(1,638–1,695)	1,666
Total < 65	80,580	2,345	(2,273–2,416)		52,800	1,387	(1,335–1,440)	
Total 65+	409,800	3,711	(3,661–3,761)		204,160	1,758	(1,724–1,792)	
Age								
65–69	162,080	4,800	(4,698–4,902)		78,320	2,213	(2,145–2,282)	
70–74	137,160	4,496	(4,392–4,600)		66,040	2,145	(2,073–2,218)	
75–79	76,300	3,341	(3,237–3,445)		40,320	1,644	(1,572–1,715)	
80–84	27,520	1,997	(1,893–2,102)		15,180	1,014	(943–1,086)	
85–89	5,880	904	(801–1,007)		3,660	506	(433–579)	
90+	820	387	(265–498)		620	268	(174–362)	
Race/ethnicity								
White	413,300	3,380	(3,335–3,425)	3,369	209,240	1,600	(1,570–1,630)	1,593
Black	54,200	4,061	(3,911–4,211)	4,130	31,060	2,117	(2,012–2,221)	2,157
Asian	2,200	1,604	(1,307–1,902)	1,531	1,920	937	(751–1,123)	888
Hispanic	9,820	2,926	(2,671–3,181)	2,920	7,120	1,895	(1,700–2,090)	1,874
N. American Native	580	2,074	(1,327–2,822)	2,146	80	240	(6.0–474)	240
Region								
Midwest	110,680	2,993	(2,915–3,071)	3,023	53,700	1,414	(1,361–1,467)	1,419
Northeast	72,480	2,608	(2,524–2,692)	2,619	41,760	1,429	(1,368–1,490)	1,441
South	230,440	4,293	(4,217–4,370)	4,286	118,060	2,033	(1,982–2,084)	2,037
West	70,100	3,135	(3,032–3,237)	3,078	37,920	1,532	(1,464–1,601)	1,497

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 10. Hospital outpatient visits by Medicare beneficiaries with erectile dysfunction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	9,860	66 (60–72)	66	13,240	87 (80–94)	87	23,180	160 (151–169)	160	17,840	116 (108–123)	116
Total < 65	3,580	115 (98–131)		4,460	129 (112–146)		7,460	217 (195–239)		6,660	175 (156–194)	
Total 65+	6,280	53 (47–59)		8,780	75 (68–82)		15,720	142 (132–152)		11,180	96 (88–104)	
Age												
65–69	3,200	79 (66–91)		4,220	110 (95–124)		6,840	203 (181–224)		4,620	131 (114–147)	
70–74	1,840	57 (45–68)		3,200	96 (81–111)		5,000	164 (144–184)		3,440	112 (95–128)	
75–79	920	41 (29–52)		740	33 (22–43)		2,840	124 (104–145)		2,000	82 (66–98)	
80–84	280	21 (10–33)		460	33 (20–47)		740	54 (36–71)		580	39 (25–53)	
85–89	40	6.7 (0–16)		140	22 (5.7–38)		240	37 (16–58)		380	53 (29–76)	
90–94	0	0		20	9.5 (0–28)		60	28 (0–60)		160	69 (21–117)	
95–97	0	0		0	0		0	0		0	0	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	6,600	53 (47–58)	53	8,540	66 (59–72)	65	16,120	132 (123–141)	131	11,980	92 (84–99)	91
Black	2,460	193 (159–227)	191	3,780	273 (234–312)	280	4,940	370 (324–416)	369	4,240	289 (250–328)	296
Asian	…	...	…	40	55 (0–130)	55	200	146 (55–236)	146	80	39 (1.0–77)	39
Hispanic	…	...	…	240	121 (52–189)	111	840	250 (175–326)	250	700	186 (125–248)	186
N. American Native	…	...	…	0	0	0	140	501 (132–869)	501	20	60 (0–177)	60
Region												
Midwest	4,020	108 (93–123)	107	4,940	128 (112–144)	129	7,100	192 (172–212)	190	5,160	136 (119–152)	131
Northeast	2,080	66 (53–78)	65	2,700	85 (71–99)	87	5,020	181 (158–203)	181	3,860	132 (113–151)	133
South	2,120	40 (33–48)	41	3,360	61 (52–71)	61	7,300	136 (122–150)	138	5,740	99 (87–110)	101
West	1,620	67 (52–82)	68	2,200	95 (77–113)	90	3,640	163 (139–186)	160	3,060	124 (104–143)	125

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 11. Hospital outpatient visits for erectile dysfunction listed as any diagnosis, 1994–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–2000					1994–1996					1998–2000				
	Count	4-Year Rate		Annualized Rate	4-Year Age-Adjusted Rate	Count	2-Year Rate		Annualized Rate	2-Year Age-Adjusted Rate	Count	2-Year Rate		Annualized Rate	2-Year Age-Adjusted Rate
Total[d]	403,193	435	(321–550)	109	432	117,636	131	(76–186)	66	129	285,557		(201–398)	150	300
Age															
18–34	*	*		*		*	*				*	*			
35–44	63,318	299	(162–436)	75		*	*				*	*			
45–54	127,949	801	(373–1,228)	200		*	*				*	*			
55–64	146,799	1,422	(749–2,094)	356		*	*				*	*			
65+	*	*		*											
Race/ethnicity															
White	242,073	347	(226–469)	87	327	77,717	113	(48–179)	56	106	164,356	232	(131–334)	116	219
Black	112,449	1,150	(597–1,704)	288	1,256	*	*		*	*	88,622	877	(368–1,386)	438	958
Region															
Midwest	106,523	492	(240–744)	123	488	*	*		*	*	*	*		*	*
Northeast	132,271	731	(397–1,066)	183	711	*	*		*	*	*	*		*	*
South	105,622	328	(142–515)	82	322	*	*		*	*	*	*		*	*
West	*	*		*	*	*	*		*	*	*	*		*	*
MSA															
MSA	340,012	477	(335–618)	119	477	109,642	160	(89–231)	80	166	230,370	311	(192–430)	156	319
Non-MSA	*	*		*	*	*	*		*	*	*	*		*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Hospital Ambulatory Medical Care Survey, 1994, 1996, 1998, 2000.

Table 12. Physician office visits for erectile dysfunction listed as any diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1992				1994			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[c]	967,388	1,101	(772–1,430)	1,101	1,238,019	1,403	(1,076–1,729)	1,403
MSA								
MSA	808,963	1,283	(826–1,659)	1,283	1,134,201	1,723	(1,297–2,149)	1,774
Non-MSA	*	*		*	*	*		*

	1996				1998			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[c]	1,810,291	1,968	(1,496–2,441)	1,968	2,641,367	2,801	(2,073–3,529)	2,801
MSA								
MSA	1,653,870	2,321	(1,724–2,917)	2,388	2,151,747	2,937	(2,101–3,773)	3,017
Non-MSA	*	*		*	*	*		*

	2000			
	Count	Rate		Age-Adjusted Rate
Total[c]	2,804,098	2,916	(2,146–3,686)	2,916
MSA				
MSA	2,370,559	3,169	(2,253–4,085)	3,249
Non-MSA	*	*		*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 13. VA users with erectile dysfunction listed as primary diagnosis, 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	69,501	2,115	68,783	1,960	74,663	2,012	82,647	2,023	90,117	2,014	94,279	1,981
Age	79,500	2,142	73,002	1,967	74,663	2,012	75,256	2,028	75,081	2,023	73,796	1,988
< 25	55	187	58	199	66	225	68	231	71	244	75	256
25–34	567	343	679	410	741	447	879	531	980	592	1,055	637
35–44	3,394	928	3,599	984	4,208	1,150	4,627	1,265	4,849	1,325	5,143	1,406
45–54	18,656	2,276	18,484	2,255	20,249	2,470	21,869	2,668	22,314	2,722	22,184	2,706
55– 64	22,332	3,576	20,168	3,230	20,542	3,290	20,238	3,241	19,878	3,183	19,428	3,111
65–74	25,459	2,643	22,149	2,299	21,522	2,234	20,652	2,144	20,261	2,103	19,600	2,034
75–84	8,787	1,290	7,624	1,119	7,090	1,041	6,716	986	6,506	955	6,110	897
85+	249	402	241	390	245	396	207	334	222	358	202	326
Race/ethnicity												
White	47,470	2,261	46,000	2,007	48,830	1,962	53,190	1,907	55,688	1,835	54,398	1,761
Black	15,895	3,364	15,825	3,281	17,195	3,542	18,275	3,745	18,873	3,863	18,326	3,846
Hispanic	2,021	2,228	2,156	2,296	2,357	2,449	2,462	2,451	2,910	2,821	2,967	2,937
Other	1,002	2,355	960	2,148	873	1,877	1,056	2,163	1,018	2,034	980	2,001
Unknown	3,113	536	3,842	643	5,408	911	7,664	1,163	11,628	1,457	17,608	1,688
Insurance Status												
No insurance/self-pay	48,450	2,023	48,234	1,914	49,284	2,000	51,275	2,078	53,517	2,112	54,091	2,146
Medicare	5,387	2,110	6,828	1,746	11,555	1,775	16,740	1,694	20,185	1,617	22,681	1,519
Medicaid	67	3,054	59	2,162	109	2,844	172	2,766	272	3,133	284	2,979
Private Insurance/HMO	15,262	2,455	13,104	2,266	12,953	2,278	13,602	2,288	15,143	2,330	16,096	2,308
Other Insurance	335	2,990	558	3,212	757	3,226	838	3,106	971	3,184	1,096	3,061
Unknown	0	0	0	0	5	573	20	1,049	29	1,027	31	1,796
Region												
Eastern	9,464	1,977	8,701	1,691	9,286	1,665	11,057	1,624	12,336	1,588	12,298	1,539
Central	12,510	2,168	13,030	2,080	13,966	2,158	15,971	2,197	18,303	2,043	20,318	1,929
Southern	25,492	2,040	24,897	1,861	29,064	2,011	32,045	1,975	37,258	2,063	40,239	2,072
Western	22,035	2,248	22,155	2,149	22,347	2,105	23,574	2,236	22,220	2,231	21,424	2,223

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

waiting lists of ED patients anticipating approval of the drug and experienced large numbers of new patient visits subsequent to its launch. Consistent with this hypothesis is a corresponding large decline in ED-related inpatient surgery rates and expenditures in Centers for Medicare and Medicaid Services (CMS) data (Table 17).

The subsequent decline in the rate of outpatient visits for ED listed as the primary diagnosis in the Medicare databases may reflect the management of ED without physiologic testing or diagnostic coding by primary care providers. Patients in these settings may have other conditions as the primary reason for their clinic visit. For example, NAMCS data on rates of office visits for ED listed as any diagnosis indicate that the age-adjusted rate of visits did not drop off from 1998 to 2000 but increased slightly (Table 12). Likewise, the rate of male Veterans Affairs (VA) patients having ED listed as the primary diagnosis remained constant from 2000 to 2003 (2,012 per 100,000 in 2000 vs 1,981 in 2003) (Table 13). However, male veterans with ED listed as any diagnosis increased by more then 2,000 per 100,000 (3,161 per 100,000 in 2000 vs 5,236 per 100,000 in 2003) (Table 14). Possible undercoding of ED in primary care settings is supported by data from the VA Pharmacy Benefits Management Group, which demonstrate that the frequency of individual veterans receiving prescriptions for specific ED drugs as a class increased ninefold from 1999 to 2003 (from 23,913, or 681 per 100,000 in 1999, to 291,884, or 6,120 per 100,000 in 2003) (Table 15).

Racial Trends

Striking racial differences in rates of outpatient visits for ED were seen in all administrative databases. African American men had the highest rates in all sampled populations; the difference between African American and Caucasian rates ranged from three to fivefold. The greatest age-adjusted discrepancies for hospital outpatient visits with ED listed as any diagnosis were seen in the National Hospital Ambulatory Medical Care Survey (NHAMCS) (Table 11). Although adjusted for age, these analyses do not control for medical comorbidities, access to healthcare, or socioeconomic and educational factors, all of which may contribute to the higher prevalence of ED and rate of outpatient visits for African American men. Hypertension and diabetes are more prevalent in ethnic minorities than in Caucasians, which may explain some of the observed differences (18-21). In the VA system, where financial access to healthcare is equal across races, the rate for African American men with ED as a primary diagnosis or all diagnoses is nearly double that of Caucasian men (Table 13). It is not known whether this is related to differences in comorbid conditions or in healthcare-seeking behavior. In contrast to findings in NHANES data (Table 7), rates of ED diagnosis did not differ notably between Caucasian and Hispanic male veterans.

Geographical Trends

Regional utilization of outpatient care for ED did not show clear patterns across databases. Rates of physician office visits by male Medicare beneficiaries were nearly 50% higher in the South than in the rest of the country. Conversely, hospital outpatient visits for this population were lowest in the South. The NAMCS ED data showed the lowest age-adjusted rates for both physician office visits and outpatient hospital visits in the South (Table 11). This geographical variation may reflect regional differences in healthcare delivery, referral patterns, or racial population distribution. In the VA system, age-adjusted rates of ED as any diagnosis increased in all regions over time. However, the East had substantially lower rates (approximately 75% lower) than other regions (Tables 13 and 14).

Age-Related Trends

Although the prevalence of ED rises with each decade of patient age, data show a pattern of differential age-related utilization for outpatient treatment. VA users with any diagnosis of ED have the highest rate between ages 55 and 64 (7,885 per 100,000 in 2003) (Table 14). In NAMCS, which includes younger patients, utilization rises sharply after age 45 and peaks in the 65–74 age range (6,025 per 100,000) (Table 16). In the Medicare population, men 80 or older have only one-half the outpatient treatment rate of men 65 to 69 (Table 9). Hospital outpatient visits for Medicare beneficiaries show a similar trend, with the exception that men under 65 have higher-than-expected utilization, which can be attributed to the confounding effect of chronic disease states that cause disability and allow early enrollment in Medicare (Table 10). The decrease in treatment-seeking among the elderly likely reflects declining patient interest

Table 14. VA users with erectile dysfunction listed as any diagnosis, 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	94,120	2,865	98,061	2,794	117,337	3,161	154,838	3,790	201,988	4,515	249,120	5,236
Age	107,879	2,907	104,224	2,808	117,337	3,161	140,432	3,784	167,011	4,500	193,121	5,203
< 25	69	234	69	236	83	283	92	314	106	360	126	428
25–34	718	433	863	521	1,057	638	1,351	816	1,639	990	2,047	1,236
35–44	4,490	1,227	4,911	1,342	6,101	1,667	7,770	2,124	9,454	2,584	11,710	3,201
45–54	24,469	2,985	25,392	3,098	30,337	3,701	37,841	4,616	45,393	5,538	52,567	6,413
55–64	30,062	4,814	28,492	4,563	31,637	5,066	37,077	5,938	43,141	6,909	49,238	7,885
65–74	35,138	3,647	32,621	3,386	35,737	3,710	41,901	4,349	50,400	5,232	58,368	6,059
75–84	12,571	1,845	11,488	1,686	11,996	1,761	13,998	2,054	16,408	2,408	18,555	2,723
85+	362	586	388	627	389	629	402	650	470	760	510	825
Race/ethnicity												
White	65,282	3,109	66,912	2,920	78,977	3,173	103,596	3,715	130,533	4,302	149,477	4,840
Black	20,606	4,361	21,301	4,416	24,813	5,111	29,815	6,109	35,822	7,332	40,694	8,540
Hispanic	2,602	2,869	2,856	3,042	3,321	3,451	3,909	3,892	4,987	4,834	5,874	5,815
Other	1,347	3,166	1,389	3,108	1,388	2,985	1,806	3,699	2,110	4,216	2,344	4,786
Unknown	4,283	738	5,603	938	8,838	1,488	15,712	2,384	28,536	3,576	50,731	4,863
Insurance Status												
No insurance/self-pay	64,909	2,710	67,587	2,682	75,431	3,062	91,781	3,720	113,099	4,464	133,255	5,286
Medicare	7,745	3,034	10,518	2,689	19,758	3,035	35,035	3,546	50,649	4,057	66,950	4,485
Medicaid	82	3,737	91	3,335	146	3,809	280	4,502	482	5,552	574	6,021
Private Insurance/HMO	20,954	3,371	19,091	3,302	20,822	3,661	26,206	4,408	35,766	5,502	45,758	6,561
Other Insurance	430	3,838	773	4,449	1,173	4,999	1,494	5,537	1,888	6,190	2,494	6,965
Unknown	0	0	1	328	7	803	42	2,202	104	3,683	89	5,156
Region												
Eastern	12,254	2,560	11,949	2,323	13,564	2,432	18,724	2,750	26,556	3,419	33,932	4,247
Central	16,333	2,830	17,672	2,822	20,968	3,240	29,359	4,038	43,546	4,862	59,240	5,625
Southern	35,016	2,802	36,150	2,702	46,592	3,224	61,257	3,775	84,219	4,664	105,465	5,430
Western	30,517	3,114	32,290	3,132	36,213	3,411	45,498	4,315	47,677	4,785	50,483	5,239

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 15. Use of prescription drugs for erectile dysfunction among veterans, count , rate[a]

	1999			2000			2001		
	Count	Rate		Count	Rate		Count	Rate	
Total	23,913	681	(673–690)	33,428	901	(891–910)	101,467	2,484	(2,469–2,499)
Age									
< 25	13	40	(18–62)	12	41	(18–64)	42	152	(106–198)
25–34	164	91	(77–105)	225	136	(118–154)	649	420	(388-453)
35–44	1,038	267	(251–283)	1,525	417	(396–438)	4,766	1,391	(1,351–1,430)
45–54	5,709	717	(698–735)	8,462	1,032	(1,010–1,054)	27,529	3,222	(3,184–3,260)
55–64	6,581	1,131	(1,103–1,158)	9,060	1,451	(1,421–1,481)	27,582	3,899	(3,853–3,945)
65–74	8,067	894	(874–913)	10,851	1,126	(1,105–1,148)	30,882	2,855	(2,824–2,887)
75–84	2,291	398	(382–414)	3,213	472	(455–488)	9,790	1,168	(1,145–1,191)
85+	50	96	(70–123)	80	129	(101–158)	227	288	(251–326)
Race/ethnicity									
White	16,262	714	(703–725)	22,123	896	(884–908)	65,240	2,364	(2,346–2,382)
Black	5,694	1,188	(1,157–1,129)	7,996	1,660	(1,623–1,696)	22,474	4,647	(4,587–4,708)
Hispanic	621	646	(595–696)	713	720	(667–773)	1,640	1,584	(1,508–1,661)
Other	322	740	(659–820)	394	874	(788–960)	1,331	2,823	(2,671–2,974)
Unknown	1,014	165	(155–175)	2,202	357	(342–372)	10,782	1,559	(1,530–1,589)
Insurance Status									
No insurance/self-pay	16,045	637	(627–647)	21,296	864	(853–876)	61,651	2,499	(2,479–2,518)
Medicare	2,801	716	(690–743)	6,015	924	(901–947)	22,592	2,286	(2,256–2,316)
Medicaid	28	1,026	(646–1406)	67	1,748	(1,329–2,167)	231	3,714	(3,235–4,193)
Private Insurance/HMO	4,833	836	(812–859)	5,697	1,002	(976–1,028)	15,966	2,686	(2,644–2,727)
Other Insurance	206	1,186	(1,024–1,348)	349	1,487	(1,331–1,643)	1,000	3,706	(3,477–3,936)
Unknown	0	0		4	459	(9–908)	27	1,416	(882–1,950)
Region									
Eastern	2,394	465	(447–484)	2,654	476	(458–494)	7,689	1,129	(1,104–1,155)
Central	5,285	844	(821–867)	8,328	1,287	(1,259–1,314)	26,577	3,656	(3,612–3,700)
Southern	6,892	515	(503–527)	10,008	693	(679–706)	33,262	2,050	(2,028–2,072)
Western	9,342	906	(888–924)	12,438	1,172	(1,151–1,192)	33,939	3,219	(3,184–3,253)

Continued on next page

Table 15 (continued). Use of prescription drugs for erectile dysfunction among veterans, count , rate[a]

	2002			2003		
	Count	Rate		Count	Rate	
Total	199,126	4,451	(4,431–4,470)	291,184	6,120	(6,098–6,142)
Age						
< 25	49	178	(128–228)	83	299	(234–363)
25–34	1,276	864	(816–911)	1,940	1,336	(1,276–1,395)
35–44	9,191	2,818	(2,761–2,876)	13,293	4,233	(4,161–4,305)
45–54	53,248	6,017	(5,966–6,068)	72,182	8,437	(8,376–8,499)
55–64	56,964	6,888	(6,831–6,944)	93,258	9,330	(9,270–9,390)
65–74	57,880	4,940	(4,900–4,981)	80,284	6,675	(6,629–6,721)
75–84	20,023	2,026	(1,998–2,054)	29,341	2,704	(2,673–2,735)
85+	495	490	(447–533)	803	627	(583–670)
Race/ethnicity						
White	120,232	4,139	(4,116–4,162)	153,784	5,551	(5,523–5,579)
Black	41,053	8,556	(8,474–8,639)	56,127	12,204	(12,103–12,305)
Hispanic	3,773	3,541	(3,428–3,654)	6,792	6,543	(6,388–6,699)
Other	2,170	4,605	(4,411–4,798)	2,897	6,601	(6,360–6,841)
Unknown	31,898	3,409	(3,372–3,446)	71,584	5,187	(5,149–5,225)
Insurance Status						
No insurance/self-pay	116,713	4,607	(4,580–4,633)	166,389	6,601	(6,569–6,632)
Medicare	47,234	3,783	(3,749–3,817)	72,461	4,854	(4,819–4,890)
Medicaid	506	5,829	(5,321–6,337)	720	7,552	(7,000–8,104)
Private Insurance/HMO	32,630	5,020	(4,965–5,074)	48,493	6,953	(6,891–7,015)
Other Insurance	1,951	6,397	(6,113–6,681)	3,024	8,445	(8,144–8,746)
Unknown	92	3,258	(2,592–3,924)	97	5,620	(4,502–6,738)
Region						
Eastern	18,113	2,332	(2,298–2,366)	26,678	3,339	(3,299–3,379)
Central	52,145	5,822	(5,772–5,872)	81,736	7,762	(7,708–7,815)
Southern	81,712	4,525	(4,494–4,556)	124,279	6,398	(6,363–6,434)
Western	47,156	4,734	(4,692–4,777)	58,491	6,070	(6,020–6,119)

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Pharmacy Benefits Management Version 3.0 (PBM), Department of Veterans Affairs.

Table 16. Physician office visits for erectile dysfunction listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000				
	Count	5-Year Rate		Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	9,461,163	10,316	(9,037–11,595)	2,063	10,287
Age					
18–34	*	*		*	
35–44	780,715	3,758	(2,129–5,387)	752	
45–54	2,331,217	15,133	(10,913–19,354)	3,027	
55–64	2,521,095	24,561	(19,105–30,017)	4,912	
65–74	2,434,590	30,127	(22,938–37,317)	6,025	
75+	833,258	16,226	(11,706–20,745)	3,245	
Race/ethnicity					
White	7,467,491	10,748	(9,227–12,269)	2,150	10,089
Black	1,140,747	11,820	(8,307–15,332)	2,364	14,350
Hispanic	694,687	7,750	(3,651–11,849)	1,550	11,212
Region					
Midwest	2,653,649	12,319	(9,642–14,997)	2,464	12,103
Northeast	1,681,436	9,313	(7,075–11,552)	1,863	9,077
South	2,669,680	8,410	(6,428–10,392)	1,682	8,222
West	2,456,398	12,055	(8,639–15,472)	2,411	12,868
MSA					
MSA	8,119,340	11,590	(10,041–13,140)	2,318	11,692
Non-MSA	1,341,823	6,194	(4,140–8,249)	1,239	5,810

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[c]Average annualized rate per year.

[d]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

in ED treatments, despite a higher prevalence of the condition (22).

Inpatient and Ambulatory Surgery Care

Penile implants were once the only efficacious treatment for ED and for many years accounted for the majority of hospitalizations and expenditures for it. Whereas expenditures for office visits related to ED have increased in the past decade, ambulatory surgery and inpatient expenses remained relatively constant from 1992 to 2001 and became a proportionally smaller overall percentage of expenditures until the most recent year studied, when they rose (Table 17). Nationally representative data indicate that inpatient and ambulatory surgery accounted for nearly three-quarters of all expenditures for ED in 1994, but less than 50% in 2000 (Table 18). Between 82% and 88% of inpatient stays for men with a primary diagnosis of ED were for penile implant (Table 19).

Despite the increasing rates of ED diagnosis, the rate of inpatient hospital stays decreased from 8.0 per 100,000 in 1994 to 4.7 per 100,000 in 2000 (Table 19). This rate reached a nadir in 1998 (3.8 per 100,000), coincident with the introduction of Viagra™, before rebounding in 2001, the most recent year surveyed. In contrast to the increase in outpatient visits, the rate of inpatient stays for ED in 2001 was approximately half what it was in 1992 (Table 20). The decline was first evident in 1998 but in the Medicare population persisted long after the introduction of Viagra™.

Table 17. Expenditures for Medicare beneficiaries for treatment of erectile dysfunction, by site of service (% of total)

	Age 65 and over							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$1,400,440	2.6%	$1,009,700	1.7%	$1,493,400	2.7%	$1,062,100	1.9%
Physician Office	$6,748,320	12.5%	$11,864,360	20.1%	$20,080,200	36.1%	$12,657,920	22.9%
Ambulatory Surgery	$15,553,520	28.9%	$19,624,500	33.2%	$14,077,760	25.3%	$15,004,880	27.1%
Emergency Room	$146,280	0.3%	$221,720	0.4%	$217,280	0.4%	$453,460	0.8%
Inpatient	$29,937,600	55.7%	$26,348,220	44.6%	$19,756,620	35.5%	$26,154,120	47.3%
TOTAL	$53,786,160		$59,068,500		$53,625,260		$55,332,480	

	Under 65							
Service Type	**1992**		**1995**		**1998**		**2001**	
Hospital Outpatient	$275,660	1.5%	$628,860	3.0%	$768,380	3.7%	$626,040	3.0%
Physician Office	$1,402,160	7.5%	$2,607,200	12.4%	$4,109,580	19.8%	$3,907,200	18.7%
Ambulatory Surgery	$3,842,800	20.7%	$6,045,000	28.8%	$5,193,840	25.0%	$6,079,580	29.1%
Emergency Room	$74,740	0.4%	$92,400	0.4%	$83,160	0.4%	$150,880	0.7%
Inpatient	$12,996,680	69.9%	$11,652,500	55.4%	$10,599,520	51.1%	$10,156,160	48.5%
TOTAL	$18,592,040		$21,025,960		$20,754,480		$20,919,860	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 18. Expenditures for erectile dysfunction, by site of service (% of total)

Service Type	**1994**		**1996**		**1998**		**2000**	
Hospital Outpatient	$6,438,236	3.5%	$7,011,462	2.7%	$13,563,958	4.7%	$12,941,222	3.9%
Physician Office	$44,778,518	24.2%	$71,307,056	27.5%	$129,426,983	45.1%	$165,872,253	50.6%
Ambulatory Surgery	$49,553,150	26.7%	$104,065,170	40.2%	$81,689,636	28.5%	$72,854,610	22.2%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$84,524,707	45.6%	$76,573,597	29.6%	$62,444,428	21.7%	$75,958,763	23.2%
TOTAL	$185,294,611		$258,957,285		$287,125,005		$327,626,849	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 19. Inpatient hospital stays for erectile dysfunction listed as primary diagnosis, by procedure rates for penile implants, count, rate[a] (95% CI), rate per visits[b] (95% CI)

	1994			1996		
	Count	Rate per 100,000 population	Rate per 100,000 visits for Erectile Dysfunction	Count	Rate per 100,000 population	Rate per 100,000 visits for Erectile Dysfunction
Total Primary Diagnosis for ED						
Prosthesis or IPP	6,285	7.1 (6.8–7.5)	88,709 (84,263–93,155)	5,066	5.5 (5.2–5.8)	85,864 (81,119–90,627)
Semi-rigid Prosthesis	1,206	1.4 (1.3–1.5)	17,022 (15,709–18,335)	859	0.9 (0.8–1.0)	14,559 (13,271–15,831)
IPP	5,079	5.8 (5.4–6.1)	71,687 (67,608–75,752)	4,208	4.6 (4.3–4.8)	71,322 (66,983–75,644)

	1998			2000		
	Count	Rate per 100,000 population	Rate per 100,000 visits for Erectile Dysfunction	Count	Rate per 100,000 population	Rate per 100,000 visits for Erectile Dysfunction
Total Primary Diagnosis for ED						
Prosthesis or IPP	2,927	3.1 (2.9–3.3)	81,396 (75,250–87,514)	3,767	3.9 (3.6–4.2)	82,573 (75,712–89,413)
Semi-rigid Prosthesis	437	0.5 (0.4–0.5)	12,152 (10,234–14,043)	639	0.7 (0.6–0.8)	14,007 (11,881–16,133)
IPP	2,490	2.6 (2.4–2.8)	69,244 (63,654–74,833)	3,128	3.2 (3.0–3.5)	68,566 (63,218–73,915)

IPP, inflatable penile prosthesis

[a]Rate per 100,000 is based on 1994–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US adult male civilian non-institutionalized population.

[b]Rate per 100,000 adult male visits is based on estimated number of visits for ED in HCUP_NIS 1994–2000.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

This trend is mirrored in the HCUP data on inpatient hospital stays, although the magnitude of the age-adjusted decline from 1994–1995 to 2000–2001 is greater in HCUP (14 per 100,000 to 8.5 per 100,000) than in Medicare (34 per 100,000 to 25 per 100,000) (Table 20 and 21).

The databases indicate racial, geographical, and age-related differences in rates of inpatient hospitalization as well. African American men have a higher rate of hospitalization than Caucasian men, and the South has the highest age-adjusted rates. Hospitalization rates are also higher in urban than in rural regions. Rates of hospitalization for younger men dropped notably more than rates for older men during the past decade (Tables 20 and 21), probably due to the better responsiveness to PDE-I in younger men. Potential explanations for the differences in hospitalization rates include the shift of implant surgery from inpatient facilities to ambulatory surgery centers; comorbid medical conditions that vary with age, race, or geography; and variation in secondary insurance coverage. Data from several sources support these explanations. The National Survey of Ambulatory Surgery measured rates of ED visits only from 1994 to 1996. Therefore, Medicare data are more useful. Age-adjusted rates of ambulatory surgery visits for ED as a primary diagnosis in Medicare beneficiaries have not increased concomitant with the reduction in inpatient hospitalizations (Table 22). Rather, the rates have paralleled those observed in inpatient Medicare beneficiaries, rising from 1992 to 1995 and then dropping in 1998 before rising again in 2001. Age-adjusted rates for ambulatory surgery visits showed the same racial and geographical trends as seen with inpatients, except for the absence of any age-related trends.

Surgical Trends

The total number of penile implants performed per year has dropped over the past decade, corresponding to the approval of pharmacological treatments for ED (alprostadil penile injections, alprostadil urethral suppositories, and oral Viagra™ in 1994, 1996, and 1998, respectively) (Table 19). Type of implant, length of stay, and hospital volume provide insight into the changing delivery of surgical care for ED. A greater percentage of penile implants are inflatable rather than semirigid or malleable. In 1994, 81% of penile prostheses implanted were inflatable, whereas in 2000, 83% were (Table 19). No randomized trials have compared treatment satisfaction and other clinically relevant outcomes for inflatable and semirigid devices. The mean number of implant surgeries performed per year at hospitals that perform at least one implant per year decreased from 22.0 in 1994 to 16.1 in 2000 (23). As the effect of surgeon and hospital volume on patient outcome is increasingly appreciated for other types of urologic surgery (23), monitoring implant outcomes as a function of provider volume may become valuable for ED surgery as well. The average length of stay for implant surgery has decreased, owing to pressure from insurers and the general trends toward reduced length of stay for all types of surgical procedures. The VA National Surgical Quality Improvement Program (NSQIP) database shows a reduction in postoperative length of stay from 2.3 days in 1998 to 1.6 days in 2003 (Table 23). HCUP data from 1994 and 2000 demonstrate that mean length of stay for a primary diagnosis or procedure for ED decreased through the 1990s from 2.8 to 2.4 days (Table 24). No regional variation in surgical practices was noted. However, African Americans and Hispanics had a higher mean length of stay than Caucasians. It is unclear whether this reflects comorbid conditions requiring longer periods of hospitalization and antibiotics or other causes.

Complications and Adverse Events of Surgical Procedures for ED

The VA NSQIP provides data on 706 veterans undergoing surgical treatment for ED in 1998–2003 (Table 23). Of these treatments, 621 (88%) occurred in either 1998 or 1999. NSQIP captures only a representative sampling (approximately 20%) of surgical procedures in VA hospitals and cannot be used to estimate total surgical volume accurately. Sampling strategies did not change between 1998 and 2003; thus, the steep decline is likely real and probably due to the availability of oral therapies. However, allocation of resources for implants is controlled regionally within the VA healthcare system, so the decrease in implants could reflect restricted access based on budgetary decisions. Total counts were too low to establish patterns of care or complications according to age, race, or region. Summary data from 1998–2003 are useful, however: the mean operating-room time for a

Table 20. Inpatient stays by Medicare beneficiaries with erectile dysfunction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	6,640	45 (40–49)	45	5,120	34 (30–38)	34	3,580	25 (21–28)	25	3,800	25 (21–28)	25
Total < 65	2,020	65 (52–77)		1,580	46 (36–56)		1,240	36 (27–45)		1,120	29 (22–37)	
Total 65+	4,620	39 (34–44)		3,540	30 (26–34)		2,340	21 (17–25)		2,680	23 (19–27)	
Age												
65–69	2,480	61 (50–72)		1,520	39 (31–48)		720	21 (14–28)		1,100	31 (23–39)	
70–74	1,480	46 (35–56)		1,360	41 (31–50)		740	24 (16–32)		740	24 (16–32)	
75–79	460	20 (12–29)		440	19 (11–28)		580	25 (16–35)		540	22 (14–30)	
80–84	180	14 (4.7–23)		160	12 (3.5–20)		240	17 (7.5–27)		200	13 (5.1–22)	
85+	20	3.4 (0–9.9)		60	9.4 (0–20)		0	0 0		40	5.5 (0–13)	
Race/ethnicity												
White	4,980	40 (35–45)	39	3,580	28 (24–32)	28	2,740	22 (19–26)	22	3,000	23 (19–27)	23
Black	1,220	96 (72–120)	99	1,080	78 (57–99)	78	600	45 (29–61)	45	600	41 (26–56)	41
Asian	…	...	…	20	27 (0–81)	27	0	0	0	20	9.8 (0–29)	9.8
Hispanic	…	...	…	300	151 (75–228)	141	100	30 (3.6–56)	36	100	27 (3.2–50)	27
N. American Native	…	...	…	0	0	0	0	0	0	20	60 (0–177)	60
Region												
Midwest	1,340	36 (27–45)	36	1,080	28 (21–35)	27	780	21 (14–28)	21	680	18 (12–24)	17
Northeast	1,080	34 (25–43)	35	700	22 (15–29)	23	620	22 (14–30)	22	760	26 (18–34)	27
South	2,660	51 (42–59)	51	2,140	39 (32–46)	38	1,500	28 (22–34)	29	1,700	29 (23–35)	30
West	1,420	59 (45–72)	57	1,040	45 (33–57)	45	640	29 (19–39)	28	540	22 (14–30)	21

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 21. Inpatient hospital stays for erectile dysfunction listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	11,931	14 (12–15)	14	9,925	11 (9.4–12)	11	7,396	7.8 (6.8–8.9)	7.8	8,158	8.5 (7.2–9.8)	8.5
Age												
18–24	*	*		*	*		*	*		*	*	
25–34	388	1.9 (1.3–2.6)		*	*		165	0.9 (0.5–1.2)		214	1.2 (0.8–1.6)	
35–44	733	3.7 (2.9–4.5)		807	3.8 (3.0–4.6)		450	2.1 (1.6–2.6)		520	2.4 (1.7–3.0)	
45–54	2,392	17 (15–20)		2,003	13 (11–15)		1,466	8.8 (7.4–10)		1,473	8.3 (6.5–10)	
55–64	3,640	38 (32–43)		3,082	31 (27–35)		2,118	20 (16–24)		2,419	22 (18–25)	
65–74	3,699	47 (40–54)		2,943	36 (30–42)		2,401	30 (24–35)		2,585	32 (27–38)	
75+	982	21 (16–26)		883	17 (14–21)		741	13 (11–16)		901	15 (13–18)	
Race/ethnicity												
White	7,077	10 (9.1–12)	9.8	5,962	8.6 (7.4–9.8)	7.9	3,991	5.7 (4.8–6.5)	5.2	4,326	6.1 (5.1–7.0)	5.6
Black	1,614	17 (14–21)	21	1,812	19 (15–23)	22	1,130	11 (8.9–14)	13	1,000	9.8 (7.5–12)	12
Hispanic	617	7.5 (5.6–9.4)	12	496	5.5 (3.7–7.3)	9.0	*	*	9.4	787	7.6 (4.9–10)	12
Region												
Midwest	1,776	8.5 (6.7–10)	8.6	1,413	6.6 (5.2–8.0)	6.4	1,167	5.4 (3.8–7.0)	5.3	1,376	6.2 (4.0–8.2)	6.2
Northeast	3,058	17 (12–22)	16	2,620	14 (9.5–19)	14	1,376	7.6 (5.0–10)	7.32	2,049	11 (6.9–16)	11
South	4,704	16 (13–19)	16	4,112	13 (11–15)	13	3,672	11 (8.8–13)	11	3,457	10 (7.8–12)	9.9
West	2,392	12 (9.4–15)	13	1,780	8.7 (6.7–11)	9.5	1,180	5.6 (4.0–7.1)	5.9	1,276	5.9 (4.6–7.2)	6.3
MSA												
Rural	1,186	5.3 (3.3–7.2)	4.8	1,093	5.3 (3.6–6.9)	4.7	789	3.8 (2.4–5.1)	3.4	705	3.3 (2.1–4.5)	2.9
Urban	10,729	19 (14–18)	17	8,825	12 (11–14)	13	6,556	9.0 (7.6–10)	9.3	7,444	10 (8.3–12)	10

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 22. Ambulatory surgery visits by Medicare beneficiaries with erectile dysfunction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	5,320	36 (31–40)	36	6,400	42 (37–47)	42	4,300	30 26–34)	30	5,080	33 (29–37)	33
Total < 65	1,040	33 (24–42)		1,500	44 (34–53)		1,020	30 (22–38)		1,340	35 (27–44)	
Total 65+	4,280	36 (31–41)		4,900	42 (36–47)		3,280	30 (25–34)		3,740	32 (28–37)	
Age												
65–69	2,080	51 (41–61)		2,100	55 (44–65)		1,320	39 (30–49)		1,840	52 (41–63)	
70–74	1,440	44 (34–55)		1,880	56 (45–68)		1,080	35 (26–45)		1,060	34 (25–44)	
75–79	540	24 (15–33)		720	32 (21–42)		500	22 (13–30)		640	26 (17–35)	
80–84	140	11 (2.7–19)		160	12 (3.5–20)		340	25 (13–36)		160	11 (3.3–18)	
85+	60	10 (0–22)		20	3.1 (0–9.3)		20	3.1 (0–9.1)		40	5.5 (0–13)	
Race/ethnicity												
White	4,420	35 (31–40)	35	5,080	39 (34–44)	39	3,480	28 (24–33)	28	3,840	29 (25–34)	29
Black	600	47 (30–64)	47	900	65 (46–84)	64	540	40 (25–56)	40	820	56 (39–73)	55
Asian	…	...	…	20	27 (0–81)	27	20	15 (0–43)	15	0	0	0
Hispanic	…	...	…	100	50 (6.0–95)	50	200	60 (23–97)	60	280	75 (35–114)	69
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	1,160	31 (23–39)	31	980	25 (18–33)	25	720	19 (13–26)	20	1,100	29 (21–37)	28
Northeast	380	12 (6.6–17)	11	380	12 (6.6–17)	12	240	8.6 (3.7–14)	8.6	460	16 (9.3–22)	14
South	2,860	55 (46–64)	55	3,900	71 (61–81)	71	2,760	51 (43–60)	51	3,000	52 (43–60)	52
West	920	38 (27–49)	37	1,100	47 (35–60)	46	560	25 (16–34)	25	460	19 (11–26)	19

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 23. Complications, by age, race/ethnicity, region, and type, within 30 days following surgery for erectile dysfunction among VA users

	1998	1999	2000	2001	2002	2003	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	All Years
Total	303	318	23	11	19	32	
Age							
≤ 39	6 (2.0)	3 (0.9)	0	1 (9.1)	0	0	
40–44	13 (4.3)	7 (2.2)	0	0	1 (5.3)	0	
45–54	77 (25.4)	86 (27.0)	11 (47.8)	5 (45.5)	3 (15.8)	4 (12.5)	
55–64	112 (37.0)	108 (34.0)	9 (39.1)	3 (27.3)	5 (26.3)	8 (25.0)	
65–74	82 (27.1)	93 (29.3)	3 (13.0)	2 (18.2)	3 (15.8)	16 (50.0)	
75–84	13 (4.3)	21 (6.6)	0	0	7 (36.8)	4 (12.5)	
Race/ethnicity							
White	212 (70.0)	209 (65.7)	17 (73.9)	8 (72.7)	11 (57.9)	14 (43.8)	
Black	65 (21.5)	80 (25.2)	3 (13.0)	2 (18.2)	4 (21.1)	5 (15.6)	
Asian	0	0	0	0	1 (5.3)	0	
N. American Native	2 (0.7)	0	0	0	0	0	
Unknown	11 (3.6)	19 (6.0)	1 (4.4)	1 (9.1)	2 (10.5)	11 (34.4)	
Region							
East	49 (16.2)	61 (19.2)	5 (21.7)	5 (45.5)	4 (21.1)	0	
Central	63 (20.8)	67	5 (21.7)	1 (9.1)	4 (21.1)	7 (21.9)	
South	130 (42.9)	113 (21.1)	11 (47.8)	3 (27.3)	5 (26.3)	18 (56.3)	
West	61 (20.1)	77 (24.2)	2 (8.7)	2 (18.2)	6 (31.6)	7 (21.9)	
30-Day Complications, unadjusted for age							
1 or More Complications	17 (5.6)	19 (6.0)	2 (8.7)	0	2 (10.5)	2 (6.3)	
Wound Events	14 (4.6)	16 (5.0)	2 (8.7)	0	2 (10.5)	1 (3.1)	
Respiratory Events	2 (0.7)	1 (0.3)	0	0	0	0	
Renal Events (Urinary Tract Infection)	0	1 (0.3)	0	0	1 (5.3)	0	
Central Nervous System Events	2 (0.7)	1 (0.3)	0	0	0	0	
Cardiac Events	1 (0.3)	0	0	0	0	0	
Other Complications	0	2 (0.6)	0	0	1 (5.3)	1 (3.1)	
Death within 30 Days	1 (0.3)	0	0	1 (9.1)	0	0	
Returns to the OR	10 (3.3)	16 (5.0)	0	0	2 (10.5)	2 (6.3)	
Operative Time (hours), mean ± SD	2.0 ± 0.9	1.9 ± 0.8	2.0 ± 1.2	2.4 ± 1.8	2.2 ± 1.5	1.8 ± 0.8	2.0 ± 0.9
Postoperative Length of Stay (days), mean ± SD	2.3 ± 4.3	1.9 ± 2.2	2.8 ± 2.6	1.8 ± 0.7	1.4 ± 0.7	1.6 ± 1.5	2.1 ± 3.3

SOURCE: VA National Surgical Quality Improvement Program (NSQIP), 1998–2003.

Table 24. Length of stay (LOS) for primary diagnosis for erectile dysfunction

	1994				1996				1998				2000			
	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)	Count	LOS (Mean)	LOS (Median)	LOS (Max)
Total[a]	11,931	2.8	2	187	9,925	2.6	2	140	7,396	2.6	1	68	8,158	2.4	1	123
Age																
18–24	97	3	3	8	64	1.6	1	6	53	2.6	3	5	47	2.4	1	11
25–34	388	3.2	2	23	143	3.1	2	21	165	2.5	2	9	214	2.2	1	23
35–44	733	2.9	2	21	807	3.6	2	140	450	3	2	14	520	2.8	2	31
45–54	2,392	3	2	187	2,003	2.3	2	29	1,466	2.7	2	49	1,473	2.2	1	22
55–64	3,640	2.6	2	65	3,082	2.1	1	22	2,118	2.4	1	35	2,419	2.2	1	23
65–74	3,699	2.6	2	28	2,943	2.8	2	73	2,401	2.6	1	48	2,585	2.6	1	123
75+	982	3.6	2	82	883	2.9	2	32	741	3.1	2	68	901	2.8	1	39
Race/ethnicity																
White	7,077	2.5	2	39	5,962	2.3	1	44	3,991	2.6	1	68	4,326	2.3	1	123
Black	1,614	3.8	2	187	1,812	3.1	2	140	1,130	3	1	35	1,000	2.7	1	39
Hispanic	617	3.2	2	50	496	3.3	2	73	539	2.8	2	24	787	2.4	1	19
Region																
Northeast	3,058	2.9	2	65	2,620	2.5	1	140	1,376	2.9	1	35	2,049	2.7	1	123
Midwest	1,776	3.2	2	187	1,413	2.7	2	29	1,167	2.5	2	17	1,376	2.4	1	39
South	4,704	2.8	2	59	4,112	2.8	2	73	3,672	2.6	1	49	3,457	2.4	1	42
West	2,392	2.2	1	82	1,780	2	1	40	1,180	2.5	2	68	1,276	2.1	1	20
MSA																
Rural	1,186	3.2	2	19	1,093	2.6	2	15	789	2.2	1	20	705	2.3	1	22
Urban	10,729	2.7	2	187	8,825	2.6	2	140	6,556	2.7	2	68	7,444	2.4	1	123

MSA, metropolitan statistical area.

US adult males 18+ civilian non-institutionalized population.

[a]Males of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample 1994, 1996, 1998, 2000.

Table 25. Emergency room visits by Medicare beneficiaries with erectile dysfunction listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	1,800	12 (9.6–15)	12	1,760	12 (9.1–14)	12	1,780	12 (9.7–15)	12	2,400	16 (13–18)	16
Total < 65	740	24 (16–31)		840	24 (17–32)		660	19 (13–26)		820	22 (15–28)	
Total 65+	1,060	9.0 (6.6–11)		920	7.8 (5.6–10)		1,120	10 (7.5–13)		1,580	14 (11–17)	
Age												
65–69	480	12 (7.1–16)		220	5.7 (2.3–9.1)		300	8.9 (4.4–13)		200	5.7 (2.1–9.2)	
70–74	140	4.3 (1.1–7.5)		240	7.2 (3.1–11)		200	6.6 (2.5–11)		560	18 (11–25)	
75–79	120	5.3 (1.1–9.5)		100	4.4 (0.5–8.3)		160	7.0 (2.1–12)		400	16 (9.2–23)	
80–84	160	12 (3.7–21)		240	17 (7.5–27)		140	10 (2.6–18)		220	15 (6.0–23)	
85–89	140	23 (6.0–41)		80	13 (0.3–25)		180	28 (9.5–46)		100	14 (1.7–26)	
90+	20	9.9 (0–29)		40	19 (0–45)		60	28 (0–60)		100	43 (5.2–81)	
Race/ethnicity												
White	1,300	10 (7.8–13)	9.9	1,200	9.2 (6.9–12)	9.4	1,200	9.8 (7.3–12)	9.8	1,580	12 (9.4–15)	12
Black	480	38 (23–53)	42	460	33 (20–47)	30	400	30 (17–43)	28	700	48 (32–64)	49
Asian	…	...	…	40	55 (0–130)	55	0	0	0	20	9.8 (0–29)	9.8
Hispanic	…	...	…	0	0	0	120	36 (7.2–64)	42	20	5.3 (0–16)	5.3
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	460	12 (7.3–18)	12	400	10 (5.8–15)	9.9	400	11 (6.1–16)	10	520	14 (8.4–19)	14
Northeast	340	11 (5.6–16)	10	400	13 (7.1–18)	12	340	12 (6.4–18)	13	380	13 (7.2–19)	12
South	860	16 (12–21)	18	780	14 (9.8–19)	15	920	17 (12–22)	17	1,200	21 (15–26)	21
West	140	5.8 (1.5–10)	3.3	180	7.8 (2.7–13)	6.9	100	4.5 (0.5–8.4)	5.4	300	12 (6.0–18)	12

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 26. Use of sildenafil, 1998–2002, by age, percent (SE)

Age	1998	1999	2000	2001	2002
Total	1.5 (0.01)	1.3(0.02)	1.5 (0.02)	2.2 (0.02)	2.9 (0.02)
18–45	0.3 (0.01)	0.3 (0.01)	0.4 (0.01)	0.6 (0.01)	0.9 (0.01)
46–55	2.0 (0.04)	1.9 (0.04)	2.3 (0.05)	3.3 (0.05)	4.3 (0.06)
56–65	4.7 (0.09)	3.7 (0.08)	4.0 (0.09)	5.3 (0.08)	6.9 (0.09)
65+	5.7 (0.13)	4.2 (0.13)	3.8 (0.11)	4.9 (0.10)	5.8 (0.11)

NOTE: Data are from national pharmacy claims. The prevalence of use is defined as having one or more sildenafil claims during respective year; SE, standard error of the prevalence estimate.

SOURCE: Adapted by permission from Macmillan Publishers LTD: International Journal of Impotence Research, Delate T, Simmons VA, Motheral BR, Patterns of use of sildenafil among commercially insured adults in the United States: 1998–2002, 16(4), 313–318, Copyright 2004.

penile implant during this period was 2.0 hours (± 0.9 hour). One or more complications occurring within 30 days was recorded in 42 of 706 men (5.9%), the most frequent complication being "wound events" (83% of all complications). This rate is similar to infection rates in published series. Approximately 4% of men required a return to the operating room within 30 days; only 2 men (0.3%) died within 30 days of the procedure.

Emergency Room Care

Emergency room (ER) care is rarely required in the management of medical problems directly related to the diagnosis or treatment of ED. The rate of ER utilization for ED as a primary diagnosis is only 1% the rate of physician office visits (16 per 100,000 vs 1,666 per 100,000, Tables 25 and 9). Acute complications of surgical treatments occur after 2% to 4% of implant surgeries and in most cases require hospitalization for removal of an infected device. Priapism is the most significant complication of pharmacological therapy, although these visits likely do not list a primary diagnosis of ED. In rare instances, men using phosphodiesterase-5 inhibitors have reported priapism. Intracavernosal injection of vasodilators such as prostaglandin E1 result in priapism in 0.35% to 4% of patients (8); for these patients, the condition usually can be resolved in the ER. Rarely, priapism associated with chronic medical conditions, such as sickle cell anemia, may prompt ER evaluation.

Some patients may use ER visits as a major point of access to healthcare, despite the fact that new-onset ED is rarely related to an emergent medical condition. This conjecture is supported by the trend in ER costs

Table 27. Relative use of sildenafil, by age and gender

	1998	1999	2000	2001	2002
Females					
18–45	1.0	0.7	0.9	1.0	1.1
46–55	1.0	0.7	0.8	0.8	0.8
56–65	1.0	0.6	0.6	0.5	0.5
65+	1.0	0.5	0.4	0.4	0.4
Males					
18–45	1.0	1.0	1.4	2.1	3.1
46–55	1.0	0.9	1.2	1.6	2.2
56–65	1.0	0.8	0.8	1.1	1.5
65+	1.0	0.7	0.7	0.9	1.0

NOTE: Change is relative to 1998; values adjusted for gender differences and age between years.

SOURCE: Adapted by permission from Macmillan Publishers LTD: International Journal of Impotence Research, Delate T, Simmons VA, Motheral BR, Patterns of use of sildenafil among commercially insured adults in the United States: 1998–2002, 16(4), 313–318, Copyright 2004.

Table 28. Specialty of sildenafil prescribers

	1998 (n = 5,801)	1999 (n = 5,128)	2000 (n = 5,862)	2001 (n = 11,010)	2002 (n = 13,428)
Primary care	58%	62%	65%	66%	69%
Urology	25%	21%	18%	16%	13%
Other specialty	16%	18%	17%	18%	18%

n=number of unique prescribers in the respective year.

NOTE: Prescribers defined as healthcare providers with one or more sildenafil claims attributed to their DEA number during their respective year.

SOURCE: Adapted by permission from Macmillan Publishers LTD: International Journal of Impotence Research, Delate T, Simmons VA, Motheral BR, Patterns of use of sildenafil among commercially insured adults in the United States: 1998–2002, 16(4), 313–318, Copyright 2004.

and rates of utilization over the past decade. Despite a decrease in the rates and expenditures for inpatient hospitalization, the yearly costs of ER treatment as a percentage of total expenditures have increased in the Medicare population (Table 17), where the rate of ER visits for ED as the primary diagnosis increased between 1992 and 2001 from 12 to 16 per 100,000 (Table 25). The rate of ER utilization by African Americans was three to four times the rate for Caucasians, and men under 65 had nearly twice the rate of older men (Table 25).

PHARMACOLOGIC MANAGEMENT OF ED

National pharmacy claims data indicate that the prevalence of Viagra™ use among males increased from 1.5% in 1998 to 2.9% in 2002 (Table 26) (24). Use increased with age—approximately 6% of men over 55 had one or more Viagra™ claims in 2002—though the greatest relative increase was in men between 18 and 45 (3.1 in 2002 vs 1.0 in 1998) (Tables 26 and 27). The vast majority of Viagra™ prescribers were primary care physicians (69% of all claims in 2002, compared with 13% for urologists) (Table 28).

Data from the Department of Veterans Affairs indicate that the number of veterans receiving prescriptions for ED treatment (excluding testosterone therapy) increased ninefold between 1999 and 2003 (Tables 15 and 29). The increase was seen across all age, race, region, and insurance categories. It was particularly striking that in 2003 among those aged 55–64, 9.3% reported having filled a prescription for ED agents in 2003. The rate of African American men filling a prescription for ED agents in 2003 (12.2%) was more than twice that for men in other racial groups. The greatest change in ED prescriptions was the marked increase in utilization of Viagra™. By 2003, approximately 85% of all pharmacologic agents prescribed for ED were Viagra™ (VA formulary policies mandated Viagra™ as the PDE-I of choice). Use of alprostadil remained stable at 427 per 100,000 men, likely reflecting contraindications to or adverse effects from Viagra™ or Viagra™ failures (Table 29). Papaverine was used in 0.05% of men during the years examined. The use of pharmacologic agents by men with ED increased from 17,458 per 100,000 in FY 1999 to 56,716 per 100,000 in FY 2003 (Table 29). That ED is underreported is reflected in the observation that many more men receive prescriptions for ED medications than carry a diagnosis of ED.

The number of men undergoing radical prostatectomy has increased markedly in the past decade, as described in the prostate cancer chapter of this compendium. Stanford and colleagues (25) demonstrated that both the level of interest in and the frequency of sexual activity declined over the 24-month period after radical prostatectomy. Nearly 60% of Medicare recipients said that they did not have erections firm enough for sexual intercourse at 24 months after radical prostatectomy, and 42% said that this was at least a moderate-to-serious problem (Table 30) (25). These individuals make up a large and increasing population at risk for ED.

In the VA system, use of ED medications by men with prostate cancer and those undergoing radical prostatectomy has increased markedly (Table 29). In men with a diagnosis of prostate cancer, the use of pharmacologic agents increased from 3,065 per 100,000 in 1999 to 9,474 per 100,000 in 2003. In 1999, 9,419 per 100,000 men filled prescriptions for ED

Table 29. Pharmacologic management of erectile dysfunction in VA users, count, age-adjusted rate[a]

	1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Erectile dysfunction medications for all males	23,913	681	33,428	901	101,467	2,484	199,126	4,451	291,184	6,120
Alprostadil	18,583	529	20,010	539	20,128	493	20,569	460	20,339	427
Papaverine	1,900	54	1,722	46	1,564	38	1,219	27	1,014	21
Sildenafil	4,224	121	12,996	350	83,280	2,039	182,141	4,071	275,254	5,785
Erectile dysfunction medications for all males with a diagnosis of erectile dysfunction	17,119	17,458	22,171	18,895	59,570	38,472	103,838	51,408	141,290	56,716
Erectile dysfunction medications for all males ≥ 40 years										
With prostate cancer	3,341	3,065	4,113	3,324	8,627	5,756	13,793	7,938	18,143	9,474
After radical prostatectomy	154	9,419	228	12,486	399	21,044	656	27,007	682	31,371
Use of sildenafil for all males ≥ 40 years										
With prostate cancer	494	453	1,152	931	5,872	3,918	11,183	6,436	15,549	8,119
After radical prostatectomy	31	1,896	106	5,805	333	17,563	493	24,430	641	29,485

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Pharmacy Benefits Management Version 3.0 (PBM), Department of Veterans Affairs.

Table 30. Distribution (percentage) of sexual function before and after radical prostatectomy in a cohort of 1,291 prostate cancer patients treated for clinically localized disease[a]

Measure	Baseline	6 Months	12 Months	24 Months
Level of interest in sexual activity				
None	6.7	25.8	12.4	12.8
A little or some	46.4	45.9	53.3	49.4
A lot	36.0	16.0	21.4	16.5
Frequency of sexual activity				
None	13.2	54.4	37.6	34.1
≥ Once a month	32.3	18.9	26.1	21.0
≥ Once a week	43.0	14.0	22.9	23.2
Erections firm enough for sexual intercourse				
No	15.8	80.2	71.8	59.9
Yes	72.7	7.9	14.7	18.5
Difficulty keeping an erection				
None	44.5	1.9	4.6	6.7
A little or some	25.8	6.4	11.3	13.7
A lot	9.7	10.2	14.5	13.0
Do not get erections	8.0	68.0	54.6	44.2
Mean sexual function score	71.5	25.6[b]	36.2[b]	38.6[b]
How big a problem is sexual function				
No problem	50.3	10.2	12.3	14.0
Small problem	20.2	15.4	20.9	22.6
Moderate-to-big problem	17.9	60.9	52.0	41.9

[a]Results are adjusted for sampling weights; percentages do not total 100% because of missing data.

[b]$P < 0.001$ for change from baseline.

SOURCE: Reprinted from Journal of the American Medical Association, 283, Stanford JL, Feng Z, Hamilton AS, Gilliland FD, Stephenson RA, Eley JW, Albertsen PC, Harlan LC, Potosky AL, Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study, 354–360, *Copyright © 2000, American Medical Association.* All rights reserved.

treatment after radical prostatectomy (Table 29). The rate increased to 31,371 per 100,000 in 2003 (Table 29). Thus, nearly one-third of the men who underwent radical prostatectomy for prostate cancer in 2003 filled a prescription for ED pharmacologic therapy, the most common being Viagra™ (93%); most of these men were relatively younger and non-Caucasian.

ECONOMIC IMPACT

Annual expenditures for ED in the United States reached nearly $330 million in 2000, increasing substantially from $185 million in 1994 (exclusive of pharmaceutical costs) (Table 18). This increase was driven by expenditures for physician office visits, which almost quadrupled between 1994 and 2000 and accounted for about 85% of the increase over the study period. Physician office visits accounted for more than half of ED expenditures in 2000. Costs also increased for ambulatory surgery and hospital outpatient services, while expenditures for inpatient services decreased slightly. Observed trends in national expenditures for ED have almost certainly been influenced by the introduction of phosphodiesterase-5 inhibitors (Viagra™, Levitra™, Cialis™) which have increased public awareness of ED and increased the number of physician office visits related to the condition. This phenomenon may also have increased usage of other services by patients for whom pharmaceutical management of ED is not an option.

Patterns of expenditures for ED in the Medicare population age 65 and older differed from those in

Table 31. Estimated annual expenditures of privately insured employees with and without a medical claim for erectile dysfunction in 2002[a]

	Annual Expenditures (per person)					
	Males without Erectile Dysfunction (N=281,277)			Males with Erectile Dysfunction (N=4,054)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$2,670	$1,036	$3,706	$3,498	$1,315	$4,813
Age						
18–34	$1,289	$654	$1,943	$2,371	$888	$3,259
35–44	$2,146	$870	$3,016	$2,957	$1,742	$4,699
45–54	$3,045	$1,207	$4,252	$3,915	$1,551	$5,466
55–64	$3,214	$1,139	$4,353	$3,918	$1,038	$4,956
Region						
Midwest	$2,582	$1,023	$3,605	$3,382	$1,308	$4,690
Northeast	$2,624	$1,117	$3,741	$3,436	$1,442	$4,878
South	$2,721	$968	$3,689	$3,563	$1,222	$4,785
West	$2,880	$1,063	$3,943	$3,771	$1,372	$5,143

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions.

SOURCE: Ingenix, 2002.

the general population (Table 17). These Medicare enrollees accounted for $55 million in expenditures in 2001. There was little change since 1992, indicating a decrease in real expenditures over the study period when inflation is taken into account. The lack of change was a function of the fact that increases in physician office and ER visit costs only slightly outpaced the decreases in costs for inpatient services, hospital outpatient services, and ambulatory surgery. Approximately 47% of costs were still for inpatient services in 2001. Because Medicare did not cover prescription drug costs during the study period, expenditures on pharmaceuticals were not captured in these data. Therefore, it is possible that the observed decreases in inpatient costs resulted from the availability of an effective pharmaceutical option. Not captured in the estimates are the national sales of Viagra™, reported to be $1.6 billion in 2005, Cialis™, reported to be $747 million in 2005, and Levitra™, reported to be $327 million in 2005 (26-28).

Expenditures for ED by Medicare enrollees under the age of 65 totaled $21 million in 2001 and have increased more slowly than inflation since 1992 (Table 17). Decreases in inpatient expenditures were offset by a doubling of costs for all other service types between 1992 and 2001. Despite these trends, inpatient services continued to constitute a plurality of ED expenditures in this population.

Individual-level expenditures for ED were estimated using risk-adjusted regression models controlling for age, work status, income, urban or rural residence, and health plan characteristics (Table 31). Among 18- to 64-year-old males with employer-provided insurance, average annual expenditures were $4,813 for those treated for ED, compared with $3,706 for similar men not treated for the condition; thus an incremental cost of $1,107 was associated with a diagnosis of ED. Pharmaceuticals such as phosphodiesterase-5 inhibitors, which have become an increasingly important source of costs related to ED, accounted for about 25% of the incremental costs. ED appeared to be more expensive for younger men than older men, the highest excess expenditures occurring among men between 35 and 44. Men in this age group with an ED diagnosis spent $872 more on pharmaceuticals than men with no ED diagnosis. Pharmaceuticals accounted for more than half of the

Table 32. Average annual work loss of males treated for erectile dysfunction, 1999 (95% CI)

			Average Work Absence (hrs)		
	Number of Workers[a]	% Missing Work	Inpatient[b]	Outpatient[b]	Total
Total	633	14%	0.2 (0–0.5)	3.4 (2.1–4.7)	3.6 (2.3–4.9)
Age					
18–29	22	18%	0	1.7 (0–3.5)	1.7 (0–3.5)
30–39	86	16%	0	5.5 (0.3–10.7)	5.5 (0.3–10.7)
40–49	164	15%	0	3.5 (0.9–6.1)	3.5 (0.9–6.1)
50–64	361	12%	0.4 (0–0.9)	2.9 (1.5–4.4)	3.3 (1.8–4.8)
Region					
Midwest	145	13%	0	3.9 (0.9–7.0)	3.9 (0.9–7.0)
Northeast	56	13%	0.6 (0–1.7)	4.3 (0–8.9)	4.8 (0.1–9.5)
South	289	12%	0.3 (0–1.0)	3.1 (1.2–4.9)	3.4 (1.5–5.4)
West	69	23%	0	5.7 (1.4–9.9)	5.7 (1.4–9.9)
Unknown	74	4%	0	0.8 (0–1.8)	0.8 (0–1.8)

[a]Individuals with an inpatient or outpatient claim for erectile dysfunction and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

excess costs in this age group. Regional differences in individual-level expenditures were negligible.

Fourteen percent of men with a diagnosis of ED missed some work, with younger men missing work more frequently than older men (Table 32). The proportion was highest in the West (23%) and lowest in the South (12%). On average, men with an ED diagnosis missed 3.6 hours of work per year; the confidence intervals were too wide to assess differences by age and region. Each outpatient visit for ED resulted in 3.4 hours of missed work; and again, data were too sparse to assess differences by age and region. The relatively small amount of work loss associated with ED is most likely due the infrequency of inpatient stays and the availability of effective pharmaceutical treatment.

The economic burden of ED is significant in the United States. While work loss is relatively low, expenditures for treatment are sizable. Although expenditures for inpatient services have been declining slightly, they have been outpaced by increases in expenditures for other services. Although excess individual-level costs were moderate for each patient, ED is relatively common—nearly 1.5% of privately insured males between the ages of 18 and 64 had at least one claim related to ED in 2002. Expenditures for ED were greater in the general population than among Medicare beneficiaries, probably due to the greater age of most Medicare enrollees. Overall, younger men with ED appear to have a more substantial economic impact than older men.

PEYRONIE'S DISEASE

DEFINITON AND DIAGNOSIS

Peyronie's disease (PD) was first described in the medical literature by de La Peyronie in 1743, although depictions of penile curvature date to antiquity. No consensus exists with regard to the etiology, prevalence, treatment, or even the definition of this condition (29). Also known as plastic induration of the penis, PD is usually associated with the presence of an inflammatory reaction and fibrotic plaque within the tunica albuginea of one or both penile corpora cavernosa. The common presenting symptoms of PD include a palpable indurated penile plaque, pain with erection, and curvature or deformity of the erect penis (pointing toward the plaque). ED can also occur due to disruption of normal mechanisms of venoocclusion that depend on the compliance of the tunica albuginea. The impact of PD on quality of life is suggested by the fact that 77% of respondents in one study complained of psychological effects from the condition, and 65% stated that the problem concerned them frequently. Pain and impotence have been recorded in about half of community-dwelling men diagnosed with PD (30).

RISK FACTORS, PREVALENCE AND INCIDENCE

Estimates of prevalence, severity, and health impact depend on populations studied, definition criteria, and assessment methods. Previous studies have shown prevalence ranging from 0.4% to 23%. The lowest estimates are based on medical record reviews of residents of Rochester, MN, and thus likely reflect the burden of illness among Caucasians (30). The highest estimate is based on histological determination of chronic inflammation and fibrosis in an autopsy series of 100 penises (31). A recent community-based German study (32) noted a patient-reported prevalence of 3.2% in men 30 to 80 years of age, while a questionnaire-based Italian study (33) revealed a prevalence of 7% in men 50 to 69. A study of 534 US men presenting for a prostate cancer screening program reported that 8.9% had a penile plaque palpable by the examining urologist (29). Only 67% of these patients reported having noticed penile curvature deformity or plaque. Men with PD based on physician diagnosis had worse scores on the five-item Sexual Health Inventory for Men (SHIM) questionnaire that measures erectile function. In univariate analysis, the prevalence of PD was associated with increased age (Odds Ratio = 2.0 for every 10-year age increase), hypertension, diabetes, and ED. A smoking history was negatively associated with PD. The prevailing theory of etiology suggests that overt or unnoticed trauma to the erect penis (34), usually during sexual intercourse, initiates an inflammatory response that is prolonged and abnormal in susceptible individuals. The role of transforming growth factor β and other growth factors in this process has been demonstrated in animal models and human plaque specimens (35, 36).

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Data that could be used to estimate the burden of disease due to PD are limited. Few administrative datasets contain enough observations to allow for thoughtful inference. A code specific to PD (607.85) was added to the ICD-9 classification system after 2001. Data presented here use an ICD-9 administrative code-based definition of PD which is thought to represent coding patterns in use prior to the introduction of the specific PD code. This definition may differ in sensitivity and specificity from data which would have been generated had the specific PD code been in existence. Because surgical management is rarely used, office visits and global utilization provide the most relevant information. Sources used in this analysis are physician office visits by Medicare beneficiaries and user rates by veterans (Tables 33 and 34).

Outpatient Care

Outpatient utilization by male Medicare beneficiaries with PD listed as the primary diagnosis is a minute fraction (1.4%) of visits for ED, as determined by age-adjusted rates in 2001 (23 per 100,000 for PD vs 1,666 per 100,000 for ED) (Tables 33 and 9). Rates of office visits were similar in earlier years. VA Information Resource Center (VIReC) data show a similar difference in period prevalence, with 31 per 100,000 VA users having any diagnosis of PD in 2001, as compared with 3,790 per 100,000 for ED

Table 33. Physician office visits by Medicare beneficiaries with Peyronie's disease listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	6,700	45 (40–50)	45	5,080	33 (29–37)	33	5,440	38 (33–42)	38	3,520	23 (19–26)	23
Total < 65	1,500	48 (37–59)		780	23 (16–30)		800	23 (16–30)		740	19 (13–26)	
Total 65+	5,200	44 (39–50)		4,300	37 (32–41)		4,640	42 (37–47)		2,780	24 (20–28)	
Age												
65–69	3,020	74 (62–86)		2,220	58 (47–68)		2,060	61 (49–73)		1,020	29 (21–37)	
70–74	1,560	48 (37–59)		1,280	38 (29–48)		1,320	43 (33–54)		760	25 (17–33)	
75–79	460	20 (12–29)		560	25 (16–34)		800	35 (24–46)		520	21 (13–29)	
80–84	120	9.2 (1.8–16)		160	12 (3.5–20)		180	13 (4.5–22)		240	16 (6.9–25)	
85–89	40	6.7 (0–16)		80	13 (0.3–25)		180	28 (9.5–46)		220	30 (12–48)	
90+	0	0		0	0		100	46 (5.6–87)		20	8.6 (0–26)	
Race/ethnicity												
White	5,840	47 (41–52)	46	4,600	35 (31–40)	36	4,920	40 (35–45)	40	3,300	25 (21–29)	25
Black	240	19 (8.2–30)	19	280	20 (9.6–31)	19	320	24 (12–36)	22	60	4.1 (0–8.7)	4.1
Asian	…	...	…	60	82 (0–176)	55	0	0	0	20	9.8 (0–29)	9.8
Hispanic	…	...	…	20	10 (0–30)	10	80	24 (0.6–47)	24	40	11 (0–25)	11
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	1,400	38 (29–47)	39	1,000	26 (19–33)	26	1,020	28 (20–35)	27	880	23 (16–30)	23
Northeast	900	28 (20–37)	28	740	23 (16–31)	23	880	32 (22–41)	31	560	19 (12–26)	19
South	3,120	60 (50–69)	59	2,320	42 (35–50)	42	2,260	42 (34–50)	43	1,460	25 (19–31)	25
West	1,260	52 (39–65)	52	1,000	43 (31–55)	41	1,200	54 (40–67)	54	580	23 (15–32)	24

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 34. VA users with Peyronie's disease as any diagnosis in 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	1,195	36	1,245	35	1,237	33	1,247	31	1,189	27	1,160	24
Age-adjusted Total	1,354	36	1,320	36	1,237	33	1,129	30	981	26	891	24
Age												
< 25	2	6	3	9	4	14	2	7	2	7	6	22
25–34	24	15	22	13	16	10	9	5	16	9	17	10
35–44	78	21	76	21	59	16	74	20	65	18	52	14
45–54	365	45	358	44	348	42	288	35	259	32	237	29
55–64	358	57	336	54	307	49	317	51	224	36	239	38
65–74	372	39	353	37	325	34	304	32	277	29	232	24
75–84	142	21	161	24	162	24	122	18	125	18	98	14
85+	14	22	11	17	16	26	14	23	12	19	9	15
Gender												
Male	1,195	36	1,245	35	1,237	33	1,247	31	1,189	27	1,160	24
Female	0	0	0	0	0	0	0	0	0	0	0	0
Race/Ethnicity												
White	837	40	895	39	858	34	869	31	780	26	726	24
Black	181	38	181	38	185	38	166	34	175	36	151	32
Hispanic	85	94	69	73	72	75	72	72	60	58	46	46
Other	14	33	12	27	22	47	17	35	16	32	14	29
Unknown	78	13	88	15	100	17	123	19	158	20	223	21
Insurance Status												
No insurance/self-pay	877	37	897	36	849	34	784	32	716	28	646	26
Medicare	89	35	117	30	203	31	253	26	279	22	299	20
Medicaid	1	46		0	1	26	1	16	2	23	2	21
Private Insurance/HMO	221	36	221	38	176	31	202	34	181	28	204	29
Other Insurance	7	62	10	58	8	34	5	19	10	33	9	25
Unknown	0	0		0	0	0	2	0	1	0		0
Region												
Eastern	155	32	158	31	133	24	196	29	204	26	172	22
Central	234	41	213	34	253	39	233	32	226	25	262	25
Southern	462	37	453	34	475	33	459	28	455	25	452	23
Western	344	35	421	41	376	35	359	34	304	31	274	28

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

Table 35. Ambulatory surgery visits by Medicare beneficiaries with Peyronie's disease listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	380	2.6 (1.4–3.7)	2.6	600	3.9 (2.5–5.4)	3.9	600	4.1 (2.7 –5.6)	4.1	620	4.0 (2.6–5.4)	4.0
Total < 65	100	3.2 (0.4–6.0)		100	2.9 (0.3–5.5)		80	2.3 (0.1–4.6)		160	4.2 (1.3–7.1)	
Total 65+	280	2.4 (1.1–3.6)		500	4.2 (2.6–5.9)		520	4.7 (2.9–6.5)		460	4.0 (2.3–5.6)	
Age												
65–69	120	2.9 (0.6–5.3)		280	7.3 (3.5–11)		220	6.5 (2.7–10)		240	6.8 (2.9–11)	
70–74	100	3.1 (0.4–5.8)		160	4.8 (1.5–8.1)		140	4.6 (1.2–8.0)		100	3.2 (0.4–6.1)	
75–79	20	0.9 (0–2.6)		20	0.9 (0–2.6)		80	3.5 (0.1–6.9)		40	1.6 (0–3.9)	
80–84	40	3.1 (0–7.3)		40	2.9 (0–6.8)		60	4.4 (0–9.3)		60	4.0 (0–8.6)	
85–89	0	0		0	0		0	0		20	2.8 (0–8.2)	
90+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	180	1.4 (0.5–2.4)	1.3	340	2.6 (1.4–3.9)	2.5	600	4.9 (3.1–6.7)	4.9	520	4.0 (2.4–5.5)	3.8
Black	160	13 (3.8–21)	14	220	16 (6.5–25)	17	0	0	0	0	0	0
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	20	10 (0–30)	10	0	0	0	20	5.3 (0–16)	5.3
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	180	4.9 (1.7–8.0)	5.4	320	8.3 (4.2–12)	8.8	200	5.4 (2.1–8.8)	5.4	60	1.6 (0–3.4)	1.6
Northeast	40	1.3 (0–3.0)	1.3	60	1.9 (0–4.0)	1.3	60	2.2 (0–4.6)	2.2	80	2.7 (0.1–5.4)	2.1
South	120	2.3 (0.5–4.1)	1.9	120	2.2 (0.4–3.9)	2.2	240	4.5 (1.9–7.0)	4.5	400	6.9 (3.9–9.9)	6.9
West	40	1.7 (0–3.9)	0.8	80	3.4 (0.1–6.8)	3.4	100	4.5 (0.5–8.4)	4.5	60	2.4 (0–5.2)	2.4

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

(0.8%) (Tables 34 and 14). Rates of office visits for PD decreased approximately 50% between 1992 and 2001 (Table 33), with declines occurring across all age and ethnic groups and geographic regions. Whether this decline (from a maximum of 45 per 100,000 in 1992) reflects a trend toward more accurate coding and a shift of patients to a primary diagnosis of ED is unclear. The true prevalence of PD is unlikely to have changed. The condition affects a younger population than ED does. Rates were highest in the Medicare beneficiaries aged 65 to 69. Among VA users, those 55 to 64 had the highest rate of diagnosis, followed by those 45 to 54. Racial differences were difficult to interpret in Centers for Medicare & Medicaid Services (CMS) data due to low numbers of ethnic minorities. Caucasian men had a much higher rate of PD-related visits than other ethnic groups, with African Americans having the lowest rate. Conversely, in the VA data, Hispanic men had the highest rate—twice that of Caucasians.

Hospital outpatient visits, ER visits, and inpatient surgical visits were exceedingly rare across all temporal, age, race, and geographic categories (< 0.1%). Age-adjusted ambulatory surgery visit rates for male Medicare beneficiaries increased from 2.6 per 100,000 in 1992 to 4.0 per 100,000 in 2001 (Table 35). This rate is approximately one-tenth that of office visits. This difference may reflect variability due to low sample size; however, another possible explanation is increased use of outpatient facilities for surgical procedures, including tunica albuginea plication, plaque incision or excision and grafting, and intralesional injections.

Veterans

VIReC provides information on both inpatient and outpatient diagnosis of PD among male users of VA medical centers (Tables 34 and 36). PD was listed under "all diagnoses" in less then 1% of male veterans. The age-adjusted period prevalence of PD listed as a primary diagnosis decreased approximately 40%, from 23 per 100,000 male veteran users in 2000 to 14 per 100,000 in 2003. As one of any diagnoses, it declined nearly one-third, from 33 per 100,000 to 24 per 100,000. It was rarely recorded in men under 45 years of age and was most common in men between 55 and 64. Higher prevalence rates were recorded in men of Hispanic ethnicity, with African American and Caucasian ethnicities having respectively lower rates. Rates were lowest in the East and the South. The reason for this variation is not known.

CONCLUSIONS

Erectile dysfunction was self-reported by nearly 1 in 5 adult men in NHANES, corresponding to 15 million Americans over the age of 20. The prevalence of ED increases with age, with more than 60% of men 70 or older (5.5 million) reporting that they are sometimes or never able to get and keep an erection adequate for satisfactory intercourse. ED may be more commonly reported in Hispanic men and in those with modifiable risk factors, including a history of diabetes, obesity, smoking, and hypertension. In most databases, African American men have rates of utilization for office visits and inpatient hospital care twice those of other racial groups, although these rates do not control for comorbid conditions or other regional and socioeconomic factors.

The treatments used for ED, as measured by hospital outpatient, ambulatory surgery, and physician office visits, as well as cost reimbursement data, suggest shifting forms of healthcare utilization. The frequency of hospital treatment for ED, including penile implants, has declined since 1992, while the diagnoses and treatment of ED in outpatient settings (especially primary care clinics) has increased. The use of diagnostic tests such as plethysmography and nocturnal penile tumescence has markedly decreased, suggesting that the diagnosis of ED is being established by history and physical examination. Age-related differences in utilization of resources for ED are evident, with lower rates of both outpatient and inpatient visits in older age groups. Pharmacologic therapy, especially with oral phosphodiesterase-5 inhibitors, as measured by VA pharmacy data, has markedly increased. Pharmacologic therapy is particularly common in men who have received a radical prostatectomy for treatment of prostate cancer (in 2003, 31% of male veterans over 40 years of age who had received a radical prostatectomy were receiving pharmacologic therapy for ED, and nearly 90% of these received phosphodiesterase-5 inhibitors). Penile implant surgery continues to be performed, despite the success of PDE-I therapy, with most patients electing inflatable devices. Inpatient length of stay

Table 36. VA users with Peyronie's disease listed as primary diagnosis in 1998–2003, count, age-adjusted rate[a]

	1998		1999		2000		2001		2002		2003	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	863	26	877	25	839	23	772	19	740	17	663	14
Age-adjusted Total	978	26	929	25	839	23	700	19	612	16	507	14
Age												
< 25	2	6	2	6	2	7	2	7	2	7	5	18
25–34	17	11	18	11	15	9	5	3	12	7	9	6
35–44	61	17	58	16	44	12	48	13	44	12	28	8
45–54	252	31	255	31	244	30	193	24	167	20	127	16
55–64	261	42	231	37	202	32	186	30	122	19	128	21
65–74	268	28	243	25	208	22	171	18	170	18	139	14
75–84	104	15	111	16	112	16	85	12	85	13	65	9
85+	12	20	10	15	12	19	9	15	10	16	5	9
Race/Ethnicity												
White	602	29	609	27	573	23	519	19	481	16	403	13
Black	132	28	137	28	138	28	117	24	129	26	97	20
Hispanic	59	65	53	56	48	50	49	49	37	36	29	29
Other	9	21	10	22	9	19	11	23	4	8	8	16
Unknown	61	11	68	11	71	12	76	12	89	11	126	12
Insurance Status												
No insurance/self-pay	642	27	640	25	578	23	494	20	447	18	378	15
Medicare	60	24	72	18	130	20	155	16	180	14	182	12
Medicaid	1	46		0	1	26	1	16	2	23	2	21
Private Insurance/HMO	156	25	157	27	124	22	118	20	107	16	97	14
Other Insurance	4	36	8	46	6	26	3	11	4	13	4	11
Unknown	0	0		0	0	0	1	0	0	0		0
Region												
Eastern	118	25	120	23	106	19	127	19	131	17	88	11
Central	179	31	160	26	160	25	151	21	156	17	177	17
Southern	324	26	306	23	309	21	258	16	251	14	230	12
Western	242	25	291	28	264	25	236	22	202	20	168	17

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

has decreased, and hospital implant volumes have decreased as well.

Men with ED incur increased healthcare expenditures due to both ED-specific therapies and other coexisting conditions. One estimate of the burden of disease is the additional cost of medical care for men with ED, estimated at $1,100 per year. Extrapolating from the population-based estimates of ED prevalence from NHANES, the cost of treatment nationwide could reach $15 billion if all men sought treatment.

Variability and reliability in administrative databases for ED is of concern, primarily due to the fact that ED is frequently diagnosed and treated in outpatient settings on the basis of patient self-reports, with little to no additional diagnostic testing. There is likely little incentive for primary care providers to code consistently for this condition, and in many databases, specific treatments for ED are not included, while some therapies such as testosterone replacement are frequently also used to treat vague symptoms of male androgen deficiency such as loss of libido or energy or for low serum testosterone levels. Updated prevalence, severity, and health-impact surveys that are representative of a national US adult population and that control for comorbid conditions are needed.

Peyronie's disease can result in considerable clinical morbidity. However, available administrative data indicate that PD reaches clinical significance in relatively few men. There is minimal use of surgical intervention for the condition, and few surgical procedures are performed for Medicare beneficiaries or VA users. For the vast majority of men diagnosed with PD, treatments are office-based. Available data are limited and it is difficult to assess accurately the true prevalence and impact of PD. This is likely due partially to the variability in diagnostic criteria used; lack of standardized symptom scales; periods of relatively asymptomatic penile plaques and deformities that may not cause patients concern or that they may not wish to address with their physicians; or the fact that PD may not be accurately diagnosed or coded in medical records. The estimates available from administrative data suggest that the prevalence of PD has actually decreased, despite the overall increase in patient and provider awareness and treatment for men's sexual health.

RECOMMENDATIONS

A better understanding of male sexual health is clearly needed. The American College of Physicians nominated this topic for review in 2005–2006 by the federal Agency for Healthcare Research and Quality's evidenced-based practice centers. This review will address the diagnosis and treatment of ED. Preliminary key questions include:

- What are accepted definitions of ED?
- What is the prevalence of underlying causes of sexual dysfunction in primary care and referral populations?
- What is the yield of measurements of blood levels of testosterone, prolactin, luteinizing hormone, and follicle-stimulating hormone for treatable causes of ED?
- What is the effectiveness of pharmaceutical treatments for patients with ED, including those with underlying medical disorders (e.g., diabetes, neuropathy)?
- What is the evidence of harms of pharmaceutical treatment for patients with ED?

Future administrative and survey research should use validated questionnaires to establish the prevalence, severity, health impact, and treatments utilized for ED and PD. Analysis should establish risk factors for ED, racial influences on the pathogenesis, and treatment-seeking behavior. Factors influencing the use of diagnostic testing should be investigated, and guidelines for appropriate and selective use are necessary. Factors that might explain patient preference for therapies, success of treatments, and relative satisfaction with oral pharmacotherapy and penile implants need to be studied. The growth of the aging male population will require economic modeling to predict future costs of evaluation and treatment. Additional research is also needed to assess aspects of male sexual health not evaluated in this chapter, including premature ejaculation, sexual desire, vitality, ejaculatory and orgasmic function, partner intimacy, psychosocial aspects, the role of testosterone replacement therapy, and male "andropause." Finally, female sexual health deserves evaluation as well. Administrative data systems and survey research are needed to capture the relevant information accurately.

REFERENCES

1. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. JAMA 1993;270:83-90.
2. United States Dept Health Human Services. Pub# PHS 87-1751. 1987;Available at:
3. Shabsigh R. Socioeconomic considerations in erectile dysfunction treatment. Urol Clin North Am 2001;28:417-22.
4. Liverman C, Blazer D, eds. Committee on assessing the need for clinical trials of testosterone replacement therapy. Washington, DC: Institute of Medicine of the National Academies, 2004.
5. Litwin MS, Nied RJ, Dhanani N. Health-related quality of life in men with erectile dysfunction. J Gen Intern Med 1998;13:159-66.
6. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822-30.
7. Lewis RW, Fugl-Meyer KS, Bosch R, Fugl-Meyer AR, Laumann EO, Lizza E, Martin-Morales A. Definitions, Classification, and Epidemiology of Sexual Dysfunction. In: Lue TF, Basson R, Rosen RC, Giuliano F, Khoury S, Montorsi F, eds. Sexual Medicine. Paris: Health Publications Ltd, 2004:37-72.
8. Lue T. Drug Therapy: Erectile Dysfunction. New England Journal of Medicine 2000;342:1802-1813.
9. Rutchik SD, Baudiere M, Wade M, Sullivan G, Rayford W, Goodman J. Practice patterns in the diagnosis and treatment of erectile dysfunction among family practice physicians. Urology 2001;57:146-50.
10. Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfuncion Erectil Masculina Study. J Urol 2001;166:569-74; discussion 574-5.
11. Panser LA, Rhodes T, Girman CJ, Guess HA, Chute CG, Oesterling JE, Lieber MM, Jacobsen SJ. Sexual function of men ages 40 to 79 years: the Olmsted County Study of Urinary Symptoms and Health Status Among Men. J Am Geriatr Soc 1995;43:1107-11.
12. Ansong KS, Lewis C, Jenkins P, Bell J. Epidemiology of erectile dysfunction: a community-based study in rural New York State. Ann Epidemiol 2000;10:293-6.
13. Jarow JP, Nana-Sinkam P, Sabbagh M, Eskew A. Outcome analysis of goal directed therapy for impotence. J Urol 1996;155:1609-12.
14. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol 1994;151:54-61.
15. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. J.A.M.A. 1999;281:537-44.
16. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. Sexual function in men older than 50 years of age: results from the health professionals follow-up study. Ann Intern Med 2003;139:161-8.
17. Saigal CS, Wessells H, Wilt T. Predictors and Prevalence of Erectile Dysfunction in a Racially Diverse Population. Arch Int Med 2005;in press.
18. Kountz D AA. Diabetes mellitus in African-Americans: Impact of race on medical complications, sexual function, and general well-being. Med Aspects Hum Sex 2001;1:13-23.
19. Henderson SO, Bretsky P, Henderson BE, Stram DO. Risk factors for cardiovascular and cerebrovascular death among African Americans and Hispanics in Los Angeles, California. Acad Emerg Med 2001;8:1163-72.
20. Geiss LS, Rolka DB, Engelgau MM. Elevated blood pressure among U.S. adults with diabetes, 1988-1994. Am J Prev Med 2002;22:42-8.
21. West SK, Klein R, Rodriguez J, Munoz B, Broman AT, Sanchez R, Snyder R. Diabetes and diabetic retinopathy in a Mexican-American population: Proyecto VER. Diabetes Care 2001;24:1204-9.
22. Ansong KS, Lewis C, Jenkins P, Bell J. Help-seeking decisions among men with impotence. Urology 1998;52:834-7.
23. Begg CB, Riedel ER, Bach PB, Kattan MW, Schrag D, Warren JL, Scardino PT. Variations in morbidity after radical prostatectomy. N Engl J Med 2002;346:1138-44.
24. Delate T, Simmons VA, Motheral BR. Patterns of use of sildenafil among commercially insured adults in the United States: 1998-2002. Int J Impot Res 2004;16:313-8.
25. Stanford JL, Feng Z, Hamilton AS, Gilliland FD, Stephenson RA, Eley JW, Albertsen PC, Harlan LC, Potosky AL. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. Jama 2000;283:354-60.
26. Pfizer Annual Report. 2005. Available at: http://www.pfizer.com/pfizer/annualreport/2005/annual/review2005.pdf.
27. Eli Lilly Annual Report. 2005. Available at: http://investor.lilly.com/annuals.cfm.
28. Bayer Annual Report. 2005. Available at: http://www.bayer.com/annualreport_2005_id0602/.
29. Mulhall JP, Creech SD, Boorjian SA, Ghaly S, Kim ED, Moty A, Davis R, Hellstrom W. Subjective and objective analysis of the prevalence of Peyronie's disease in a population of men presenting for prostate cancer screening. J Urol 2004;171:2350-3.
30. Lindsay MB, Schain DM, Grambsch P, Benson RC, Beard CM, Kurland LT. The incidence of Peyronie's disease in Rochester, Minnesota, 1950 through 1984. J Urol 1991;146:1007-9.
31. Smith BH. Subclinical Peyronie's disease. Am J Clin Pathol 1969;52:385-90.
32. Schwarzer U, Sommer F, Klotz T, Braun M, Reifenrath B, Engelmann U. The prevalence of Peyronie's disease: results of a large survey. BJU Int 2001;88:727-30.

33. La Pera G, Pescatori ES, Calabrese M, Boffini A, Colombo F, Andriani E, Natali A, Vaggi L, Catuogno C, Giustini M, Taggi F. Peyronie's disease: prevalence and association with cigarette smoking. A multicenter population-based study in men aged 50-69 years. Eur Urol 2001;40:525-30.
34. Jarow JP, Lowe FC. Penile trauma: an etiologic factor in Peyronie's disease and erectile dysfunction. J Urol 1997;158:1388-90.
35. Mulhall JP, Thom J, Lubrano T, Shankey TV. Basic fibroblast growth factor expression in Peyronie's disease. J Urol 2001;165:419-23.
36. El-Sakka AI, Hassoba HM, Chui RM, Bhatnagar RS, Dahiya R, Lue TF. An animal model of Peyronie's-like condition associated with an increase of transforming growth factor beta mRNA and protein expression. J Urol 1997;158:2284-90.

CHAPTER 16

Male Urethral Stricture Disease

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Male Urethral Stricture Disease

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INTRODUCTION

The true incidence of male urethral stricture disease is unknown, despite the fact that urethral strictures may have great negative impact on patients. The majority of stricture patients suffer from moderate complications such as irritative voiding symptoms, recurrent urinary tract infections, or the need for repeated urethral procedures (e.g., dilation or urethrotomy) (1, 2). A minority suffer severe sequelae such as acute urinary retention, renal failure, urethral carcinoma, Fournier's gangrene (3), or bladder failure resulting from long-standing obstruction (2). Table 1 lists ICD-9 and CPT-4 codes used to identify urethral stricture disease and related procedures.

DEFINITION AND DIAGNOSIS

Male urethral stricture disease encompasses a spectrum of divergent ailments that cause obliteration of the urethral lumen and slowing or cessation of urinary flow. Strictures are usually described according to their location (e.g., fossa navicularis, penile urethra, bulbar urethra, membranous urethra, prostatic urethra, or bladder neck). Bulbar urethral strictures represent the overwhelming majority of cases, while prostatic urethral strictures are vanishingly rare.

The etiology of strictures is also varied. Fossa navicularis and distal penile urethral strictures can occur as a result of lichen sclerosis (a.k.a., balanatis xerotica obliterans), an idiopathic inflammatory disease of the glans penis. Penile urethral strictures may be post-surgical after repair of hypospadias. Bulbar strictures are most often idiopathic, but may also be due to gonococcal infection, direct trauma (straddle injury), or as complication of prostatic irradiation for cancer.

Most strictures are treated by general-practice urologists with dilation or direct-vision internal urethrotomy (DVIU), although these have less than a 50% durable cure rate as initial therapy and an even lower cure rate once an initial procedure has failed. Selected general urologists and specialty referral centers treat strictures with open urethroplasty techniques, which generally have a lifetime success rate in the range of 75% to 100%, depending on the length and location of stricture.

In addition to the burden of the disease itself, therapy for strictures can sometimes be associated with further complications. For example, urethrotomy can be associated with complications such as bleeding (in 4% to 6% of cases), infection (8% to 9%), incontinence (1%), impotence (1%), and a failure rate of up to 100% after repeated use (4, 5). Until definitively treated with urethroplasty, strictures tend to recur after urethrotomy or dilation (6-8), further adding to their impact on patients. Even after definitive urethroplasty, urethral strictures can cause problems for the patient. Rates of surgical complications range from 7% (anastomotic urethroplasty) to 33% (fasciocutaneous urethroplasty) after open urethral surgery (9). One study showed that the rate of erectile dysfunction after anastomotic urethroplasty could be as high as 27% (10).

Despite an emerging understanding of the burden of urethral stricture on individual patients, little is

Table 1. Codes used in the diagnosis and management of male urethral stricture

Males with one or more of the following:	
ICD-9 diagnosis codes	
598	Urethral stricture
598.0	Urethral stricture due to infection
598.01	Urethral stricture due to infective diseases classified elsewhere
598.1	Traumatic urethral stricture
598.2	Postoperative urethral stricture
598.8	Other specified causes of urethral stricture
598.9	Urethral stricture, unspecified
CPT procedure codes	
52283	Cystourethroscopy, with steroid injection into stricture
52275	Cystourethroscopy, with internal urethrotomy; male
52276	Cystourethroscopy with direct vision internal urethrotomy
52281[a]	Cystourethroscopy, with calibration and/or dilation of urethral stricture or stenosis, with or without meatotomy, with or without injection procedure for cystography, male or female
52282	Cystourethroscopy, with insertion of urethral stent
53000	Urethrotomy or urethrostomy, external (separate procedure); pendulous urethra
53010	Urethrotomy or urethrostomy, external (separate procedure); perineal urethra, external
53020[a]	Meatotomy, cutting of meatus (separate procedure); except infant
53025[a]	Meatotomy, cutting of meatus (separate procedure); infant
53400	Urethroplasty; first stage, for fistula, diverticulum, or stricture (eg, Johannsen type)
53405	Urethroplasty; second stage (formation of urethra), including urinary diversion
53410	Urethroplasty, one-stage reconstruction of male anterior urethra
53415	Urethroplasty, transpubic or perineal, one stage, for reconstruction or repair of prostatic or membranous urethra
53420	Urethroplasty, two-stage reconstruction or repair of prostatic or membranous urethra; first stage
53425	Urethroplasty, two-stage reconstruction or repair of prostatic or membranous urethra; second stage
53431	Urethroplasty with tubularization of posterior urethra and/or lower bladder for incontinence (eg, Tenago, Leadbetter procedure)
53450	Urethromeatoplasty, with mucosal advancement
53600[a]	Dilation of urethral stricture by passage of sound or urethral dilator, male; initial
53601[a]	Dilation of urethral stricture by passage of sound or urethral dilator, male; subsequent
53605[a]	Dilation of urethral stricture or vesical neck by passage of sound or urethral dilator, male, general or conduction (spinal) anesthesia
53620[a]	Dilation of urethral stricture by passage of filiform and follower, male; initial
53621[a]	Dilation of urethral stricture by passage of filiform and follower, male; subsequent
53640[a]	Passage of filiform and follower for acute vesical retention, male

[a]Included only in definition of hospital outpatient and physician office visits.

known about the burden of the disease on society as a whole. This chapter presents results from an analysis of public and private healthcare data on disease rates, treatments, and costs of male urethral stricture disease in America.

RISK FACTORS

Sexually Transmitted Disease (STD)

Urethral stricture is a common sequela of sexually transmitted diseases in men, resulting from a chronic inflammatory process (11). The risk of urethral stricture is increased in men who have a history of chlamydia or gonorrhea (12-14).

Race

Some, but not all, of the datasets analyzed in this project indicate that African Americans may have higher stricture rates than Caucasians have. (In general, sample numbers for Asian, Hispanic, and Native American patients are too small to permit accurate conclusions.) Inpatient samples from Healthcare Cost and Utilization Project (HCUP) data (Table 2) show substantial racial variations, as do inpatient and outpatient samples from Medicare (Tables 3 and 4). Caution must always be used when interpreting Medicare data, as most Medicare patients are over 65 years of age, so the rate of strictures in younger patients may be non-representative. This racial variation in incidence has implications for both the etiology of strictures and funding for programs to investigate stricture disease in susceptible populations.

Age

A clear trend of increasing incidence of treatment for urethral stricture with age is seen across multiple datasets, likely indicating a true increase in urethral stricture disease with age, with a marked increase in persons over the age of 55 (Figure 1).

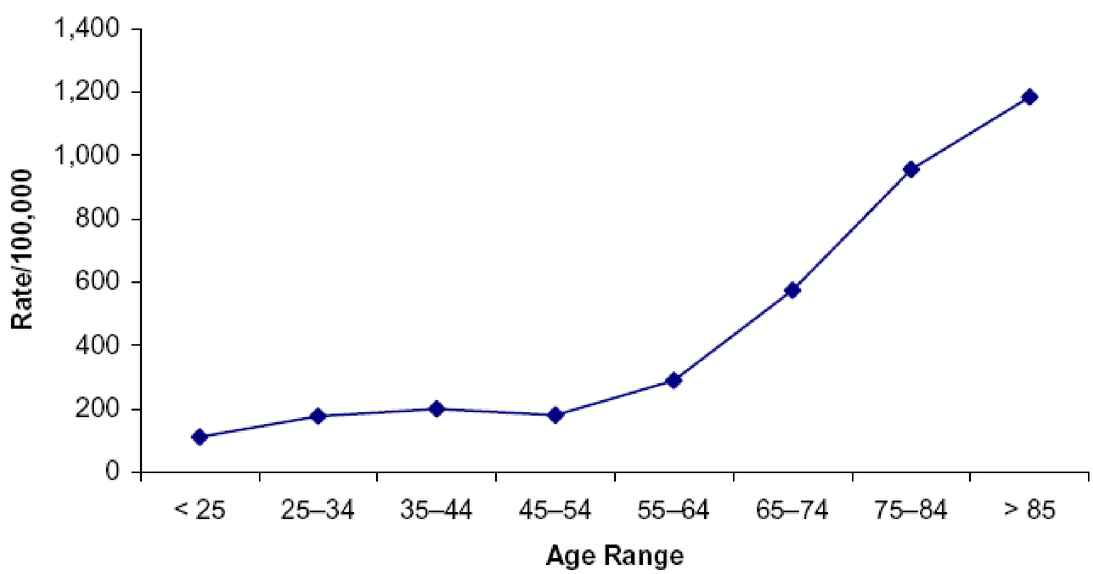

Figure 1. Male dual VA-Medicare users with a diagnosis of urethral stricture in 2002, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC) and Carrier and Outpatient and MedPar Files, CMS.

Table 2. Inpatient hospital stays for males with urethral stricture listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b] (95% CI)

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	7,004	5.7 (5.4–6.3)	5.7	5,235	4.1 (3.7–4.5)	4.1	4,932	3.8 (3.4–4.1)	3.8	5,035	3.8 (3.1–4.4)	3.8
Age												
<18	408	1.2 (0.7–1.7)		227	0.6 (0.3–0.9)		239	0.6 (0.4–0.9)		145	0.4 (0.2–0.6)	
18–24	241	2.0 (1.4–2.5)		171	1.4 (0.8–2.0)		*	*		218	1.7 (0.8–2.5)	
25–34	552	2.8 (2.1–3.4)		376	1.9 (1.4–2.4)		355	1.8 (1.4–2.3)		468	2.6 (1.6–3.5)	
35–44	618	3.1 (2.4–3.8)		474	2.2 (1.7–2.8)		560	2.6 (2.0–3.2)		650	3.0 (2.1–3.9)	
45–54	599	4.3 (3.3–5.2)		540	3.5 (2.7–4.3)		539	3.2 (2.6–4.0)		667	3.7 (2.8–4.7)	
55–64	725	7.6 (6.0–9.1)		543	5.5 (4.2–6.7)		500	4.7 (3.6–5.8)		649	5.8 (4.3–7.3)	
65–74	1,685	21 (18–25)		1,293	16 (13–18)		895	11 (9.2–13)		877	11 (8.7–13)	
75–84	1,545	41 (34–48)		1,159	27 (23–32)		1,202	26 (22–31)		905	19 (15–22)	
85+	630	70 (56–84)		452	52 (40–64)		493	50 (39–61)		457	45 (35–55)	
Race/ethnicity												
White	3,945	4.3 (3.7–4.9)	3.9	3,042	3.3 (2.9–3.6)	2.9	2,617	2.8 (2.4–3.1)	2.5	2,679	2.8 (2.2–3.5)	2.6
Black	1,078	7.3 (5.9–8.7)	10	770	5.0 (4.1–5.9)	6.9	833	5.3 (4.2–6.8)	6.9	761	4.8 (3.8–5.8)	6.1
Hispanic	361	2.8 (2.0–3.6)	5.0	349	2.4 (1.6–3.3)	3.7	339	2.2 (1.3–3.0)	4.3	398	2.4 (1.7–3.2)	3.8
Region												
Midwest	1,560	5.3 (3.9–6.7)	5.4	1,199	4.0 (3.1–4.9)	4.0	1,144	3.7 (3.0–4.4)	3.7	1,063	3.4 (2.5–4.3)	3.5
Northeast	2,427	9.8 (7.7–12)	9.3	1,546	6.2 (4.9–7.6)	5.9	1,209	4.9 (3.9–5.9)	4.7	1,178	4.8 (3.7–5.8)	4.4
South	2,115	5.1 (4.3–5.9)	5.1	1,783	4.0 (3.4–4.6)	4.0	1,716	3.8 (3.1–4.5)	3.8	1,892	4.0 (2.7–5.4)	4.0
West	903	3.2 (2.4–4.1)	3.4	707	2.4 (2.0–2.9)	2.6	862	2.9 (2.2–3.5)	3.0	902	3.0 (1.5–4.4)	3.1
MSA												
Rural	876	2.8 (2.1–3.5)	2.5	776	2.7 (2.1–3.3)	2.5	578	2.0 (1.5–2.4)	1.8	540	1.8 (1.4–2.3)	1.7
Urban	6,112	6.6 (5.8–7.5)	6.9	4,430	4.5 (4.0–4.9)	4.6	4,335	4.3 (3.8–4.7)	4.4	4,495	4.3 (3.5–5.1)	4.4

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 3. Inpatient stays by male Medicare beneficiaries with urethral stricture listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	3,760	25 (22–29)		2,340	15 (13–18)		2,020	14 (11–17)		1,260	8.2 (6.2–10)	
Total < 65	320	10 (5.2–15)		240	7.0 (3.0–11)		320	9.3 (4.7–14)		220	5.8 (2.4–9.2)	
Total 65+	3,440	29 (25–34)	33	2,100	18 (14–21)	20	1,700	15 (12–19)	16	1,040	9.0 (6.5–11)	9.4
Age												
65–69	660	16 (11–22)		380	9.9 (5.4–14)		280	8.3 (3.9–13)		160	4.5 (1.4–7.7)	
70–74	640	20 (13–27)		320	9.6 (4.9–14)		340	11 (5.8–16)		160	5.2 (1.6–8.8)	
75–79	800	35 (24–46)		620	27 (18–37)		420	18 (11–26)		360	15 (7.9–21)	
80–84	680	52 (34–69)		380	27 (15–40)		380	28 (15–40)		180	12 (4.1–20)	
85–89	420	70 (40–101)		220	35 (14–55)		220	34 (14–54)		100	14 (1.7–26)	
90–94	240	118 (51–186)		160	76 (23–128)		20	9.3 (0–27)		80	35 (0.9–68)	
95–97	0	0		20	53 (0–156)		40	101 (0–240)		0	0	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	2,660	21 (18–25)	21	1,680	13 (10–16)	13	1,320	11 (8.2–13)	11	880	6.7 (4.7–8.7)	6.3
Black	920	72 (51–93)	77	480	35 (21–49)	35	520	39 (24–54)	42	260	18 (8.1–27)	22
Asian	…	...	…	0	0	0	0	0	0	20	9.8 (0–29)	9.8
Hispanic	…	...	…	80	40 (1.0–80)	30	80	24 (0.6–47)	24	40	11 (0–25)	11
N. American Native	…	...	…	20	99 (0–293)	99	0	0	0	20	60 (0–177)	60
Region												
Midwest	760	20 (14–27)	23	520	13 (8.3–19)	12	320	8.7 (4.4–12.9)	8.1	200	5.3 (2.0–8.5)	4.7
Northeast	1,260	40 (30–50)	44	700	22 (15–29)	22	600	22 (14–29)	22	240	8.2 (3.6–13)	7.5
South	1,260	24 (18–30)	20	920	17 (12–22)	17	760	14 (9.7–19)	14	460	7.9 (4.7–11)	7.9
West	320	13 (6.7–20)	14	80	3.4 (0.1–6.8)	4.3	280	13 (5.9–19)	13	280	11 (5.4–17)	11

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, MedPAR Files, 1992, 1995, 1998, 2001.

Table 4. Hospital outpatient visits by male Medicare beneficiaries with urethral stricture listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992				1995				1998				2001			
	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate	Count	Rate		Age-Adjusted Rate
Total[d]	5,540	37	(33–42)		3,120	20	(17–24)		2,800	19	(16–23)		3,260	21	(18–24)	
Total < 65	560	18	(11–25)		620	18	(12–24)		900	26	(19–34)		760	20	(14–26)	
Total 65+	4,980	42	(37–48)	47	2,500	21	(18–25)	23	1,900	17	(14–21)	17	2,500	22	(18–25)	22
Age																
65–69	800	20	(14–26)		440	11	(6.6–16)		520	15	(9.5–21)		600	17	(11–23)	
70–74	1,300	40	(30–50)		380	11	(6.3–16)		580	19	(12–26)		720	23	(16–31)	
75–79	1,380	61	(47–75)		900	40	(28–51)		300	13	(6.5–20)		660	27	(18–36)	
80–84	660	50	(33–68)		520	37	(23–52)		320	23	(12–35)		220	15	(6.0–23)	
85–89	300	50	(25–76)		220	35	(14–55)		160	25	(7.5–42)		280	39	(18–59)	
90–94	540	267	(166–367)		40	19	(0–45)		20	9.3	(0–27)		20	8.6	(0–26)	
95–97	0	0			0	0			0	0			0	0		
98+	0	0			0	0			0	0			0	0		
Race/ethnicity																
White	2,960	24	(20–27)	22	1,620	12	(9.7–15)	12	1,700	14	(11–17)	13	2,180	17	(14–20)	16
Black	2,440	191	(157–225)	208	1,180	85	(63–107)	90	840	63	(44–82)	66	600	41	(26–56)	44
Asian	…	...		…	0	0		0	20	15	(0–43)	15	0	0		0
Hispanic	…	...		…	180	91	(31–150)	101	160	48	(15–81)	48	200	53	(20–86)	59
N. American Native	…	...		…	0	0		0	20	72	(0–211)	72	120	360	(72–649)	300
Region																
Midwest	1,560	42	(33–51)	40	1,180	31	(23–38)	24	960	26	(19–33)	25	880	23	(16–30)	22
Northeast	780	25	(17–32)	23	400	13	(7.1–18)	15	560	20	(13–28)	22	560	19	(12–26)	20
South	2,600	50	(41–58)	52	1,020	19	(13–24)	20	700	13	(8.7–17)	13	980	17	(12–22)	17
West	580	24	(15–33)	23	400	12	(9.7–25)	19	480	21	(13–30)	21	820	33	(23–43)	35

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Geographic Location

Few datasets include sample sizes large enough to permit inferences about the effect of geographic location on the incidence of strictures, but analysis of HCUP inpatient data indicates that the incidence was 2.6 times higher in urban hospitals than in rural hospitals (Table 2). This could reflect either a true increase in incidence in the urban setting or a tendency to refer patients with urethral stricture to urban medical centers for definitive treatment. No clear trends in diagnosis rates were seen across the regions of the United States.

TREATMENT

Retrograde Urethrogram

The rate of retrograde urethrograms performed for patients over 65 years of age with a diagnosis of urethral stricture disease was 6,557 per 100,000 in 2001 (Table 5). This means that 6.5% of patients with a diagnosis of urethral stricture disease who were over the age of 65 had a retrograde urethrogram in that year.

Dilation

Analyzed by CPT procedure code, the rate of urethral dilations in the office setting in 2001 ranged from 0 to 35,304 per 100,000 Medicare beneficiaries 65 and older with a diagnosis of urethral stricture (Table 6). For comparison purposes, the rate of ureteroscopies performed in the same population in 1998 in all medical settings was 8,372 per 100,000 (15). Office dilation became much less common after 1992, decreasing in most cases by 2001.

Associated Illness

Although causation cannot be determined from the datasets, the percentage of men with urethral stricture disease who also had a diagnosis of urinary tract infection in 2001 was notably high at 42% (Table 7). Approximately 11% of men with a urethral stricture diagnosis also had a diagnosis of urinary incontinence in the same year (Table 8).

PREVALENCE AND INCIDENCE

Data from the Veterans Affairs (VA) show that the unadjusted rate of urethral stricture for all diagnoses was 274 per 100,000 male VA users in 1998 (Table 9). This rate declined to 193 per 100,000 by 2003. The rate of stricture diseases climbs sharply after the age of 55 (Figure 1).

Even with complex analysis of large datasets, the true prevalence of urethral stricture is only estimable. In a population of older veterans, prevalence was found to be as high as 0.6%. However, even this is likely to undercount the true prevalence of urethral stricture disease, because most of the patients in the VA datasets are older than the general population. In 2000, urethral stricture resulted nationally in thousands of inpatient, outpatient, and emergency room visits, tens of thousands of ambulatory surgery visits, and hundreds of thousands of office visits. Urethral strictures resulted in a 6.5% rate of affected patients undergoing radiographic studies (retrograde urethrogram) and a rate of urethral dilation that exceeds even that of commonly performed procedures such as ureteroscopy for stones (Table 5). Patients affected by stricture had a high rate of untoward associated sequelae, including urinary tract infection (42%) and incontinence (11%) (Tables 7 and 8). Urethral strictures are also associated with urethral carcinoma, and while not reported in the datasets analyzed here, urethral carcinoma must be listed as one of the many possible negative sequelae of the disease.

Multiple datasets indicate that the prevalence of stricture disease is decreasing over time. The reasons for this are unknown, but two hypotheses are (1) decreased incidence of *de novo* stricture disease and (2) decreased incidence of recurrent stricture disease due to more effective primary treatment. Better treatment of infectious urethritis may be decreasing its incidence, although separate specific study would be needed to determine the etiology accurately. It is also probable that increasingly successful surgical treatments of urethral stricture such as buccal mucosal urethroplasty are decreasing the persistence of the disease, thereby resulting in a lower incidence of strictures over time.

Table 5. Use of retrograde urethrocystography[a] or injection procedure for urethrogram[b] among males 65 years and older with urethral stricture, in any setting, count[c], rate[d] (95% CI), age-adjusted rate[e]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[f]	13,840	7,322 (6,797–7,847)		12,060	7,157 (6,607–7,708)		10,580	7,774 (7,137–8,410)		8,200	6,557 (5,944–7,170)	
Age												
65–69	4,040	10,504 (9,134–11,875)		2,980	9,324 (7,897–10,751)		2,520	10,535 (8,796–12,274)		1,980	9,340 (7,590–11,090)	
70–74	4,000	8,368 (7,257–9,479)		3,720	8,832 (7,621–10,043)		2,760	8,550 (7,187–9,913)		2,360	8,049 (6,658–9,441)	
75–79	2,880	6,135 (5,164–7,107)		2,540	6,144 (5,109–7,179)		2,720	7,902 (6,627–9,178)		1,960	6,347 (5,130–7,565)	
80–84	1,780	5,414 (4,319–6,509)		1,680	5,280 (4,180–6,380)		1,480	5,777 (4,500–7,053)		1,100	4,622 (3,429–5,815)	
85–89	800	4,884 (3,407–6,361)		760	5,080 (3,509–6,651)		760	5,094 (3,519–6,669)		560	3,911 (2,493–5,328)	
90–94	280	5,109 (2,500–7,719)		220	4,198 (1,775–6,622)		320	8,290 (4,404–12,176)		180	3,766 (1,360–6,172)	
95–97	0	0		80	10,256 (769–19,744)		20	2,222 (0–6,556)		40	7,143 (0–16,607)	
98+	0	0		0	0		0	0		0	0 0	
Race/ethnicity												
White	11,380	7,204 (6,634–7,775)	7,204	10,280	7,117 (6,524–7,710)	7,117	8,840	7,619 (6,937–8,302)	7,533	7,060	6,717 (6,041–7,394)	6,736
Black	1,600	8,073 (6,377–9,768)	7,871	1,360	8,047 (6,213–9,882)	8,047	1,160	8,555 (6,453–10,656)	9,440	580	4,715 (3,041–6,390)	4,553
Asian	…	...	…	20	2,381 (0–7,024)	2,381	40	4,878 (0–11,463)	2,439	60	4,054 (0–8,581)	4,054
Hispanic	…	...	…	120	6,122 (1,378–10,867)	6,122	400	11,696 (6,871–16,520)	12,281	220	6,707 2,866–10,549)	6,098
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	3,720	7,626 (6,572–8,680)	7,790	3,120	7,166 (6,082–8,250)	6,982	2,880	7,912 (6,673–9,151)	7,857	1,680	5,125 (4,057–6,193)	5,003
Northeast	2,760	7,697 (6,464–8,929)	7,418	2,400	7,528 (6,233–8,824)	7,654	1,920	7,339 (5,925–8,754)	7,187	1,440	6,338 (4,921–7,755)	6,514
South	5,780	7,585 (6,744–8,427)	7,559	4,700	6,924 (6,070–7,778)	6,865	3,800	7,244 (6,252–8,235)	7,396	3,460	7,257 (6,214–8,299)	7,173
West	1,520	6,022 (4,711–7,334)	6,181	1,740	7,831 (6,251–9,410)	8,101	1,860	10,043 (8,105–11,982)	9,935	1,560	8,117 (6,389–9,844)	8,429

…data not available.

[a]CPT 74450 or ICD-9 87.76.

[b]CPT 51610.

[c]Unweighted counts multiplied by 20 to arrive at values in the table.

[d]Rate per 100,000 male Medicare beneficiaries 65 years and older with urethral stricture.

[e]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[f]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 6. Use of procedures during physician office visits by male Medicare beneficiaries with urethral stricture listed as primary diagnosis, count[a], rate[b]

CPT Code	Procedure	1992		1995		1998		2001	
		Count	Rate	Count	Rate	Count	Rate	Count	Rate
52281	Cystourethroscopy and urethral dilation	48,460	25,616	50,360	29,870	45,560	33,456	44,180	35,304
53600	Urethral dilation with sound, initial	38,560	20,383	25,220	14,958	16,640	12,219	12,360	9,877
53601	Urethral dilation with sound, subsequent	49,960	26,409	38,720	22,966	27,040	19,856	24,600	19,658
53620	Urethral dilation with filiform and followers, initial	15,860	8,384	11,800	6,999	9,000	6,609	8,100	6,473
53621	Urethral dilation with filiform and followers, subsequent	13,300	7,030	11,080	6,572	7,520	5,522	7,140	5,706
53640	Urethral dilation with filiform and followers for acute vesical retention	1,200	634	1,620	961	0	0	0	0

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries 65 years and older with urethral stricture.

NOTE: Counts less than 600 should be interpreted with caution

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 7. Male Medicare beneficiaries with a diagnosis of urethral stricture and urinary tract infection (UTI) in the same year, count[a], percent[b]

	1992		1995		1998		2001	
	Count	Percent	Count	Percent	Count	Percent	Count	Percent
Total[c]	58,040	35%	54,020	37%	49,560	42%	46,400	42%
Age								
65–69	10,440	31%	9,560	34%	7,840	38%	7,320	40%
70–74	13,400	32%	12,680	35%	11,000	39%	10,780	42%
75–79	14,660	36%	13,180	36%	12,640	42%	11,480	42%
80–84	10,660	37%	10,640	38%	9,740	44%	8,620	41%
85–89	6,280	43%	5,420	42%	6,120	47%	5,780	45%
90–94	2,060	45%	2,080	44%	1,780	51%	2,100	49%
95–97	320	48%	360	58%	320	43%	220	44%
98+	220	58%	100	56%	120	75%	100	71%
Race/ethnicity								
White	47,140	34%	45,740	36%	41,400	41%	38,520	42%
Black	7,680	44%	5,920	40%	5,460	46%	4,760	44%
Asian	...	...	200	26%	280	37%	600	46%
Hispanic	…	…	900	52%	1,640	56%	1,520	52%
N. American Native	…	…	80	67%	20	20%	20	20%
Region								
Midwest	14,400	34%	13,900	36%	12,380	39%	10,780	37%
Northeast	10,520	33%	9,300	34%	9,860	44%	8,380	43%
South	24,960	38%	22,120	37%	19,120	42%	18,260	43%
West	7,280	33%	7,480	38%	6,720	41%	7,520	44%

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Percent of males with urethral stricture who also have diagnosis of urinary tract infection.

[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 8. Male Medicare beneficiaries with a diagnosis of urethral stricture and urinary incontinence in the same year, count[a], percent[b]

	1992		1995		1998		2001	
	Count	Percent	Count	Percent	Count	Percent	Count	Percent
Total[c]	13,220	8%	11,940	8%	11,200	9%	11,760	11%
Age								
65–69	1,680	5%	1,880	7%	1,660	8%	1,440	8%
70–74	3,160	8%	2,860	8%	2,320	8%	2,600	10%
75–79	3,020	7%	2,700	7%	3,000	10%	2,620	10%
80–84	2,960	10%	2,660	10%	2,160	10%	2,700	13%
85–89	1,600	11%	1,180	9%	1,640	13%	1,580	12%
90–94	660	14%	540	11%	340	10%	740	17%
95–97	100	15%	100	16%	80	11%	60	12%
98+	40	11%	20	11%	0	0%	20	14%
Race/ethnicity								
White	10,900	8%	10,560	8%	9,560	9%	9,560	10%
Black	1,580	9%	1,060	7%	1,120	10%	1,440	13%
Asian	...	...	40	5%	100	13%	240	18%
Hispanic	…	…	60	3%	280	10%	260	9%
N. American Native	…	…	0	0%	0	0%	20	20%
Region								
Midwest	3,860	9%	3,120	8%	2,940	9%	2,680	9%
Northeast	1,880	6%	2,180	8%	2,240	10%	2,340	12%
South	5,360	8%	4,980	8%	4,400	10%	4,720	11%
West	2,060	9%	1,520	8%	1,500	9%	1,840	11%

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Percent of males with urethral stricture who also have diagnosis of urinary incontinence.

[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

Table 9. Male VA users with a diagnosis of urethral stricture, 1998–2003, count, rate[a] (95% CI)

	1998			1999			2000			2001			2002			2003		
	Count	Rate		Count	Rate		Count	Rate		Count	Rate		Count	Rate		Count	Rate	
Total	8,992	274	(268–279)	9,229	263	(258–268)	9,397	253	(248–258)	9,003	220	(216–225)	9,156	205	(200–209)	9,201	193	(189–197)
Age																		
< 25	15	41	(20–62)	21	64	(37–91)	16	55	(28–81)	14	51	(24–77)	7	25	(7–44)	7	25	(7–44)
25–34	133	70	(58–82)	147	82	(69–95)	131	79	(66–93)	132	86	(71–100)	118	80	(65–94)	123	85	(70–100)
35–44	444	111	(101–121)	415	107	(96–117)	380	104	(93–114)	383	112	(101–123)	310	95	(84–106)	305	97	(86–108)
45–54	1,290	172	(163–181)	1,278	160	(152–169)	1,298	158	(150–167)	1,311	153	(145–162)	1,292	146	(138–154)	1,202	141	(133–148)
55–64	1,424	261	(247–274)	1,521	261	(248–274)	1,601	256	(244–269)	1,506	213	(262–290)	1,736	210	(200–220)	1,876	188	(179–196)
65–74	3,242	389	(375–402)	3,207	355	(343–368)	3,071	319	(308–331)	2,794	258	(249–268)	2,729	233	(224–242)	2,625	218	(210–227)
75–84	2,186	452	(433–471)	2,361	410	(393–427)	2,598	381	(367–396)	2,565	306	(294–318)	2,633	266	(256–277)	2,657	245	(236–254)
85+	258	577	(506–647)	279	537	(474–599)	302	488	(433–543)	298	378	(335–421)	331	328	(292–363)	406	317	(286–348)
Gender																		
Male	8,992	274	(268–279)	9,229	263	(275–287)	9,397	253	(248–258)	9,003	220	(216–225)	9,156	205	(200–209)	9,201	193	(189–197)
Female	0	0		0	0		0	0		0	0		0	0		0	0	
Race/ethnicity																		
White	6,400	305	(297–312)	6,587	287	(281–294)	6,683	268	(262–275)	6,477	232	(227–238)	6,463	213	(208–218)	6,283	203	(198–208)
Black	1,987	420	(402–439)	2,041	423	(405–442)	2,035	419	(401–437)	1,800	369	(352–386)	1,805	369	(352–387)	1,716	360	(343–377)
Hispanic	235	259	(226–292)	228	243	(211–274)	245	255	(223–286)	210	209	(181–237)	246	238	(237–305)	229	227	(197–256)
Other	99	233	(187–279)	95	213	(170–255)	93	200	(159–241)	100	205	(165–245)	84	168	(131–204)	82	167	(131–204)
Unknown	271	47	(41–52)	278	47	(41–52)	341	57	(51–64)	416	63	(57–69)	558	70	(64–76)	891	85	(80–91)
Insurance Status																		
No insurance/ self-pay	5,773	241	(235–247)	5,859	232	(227–238)	5,480	222	(217–228)	4,735	192	(186–197)	4,549	180	(174–185)	4,398	174	(169–180)
Medicare	1,052	412	(387–437)	1,462	374	(355–393)	2,306	354	(340–369)	2,938	297	(287–308)	3,250	260	(251–269)	3,573	239	(232–247)
Medicaid	4	182	(4–361)	12	440	(191–689)	13	339	(155–524)	23	370	(219–521)	26	300	(184–415)	30	315	(202–427)
Private Insurance/HMO	2,139	344	(329–359)	1,858	321	(307–336)	1,558	274	(260–288)	1,243	209	(197–221)	1,270	195	(185–206)	1,131	162	(153–172)
Other Insurance	24	214	(128–300)	38	219	(149–288)	39	166	(114–218)	64	237	(179–295)	59	193	(144–243)	67	187	(142–232)
Unknown	0	0		0	0		1	115	0	0	0		2	71	0	2	116	0
Region																		
Eastern	1,118	234	(220–247)	1,080	210	(197–222)	1,235	221	(209–234)	1,168	172	(162–181)	1,310	169	(160–178)	1,448	181	(172–191)
Central	1,443	250	(237–263)	1,513	242	(229–254)	1,445	223	(212–235)	1,559	214	(204–225)	1,763	197	(188–206)	2,039	194	(185–202)
Southern	3,987	319	(309–329)	4,192	313	(304–323)	4,218	292	(283–301)	4,007	247	(239–255)	4,078	226	(219–233)	3,890	200	(194–207)
Western	2,444	249	(239–259)	2,444	237	(228–246)	2,499	235	(226–245)	2,269	215	(206–224)	2,005	201	(192–210)	1,824	189	(181–198)

[a]Rate per 100,000 veterans using the VA system, age-adjusted to 2000.

SOURCE: Inpatient and Outpatient Files, VA Information Resource Center (VIReC), Veterans Affairs Health Services Research and Development Service Resource Center.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

The HCUP dataset shows that the rate of hospitalizations for urethral stricture was 3.8 per 100,000 population in 2000 (Table 2). This represents a nearly 50% decrease since 1994, when the rate was 5.7 per 100,000. This rate is considerably lower than that of other urologic diseases such as urolithiasis (71 per 100,000 in 2000) (15). The rate of hospitalizations peaks at age 55 and appears to be higher in both urban and African American populations.

Medicare data show a higher rate of hospitalization for stricture disease in beneficiaries 65 and older, 9.0 per 100,000 in 2001 (Table 3). As in the HCUP data, a higher rate of hospitalizations in older patients is confirmed. The rate in patients under 65 years of age (comprising primarily disabled and dialysis-dependent individuals) was 5.8 per 100,000. The downward trend in incidence over time seen in HCUP is confirmed, with a threefold decrease between 1992 and 2001.

Outpatient Care

The rate of hospital outpatient visits for Medicare beneficiaries (most of whom, as noted, are over age 65) was 21 per 100,000 in 2001 (Table 4). This rate is only half the rate of visits for urolithiasis in this population (15).

Physician Office Visits

Physician office visits by males with urethral stricture disease were determined using pooled data from the National Ambulatory Medical Care Survey, 1992–2000. The annualized rate was 229 per 100,000 (Table 10), far lower than the rate for urolithiasis (15). The rate of physician office visits by male Medicare beneficiaries was 312 per 100,000 in 2001 (Table 11).

Table 10. Physician office visits for males with urethral stricture listed as any diagnosis, 1992–2000 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1992–2000				
	Count	5-Year Rate		Annualized Rate	5-Year Age-Adjusted Rate
Total[d]	1,460,899	1,146	(858–1,434)	229	1,138
Age					
< 65	870,812	762	(476–1,048)	152	
65+	590,087	4,465	(3,198–5,731)	893	
Race/ethnicity					
White	1,026,894	1,106	(794–1,417)	221	1,049
Black	*	*		*	*
Other	*	*		*	*
MSA					
MSA	1,114,540	1,144	(849–1,440)	229	1,145
Non-MSA	*	*		*	*

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Average annualized rate per year.

[c]Age-adjusted to the US Census-derived age distribution of the midpoint of years.

[d]Persons of missing or unavailable race and ethnicity, and missing MSA are included in the total.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 11. Physician office visits by male Medicare beneficiaries with urethral stricture listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	73,940	496 (480–512)		63,040	414 (400–429)		53,260	368 (354–382)		48,040	312 (299–324)	
Total < 65	5,180	166 (146–186)		4,780	139 (121–156)		4,740	138 (120–155)		5,000	131 (115–148)	
Total 65+	68,760	584 (565–604)	636	58,260	495 (477–513)	526	48,520	439 (422–457)	459	43,040	371 (355–386)	382
Age												
65–69	11,140	274 (251–296)		10,000	260 (237–282)		8,180	242 (219–266)		6,560	185 (165–205)	
70–74	17,860	549 (513–585)		14,800	444 (412–476)		10,380	340 (311–370)		9,560	311 (283–338)	
75–79	17,440	770 (720–821)		14,220	627 (581–673)		12,760	559 (516–602)		11,100	452 (415–490)	
80–84	12,820	979 (903–1,054)		11,380	819 (752–886)		10,100	733 (669–797)		8,300	555 (501–608)	
85–89	7,040	1,181 (1,058–1,303)		5,680	892 (788–995)		5,620	864 (763–964)		5,420	749 (660–838)	
90–94	2,060	1,017 (822–1,213)		1,840	870 (694–1,047)		1,340	623 (474–772)		1,720	742 (586–899)	
95–97	280	693 (332–1054)		300	796 (395–1,196)		80	202 (5.1–399)		280	729 (349–1109)	
98+	120	316 (63–569)		40	90 (0–214)		60	125 (0–268)		100	184 (22–346)	
Race/ethnicity												
White	57,920	461 (444–478)	456	50,480	388 (373–403)	390	42,520	348 (333–362)	344	39,860	305 (291–318)	303
Black	11,520	903 (829–976)	917	9,360	676 (615–737)	656	7,800	584 (527–642)	614	5,820	397 (351–442)	414
Asian	…	...	…	220	302 (123–480)	357	420	306 (176–437)	350	420	205 (118–292)	224
Hispanic	…	...	…	1,180	594 (443–745)	655	1,460	435 (335–534)	453	880	234 (165–303)	229
N. American Native	…	...	…	40	199 (0–472)	298	20	72 (0–211)	72	20	60 (0–177)	60
Region												
Midwest	18,260	492 (460–524)	494	15,520	403 (374–431)	410	13,600	368 (340–395)	376	11,480	302 (278–327)	297
Northeast	17,440	550 (514–586)	562	14,280	449 (416–482)	443	10,800	389 (356–421)	386	8,900	305 (276–333)	292
South	26,760	511 (484–538)	507	23,220	423 (399–448)	420	20,000	373 (350–396)	373	19,800	341 (320–362)	346
West	9,020	373 (339–408)	359	8,220	354 (320–389)	353	7,880	352 (318–387)	336	7,000	283 (253–312)	287

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 12. Ambulatory surgery visits for males with urethral stricture listed as any diagnosis, 1994–1996 (merged), count, rate[a] (95% CI), annualized rate[b], age-adjusted rate[c]

	1994–1996				
	Count	3-Year Rate		Annualized Rate	3-Year Age-Adjusted Rate
Total	227,322	180	(163–197)	60	179
Age					
0–2	8,035	131	(55–207)	44	
3–10	27,158	167	(130–204)	56	
11–17	6,666	50	(22–78)	17	
18–34	20,668	64	(45–82)	21	
35–44	22,198	108	(74–142)	36	
45–54	26,188	177	(124–229)	59	
55–64	34,910	357	(257–457)	119	
65–74	39,404	489	(383–595)	163	
75–84	32,799	812	(632–991)	271	
85+	9,296	1,079	(578–1,580)	360	
Region					
Midwest	76,431	256	(221–292)	85	257
Northeast	54,798	222	(167–277)	74	220
South	74,448	172	(145–199)	57	168
West	21,645	76	(57–95)	25	76

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 is based on 1994, 1995, 1996 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population

[b]Average annualized rate per year.

[c]Grouped years age-adjusted to the US Census-derived age distribution of the midpoint of years. Individual years age-adjusted to the US Census-derived age distribution of the year under analysis.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Survey of Ambulatory Surgery, 1994, 1995, 1996.

Ambulatory Surgery Visits

The annualized rate of ambulatory surgery center visits, based on pooled data for 1994–1996 from the National Survey of Ambulatory Surgery, was 60 per 100,000 (Table 12). There is a bimodal distribution in incidence, with the first peak in patients under the age of 10 and the second peak steadily increasing in patients after age 35.

Emergency Room Care

The rate of emergency room visits by male Medicare beneficiaries with urethral strictures was relatively low, 6.9 per 100,000 in 2001 (Table 13).

ECONOMIC IMPACT

Stricture disease is expensive—expenditures for the disease reached almost $200 million in 2000 (which is not inflation-adjusted). Lifetime treatments with (usually repeated) direct visual internal urethrotomy (DVIU) have been estimated to cost an average of $17,747 per patient in the United States, and the lifetime costs of immediate urethral reconstruction have been estimated at $16,444 (16). British reports put the cost of DVIU or dilation at $3,375, compared with $7,522 for one-stage urethroplasty and $15,555 for two-stage urethroplasty (8).

The estimated total annual expenditure for male urethral stricture disease was $191 million in 2000 (Table 14). These costs are much lower than those of more common urologic diseases such as nephrolithiasis, which cost $2.1 billion in 2000 (15). Although total costs for the treatment of urethral stricture in males in the United States have generally increased since 1994, they have fluctuated, peaking at $207 million in 1998 (Table 14). Spending on all service categories varied over the study period, with the exception of physician office visits, which

Table 13. Emergency room visits by male Medicare beneficiaries with urethral stricture listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	2,740	18 (15–21)		2,480	16 (13–19)		1,840	13 (10–15)		1,060	6.9 (5.0–8.7)	
Total < 65	240	7.7 (3.3–12)		220	6.4 (2.6–10)		200	5.8 (2.2–9.4)		200	5.3 (2.0–8.5)	
Total 65+	2,500	21 (18–25)	23	2,260	19 (16–23)	21	1,640	15 (12–18)	16	860	7.4 (5.2–9.6)	7.9
Age												
65–69	540	13 (8.3–18)		320	8.3 (4.2–12)		220	6.5 (2.7–10)		180	5.1 (1.8–8.4)	
70–74	440	14 (7.9–20)		420	13 (7.2–18)		200	6.6 (2.5–11)		120	3.9 (0.8–7.0)	
75–79	640	28 (18–38)		640	28 (18–38)		300	13 (6.5–20)		160	6.5 (2.0–11)	
80–84	300	23 (11–35)		440	32 (18–45)		480	35 (21–49)		140	9.4 (2.4–16)	
85–89	460	77 (46–109)		280	44 (21–67)		340	52 (27–77)		160	22 (6.8–38)	
90–94	80	39 (1.0–78)		120	57 (11–102)		80	37 (0.9–73)		100	43 (5.2–81)	
95–97	40	99 (0–235)		0	0		20	51 (0–149)		0	0	
98+	0	0		40	90 (0–214)		0	0		0	0	
Race/ethnicity												
White	2,060	16 (13–20)	17	1,980	15 (12–18)	15	1,420	12 (8.9–14)	12	780	6.0 (4.1–7.8)	6.0
Black	640	50 (33–68)	47	420	30 (17–43)	29	300	22 (11–34)	18	220	15 (6.1–24)	14
Asian	…	...	…	20	27 (0–81)	27	0	0	0	0	0	0
Hispanic	…	...	…	20	10 (0–30)	10	40	12 (0–28)	18	0	0	0
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	880	24 (17–31)	24	860	22 (16–29)	19	500	14 (8.2–19)	16	180	4.7 (1.6–7.8)	4.2
Northeast	560	18 (11–24)	17	480	15 (9.1–21)	16	500	18 (11–25)	18	180	6.2 (2.1–10)	5.5
South	1,100	21 (15–27)	21	880	16 (11–21)	16	680	13 (8.4–17)	12	540	9.3 (5.8–13)	10
West	160	6.6 (2.0–11)	5.8	260	11 (5.1–17)	13	140	6.3 (1.6–11)	5.4	140	5.7 (1.5–9.9)	4.8

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 14. Expenditures for male urethral stricture, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$3,985,122	2.3%	$4,339,936	2.3%	$8,002,002	3.9%	$5,081,869	2.7%
Physician Office	$9,210,826	5.3%	$14,957,752	8.0%	$17,114,631	8.3%	$22,683,608	11.9%
Ambulatory Surgery	$130,472,080	74.5%	$142,088,620	76.0%	$152,419,401	73.7%	$132,300,099	69.2%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$31,519,724	18.0%	$25,656,338	13.7%	$29,305,944	14.2%	$31,008,773	16.2%
TOTAL	$175,187,753		$187,042,646		$206,841,978		$191,074,350	

SOURCE: National Ambulatory Medical Care Survey; National Hospital Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

increased by almost 150% between 1994 and 2000 and were responsible for the majority of the increase in total expenditures. Despite the increasingly large proportion of expenditures being for physician office visits, ambulatory surgery still accounted for nearly 70% of spending for the treatment of urethral stricture in males in 2000.

Individual-level expenditures for urethral stricture were estimated using risk-adjusted regression models controlling for age, work status, income, urban or rural residence, and health plan characteristics (Table 15).The annual healthcare expenditure of an insured male with urethral stricture diseases is almost three times that of an insured male without stricture disease ($3,713 vs $10,472). Thus, an incremental cost of $6,759 is associated with treatment of urethral stricture. Although pharmaceutical costs were similar for men with and without stricture, medical costs were almost 3.5 times higher among men treated for the condition. This result is not unexpected, as treatment of urethral stricture does not rely heavily on pharmaceuticals and typically consists of widening the urethra through dilation, insertion of a urethral stent, urethrotomy, or open urethroplasty (in severe cases). Individual-level expenditures among men with urethral stricture appear to increase with age, although the relationship was not found to be monotonic: pharmaceutical expenditures peaked in the 55- to 64-year-old group, and medical expenditures peaked in the 45- to 54-year-

Table 15. Estimated annual expenditures for privately insured male employees with and without a medical claim for urethral stricture, 2002[a]

	Annual Expenditures (per person)					
	Males without Urethral Stricture (N=284,831)			Males with Urethral Stricture (N=500)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$2,677	$1,036	$3,713	$9,227	$1,245	$10,472
Age						
18–34	$1,287	$658	$1,945	$4,262	$870	$5,132
35–44	$2,137	$879	$3,016	$9,088	$898	$9,986
45–54	$3,047	$1,217	$4,264	$11,848	$859	$12,707
55–64	$3,239	$1,129	$4,368	$9,187	$1,921	$11,108
Region						
Midwest	$2,587	$1,028	$3,615	$8,918	$1,247	$10,165
Northeast	$2,610	$1,119	$3,729	$8,997	$1,349	$10,346
South	$2,730	$968	$3,698	$9,411	$1,151	$10,562
West	$2,940	$1,064	$4,004	$10,134	$1,309	$11,443

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions.

SOURCE: Ingenix, 2002.

Table 16. Expenditures for male Medicare beneficiaries for treatment of urethral stricture, by site of service (% of total)

	Age 65 and over							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$846,600	2.4%	$422,500	1.2%	$613,700	1.6%	$537,500	1.7%
Physician Office	$2,269,080	6.4%	$2,505,180	6.9%	$2,474,520	6.5%	$3,012,800	9.8%
Ambulatory Surgery	$17,436,160	48.9%	$22,431,600	62.1%	$23,789,340	62.9%	$19,983,600	64.9%
Emergency Room	$592,500	1.7%	$806,820	2.2%	$836,400	2.2%	$538,360	1.7%
Inpatient	$14,547,760	40.8%	$9,928,800	27.5%	$10,101,400	26.7%	$6,713,200	21.8%
TOTAL	$35,692,100		$36,094,900		$37,815,360		$30,785,460	
	Under 65							
Service Type	1992		1995		1998		2001	
Hospital Outpatient	$0	0.0%	$57,040	2.0%	$236,700	5.6%	$169,480	3.7%
Physician Office	$155,400	7.2%	$200,760	7.2%	$255,960	6.1%	$370,000	8.1%
Ambulatory Surgery	$2,000,880	92.8%	$2,527,560	90.7%	$3,722,320	88.3%	$4,028,680	88.2%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	---	0.0%	---	0.0%	---	0.0%	---	0.0%
TOTAL	$2,156,280		$2,785,360		$4,214,980		$4,568,160	

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998, 2001.

old group. Costs did not exhibit substantial regional variation.

Total expenditures for urethral stricture in male Medicare enrollees age 65 and older decreased from $36 million in 1992 to $31 million in 2001 (Table 16). The decrease was driven almost exclusively by a decline in inpatient spending. Similar to the proportion in the general population, ambulatory surgery costs made up about 65% of Medicare expenditures for urethral stricture in 2001 and have fluctuated over time. Among male Medicare enrollees under the age of 65, expenditures more than doubled between 1992 and 2001, although total costs in 2001 were only about $4.6 million. Ambulatory surgery also dominated expenditures in this group, accounting for nearly 90% of the costs in 2001.

Twenty-four percent of men diagnosed with urethral stricture missed some work. On average, each male diagnosed with urethral stricture missed 2.3 hours for inpatient visits and 9.2 hours for outpatient stays—a total of nearly 12 hours of work missed per diagnosis (Table 17). Each outpatient visit for urethral stricture resulted in about 5 hours of missed work (Table 18). Men in the South and the West also appeared to miss more hours of work for each outpatient visit than did men in other regions.

OVERALL BURDEN OF URETHRAL STRICTURE

Urethral stricture places a moderate burden on the US healthcare system, with total expenditures amounting to nearly $200 million in 2000. Expenditures were modest for Medicare enrollees 65 years of age and older and were insignificant among Medicare enrollees under 65 years of age. At the individual level, diagnosis of urethral stricture was associated with increased costs almost entirely accounted for by medical services. About one-quarter of men with claims for urethral stricture missed some work.

LIMITATIONS

By definition, all statistical analyses require assumptions and manipulations of data that may not be accurate. The limitations of the datasets analyzed in this project were discussed above (17). In general, however, we have attempted to remove sources of error in analyzing these datasets. For example, the numbers of patients with urethral stricture were generally lower than the numbers of patients with other urologic diseases, and in those cases where patient counts were too low to allow statistical significance, data analysis was not reported. Improved data collection methods will help to better analyze the impact of such relatively rare diseases in the future.

Table 17. Average annual work loss of males treated for urethral stricture, 1999 (95%CI)

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs) Inpatient[b]	Outpatient[b]	Total
Total	100	24%	2.3 (0–6.3)	9.2 (3.5–15)	11.6 (4.7–18)
Age					
18–29	7	0%	0	0	0
30–39	21	29%	0	11 (0–28)	11 (0–28)
40–49	29	21%	6.9 (0–21)	5.8 (0–13)	12.7 (0–28)
50–64	43	28%	0.7 (0–1.9)	12.2 (2.4–22)	13 (3.2–23)
Region					
Midwest	31	23%	0	2.4 (0.3–4.5)	2.4 (0.3–4.5)
Northeast	11	9%	0	1.5 (0–4.7)	1.5 (0–4.7)
South	37	30%	5.4 (0–16)	15.4 (2.1–29)	20.8 (4.1–37)
West	12	8%	0	10 (0–32)	10 (0–32)
Unknown	9	44%	3.6 (0–9.8)	16 (0–41)	19.6 (0–43)

[a]Individuals with an inpatient or outpatient claim for urethral stricture and for whom absence data were collected. Work loss is based on reported absenses contiguous to admission and discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

Source: Marketscan Health and Productivity Management, 1999.

Table 18. Average work loss[a] associated with a hospital stay or an ambulatory care visit for male urethral stricture (95% CI)

	Number of Inpatient Stays	Average Hours Missed for Inpatient Stays	Number of Outpatient Visits	Average Hours Missed for Outpatient Visits
Total	4	58 (0–210)	180	5.1 (2–8)
Age				
18–29	…	…	9	0
30–39	…	…	54	4.3 (0–9)
40–49	1	200 …	51	3.3 (0–8)
50–64	3	11 (0–41)	66	8.0 (2–14)
Region				
Midwest	...	...	53	1.4 (0–3)
Northeast	1	0	28	0.6 (0–2)
South	1	200 …	69	8.2 (2.9–14)
West	…	…	20	6.0 (0–18)
Unknown	2	16 (0–118)	10	14.4 (0–36)

…data not available.

[a]Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of outpatient visit.

SOURCE: Marketscan Health and Productivity Management, 1999.

In addition, some datasets, including those maintained by the VA and Medicare, underestimate the rate of urethral strictures because they tend not to capture younger patients, who are more typically affected by strictures after trauma, after hypospadias surgery, or as a result of balanitis xerotica obliterans.

CONCLUSIONS

Male urethral stricture disease occurs at a rate as high as 0.6% in some susceptible populations and results in more than 5,000 inpatient visits yearly. Office visits for urethral stricture numbered almost 1.5 million per year between 1992 and 2000. The total cost of male urethral stricture diseases in 2000 was almost $200 million, and the yearly individual cost of the disease averaged more than $6,000. Urethral stricture disease appears to be more common in the elderly and in African American patients, and by most measures, the prevalence of urethral stricture disease has decreased over time. Patients with urethral stricture disease appear to have very high rates of urinary tract infection (41%) and incontinence (11%). Demographic data such as those analyzed here have not previously been available and should help in the understanding of this disease.

REFERENCES

1. Romero Perez P, Mira Llinares A. Complications of the lower urinary tract secondary to urethral stenosis. Actas Urol Esp 1996;20:786-93.
2. Romero Perez P, Mira Llinares A. Male urethral stenosis: review of complications. Arch Esp Urol 2004;57:485-511.
3. Hodonou R, Hounnasso PP, Gbessi DG, Akpo C. Penile-perineal-scrotal gangrene. Epidemiologic, diagnostic, and therapeutic features. Report of 32 cases. Prog Urol 2000;10:271-6.
4. Chilton CP, Shah PJ, Fowler CG, Tiptaft RC, Blandy JP. The impact of optical urethrotomy on the management of urethral strictures. Br J Urol 1983;55:705-10.
5. Kinder PW, Rous SN. The treatment of urethral stricture disease by internal urethrotomy: a clinical review. J Urol 1979;121:45-6.
6. Heyns CF, Steenkamp JW, De Kock ML, Whitaker P. Treatment of male urethral strictures: is repeated dilation or internal urethrotomy useful? J Urol 1998;160:356-8.
7. Pansadoro V, Emiliozzi P. Internal urethrotomy in the management of anterior urethral strictures: long-term followup. J Urol 1996;156:73-5.
8. Greenwell TJ, Castle C, Andrich DE, MacDonald JT, Nicol DL, Mundy AR. Repeat urethrotomy and dilation for the treatment of urethral stricture are neither clinically effective nor cost-effective. J Urol 2004;172:275-7.
9. Andrich DE, Dunglison N, Greenwell TJ, Mundy AR. The long-term results of urethroplasty. J Urol 2003;170:90-2.
10. Coursey JW, Morey AF, McAninch JW, Summerton DJ, Secrest C, White P, Miller K, Pieczonka C, Hochberg D, Armenakas N. Erectile function after anterior urethroplasty. J Urol 2001;166:2273-6.
11. De Schryver A, Meheus A. Epidemiology of sexually transmitted diseases: the global picture. Bull World Health Organ 1990;68:639-54.
12. Greenberg SH. Male reproductive tract sequelae of gonococcal and nongonococcal urethritis. Arch Androl 1979;3:317-9.
13. Osoba AO. Sexually transmitted diseases in tropical Africa. A review of the present situation. Br J Vener Dis 1981;57:89-94.
14. Pandhi D, Reddy BS. Watering can perineum--a forgotten complication of gonorrhoea. J Eur Acad Dermatol Venereol 2002;16:486-7.
15. Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: urolithiasis. J Urol 2005;173:848-57.
16. Rourke KF, Jordan GH. Primary urethral reconstruction: the cost minimized approach to the bulbous urethral stricture. J Urol 2005;173:1206-10.
17. Litwin MS, Saigal CS, Yano EM, Avila C, Geschwind SA, Hanley JM, Joyce GF, Madison R, Pace J, Polich SM, Wang M. Urologic diseases in America Project: analytical methods and principal findings. J Urol 2005;173:933-7.

CHAPTER 17

Testicular Cancer

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Testicular Cancer

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INTRODUCTION

The incidence of testicular cancer is increasing. In 2005, approximately 8,000 new cases were diagnosed in the United States (1). Although it constitutes less than 1% of all malignancies in males, testicular cancer is the most common cancer in men 20 to 34 years of age. Because of advances in therapy, overall survival rates are high—and the management of testicular cancer represents a paradigm for successful multimodality therapy.

Modifications in both surgical and radiation techniques, as well as improved methods of employing systemic chemotherapy, have substantially diminished the morbidity of therapy. Nonetheless, the sequelae of multimodality therapy are not insignificant and can have broad and far-reaching consequences with regard to general health, reproduction, and economic productivity.

The small numbers of cases, changing treatment practices coupled with an absence of standardized therapy, the young age of affected patients, and the relative paucity of these patients in databases makes evaluation of trends in the treatment of testicular cancer difficult. The diagnostic and procedure codes commonly associated with the disease are listed in Table 1. The narrow scope of these codes underscores the limitations to collecting and analyzing information. More comprehensive and detailed data are needed to provide a better understanding of the impact of this cancer on health and prosperity.

DEFINITIONS AND DIAGNOSIS

The term *testicular cancer* characteristically refers to seminomatous and non-seminomatous germ cell tumors, as these constitute nearly 98% of primary neoplasms of the testes (2). These malignancies arise in the germinal cells of the testes. Other tumors can arise from stromal, mesenchymal, and adnexal elements of the testes, but such tumors are exceedingly uncommon and generally carry an excellent prognosis. Metastatic spread of other cancers to the testes is rare, although involvement by lymphoma and leukemia may occur. Diagnosis is usually made on physical examination and confirmed with scrotal ultrasound.

Histologic Classification

Seminomas are the most common testicular germ cell tumor (3). They are derived from spermatogenic cells within the seminiferous tubules and recapitulate certain aspects of spermatogenesis. Although they are subclassified by histology, their management is relatively uniform across the subtypes. *Non-seminomatous germ cell tumors* (NSGCTs) are also derived from spermatogenic cells. They are progeny of pluripotent embryonic cells formed from germ cells through the process of parthenogenesis. They encompass a variety of histologic patterns and can develop as a single entity or as a combination of choriocarcinoma, embryonal, teratoma, and yolk sac elements. NSGCTs can occur in conjunction with seminomas. Each subtype behaves differently, and this has implications for prognosis, as well as for therapy. Diagnosis is based on tissue removed during

Table 1. Codes used in the diagnosis and management of testicular cancer

Males with one or more of the following:	
ICD-9 diagnosis codes	
186	Malignant neoplasm of testis
186.0	Malignant neoplasm of undescended testis
186.9	Malignant neoplasm of other and unspecified testis
CPT procedure codes	
38564	Limited lymphadenectomy for staging (separate procedure); retroperitoneal (aortic and/or splenic)
38780	Retroperitoneal transabdominal lymphadenectomy, extensive, including pelvic, aortic, and renal nodes (separate procedure)
54530	Orchiectomy, radical, for tumor; inguinal approach
54535	Orchiectomy, radical, for tumor; with abdominal exploration

radical orchiectomy or, rarely, when a metastatic site is biopsied.

Serum Tumor Markers

In addition to histopathologic classifications, some testicular tumors are associated with the production of α-fetoprotein (AFP) by trophoblastic cells and β-human chorionic gonadotrophin (HCG) by syncytiotrophoblasts (4). Serologic measurements of HCG and AFP are used in the diagnosis and management of testicular cancer. AFP is never produced by pure seminomas or choriocarcinomas. HCG production is seen in all choriocarcinomas, most embryonal tumors, and occasional seminomas. Both AFP and HCG can be used to monitor response to therapy when they are present at the time of initial diagnosis. In addition, measurements of the enzyme lactate dehydrogenase (LDH) are often used in prognostication, as LDH correlates with tumor burden.

Staging

Once a diagnosis of testicular cancer is made (almost always after radical orchiectomy: the removal of the testis and spermatic cord), treatment decisions are primarily based on clinical staging, which usually consists of computed tomography (CT) imaging of the chest, abdomen, and pelvis. Patterns of metastatic spread in testicular cancer are very predictable, and the reproducibility of expected "landing sites" aids

Table 2. Staging systems for testicular cancer

Conventional Clinical Staging System	AJCC Staging System	
	Primary tumor (T)	
I: Confined to testis	pTX:	Primary tumor cannot be assessed
	pT0:	No evidence of primary tumor
	pTis:	Intratubular germ cell neoplasia (carcinoma *in situ*)
	pT1:	Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invadeinto the tunica albuginea but not the tunica vaginalis
	pT2:	Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis
	pT3:	Tumor invades the spermatic cord with or without vascular/lymphatic invasion
	pT4:	Tumor invades the scrotum with or without vascular/lymphatic invasion
	Regional lymph nodes (N)	
II: Retroperitoneal Spread	NX:	Regional lymph nodes cannot be assessed
IIa: positive nodes, no node > 2 cm	N0:	No regional lymph node metastasis
IIb: positive nodes between 2 and 5 cm	N1:	Metastasis with a lymph node mass 2 cm or less in greatest dimension; or
IIc: positive nodes > 5 cm		multiple lymph nodes, none more than 2 cm in greatest dimension
	N2:	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or multiple lymph nodes, any one mass greater than 2 cm but not more than 5 cm in greatest dimension
	N3:	Metastasis with a lymph node mass more than 5 cm in greatest dimension
	Distant metastasis (M)	
III. Metastatic: supraclavicular or mediastinal	MX:	Distant metastasis cannot be assessed
	M0:	No distant metastasis
	M1:	Distant metastasis
	M1a:	Non-regional nodal or pulmonary metastasis
	M1b:	Distant metastasis other than to non-regional lymph nodes and lungs
	Serum Tumor Markers (S)	
	SX:	Marker studies not available or not performed
	S0:	Marker study levels within normal limits
	S1:	LDH < 1.5 x normal; and hCG < 5,000 mIu/ml; and AFP < 1,000 ng/ml
	S2:	LDH 1.5–10 x normal; or hCG 5,000–50,000 mIu/ml; or AFP 1,000–10,000 ng/ml
	S3:	LDH > 10 x normal; or hCG > 50,000 mIu/ml; or AFP > 10,000 ng/ml

SOURCE: Testis. In: American Joint Committee on Cancer.: AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, Copyright 2002, 317–322.

Table 3. Percent distribution of treatment modalities by histologic type of disease and stage of testicular cancer[a]

	1985–1986[b]		1990–1991[c]		1995–1996[d]	
	Early	Advanced	Early	Advanced	Early	Advanced
Seminoma						
Surgery Alone						
Excision of testicle without LND	4.7	1.4	13.9	3.3	16.8	4.4
Excision of testicle with LND	3.7	1.4	1.0	1.4	0.6	0.7
Orchiectomy, NOS	3.5	2.7	3.6	0.7	3.5	1.7
Surgery, NOS	3.9	0	0.5	0	0.1	0.2
Surgery and radiation						
Excision of testicle without LND	25.3	18.9	57.4	15.6	61.2	20.4
Excision of testicle with LND	12.0	8.1	2.2	2.5	1.7	1.2
Orchiectomy, NOS	17.2	9.5	12.4	5.8	11.1	4.9
Surgery, NOS	20.9	6.8	1.1	1.1	0.1	0.7
Surgery and chemotherapy						
Excision of testicle without LND	0.5	10.8	1.7	30.1	1.2	38.4
Excision of testicle with LND	0.5	5.4	0.3	4.3	0.1	4.1
Orchiectomy, NOS	0.8	2.7	0.8	8.7	0.6	7.3
Surgery, NOS	0.5	6.8	0.1	2.9	0	1.7
Other treatment modalities	5.7	21.6	4.0	22.1	1.9	13.6
No treatment indicated	0.7	4.1	1.1	1.4	0.5	0.5
Total	100	100	100	100	100	100
Cases, n	593	74	2,393	276	3,391	411
Nonseminomatous Germ Cell Tumor						
Surgery Alone						
Excision of testicle without LND	18.3	2.7	35.2	2.6	45.3	5.9
Excision of testicle with LND	12.6	1.6	21.4	3.2	17.6	3.6
Orchiectomy, NOS	13.3	2.1	9.2	2.1	9.5	1.6
Surgery, NOS	25.6	5.3	2.4	1.3	2.4	0.8
Surgery and radiation						
Excision of testicle without LND	0.7	0	0.4	0.1	0.6	0.1
Excision of testicle with LND	0.3	0	0	0	0.1	0
Orchiectomy, NOS	0.3	0	0.1	0	0.1	0
Surgery, NOS	0.3	0	0	0.1	0	0
Surgery and chemotherapy						
Excision of testicle without LND	5.6	28.3	13.6	38.4	15.0	45.6
Excision of testicle with LND	5.6	14.4	6.5	20.6	2.8	17.9
Orchiectomy, NOS	4.3	13.9	5.2	10.4	3.9	12.1
Surgery, NOS	8.0	18.7	1.2	7.0	0.5	3.5
Other treatment modalities	1.7	11.8	4.0	13.4	1.8	8.5
No treatment indicated	3.3	1.1	0.9	0.8	0.5	0.4
Total	100	100	100	100	100	100
Cases, n	301	187	1,207	719	1,542	827

…data not available.

LND, lymph node dissection; NOS, not otherwise specified.

[a]Early stage: 1985–1986 American Joint Committee on Cancer (AJCC) Stage I and II; 1990–1991 AJCC Stage I, II, and III; 1995–1996 AJCC Stage I, II NI; Advanced Stage: 1985–1986 AJCC Stage III and IV; 1990–1991 AJCC Stage IV; 1995–1996 AJCC Stage II (N2 or higher) and III.

[b]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 2nd edition.

[c]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 3rd edition.

[d]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 4th edition.

SOURCE: Reprinted from Cancer, 86, Steele, GS, Richie, JP, Stewart AK, and Menck HR, The National Cancer Data Base report on patterns of care for testicular carcinoma,1985–1996, 2,171–2,184, Copyright 1999, with permission from Wiley.

tremendously with staging and treatment decision-making (5). In the simplest form, staging is divided into localized (testis only), retroperitoneal (minimal or bulky), and extralymphatic/extraretroperitoneal metastatic disease. The staging data are combined with levels of serologic tumor markers to guide management. The prevalence of several different staging schemas, as well as the complexity of the chosen tumor, nodes, and metastases (TNM) system, has confounded data acquisition and outcome reporting. The staging systems for testicular cancer referenced in this chapter and accepted by most practicing urologists are summarized in Table 2. Accurate clinical staging is crucial, as it is the basis for management decision-making.

The onset of testicular cancer is insidious, and there are few symptoms (5). Testicular tumors are usually discovered after the patient or his sexual partner palpates an abnormal mass. Patients may experience sensations of testicular heaviness or aching or may develop a reactive hydrocele. Rarely, pain is a presenting symptom. Occasionally, a patient presents with signs or symptoms of metastatic disease, including back pain, hydroureteronephrosis, and constitutional symptoms. The formal diagnosis of testicular cancer is based on histopathologic evaluation of the testis after orchiectomy or, rarely, biopsy of a retroperitoneal mass or subclavian lymph node (if the patient presents with metastatic disease and palpably normal testes). Such extraprimary/extragonadal disease constitutes less than 5% of cases.

When an obvious mass is present, no further diagnostic imaging is necessary, and the patient is brought to surgery for an orchiectomy. If the mass is subtle, ultrasonography may be performed to confirm its presence. Imaging of the chest and retroperitoneum is paramount for clinical staging and management decision-making, although it offers little with regard to diagnosis. Serum tumor markers are drawn prior to orchiectomy to aid with management. Occasionally, they can assist with diagnosis, as AFP is never produced by pure seminomas or choriocarcinomas. Prior to initial treatment, many physicians classify patients into "good," "intermediate," or "poor" prognostic groups to aid with management and help predict the probability of cure. Given the potential morbidity of treatment, many patients are advised to bank sperm prior to initiating treatment.

Screening

Other than genital examinations during routine physical examination, no formal screening algorithm exists for testicular cancer. Routine ultrasound examinations and serologic testing are not cost-effective. Moreover, most men of the ages at greatest risk for developing testicular cancer do not routinely see a physician because of their general good health and because of limited access to healthcare, since many are students and hence are more likely to be uninsured.

Many men are hesitant to see a physician for evaluation even after self-detection of a testicular mass, because of the obvious fear of undergoing orchiectomy. Hence, a delay in diagnosis is not uncommon. Fortunately, current multimodal treatment yields excellent survival rates for men with all stages of the disease. Despite advocacy by some in the urologic community for men to perform monthly self-examinations of the testes (analogous to monthly breast examinations by women) to enable early diagnosis, evidence does not support this recommendation (6).

RISK FACTORS

Risk factors postulated for testicular cancer include cryptorchidism, trauma, prenatal exposure to hormones, familial and genetic factors, and occupational exposure (7). Interestingly, while the incidence of testicular cancer is increasing, the rate of increase in incidence is slowing. The reason for this deceleration is unclear. No formal prevention programs exist for testicular cancer, and cryptorchidism rates have remained stable for the past two decades (8). It is also unlikely that the gene pool has changed dramatically enough to decrease malignant transformation. Hence, none of these factors is likely responsible.

However, programs directed at increasing awareness and limiting the risk of trauma during driving, sports, and other leisure activities that may result in testicular trauma have been instituted. Moreover, these programs are coincidentally aimed at men in the age groups most susceptible to testicular cancer. Awareness of the dangers of prenatal and occupational exposure to toxins and hormones has also been enhanced. These factors may explain the slowing of the rate of increase in testicular cancer incidence.

TREATMENT

Once a diagnosis of testicular cancer is made, clinical staging is performed (Table 2). Several factors, including histopathology, serologic biomarkers, stage of disease, and the preference (or bias) of the providing physician and patient, dictate how an individual testicular cancer is treated. Treatment can involve any or all of the following: surgery, radiotherapy, chemotherapy, and surveillance. A recent review and consensus statement by the European Germ Cell Cancer Consensus Group provides excellent background material (9).

Surgery

Within the lexicon of testicular cancer therapies, surgery can refer to either radical orchiectomy or retroperitoneal lymph node dissection (RPLND), which involves resection of retroperitoneal lymphatic tissue for both staging and therapeutic purposes. This can occur *de novo* or after chemotherapy to remove a residual mass. Although almost all testicular cancer patients undergo orchiectomy, a small minority have an RPLND, and the extent of RPLND has changed, as has the indication for adjuvant systemic therapy post-RPLND (10). This complicates data analysis, as many databases refer to surgical treatment without specifying the type and scope of procedure or separating single- from combination-modality therapy.

Radiotherapy

Radiotherapy is limited to the treatment of seminoma and is used in several situations (9). For clinically localized disease (no lymphadenopathy on CT scanning), post-orchiectomy adjuvant therapy currently involves 20Gy of radiation to the infradiaphragmatic para-aortal and para-caval lymphatics. Alternatives include surveillance (given a nearly 100% cure rate with salvage therapy) with administration of irradiation or chemotherapy in cases of relapse. Radiotherapy is also used for patients with clinical stage IIA/B seminoma, in which 30–36Gy is given to the infradiaphragmatic para-aortal and para-caval and ipsilateral iliac lymphatics. The recommended dose and field of abdominal radiotherapy have changed frequently in recent decades.

Systemic Therapy

Cisplatin-based chemotherapy is highly effective for the treatment of testicular cancer and can be used in several settings (9). For NSGCT, chemotherapy is used whenever tumor markers remain elevated post-orchiectomy. In addition, it can be used in clinical stage I tumor-marker-negative disease (with the exception of teratoma) as an alternative to surgery or surveillance, or for salvage therapy after post-surveillance relapse. Chemotherapy can also be utilized as an alternative to surgery in NSGCT for clinical stage IIA/B tumor-marker-negative disease. Chemotherapy is standard for all clinical stage IIC or greater NSGCT. For seminomas, chemotherapy is standard for all clinical stage IIC or greater tumors. It can also be used as an alternative to radiotherapy for clinical stage IIA/B seminomas. Finally, chemotherapy can be used as an adjuvant to RPLND if positive nodes are found at the time of resection.

Observation

Given the success rates of salvage therapy, some patients with clinical stage I tumor-marker-negative disease undergo close surveillance as primary treatment. This places tremendous responsibility on the patient and the physician, as monthly scans and blood tests are initially required.

Changes in Treatment Approaches

The National Cancer Data Base (NCDB), a joint project of the American Cancer Society and the American College of Surgeons, includes information that can be used to monitor changes in treatment approaches for testicular cancer between 1985 and 1996 (11). These changes are summarized in Table 3 and illustrated graphically in Figures 1a and 1b.

The management of seminoma has remained relatively consistent over the past decade. Approximately 75% of patients in the NCDB underwent radiotherapy after radical orchiectomy (11). However, a growing proportion of patients with clinical stage I disease are being treated initially by surgery alone (an increase from 15.8% in 1985–1986 to 21% in 1995–1996) (3). The use of surgery and

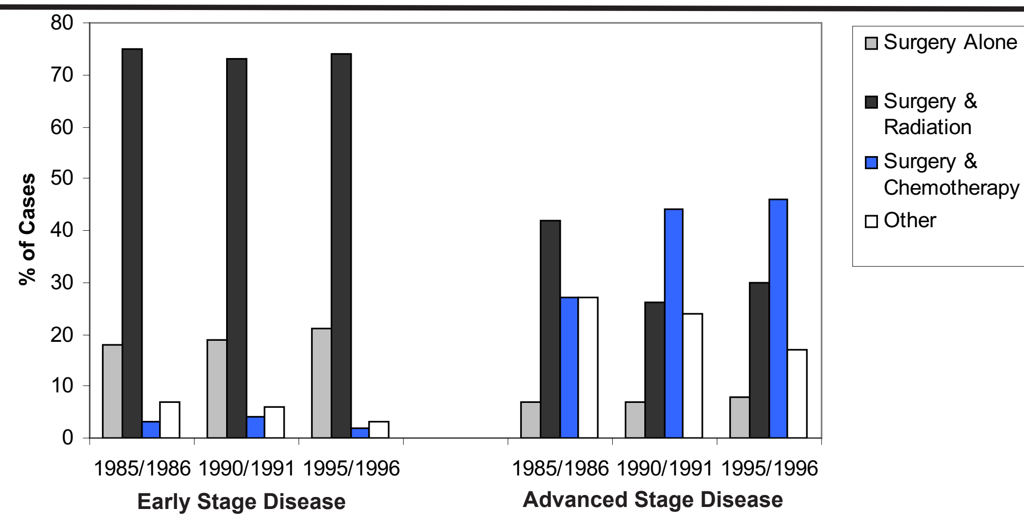

Figure 1a. Changing patterns of seminoma treatment by early or advanced stage in patients diagnosed in 1985–1996.

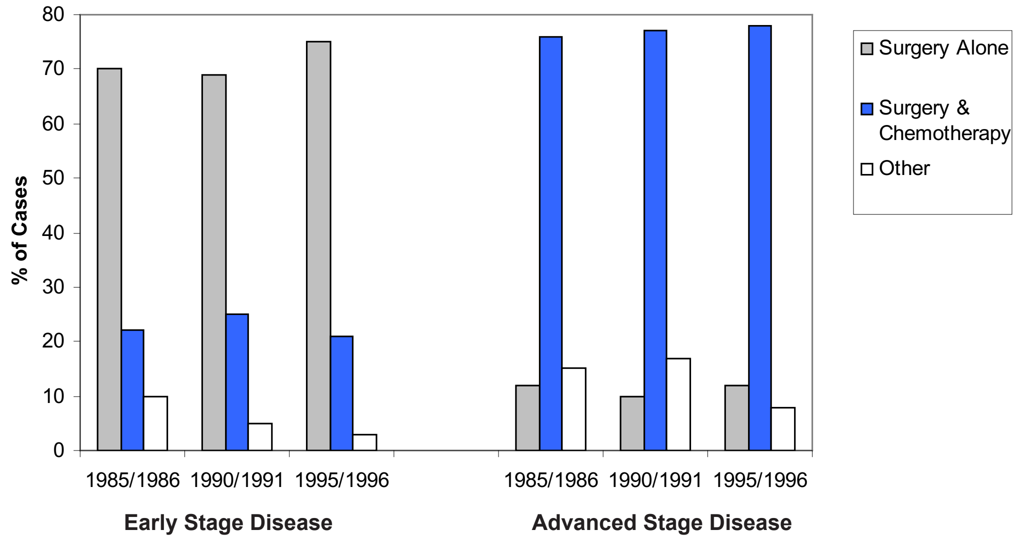

Figure 1b. Changing patterns of nonseminoma treatment by early or advanced stage for patients diagnosed in 1985–1996.

SOURCE: Adapted from Cancer, 86, Steele, GS, Richie, JP, Stewart AK, and Menck HR, The National Cancer Data Base report on patterns of care for testicular carcinoma,1985–1996, 2,171–2,184, Copyright 1999, with permission from Wiley.

radiation remained stable at 76% in 1985–1986 to 74% in 1995–1996 during the period studied. As expected, the use of lymphadanectomy in seminoma is rare, at 0.6%. Chemotherapy is becoming the standard treatment for advanced seminoma after orchiectomy; its rate of use increased from 25.7% in 1985–1986 to 51.5% in 1995–1996 (Table 3) (11). Consequently, the rate of use of radiotherapy in higher-stage disease decreased from 43.3% in 1985–1986 to 27.2% in 1995–1996 (3).

For patients with early-stage NSGCT, the NCDB data revealed an increase in the use of surgery as a single-modality therapy (from 69.8% in 1985–1986 to 75% in 1995–1996) (Table 3). While the use of RPLND increased (from 12.6% in 1985–1986 to 17.6 in 1995–1996), so did orchiectomy as a single therapy (from 18.3% in 1985–1986 to 45% in 1995–1996), again reflecting the use of surveillance as a primary treatment, followed by salvage therapy if necessary (3). The increase in RPLND is not surprising, since refinements in technique have diminished the morbidity of this operation. The rate of use of chemotherapy in early disease has remained relatively stable at 22–23%. However, its rate of use for advanced NSGCT increased from 75% in 1985–1986 to 79% in 1995–1996 (3). This primarily reflects improved methods of supporting patients that make chemotherapy more tolerable. Certain aspects of therapy are not covered in the NCDB, including the use of laparoscopy and changes in the dosing of chemotherapeutic agents. These are expected to have a profound effect on management in the next decade.

PREVALENCE AND INCIDENCE

Testicular cancer constitutes less than 1% of all male cancers (12). According to the Surveillance, Epidemiology, and End Results (SEER) database, the age-adjusted incidence rate of testicular cancer from 1997 to 2001 was estimated to be 5.5 per 100,000 population. The lifetime prevalence count of testicular cancer on January 1, 2001, was 157,349. These data, as well as the racial disparity in testicular cancer between Caucasian and African American men, are clearly delineated in Table 4.

The overall incidence of testicular cancer in the United States has been steadily increasing (12). SEER data show although that the overall incidence of testicular germ cell tumors rose 46% between 1975 and 2001, from 3.7 per 100,000 to 5.4 per 100,000 population, the absolute change is relatively small (Table 5). This corresponds to an annual change of 1.5% across all populations under study. However, the rate of increase in incidence appears to be leveling. Over the past three decades, it has decreased from 22% to 15% to 4%, respectively. No formal testicular cancer prevention programs exist, so there is no obvious explanation for this diminution. It is possible that the

Table 4. Incidence and prevalence rates[a] for testicular cancer, by race/ethnicity, 1997–2001

	All Races	White Males	Black Males
Age-adjusted incidence rates			
All ages	5.5	6.5	1.5
< 65	6.2	7.2	1.6
65+	0.9	1.1	*
Prevalence Counts of Testicular Cancer on Jan 1, 2001			
All	157,349	150,181	2,948

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 men of the same stratum.

SOURCE: Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L., Mariotto A,Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2001, National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/csr/1975_2001/, 2004.

Table 5. Incidence rates[a] for testicular cancer, age-adjusted, by age

	All	< 50	≥ 50
Year of Diagnosis			
1975	3.7	4.2	2.4
1976	3.4	4.2	1.5
1977	4.3	5.1	2.2
1978	3.6	4.2	1.8
1979	3.9	4.5	2.2
1980	4.4	5.3	1.9
1981	4.2	5.1	1.8
1982	4.4	5.2	2.3
1983	4.6	5.5	2.2
1984	4.4	5.3	1.9
1985	4.5	5.5	1.8
1986	4.8	5.8	2.2
1987	5.0	6.3	1.8
1988	4.6	5.8	1.5
1989	5.5	6.7	2.2
1990	5.1	6.3	2.1
1991	5.1	6.2	2.1
1992	5.2	6.4	1.9
1993	5.1	6.4	1.6
1994	5.5	6.7	2.1
1995	4.6	5.6	1.8
1996	5.2	6.6	1.7
1997	5.4	6.5	2.4
1998	5.6	7.1	1.6
1999	5.4	6.8	1.8
2000	5.7	7.1	2.0
2001	5.4	6.7	2.0
1997–2001	5.5	6.9	2.0

[a]Seer 9 areas. Rates are per 100,000 and are age-adjusted to the 2000 standard population by 5-year age groups.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

decrease is the indirect result of changes in behavior that influence risk factors, most specifically, programs directed at preventing trauma and at awareness of the hazards of maternal hormone exposure, although this has never been definitively studied.

Age

Testicular cancer is being diagnosed at an earlier age. Among men under 50 years of age in the SEER database (Table 5), the incidence of testicular cancer increased from 4.2 per 100,000 to 6.7 per 100,000 between 1975 and 2001. During the same period, the incidence in men older than 50 decreased from 2.4 per 100,000 to 2.0 per 100,000. This reflects a shift in diagnosis to younger men and is demonstrated by the SEER data, in which testicular cancer incidence is stratified by age at diagnosis (Table 6). McKiernan et al. reviewed similar SEER data from 1973–1995 and found that birth cohort was strongly associated with the relative risk of testicular cancer (12). They also demonstrated that the peak age at diagnosis has decreased for each successive birth cohort (Figure 2). This shift may reflect improved physician education, a greater emphasis on making young and teenage boys more aware of their own health issues, and the dissemination of self-examination programs. As noted later in this chapter, however, the lack of stage migration at the time of diagnosis casts doubt on the success of self-examination programs.

Table 6. Incidence rates[a] for testicular cancer, 1997–2001, age-adjusted and age-specific rates, by race/ethnicity

	All Males	White Males	Black Males
Age-specific Rates			
Age at Diagnosis			
<1	…	…	…
1–4	…	…	
5–9	…	…	…
10–14	…	…	
15–19	3.3	3.9	…
20–24	9.4	11.3	…
25–29	11.9	14.4	…
30–34	13.6	16.2	…
35–39	12.2	14.3	4.0
40–44	10.2	12.0	…
45–49	6.8	7.8	…
50–54	4.1	4.7	…
55–59	2.1	2.3	…
60–64	1.6	1.8	…
65–69	…	…	…
70–74	…	…	…
75–79	…	…	…
80–84	…	…	…
85+	…	…	…
Age-adjusted Rates			
Age at Diagnosis			
All ages	5.5	6.5	1.5
< 65	6.2	7.2	1.6
65+	0.9	1.1	…

…data not available.

[a]SEER 9 areas. Rates are per 100,000 and are age-adjusted to the 2000 standard population by 5-year age groups.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Ethnicity

It has long been known that there is a disparity in the incidence and prevalence of testicular cancer between Caucasians and African Americans in the United States. SEER data indicate that the lifetime risk of being diagnosed with testicular cancer is four times greater for Caucasians than for African Americans (Table 7). The age-adjusted incidence in 1997–2001 for Caucasians was 6.2 per 100,000 population (7.0 for non-Hispanic Caucasians), while that for African Americans was 1.5 per 100,000 (Table 8). The age-adjusted incidence in Hispanic and Asian/Pacific Islander and North American Native populations fell between these rates. Prevalence of testicular cancer is displayed in Table 9.

Biggs and Schwartz examined relationships between race and ethnicity and testicular cancer, using 16,086 cases from the SEER database (13). The characteristics of the patients are summarized in Table 10. African American, North American Native, Hawaiian American, and Hispanic patients were more likely than Caucasians to be diagnosed with late-stage testicular cancer. In addition, a slightly greater percentage of Native American, Hawaiian American, and Hispanic men had NSGCTs. It is unclear whether this represents a sampling bias or a true biological and genetic difference. In all populations, testicular cancer is more common in men under 40 years of age.

Table 7. Percent of males diagnosed with testicular cancer after 10, 20, and 30 years and during remaining lifetime, given freedom from cancerat current age, by race/ethnicity

	All Males			
	> 10 years	**> 20 years**	**> 30 years**	**Eventually**
Current Age				
0	0	0.30	0.12	0.35
10	0.02	0.12	0.24	0.36
20	0.10	0.22	0.29	0.34
30	0.12	0.19	0.22	0.24
40	0.08	0.11	0.12	0.12
50	0.03	0.04	0.05	0.05
60	0.01	0.02	0.02	0.02
Lifetime Risk of Being Diagnosed =	0.35%	**Lifetime Risk of Dying =**	0.02%	
	White Males			
	> 10 years	**> 20 years**	**> 30 years**	**Eventually**
Current Age				
0	0	0.03	0.15	0.42
10	0.03	0.15	0.28	0.42
20	0.12	0.26	0.34	0.40
30	0.14	0.23	0.26	0.28
40	0.09	0.12	0.13	0.14
50	0.03	0.05	0.05	0.06
60	0.01	0.02	0.02	0.02
Lifetime Risk of Being Diagnosed =	0.42%	**Lifetime Risk of Dying =**	0.02%	
	Black Males			
	> 10 years	**> 20 years**	**> 30 years**	**Eventually**
Current Age				
0	0	0.01	0.03	0.10
10	0.01	0.03	0.06	0.10
20	0.02	0.05	0.07	0.09
30	0.03	0.05	0.06	0.07
40	0.02	0.03	0.04	0.04
50	0.01	0.02	0.02	0.02
60	0.01	0.01	0.01	0.01
Lifetime Risk of Being Diagnosed =	0.10%	**Lifetime Risk of Dying =**	0.01%	

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 8. Age-adjusted incidence[a] rates for testicular cancer, 1997–2001, by race/ethnicity

	Rate per 100,000 persons 1997–2001	**Annual Percent Change Trend 1992–2001**
Race/ethnicity		
Total	5.2	1.2[c]
White	6.2	1.3[c]
White Hispanic[b]	3.7	1.0
White Non-Hispanic[b]	7.0	1.8[c]
Black	1.5	6.4[c]
Asian/Pacific Islander	2.1	2.3
N. American Native/Alaska Native	2.3	…
Hispanic[b]	3.6	1.1

…data not available.

[a]Incidence data are from the 12 SEER areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, and Alaska Native Registry.

[b]Hispanic and Non-Hispanic are not mutually exclusive from Whites, Blacks, Asian/Pacific Islanders,and American Indians/Alaska Natives. Incidence data for Hispanics and Non-Hispanics do not include cases from Detroit, Hawaii, and Alaska Native Registry.

[c]The annual percent of change is significantly different from zero ($p < 0.05$).

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

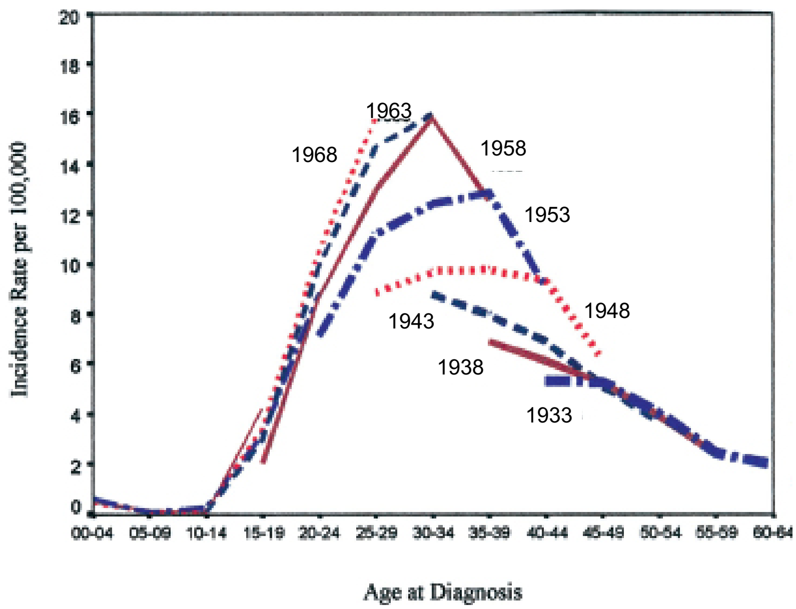

Figure 2. Testicular cancer rates by birth cohort vs age at diagnosis.

SOURCE: Adapted from Journal of Urology, 162, McKiernan JM, Goluboff ET, Liberson GL, Golden R, and Fisch H, Rising risk of testicular cancer by birth cohort in the United States from 1973–1995, 361–363, Copyright 1999, with permission from American Urological Association.

Between 1975 and 2001, the incidence of testicular cancer among Caucasian men rose 54%, from 4.1 per 100,000 to 6.3 per 100,000 (Table 11). As expected, this was most notable in men younger than 50 years of age, among whom the incidence increased from 4.7 per 100,000 to 7.9 per 100,000. In men older than 50, the incidence declined by 15%. Among African American men, the overall incidence of testicular cancer remained stable between 1973 and 1998 at about 1.0 per 100,000 (2). Data on the changes in incidence in other ethnic groups is limited, although Paltoo and Chu found that testicular cancer rates in American Indian and Native Alaskan men stabilized at 2.2 per 100,000 throughout the 1990s (8).

Histology

Changes in the incidence of testicular germ cell tumors among Caucasian and African American men stratified by histologic subtypes are illustrated in Figure 3. McGlynn et al. analyzed SEER data from 1973 to 1998 and found that seminoma and non-seminoma have distinguishable incidence patterns among Caucasian and African American racial groups (2). They demonstrated that for Caucasian men, only the incidence of seminoma was increasing. The incidence of NSGCT was decreasing. In addition, the ratio of seminoma to non-seminoma among Caucasian men changed from 50:50 in 1973–1978 to 60:40 in 1994–1998. In African American men, seminoma also showed continued increasing incidence, coupled with an overall decrease in NSGCT (despite a small upward surge in the final period under study). The seminoma to non-seminoma ratio in African American men increased from 60:40 to 70:30. The divergent trends in the incidence of seminoma and NSGCT may be the result of changes in underlying risk factors and etiologic causes, alterations in biology, refinements in histologic evaluation, or changes in diagnostic practices, including coding practices (i.e., the classification for mixed germ cell was introduced as an ICD-9 code in 1990).

Biggs and Schwartz evaluated the relationships between histology and ethnicity in their examination of 16,086 cases from the SEER database (Table 10) (13). Seminomas constituted an average of 56% of the cases under study, ranging from a low of 51% (Hispanic Americans) to a high of 70% (Japanese Americans). Among the NSGCT subtypes, mixed germ cell

Table 9. Estimated testicular cancer prevalence counts[a] on January 1, 2001 in the United States, by race/ethnicity and years since diagnosis

Years Since Diagnosis	0 to < 5	5 to < 10	10 to < 15	15 to < 20	20 to < 25	0 to < 11[e]	0 to < 26[e]	≥ 26[f]	Complete[g]
Race/ethnicity									
Total[b]	36,654	31,755	29,060	21,694	15,575	74,666	136,928	20,421	157,349
White[b]	34,466	30,101	28,019	20,927	15,006	70,615	130,559	19,622	150,181
Black[b]	1,021	622	417	367	256	1,723	2,747	201	2,948
Asian/Pacific Islander[c]	562	494	…	…	…	1,122	…	…	…
Hispanic[d]	3,236	2,389	…	…	…	5,990	…	…	…

…data not available.

[a]US 2001 cancer prevalence counts are based on 2001 cancer prevalence proportions from the SEER registries and 1/1/2001 US population estimates based on the average of 2000 and 2001 population estimates from the US Bureau of the Census. Prevalence was calculated using the First Malignant Primary Only for a person.

[b,c,d]Statistics based on (b) SEER 9 Areas, (c) SEER 11 Areas, and (d) SEER 11 Areas excluding Hawaii and Detroit.

[e]Maximum limited-duration prevalence: 26 years for 1975–2001 SEER 9 data; 11 years for 1990–2001 SEER 11 data (used to calculate prevalence for Hispanics and Asian/ Pacific Islanders.

[f,g](f)Cases diagnosed 26 years or more ago were estimated using the completeness index method (Capocaccia et. al. 1997. Merrill et. al 2000); (g) Complete prevalence is obtained by summing 0 to < 26 and ≥ 26.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 10. Characteristics of testicular cancer patients, by age and race/ethnicity

Characteristic	Non-Hisp. White (n=13,922)	African Am. (n=329)	Native Am. (n=89)	Chinese (n=129)	Japanese (n=141)	Filipino (n=60)	Hawaiian (n=94)	Hisp. White (n=1,322)	Total (n=16,086)
Age at Diagnosis									
15–19	598 (4%)	13 (4%)	6 (7%)	1 (1%)	2 (1%)	1 (2%)	6 (6%)	107 (8%)	734 (5%)
20–29	4,572 (33%)	101 (31%)	43 (48%)	41 (32%)	39 (28%)	27 (45%)	42 (45%)	575 (44%)	5,443 (34%)
30–39	5,185 (37%)	137 (42%)	25 (29%)	50 (39%)	60 (43%)	19 (32%)	33 (35%)	426 (32%)	5,935 (37%)
40–49	2,354 (17%)	55 (17%)	10 (11%)	25 (19%)	28 (20%)	8 (13%)	8 (9%)	150 (11%)	2,638 (16%)
50–59	767 (6%)	13 (4%)	3 (3%)	10 (8%)	6 (4%)	2 (3%)	3 (3%)	41 (3%)	845 (5%)
60+	446 (3%)	10 (3%)	2 (2%)	2 (2%)	6 (4%)	3 (5%)	2 (2%)	20 (2%)	491 (3%)
Stage at Diagnosis									
Localized	9,084 (65%)	202 (61%)	51 (57%)	98 (76%)	100 (71%)	43 (72%)	47 (50%)	841 (64%)	10,466 (65%)
Regional	2,896 (21%)	65 (20%)	13 (15%)	16 (12%)	25 (18%)	10 (17%)	22 (23%)	248 (19%)	3,295 (21%)
Distant	1,640 (12%)	53 (16%)	24 (27%)	12 (9%)	15 (11%)	6 (10%)	25 (27%)	213 (16%)	1,988 (12%)
Unstaged	302 (2%)	9 (3%)	1 (1%)	3 (2%)	1 (1%)	1 (2%)	0	20 (2%)	337 (2%)
Histology									
Seminoma	7,779 (56%)	197 (60%)	47 (53%)	84 (65%)	99 (70%)	39 (65%)	49 (52%)	678 (51%)	8,972 (56%)
NSGCT	5,995 (43%)	119 (36%)	40 (45%)	39 (30%)	42 (30%)	20 (33%)	44 (47%)	635 (48%)	6,934 (43%)
Embryonical	2,318 (17%)	33 (10%)	12 (13%)	15 (12%)	12 (9%)	6 (10%)	16 (17%)	182 (14%)	2,594 (16%)
Yolk Sac	118 (1%)	3 (1%)	1 (1%)	0	0	0	2 (2%)	14 (1%)	238 (1%)
Teratoma	447 (3%)	8 (2%)	4 (4%)	3 (2%)	5 (4%)	0	5 (5%)	50 (4%)	533 (3%)
Choriocarcinoma	124 (1%)	7 (2%)	3 (3%)	3 (2%)	0	0	1 (1%)	11 (1%)	149 (1%)
Mixed Germ Cell	2,988 (21%)	68 (21%)	20 (22%)	18 (14%)	25 (18%)	14 (23%)	20 (21%)	378 (29%)	3,531 (22%)
Non-germ cell	146 (1%)	13 (4%)	2 (2%)	6 (5%)	0	1 (2%)	1 (1%)	9 (1%)	180 (1%)

NSGCT, non-seminomatous germ cell tumor.

SOURCE: Reprinted from Springer and Klurer Acadameic Publishers, Cancer Causes and Control, 15(5),2004, 437–444, Differences in testis cancer survival by race and ethnicity: a population based study, 1973–1999 (US), Biggs ML, Schwartz SM, Table 1, with kind permission from Springer Science and Business Media.

Table 11. Incidence rates[a] for testicular cancer, among white males, age-adjusted, by age

	White Males		
	All	< 50	50+
Year of Diagnosis			
1975	4.1	4.7	2.6
1976	3.8	4.5	1.7
1977	4.9	5.8	2.4
1978	3.9	4.6	2.1
1979	4.3	5.1	2.3
1980	4.9	6.0	2.1
1981	4.8	5.8	2.1
1982	5.0	6.0	2.4
1983	5.2	6.3	2.5
1984	5.0	6.4	2.1
1985	5.1	6.3	2.1
1986	5.6	6.8	2.3
1987	5.7	7.1	1.9
1988	5.4	6.9	1.7
1989	6.3	7.8	2.5
1990	6.0	7.4	2.3
1991	5.7	7.0	2.3
1992	6.1	7.6	2.1
1993	6.0	7.5	1.9
1994	6.3	7.8	2.3
1995	5.3	6.5	2.1
1996	6.2	7.8	1.9
1997	6.3	7.7	2.7
1998	6.6	8.4	1.8
1999	6.3	8.0	2.0
2000	6.7	8.4	2.3
2001	6.3	7.9	2.2
1997–2001	6.5	8.1	2.2

[a]Seer 9 areas. Rates are per 100,00 and are age-adjusted to the 2000 standard population by 5-year age groups.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

(mean 22%; range 14%–29%) was the most common, followed by embryonal (mean 16%; range 9%–17%), then teratoma (mean 3%; range 0%–5%), and finally choriocarcinoma and yolk sac (mean 1% each; ranges 0%–3% and 0%–2%, respectively). This order of histologic frequency (mixed, embryonal, teratoma, choriocarcinoma and yolk sac) was found across all ethnic groups. African American, Native American, Hawaiian American, and Hispanic testicular cancer patients were more likely than Caucasian patients to have more-aggressive NSGCTs.

Steele et al. examined testicular cancer data from the NCDB collected between 1985 and 1996 (11). The incidence of testicular cancer divided by histologic subtype in this database is summarized in Table 12. The percentage of seminoma remained stable at approximately 55% over the ten years of collected data, while the percentage of embryonal tumors and choriocarcinomas decreased from 18.9% to 11.4% and 5.2 to 2.5%, respectively, and the percentage of teratomas increased from 16.4% to 22.3%. In addition, the percentage of non–germ-cell tumors increased from 5.2% to 7.2%. It is unclear whether this represents a true transformation in the percentage of histologic subtypes as opposed to changes in histopathologic

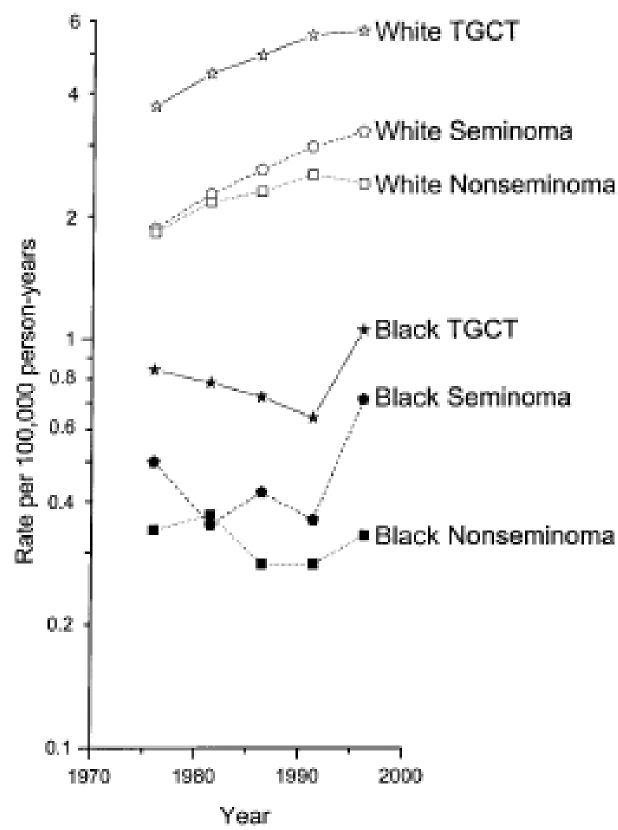

Figure 3. Incidence of testicular germ cell tumors (TGCTs) in the SEER Program from 1973–1978 to 1994–1998, race/ethnicity and tumor type.

SOURCE: Adapted from Cancer, 97,McGlynn K, Devesa SS, Sigurdson AJ, Brown, LM, Tsao L, and Tarone RE, Trends in the incidence of testicular germ cell tumors in the United States, 63–70, Copyright 2003, with permission from Wiley.

Table 12. Testicular tumor characteristics

	1985–1986[a]		1990–1991[b]		1995–1996[c]	
	Cases	Percent	Cases	Percent	Cases	Percent
Anatomic site						
Undescended testis	39	1.7	138	2.4	160	2.1
Descended testis	56	2.5	278	4.9	2,187	29.3
Testis, NOS	2,185	95.8	5,261	92.7	5,105	68.5
Total	2,280	100	5,677	100	7,452	100
Histology						
Seminoma, NOS	1,219	53.5	3,029	53.4	4,171	56.0
Spermatocytic seminoma	14	0.6	31	0.5	40	0.5
Embryonal carcinoma	430	18.9	846	15.4	853	11.4
Malignant teratoma	373	16.4	1,203	21.2	1,659	22.3
Choriocarcinoma	118	5.2	210	3.7	184	2.5
Nongerm cell tumors	118	5.2	322	5.7	537	7.2
Unspecified	8.0	0.4	6.0	0.1	8.0	0.1
Total	2,280	100	5,677	100	7,452	100
AJCC stage						
I	779	64.2	3,141	65.0	4,800	73.4
II	156	12.9	295	6.1	1,107	16.9
III	108	8.9	324	6.7	633	9.7
IV	170	14.0	1,069	22.1	…	…
Total	1,213	100	4,829	100	6,540	100
Unknown	1,067	46.8	848	14.9	912	12.2
Total	2,280	100	5,677	100	7,452	100

…data not available.

NOS = not otherwise specified; AJCC: American Joint Committee on Cancer.

[a]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 2nd edition.

[b]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 3rd edition.

[c]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 4th edition.

SOURCE: Reprinted from Cancer, 86, Steele, GS, Richie, JP, Stewart AK, and Menck HR, The National Cancer Data Base report on patterns of care for testicular carcinoma, 1985–1996, 2,171–2,183, Copyright 1999, with permission from Wiley.

Table 13. Percent distribution of AJCC stage at diagnosis, by disease histology

	1985–1986[a]		1990–1991[b]		1995–1996[c]	
	Seminoma	NSGCT	Seminoma	NSGCT	Seminoma	NSGCT
Stage of Diseased						
Early	88.9	61.7	89.7	62.7	89.2	65.1
Advanced	11.1	39.3	10.3	37.3	10.8	34.9
Total	100	100	100	100	100	100
Cases, n	667	488	2669	1926	3802	2369

…data not available.

NOS = not otherwise specified; AJCC = American Joint Committee on Cancer.

[a]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 2nd edition.

[b]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 3rd edition.

[c]Cases staged according to the American Joint Committee on Cancer *Manual for Staging of Cancer*, 4th edition.

[d]Early stage: 1985–1986 American Joint Committee on Cancer Stage I and II; 1990–1991 American Joint Committee on Cancer Stage I, II, and III; 1995–1996 American Joint Committee on Cancer Stage I and II N1. Advanced stage: 1985–1986 American Joint Committee on Cancer Stage IIIand IV; 1990–1991 American Joint Committee on Cancer Stage IV; 1995–1996 American Joint Committee on Cancer Stage II (N2 or higher) and III.

SOURCE: Reprinted from Cancer, 86, Steele, GS, Richie, JP, Stewart AK, and Menck HR, The National Cancer Data Base report on patterns of care for testicular carcinoma, 1985–1996, 2,171–2,183, Copyright 1999, with permission from Wiley.

Table 14. Survival rates for testicular cancer, 1995–2000[a] by race, stage, and age, percent

	All Males			White Males			Black Males		
	All	< 50	≥ 50	All	< 50	≥ 50	All	< 50	≥ 50
All Stages (n)	4,148	3,827	321	3,822	3,521	301	121	113	8
Localized	70	71	67	71	71	68	63	65	38
Regional	18	18	17	18	18	17	20	20	13
Distant	10	10	13	10	10	13	16	13	50
Unstaged	1	1	2	1	1	2	2	2	…

…data not available.

[a]Rates are from SEER 9 areas. Rates are per 100,000 and are age-adjusted to the 2000 standard population by 5-year age groups. They are based on data from population-based registries in Connecticut, Puerto Rico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland. Rates are based on follow up of patients into 2001.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

analysis, or whether it reflects the 3.25-fold increase in patients entered into the database between 1985 and 1996. It is also unclear why these data differ from the SEER data. It is possible that the NCDB and the SEER data were influenced differently by changes in coding practices during the period of data collection.

Stage

Distribution by stage at diagnosis in the NCDB is summarized in Table 12. From 1985 to 1991, the proportion of tumors presenting as stage I remained relatively stable at approximately 65%, whereas the percentage of stage II and III tumors decreased from 12.9% to 6.1% and 8.9% to 6.7%, respectively. Stage IV tumors increased from 14% to 22% during the same period. This is an unexpected finding. With increased physician and patient education and awareness, as well as self-examination programs, one would expect a stage migration, i.e., an increasing percentage of localized tumors (stage I) coupled with diminishing rates of disseminated disease (stages II–IV). Several factors may explain these findings. Nearly half of the patients in the NCDB had an unknown stage; this rate decreased to 12.2% by 1995–1996. In addition, considerable changes in staging practices occurred during the 11 years of data acquisition. However, when the NCDB data are further divided into "early" and "advanced" disease (Table 13), there still appears to be little change in stage distribution over time. These data do confirm that more seminomas than NSGCTs are discovered earlier in their course.

The stage distribution of all 4,148 men in the SEER database from 1995 to 2000 showed 70% localized, 18% with regional spread, 10% with distant spread, and 1% unstaged (Table 14). Caucasian men were more likely to present with localized disease than were African American men (71% vs 63%), who, conversely, were more likely to have metastatic disease (20% vs 18% and 16% vs 10% for regional and distant spread, respectively). Biggs and Schwartz evaluated the relationships between stage and ethnicity in the SEER database (Table 10) (13) and found that, on average, 65% of patients presented with localized disease, which is similar to findings in the NCDB data. However, African American, Native American, Hawaiian American, and Hispanic testicular cancer patients were more likely than Caucasians to be diagnosed with late-stage disease. Overall, 21% of the patients in the database examined by Biggs and Schwartz presented with regional metastases, 12% with distant metastases, and 2% without formal staging (Table 10). The differences between these findings and those of the NCDB could be the result of differences in nomenclature, biological differences in the tumors of the study populations, or disparity in other social factors, including healthcare access and usage. Interestingly, in the SEER analysis, men of Asian ancestry (China, Japan, and the Philippines) had the highest incidence of localized disease, whereas Hawaiians, who share some genetic heritage with this population, had the lowest. This may reflect access to

Table 15. Survival rates[a,b] for testicular cancer, by race/ethnicity, diagnosis year, stage, and age

	All Males			White Males			Black Males		
	All	**< 50**	**≥ 50**	**All**	**< 50**	**≥ 50**	**All**	**< 50**	**≥ 50**
5-Year Relative Survival Rates									
Year of Diagnosis									
1960–1963[a]	…	…	…	63.0	…	…	…	…	…
1970–1973[a]	…	…	…	72.0	…	…	…	…	…
1974–1976[b]	78.7	78.1	82.9	78.8	78.2	83.3	75.9[d]	…	…
1977–1979[b]	87.5	88.6	77.1	87.9	89.0	78.1	66.2[d]	…	…
1980–1982[b]	91.9	91.9	91.8	92.1	92.0	92.7	89.7[d]	89.2[d]	…
1983–1985[b]	91.0	91.8	82.3	91.3	92.3	80.7	87.9[d]	84.3[d]	…
1986–1988[b]	95.2	95.3	93.5	95.7	95.7	94.4	…	…	…
1989–1991[b]	95.4	95.5	93.8	95.9	95.8	94.8	89.8[d]	93.6[d]	…
1992–1994[b]	95.4	95.7	90.4	95.6	95.9	60.1	85.2[d]	84.5[d]	…
1995–2000[b]	95.9[c]	96.4[c]	88.3	96.2[c]	96.7[c]	89.4	87.3	90.4	…
1995-2000[b]									
All Stages	95.9	96.4	88.3	96.2	96.7	89.4	87.3	90.4	…
Localized	99.4	99.4	97.0	99.4	99.4	97.6	96.5[d]	99.6	…
Regional	95.9	96.4	89.9[d]	96.1	96.5	90.6[d]	…	…	…
Distant	71.8	75.1	38.7[d]	73.1	76.6	39.5[d]	…	…	…
Unstaged	89.1	91.6	…	90.2	93.0	…	…	…	…
5-Year Relative Survival Rates, 1995–2000[b]									
Age at Diagnosis									
< 45	96.5	…	…	96.7	…	…	…	…	…
45–54	94.5	…	…	95.3	…	…	…	…	…
55–64	87.2	…	…	87.9	…	…	…	…	…
65–74	74.2[d]	…	…	75.9[d]	…	…	…	…	…
75+	…	…	…	…	…	…	…	…	…
< 65	96.1	…	…	96.4	…	…	…	…	…
65+	73.9[d]	…	…	77.6[d]	…	…	…	…	…

…data not available.

[a]Rates are based on End Results data from a series of hospital registries and one population-based registry.

[b]Rates are from SEER 9 areas. They are based on data from population-based registries in Connecticut, Puerto Rico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland. Rates are based on follow up of patients into 2001.

[c]The difference in rates between 1974–1976 and 1995–2000 is statistically significant ($p < 0.05$).

[d]The standard error of the survival rate is between 5–10 percentage points.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 16. Survival rates[a] for testicular cancer, by year of diagnosis

	1976–1979	1980–1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
Survival Rates																		
1-year	93.3	96.0	97.1	98.1	98.1	98.9	98.2	98.2	98.4	97.9	96.8	97.7	98.3	97.9	97.4	98.2	97.0	97.7
2-year	88.6	92.7	94.0	96.7	97.3	96.6	95.7	96.7	96.9	96.7	95.9	96.5	97.5	96.4	95.7	96.6	96.1	
3-year	86.5	92.1	93.4	96.5	96.3	95.8	95.0	96.3	95.8	95.6	95.2	95.9	96.4	96.0	95.2	96.2		
4-year	85.6	91.5	92.8	95.8	95.6	95.2	94.8	96.3	95.3	95.6	95.2	95.9	96.4	96.0	94.9			
5-year	85.1	91.2	92.5	95.5	95.3	94.8	94.7	96.3	95.3	95.3	95.2	95.7	96.3	96.0				
6-year	84.8	90.9	92.3	95.4	94.6	94.6	94.6	96.0	95.1	94.9	95.2	95.7	96.3					
7-year	84.7	90.8	92.3	95.4	94.5	94.4	94.3	95.9	95.1	94.8	95.2	95.6						
8-year	84.6	90.5	91.5	95.4	94.5	93.5	94.2	95.9	94.8	94.0	95.0							
9-year	84.5	90.0	91.5	95.2	94.5	93.5	96.8	95.9	94.6	94.0								
10-year	83.8	89.9	91.4	94.7	94.5	93.4	96.8	95.9	94.5									
11-year	83.3	89.9	90.6	94.7	94.4	93.3	96.8	95.9										
12-year	92.1	89.8	90.6	94.2	94.4	93.3	96.8											
13-year	92.8	89.7	89.9	94.2	93.7	93.3												
14-year	82.1	89.2	89.0	94.0	93.6													
15-year	81.9	88.7	88.9	94.0														
16-year	81.5	88.5	88.5															
17-year	80.9	88.0																
18-year	80.4	87.6																
19-year	79.9																	
20-year	79.7																	

[a]Rates from the SEER 9 areas are rates expressed as percents.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Table 17. Completeness of follow-up, number of testicular cancer deaths, and Kaplan Meier estimates of 5-year cause-specific survival among testicular cancer patients by race/ethnicity, 12 SEER registries, 1973–1999

Characteristic	Non-Hisp. White (n=13,922)	African Am. (n=329)	Native Am. (n=89)	Chinese (n=129)	Japanese (n=141)	Filipino (n=60)	Hawaiian (n=94)	Hisp. White (n=1,322)	Total (n=16,086)
Completeness of follow-up	87%	80%	89%	88%	92%	85%	85%	86%	87%
Number of testicular cancer deaths	728	35	12	7	6	5	15	78	886
5-Year Survival									
1973–1989	0.93	0.87	0.85	0.94	0.90	0.94	0.77	0.91	0.92
1990–1999	0.97	0.90	0.90	0.99	0.99	0.92	0.92	0.95	0.97
1973–1999	0.95	0.89	0.89	0.97	0.95	0.93	0.84	0.94	0.95

SOURCE: Reprinted from Springer and Klurer Acadameic Publishers, Cancer Causes and Control, 15(5),2004, 437–444, Differences in testis cancer survival by race and ethnicity: a population based study, 1973–1999 (US), Biggs ML, Schwartz SM, Table 2, with kind permission from Springer Science and Business Media.

healthcare on the Hawaiian Islands, as well as dietary and other environmental factors.

Survival

When considering the epidemiologic data, it is important to recognize the difference between mortality, the deaths in the general population due to the specific disease, and survival, which is limited to the patient cohort with the disease. Five-year relative survival rates by race, year of diagnosis, stage, and age from the SEER database are summarized in Table 15. From 1974 to 2000, five-year survivals rates increased successively, reaching the most recent level of 95.9%. This may be explained in part by a stage migration to earlier presentation of disease (14). African American men with testicular cancer experienced a decrease in survival rates between 1989–1991 and 1992–1994, from 89.8% to 85.2%. This was a temporary downturn, however, and in the 1995–2000 dataset survival of African American men increased to 87.3%. Possible explanations include differential access to medical care.

Table 15 also demonstrates that survival rates are best for patients who present with localized disease. When stratified by stage at presentation, men diagnosed between 1995 and 2000 with localized disease had survival rates of 99.4%, compared with 95.9% and 71.8% for regional and distant disease, respectively. Men diagnosed at a younger age also have better survival rates. In the 1995–2000 cohort, men younger than 50 years of age had five-year relative survival rates of 96.4%, compared with 88.3% for men older than 50. Finally, men diagnosed more recently had better survival rates. A man diagnosed in 1995 had a 95.9% chance of five-year survival, while the rate for a man diagnosed in 1974 was 78.7%.

Table 18. Multivariate adjusted hazard ratios for association of race/ethnicity with death from testicular cancer

Adjustment	Non-Hisp. White (n=13,922)	African Am. (n=329)	Native Am. (n=89)	Chinese (n=129)	Japanese (n=141)	Filipino (n=60)	Hawaiian (n=94)	Hisp. White (n=1,322)
Histology, period of diagnosis	1.0	2.6	2.9	1.3	1.4	2.1	3.6	1.6
Histology, period of diagnosis, stage	1.0	2.3	2.1	1.6	1.1	3.6	2.4	1.4

SOURCE: Reprinted from Springer and Klurer Acadameic Publishers, Cancer Causes and Control, 15(5), 2004, 437–444, Differences in testis cancer survival by race and ethnicity: a population based study, 1973–1999 (US), Biggs ML, Schwartz SM Table 4, with kind permission from Springer Science and Business Media.

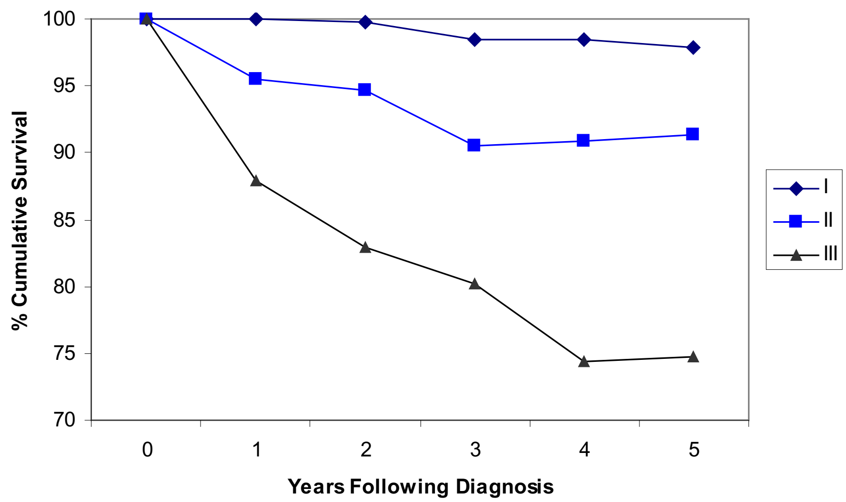

Figure 4a. Relative survival of seminoma patients by cancer stage for cases diagnosed in 1985–1991.

Stage I represents 1,796 patients; Stage II represents 158 patients; and Stage III represents 117 patients.

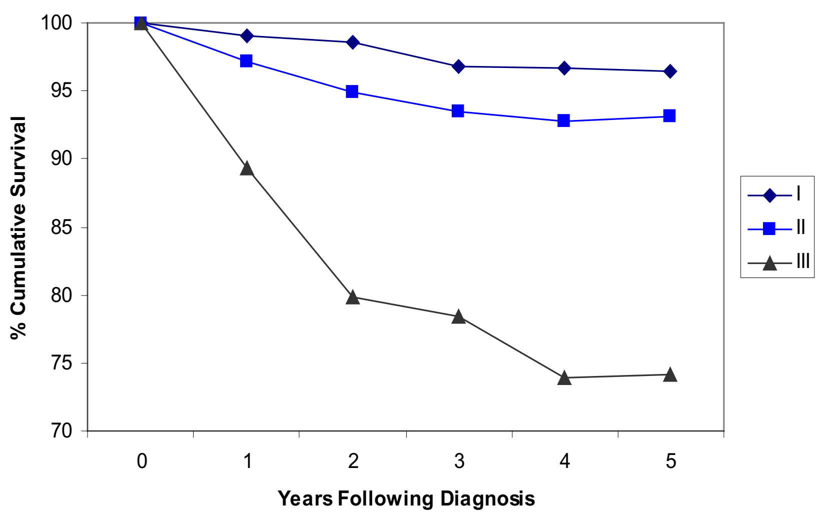

Figure 4b. Relative survival of nonseminoma patients by cancer stage for cases diagnosed in 1985–1991.

Stage I represents 801; Stage II represents 129 patients; and Stage III represents 202 patients.

SOURCE: Adapted from Cancer, 86, Steele GS, Richie JP, Stewart AK, and Menck HR, The National Cancer Data Base report on patterns of care for testicular carcinoma, 1985–1996, 2,171–2,183,. Copyright 1999, wiht permission from Wiley.

Survival rates by year of diagnosis from 1976 to 2000 are given in Table 16.

Biggs and Schwartz evaluated the relationship between survival and ethnicity in their examination of 16,086 cases from the SEER database between 1973 and 1999 (Table 17) (13). Survival rates after a diagnosis of testicular cancer were high, with only 886 deaths among 16,086 patients. After multivariate analysis was performed to control for stage, histology, and period of diagnosis (Table 18), African American,

Table 19. United States death rates[a] for testicular cancer, age-adjusted, by race and age

	All Males			White Males			Black Males		
	All	< 50	≥ 50	All	< 50	≥ 50	All	< 50	≥ 50
Year of Diagnosis									
1975	0.7	0.7	0.7	0.8	0.8	0.8	…	…	…
1976	0.7	0.7	0.7	0.8	0.8	0.7	0.4	…	…
1977	0.6	0.7	0.6	0.7	0.7	0.6	…	…	…
1978	0.6	0.6	0.5	0.6	0.6	0.6	0.2	…	…
1979	0.5	0.5	0.6	0.5	0.5	0.6	0.4	…	…
1980	0.5	0.4	0.5	0.5	0.5	0.5	…	…	…
1981	0.4	0.4	0.4	0.4	0.4	0.4	…	…	…
1982	0.4	0.4	0.4	0.4	0.4	0.4	…	…	…
1983	0.4	0.4	0.4	0.4	0.4	0.4	…	…	…
1984	0.3	0.3	0.4	0.4	0.4	0.4	…	…	…
1985	0.4	0.3	0.4	0.4	0.3	0.4	…	…	…
1986	0.3	0.3	0.3	0.3	0.4	0.4	…	…	…
1987	0.3	0.4	0.3	0.4	0.3	0.3	…	…	…
1988	0.3	0.3	0.4	0.3	0.3	0.4	…	…	…
1989	0.3	0.3	0.3	0.3	0.3	0.3	0.2	…	…
1990	0.3	0.3	0.2	0.3	0.3	0.2	…	…	…
1991	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
1992	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
1993	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
1994	0.3	0.3	0.2	0.3	0.3	0.2	…	…	…
1995	0.2	0.2	0.2	0.3	0.3	0.3	…	…	…
1996	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
1997	0.2	0.2	0.2	0.3	0.3	0.3	…	…	…
1998	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
1999	0.3	0.3	0.3	0.3	0.3	0.3	…	…	…
2000	0.2	0.3	0.2	0.3	0.3	0.2	0.2	…	…
2001	0.2	0.2	0.3	0.3	0.3	0.2	…	…	…
1997–2001	0.3	0.3	0.3	0.3	0.3	0.3	0.2	0.1	0.2

…data not available.

[a]NHS public use data file for the total US. Rates are per 100,000 and are age-adjusted to the International Agency for Researchon Cancer (IARC) world standard population.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Native American, Filipino, and Hawaiian men were found to have a 2- to 3.5-fold greater risk of dying than non-Hispanic Caucasian men. The risk of dying was 40% higher for Hispanic men than for non-Hispanics. Still, because of the high survival rates, these differences translate into a small absolute number of deaths. The authors postulate that the observed disparities may reflect biological differences in the tumor, patient comorbidities, or differences for which race is a proxy, including social, economic, and health insurance status; treatment options and uptake; healthcare access and utilization; and environment, cultural, and lifestyle factors (13).

Men with seminomas have better survival rates than do those with NSGCT. Survival data based on stage and divided between seminoma and NSGCT from the National Cancer Data Base (NCDB) are shown graphically in Figures 4a and 4b (11). The five-year survival rate for seminoma is 97.9%, and that for NSGCT is 96.5%. Although this may represent a difference in tumor biology and behavior between the two types of testicular cancer, it may also result from the finding that men with seminoma generally present at an earlier stage (Table 13).

Table 20. Age-adjusted death rates[a] for testicular cancer, 1997–2001, by race/ethnicity

Race/ethnicity	Rate per 100,000 persons 1997–2001	Annual Percent Change Trend 1992–2001
Total	0.3	-1.3
White	0.3	-1.4
White Hispanic[b]	0.2	-4.0
White Non-Hispanic[b]	0.3	-0.8
Black	0.2	2.3
Asian/Pacific Islander	…	…
N. American Native/Alaska Native	…	…
Hispanic[b]	0.2	-3.9

…data not available.

[a]Mortality data are analyzed from public use file provided by the National Center for Health Statistics (NCHS).

[b]Hispanic and Non-Hispanic are not mutually exclusive from Whites, Blacks, Asian/Pacific Islanders, and N. American Natives/Alaska Natives. Incidence data for Hispanics and Non-Hispanics do not include cases from Detroit, Hawaii, and Alaska Native Registry.

SOURCE: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 9 Regs Public-Use, (1973–2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.

Mortality

Testicular tumors are exceedingly curable, and mortality is very low. SEER data from 1997–2001 place the age-adjusted death rate from testicular cancer for American men at 0.3 per 100,000 (Table 19). The overall death rate from testicular germ cell tumors decreased by 71% between 1975 and 2001, from 0.7 per 100,000 to 0.2 per 100,000. During this period, the death rate decreased from 0.8 per 100,000 to 0.3 per 100,000 for Caucasian men and from 0.4 per 100,000 to 0.2 per 100,000 for African American men. These findings indicate that Caucasian males have a higher lifetime risk of dying from testicular cancer than do African Americans males (0.02% vs 0.01%) (Table 7).

Age-adjusted mortality rates from SEER for 1997–2001 for different ethnic groups are shown in Table

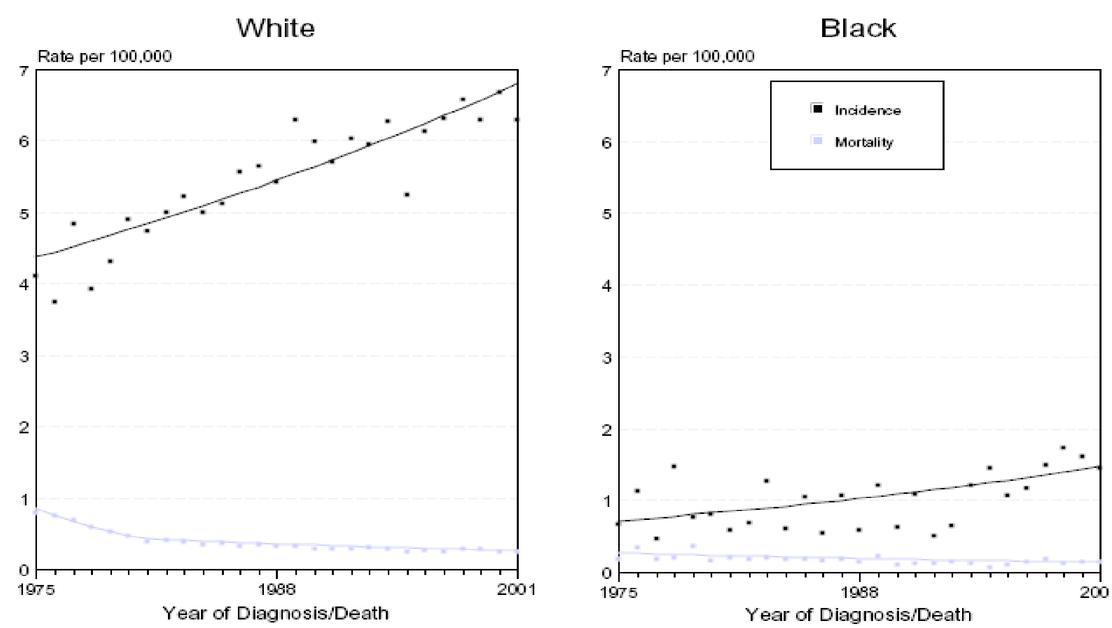

Figure 5. Incidence and death rates for testicular cancer, by race.

SOURCE: SEER 9 areas and NCHS public use data file for the total US. Rates are age-adjusted to the 2000 US standard million population by 5-year age groups. Regression lines are calculated using the Joinpoint Regression Program Version 2.7, September 2003, National Cancer Institute.

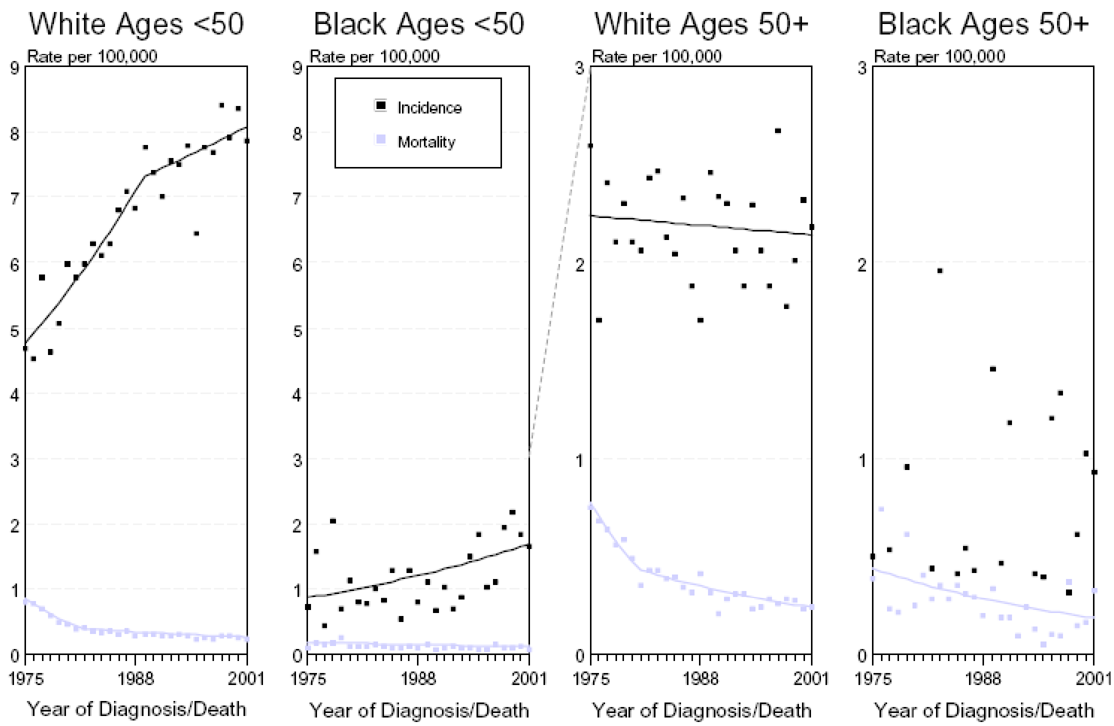

Figure 6. Incidence and death rates for testicular cancer, by age and race.

Regression line could not be calculated for the black ages 50+ incidence rates due to years with a rate of zero.

SOURCE: SEER 9 areas and NCHS public use data file for the total US. Rates are age-adjusted to the 2000 US standard million population by 5-year age groups. Regression lines are calculated using the Joinpoint Regression Program Version 2.7, September 2003, National Cancer Institute.

20. Caucasian men in the database had the highest mortality rates, at 0.3 per 100,000. However, from 1992 to 2001, the annual mortality rate for Caucasian men declined by 1.3%. While the annual mortality rate for African American men was lower than that for Caucasians, it increased by 2.3% between 1992 and 2001. No clear explanation for this divergence is apparent. It seems unlikely that the biology of testicular cancer in African American men has changed to make it more deadly. However, it is plausible that changes in epigenetic factors such as diet or environmental exposure could be worsening the prognosis. It is also possible that access to medical care or the treatment provided to African American men deteriorated over the decade under study. In fact, five-year relative survival rates for African American men declined between 1992 and 1994 (they have subsequently rebounded), as evidenced in Table 15.

SEER data for the incidence of testicular cancer and death rates among American men are presented in Figures 5 and 6. Incidence increased between 1975 and 2001, although the rate of increase slowed. The percentage increase was greater for Caucasians than for African Americans and was greatest in men under 50. During the same period, death rates fell. This decrease was greater for Caucasians than for African Americans, although overall mortality (much like incidence) is greater for American men of European descent. In the 1990s, there was a temporary increase in the annual percentage mortality rate for African American men, the only racial group to experience such a setback. Still, overall mortality from testicular cancer is quite low.

Table 21. Inpatient hospital stays for testicular cancer listed as primary diagnosis, count, rate[a] (95% CI), age-adjusted rate[b]

	1994			1996			1998			2000		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[c]	2,230	1.8 (1.6–2.0)	1.8	1,890	1.5 (1.3–1.7)	1.5	1,993	1.5 (0.9–2.2)	1.5	1,907	1.4 (1.2–1.6)	1.4
Age												
<18	*	*		*	*		*	*		*	*	
18–24	407	3.3 (2.4–4.2)		296	2.4 (1.7–3.1)		414	3.3 (1.5–5.1)		396	3.0 (2.2–3.8)	
25–34	951	4.7 (3.8–5.6)		771	3.9 (3.1–4.7)		732	3.8 (2.0–5.6)		647	3.5 (2.8–4.3)	
35–44	561	2.8 (2.3–3.4)		483	2.3 (1.8–2.8)		522	2.4 (1.4–3.4)		553	2.5 (2.0–3.1)	
45–54	158	1.1 (0.7–1.6)		*	*		*	*		151	0.8 (0.5–1.2)	
55–64	*	*		*	*		*	*		*	*	
65–74	*	*		*	*		*	*		*	*	
75–84	*	*		*	*		*	*		*	*	
85+	*	*		*	*		*	*		*	*	
Race/ethnicity												
White	1,526	1.7 (1.4–1.9)	1.7	1,221	1.3 (1.1–1.5)	1.3	1,333	1.4 (0.6–2.2)	1.5	1,027	1.1 (0.9–1.3)	1.1
Hispanic	176	1.4 (0.8–1.8)	1.1	138	1.0 (0.5–1.4)	0.9	*	*	1.1	289	1.8 (1.0–2.5)	1.5
Region												
Midwest	489	1.7 (1.2–2.1)	1.7	477	1.6 (1.2–2.0)	1.6	349	1.1 (0.7–1.6)	1.2	392	1.3 (0.9–1.6)	1.3
Northeast	686	2.8 (2.1–3.5)	2.8	345	1.4 (0.9–1.9)	1.4	*	*	3.0	334	1.4 (1.0–1.8)	1.4
South	579	1.4 (1.1–1.7)	1.4	610	1.4 (1.1–1.7)	1.4	455	1.0 (0.8–1.2)	1.0	575	1.2 (0.9–1.6)	1.2
West	475	1.7 (1.3–2.1)	1.7	458	1.6 (1.0–2.1)	1.5	443	1.5 (1.0–2.0)	1.4	606	2.0 (1.4–2.6)	2.0
MSA												
Rural	188	0.6 (0.4–0.8)	0.6	187	0.6 (0.4–0.9)	0.7	*	*	*	194	0.7 (0.4–0.9)	0.7
Urban	2,034	2.2 (1.9–2.5)	2.2	1,695	1.7 (1.4–2.0)	1.7	1,863	1.8 (1.0–2.7)	1.8	1,713	1.6 (1.4–1.9)	1.6

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 is based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[c]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Inpatient Care

Testicular cancer patients may require inpatient hospitalization for surgery (i.e., RPLND), chemotherapy, or any of the potential side effects of either. Currently, orchiectomy rarely requires hospitalization. According to the Healthcare Cost and Utilization Project (HCUP), the rate of national inpatient hospitalizations for testicular cancer as a primary diagnosis was 1.8 per 100,000 (2,230 admissions) in 1994 and 1.4 per 100,000 (1,907 admissions) in 2000 (Table 21). The age-adjusted hospitalization rate decreased slightly for Caucasian men and increased slightly for Hispanic men. No HCUP data are available for African American men with testicular cancer.

Hospitalization rates were highest in the 25- to 34-year-olds, followed by 18- to 24-year-olds, 35- to 44-year-olds, and 45- to 54-year-olds. This reflects the age distribution of men with testicular cancer. Little geographic variation exists, except in the Northeast, where hospitalization rates were nearly double those of all other regions in 1994. It is unclear whether this disparity results from financial considerations or differences in management practices by physicians in that geographical region. Admission rates were highest in urban areas, most likely reflecting the treatment of many testicular cancer patients in tertiary care centers of excellence for both complex surgery and chemotherapy.

The steady decline in hospitalizations in the HCUP data likely reflects (1) improved surgical technique, (2) trends among surgeons to shorten post-operative hospital stays, (3) outpatient orchiectomies, (4) decreases in the number of cycles of chemotherapy as primary treatment and the forgoing of some as adjuvant to RPLND, (5) greater reliance on outpatient chemotherapy, (6) improved management and support of patients receiving chemotherapy, and (7) increasing utilization of surveillance as a primary modality of treatment.

Outpatient Care

An individual with testicular cancer may be seen in the outpatient setting during diagnosis, treatment, and follow-up. This includes initial work-up, before and after orchiectomy, before and after any secondary surgeries (i.e., RPLND), during radiation and chemotherapy, and during surveillance for recurrence. Emergency room visits are exceeding rare; consequently, there is insufficient information on which to base any conclusions.

Physician Office Visits

In the Medicare data for 1992, 1995, 1998, and 2001, physician office visit rates increased significantly from 1992 to 1998 and then remained stable for men younger than 65 years of age (Table 22). For men older than 65, the age-adjusted rate varied minimally from 1992 to 2001. Variability was seen across geographic regions and racial/ethnic strata. Greater reliance on outpatient care resulted, not surprisingly, in increased physician office visits (corresponding to the decrease in inpatient hospitalizations (Table 21)).

Data regarding physician office visits by African American and Hispanic men are difficult to interpret due to small sample size; low counts preclude drawing firm conclusions regarding trends. However, for African American men, the rates of physician office visits fell steadily from 1992 to 2001 (with one exception, in 1998), with an overall ultimate decrease of 50%. A similar trend was seen in Hispanic men, for whom the number of physician office visits nearly tripled from 1995 to 1998, then subsequently fell by 40%. These racial/ethnic differences are difficult to explain but may be tied to the decreased survival rates for African American men in the 1990s mentioned earlier (Table 15). We have already noted that non-Caucasian testicular cancer patients present with later-stage disease (Table 10). Perhaps, in addition, non-Caucasian men are now presenting with more-aggressive tumors that require greater amounts of in-hospital care and are associated with worse survival outcomes.

Alternatively, the high rates of hospitalization and low rates of outpatient visits by non-Caucasian men with testicular cancer may reflect a reluctance of physicians to use surveillance or outpatient chemotherapy for minority populations. In addition, it is possible that the non-Caucasian men are more comfortable receiving more aggressive, definitive, and/or in-patient care and opt against outpatient

Table 22. Physician office visits by Medicare beneficiaries with testicular cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	4,360	29 (25–33)		6,080	40 (35–44)		5,940	41 (36–46)		6,240	40 (36–45)	
Total < 65	1,840	59 (47–71)		2,440	71 (58–83)		2,920	85 (71–99)		3,180	84 (71–97)	
Total 65+	2,520	21 (18–25)	23	3,640	31 (26–35)	31	3,020	27 (23–32)	27	3,060	26 (22–31)	26
Age												
65–69	660	16 (11–22)		1,440	37 (29–46)		680	20 (13–27)		1,240	35 (26–44)	
70–74	520	16 (9.8–22)		640	19 (13–26)		1,200	39 (29–49)		720	23 (16–31)	
75–79	740	33 (22–43)		1,000	44 (32–56)		520	23 (14–32)		700	29 (19–38)	
80–84	200	15 (5.8–25)		260	19 (8.6–29)		280	20 (9.7–31)		120	8.0 (1.6–14)	
85–89	160	27 (8.2–46)		100	16 (1.9–30)		340	52 (27–77)		120	17 (3.3–30)	
90–94	240	118 (51–186)		180	85 (29–141)		0	0		160	69 (21–117)	
95–97	0	0		20	53 (0–156)		0	0		0	0	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	3,840	31 (26–35)	30	5,300	41 (36–46)	41	5,400	44 (39–49)	44	5,620	43 (38–48)	43
Black	280	22 (10–33)	24	300	22 (11–33)	16	320	24 (12–36)	25	180	12 (4.2–20)	12
Asian	…	...	…	0	0	0	0	0	0	0	0	0
Hispanic	…	...	…	40	20 (0–48)	20	160	48 (15–81)	54	120	32 (6.4–58)	32
N. American Native	…	...	…	0	0	0	0	0	0	40	120 (0–285)	120
Region												
Midwest	860	23 (16–30)	25	1,700	44 (35–53)	43	1,440	39 (30–48)	40	1,340	35 (27–44)	37
Northeast	1,700	54 (42–65)	48	880	28 (19–36)	26	820	30 (20–39)	29	1,780	61 (48–74)	60
South	1,360	26 (20–32)	27	1,980	36 (29–43)	34	2,480	46 (38–54)	49	2,540	44 (36–51)	42
West	440	18 (11–26)	19	1,520	66 (51–80)	75	1,140	51 (38–64)	43	580	23 (15–32)	23

…data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.
[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.
[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 23. Hospital outpatient visits by Medicare beneficiaries with testicular cancer listed as primary diagnosis, count[a], rate[b] (95% CI), age-adjusted rate[c]

	1992			1995			1998			2001		
	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate	Count	Rate	Age-Adjusted Rate
Total[d]	1,800	12 (9.6–15)		820	5.4 (3.7–7.0)		1,060	7.3 (5.4–9.3)		460	3.0 (1.8–4.2)	
Total < 65	1,320	42 (32–52)		520	15 (9.3–21)		900	26 (19–34)		200	5.3 (2.0–8.5)	
Total 65+	480	4.1 (2.4–5.7)	4.2	300	2.5 (1.3–3.8)	2.4	160	1.4 (0.4–2.5)	1.4	260	2.2 (1.0–3.5)	2.2
Age												
65–69	100	2.5 (0.3–4.6)		180	4.7 (1.6–7.7)		80	2.4 (0.1–4.7)		120	3.4 (0.7–6.1)	
70–74	140	4.3 (1.1–7.5)		40	1.2 (0–2.8)		20	0.7 (0–1.9)		60	1.9 (0–4.2)	
75–79	160	7.1 (2.2–12)		60	2.6 (0–5.6)		60	2.6 (0–5.6)		80	3.3 (0.1–6.4)	
80–84	80	6.1 (0.2–12)		20	1.4 (0–4.2)		0	0		0	0	
85–89	0	0		0	0		0	0		0	0	
90–94	0	0		0	0		0	0		0	0	
95–97	0	0		0	0		0	0		0	0	
98+	0	0		0	0		0	0		0	0	
Race/ethnicity												
White	1,660	13 (10–16)	13	740	5.7 (3.9–7.5)	5.5	900	7.4 (5.2–9.5)	7.4	380	2.9 (1.6–4.2)	2.9
Black	20	1.6 (0–4.6)	1.6	20	1.4 (0–4.3)	1.4	20	1.5 (0–4.4)	1.5	60	4.1 (0–8.7)	4.1
Asian	…	...	…	0	0	0	20	15 (0–43)	15	0	0	0
Hispanic	…	...	…	20	10 (0–30)	10	120	36 (7.2–64)	36	20	5.3 (0–16)	5.3
N. American Native	…	...	…	0	0	0	0	0	0	0	0	0
Region												
Midwest	680	18 (12–25)	19	440	11 (6.6–16)	10	180	4.9 (1.7–8.1)	4.9	120	3.2 (0.6–5.7)	3.2
Northeast	540	17 (11–23)	16	180	5.7 (1.9–9.4)	5.7	80	2.9 (0.1–5.7)	2.9	80	2.7 (0.1–5.4)	2.7
South	200	3.8 (1.5–6.2)	3.8	80	1.5 (0–2.9)	1.5	620	12 (7.5–16)	12	120	2.1 (0.4–3.7)	2.1
West	380	16 (8.7–23)	15	120	5.2 (1.0–9.3)	6.0	160	7.2 (2.2–12)	7.2	120	4.8 (1.0–8.7)	4.8

…data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 male Medicare beneficiaries in the same demographic stratum.

[c]Age-adjusted to the US Census-derived age distribution of the year under analysis.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998, 2001.

Table 24. Use of chemotherapy during inpatient hospital stays for testicular cancer listed as primary diagnosis, count, rate[a] (95% CI), rate per 100,000 visits[b] (95% CI)

	1994			1996		
	Count	Rate	Rate per 100,000 visits for Testicular Cancer	Count	Rate	Rate per 100,000 visits for Testicular Cancer
Total	2,230	1.8 (1.6–2.0)		1,890	1.5 (1.3–1.7)	
Infusion of Chemotherapy Performed	364	0.3 (0.2–0.4)	16,323 (11,883–20,807)	298	0.2 (0.2–0.3)	15,767 (11,376–20,159)

	1998			2000		
	Count	Rate	Rate per 100,000 visits for Testicular Cancer	Count	Rate	Rate per 100,000 visits for Testicular Cancer
Total	1,993	1.5 (0.9–2.2)		1,907	1.4 (1.2–1.6)	
Infusion of Chemotherapy Performed	336	0.3 (0.2–0.3)	16,859 (11,139–22,529)	295	0.2 (0.2–0.3)	15,469 (10,383–20,556)

[a]Rate per 100,000 is based on 1994–2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male civilian non-institutionalized population.

[b]Rate per 100,000 male visits testicular cancer in HCUP_NIS 1994–2000.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 25. Estimated annual expenditures of privately insured employees with and without a medical claim for testicular cancer in 2002[a]

	Annual Expenditures (per person)					
	Males Age 18–54 without Testicular Cancer (N=285,095)			Males Age 18–54 with Testicular Cancer (N=236)		
	Medical	Rx Drugs	Total	Medical	Rx Drugs	Total
Total	$2,682	$1,035	$3,717	$8,816	$1,137	$9,953
Age						
18–34	$1,288	$654	$1,942	$6,905	$875	$7,780
35–44	$2,149	$875	$3,024	$6,443	$1,193	$7,636
45–54	$3,067	$1,211	$4,278	$9,680	$1,941	$11,621
Region						
Midwest	$2,584	$1,022	$3,606	$8,492	$1,126	$9,618
Northeast	$2,611	$1,122	$3,733	$8,580	$1,232	$9,812
South	$2,747	$969	$3,716	$9,029	$1,057	$10,086
West	$2,920	$1,058	$3,978	$9,596	$1,174	$10,770

Rx, Prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 2002. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments) and binary indicators for 28 chronic disease conditions. Predicted expenditures for males age 55 to 64 are omitted due to small sample size.

SOURCE: Ingenix, 2002.

treatment. Either way, this disparity requires further study.

Hospital Outpatient Visits

In the Medicare data for 1992, 1995, 1998, and 2001, age-adjusted outpatient hospital visit rates fell consistently from 1992 to 1998 before rebounding slightly in 2001, for an overall decrease of 48% (Table 23). The decrease was most notable in men younger than 65 years of age (an 88% decrease). Outpatient visits from 1992 to 2001 decreased by 83% in the Midwest and Northeast, 68% in the West, and 45% in the South. There is no clear explanation for this variation.

Caucasians experienced a drop in outpatient hospital visits of 78%. A decrease would be expected for men on surveillance and outpatient chemotherapy, as these treatments commonly taking place in physicians' offices. Table 24 confirms that inpatient chemotherapy is declining. From 1994 to 2000, the rate of inpatient chemotherapy infusions decreased by 33%.

An increase in hospital outpatient visits would also be expected if there were an increase in the number of men receiving radiotherapy. Hence, when the data presented in Table 23 are combined with the inpatient hospital and physician office visit data presented earlier, one can postulate that Caucasian testicular cancer patients are receiving increasing surveillance and in-office chemotherapy treatments, whereas non-Caucasians are receiving less surveillance and more primary therapy, including radiation and procedures that require hospitalization, such as surgery and high-dose chemotherapy.

ECONOMIC IMPACT

According to data from the Ingenix dataset for 2002, the estimated annual expenditure for privately insured individuals between the ages of 18 and 54 with a diagnosis of testicular cancer was $9,953 (Table 25). Of this, $8,816 was for medical costs, and $1,137 was for prescription medications. The annual expenditure for males aged 18 to 54 without testicular cancer was $3,717. The difference of $6,236 (after controlling for differences in age distribution, median household income, type of health insurance, and 28 comorbid conditions) may be attributed to expenditures either directly or indirectly related to testicular cancer.

Men 45 to 54 years of age had the highest annual expenditure (Table 25), although sample sizes were small. Moreover, this age group had an increase in medication costs, which were 70% greater than the mean medication costs for all age groups. This may reflect a greater use of chemotherapy in the older patient population and a greater reliance on surgery and/or observation in younger patients. When stratified by region, costs were fairly consistent and generally correlated with expenditures of men without testicular cancer (Table 25).

National estimates of annual medical expenditures place the total cost of treating testicular cancer at $21.8 million in 2000 (exclusive of medications) (Table 26), an increase of 10% over the total in 1994. Between 1994 and 2000, the percentage of total costs attributed to hospital outpatient visits remained stable at 7.7% to 8.7%, the percentage of ambulatory surgery costs remained stable at 14.9% to 16.8%, and inpatient costs decreased slightly, from 77.4% to 74.6%. Again, this reflects the trends already discussed, with care being transferred to the office and outpatient settings.

Table 26. Expenditures for testicular cancer, by site of service (% of total)

Service Type	1994		1996		1998		2000	
Hospital Outpatient	$1,521,508	7.7%	$1,638,654	8.7%	$1,740,460	8.4%	$1,885,498	8.7%
Physician Office	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Ambulatory Surgery	$2,941,777	14.9%	$3,168,275	16.9%	$3,365,113	16.2%	$3,645,539	16.8%
Emergency Room	---	0.0%	---	0.0%	---	0.0%	---	0.0%
Inpatient	$15,300,472	77.4%	$13,966,091	74.4%	$15,642,173	75.4%	$16,214,464	74.6%
TOTAL	$19,763,756		$18,773,020		$20,747,745		$21,745,500	

SOURCE: National Ambulatory and Medical Care Survey; National Hospital and Ambulatory Medical Care Survey; Healthcare Cost and Utilization Project; Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 27. Mean inpatient cost per child admitted with testicular cancer listed as primary diagnosis, count, mean cost[a] (95% CI)

	1999			2000			2001		
	Count	Mean Cost		Count	Mean Cost		Count	Mean Cost	
Total	23	$9,177	(6,282–12,073)	23	$20,603	(10,141–31,066)	44	$21,892	(8,574–35,210)
Age									
0–2	2	$3,955	(2,748–5,162)	5	$18,629	(0–51,259)	9	$5,663	(3,760–7,565)
3–10	6	$9,817	(639–18,995)	2	$12,895	(0–66,586)	6	$10,390	(3,009–17,771)
11–17	14	$9,737	(6,012–13,462)	15	$23,445	(9,003–37,886)	26	$22,850	(7,664–38,035)
18–24	1	$7,947	...	1	$3,272	…	3	$85,286	(0–397,727)
Race/ethnicity									
White	19	$9,907	(6,698–13,115)	12	$14,138	(3,672–24,603)	28	$15,030	(9,324–20,736)
Black	1	$11,700		6	$32,129	(0–68,690)	5	$46,139	(0–147,741)
Asian	1	$0		1	$65,623	…	1	$3,861	…
Hispanic	0	$0		2	$7,270	(0–17,023)	7	$39,275	(0–117,340)
N. American Native	0	$0		0	$0		0	$0	
Missing	1	$0		1	$22,515	…	3	$10,975	(0–26,967)
Other	1	$11,151		1	$8,774	…	0		
Region									
Midwest	7	$8,484	(2,457–14,510)	9	$23,815	(839–46,792)	14	$11,991	(2,670–21,311)
Northeast	2	$8,752	(0–19,102)	1	$3,272	…	3	$82,816	(0–400,428)
South	9	$10,291	(4,837–15,746)	11	$20,520	(5,235–35,804)	20	$22,382	(2,877–41,887)
West	4	$10,391	(0–24,094)	2	$15,276	(0–107,250)	7	$14,184	(5,690–22,677)
Missing	1	$0		0	$0		0	$0	

…data not available.

[a]Calculated using adjusted ratio of costs to charges, including variable and fixed cost among participating children's hospitals.

SOURCE: National Association of Children's Hospitals and Related Institutions, 1999–2001.

Testicular cancer is rare in pre-pubertal males. However, data from the National Association of Children's Hospitals and Related Institutions (NACHRI) database indicate that the mean inpatient cost per child with testicular cancer listed as a primary diagnosis was $21,892 in 2001, a 2.3-fold increase over the cost in 1999 (Table 27). In summary data from 1999–2001, increases in costs correlated directly with increases in age: males 11 years of age and older with a primary diagnosis of testicular cancer had costs nearly three times greater than those for patients 10 and under. This may be due to the fact that older children admitted to inpatient facilities had a higher proportion of recurrent cancers involving more-intensive care, while younger patients were admitted for their initial cancer procedure.

Marketscan data from 1999 allow assessment of the impact of a diagnosis of testicular cancer on employment (Table 28). Most men with testicular cancer are in the age range where they would be either enrolled in school or employed. Market scan data indicate that 16% percent of men with testicular cancer missed work for treatment of the disease. An average of 0.7 hour of work was missed for inpatient hospitalization, and 7.7 hours were missed for outpatient visits. Hence, the average total hours of work missed was 8.4. This suggests that most of the men with testicular cancer were under surveillance or underwent primary treatment prior to 1999, either of which would result in only occasional follow-up visits to a physician's office. Overall, the impact of testicular cancer on the workplace seems limited.

CONCLUSIONS

Testicular cancer is relatively uncommon, constituting less than 1% of all male malignancies. Still, it is currently the most common cancer in men 20 to 34 years of age. Although the incidence of testicular cancer in the United States continues to rise, the rate of increase is slowing. The reasons for this are unknown, although there is speculation that an increase in environmental endocrine disruptions may play a role (15).

Fortunately, testicular tumors are exceedingly curable. Their successful treatment represents a

Table 28. Average annual work loss of males treated for testicular cancer

	Number of Workers[a]	% Missing Work	Average Work Absence (hrs) Inpatient[b]		Outpatient[b]		Total	
Total	45	16%	0.7	(0–2.1)	7.7	(0–19.5)	8.4	(0–20.3)
Age								
18–29	5	0%	0		0		0	
30–39	16	19%	2	(0–6.3)	0.8	(0–1.9)	2.8	(0–7.1)
40–49	18	17%	0		17.9	(0–48.6)	17.9	(0–48.6)
50–64	6	17%	0		1.8	(0–6.5)	1.8	(-0–6.5)
Region								
Northeast	4	0%	0		0		0	
North Central	15	13%	0		1.3	(0–3.1)	1.3	(0–3.1)
South	18	17%	1.8	(0–5.5)	2.9	(0–8.5)	4.7	(0–11.2)
West	5	40%	0		54.7	(0–198.3)	54.7	(0–198.3)
Unknown	3	0%	0		0		0	

[a]Individuals with an inpatient or outpatient claim for testicular cancer and for whom absence data were collected. Work loss based on reported absences contiguous to the admission or discharge dates of each hospitalization or the date of the outpatient visit.

[b]Inpatient and outpatient include absences that start or stop the day before or after a visit.

SOURCE: Marketscan Health and Productivity Management, 1999.

medical triumph and underscores the strength of multimodality therapy. Overall, the death rate from testicular cancer continues to decrease. However, African American men have experienced a slight decline in survival, possibly due to differences in access to care.

Modifications in surgical technique and radiotherapy, as well as improved methods of employing systemic chemotherapy, have substantially diminished the morbidity of therapy. More patients are being treated with surveillance for early-stage disease. In Caucasian men, who are the vast majority of testicular cancer patients, care has shifted to the outpatient setting. Because of these successes, however, the treatment paradigms for testicular cancer are changing. As a result, there is little standardization in treatment approaches. This, coupled with the relative rarity of testicular cancer and subsequent limited database information, makes evaluation for a project such as Urologic Diseases in America very difficult. There is a need to collect more-comprehensive, detailed information so that the burden of testicular cancer on patients and the economy can be better evaluated.

Several recent high-profile celebrity and athlete cases of testicular cancer and their attendant publicity have increased awareness of the disease. This may mitigate fear and embarrassment and encourage men to seek care.

RECOMMENDATIONS

The underlying limitations to this analysis are that testicular cancer is a relatively rare disease and it occurs in young men, a population that is not routinely captured in database studies. The following efforts could improve data collection and analysis.

Classification and Coding

- ICD and CPT codes should be more detailed, and greater attention should be given to the therapeutic management options most germane to testicular cancer: surveillance, specifying orchiectomy for testicular cancer and differentiating *de novo* and post-chemotherapeutic RPLND, and denoting when radiotherapy and chemotherapy are given as a primary treatment or in the salvage setting.
- The underlying causes of infertility in men with testicular cancer (for example, innate, post-RPLND anejaculation, and/or chemotoxicity) should be detailed more thoroughly in database studies.
- Terminology and coding need to be standardized.

Data Collection

- Data should be collected with attention to accurate staging information.
- An objective and standardized staging system (see Table 2) should be used.
- Terms such as "early" and "late" disease are subjective and should be discouraged.
- Clinical and pathologic staging data should be separated and detailed individually.
- Data should be collected with attention to histology.
- Data should be collected with strict regard to risk stratification, which takes into consideration clinical, radiographic, serologic, and pathologic features.

Impact on Education

- Since many men with testicular cancer are enrolled in college or other educational institutions, the impact of a diagnosis on education should be evaluated. Relevant questions include:
    - How much school is missed? Is graduation delayed?
    - What is the financial impact of missing school after tuition has been paid?

Racial/Ethnic Data

Several disturbing and provocative findings with regard to racial disparities need to be addressed:

- Why did African American men experience a decline in survival rates in the 1990s?
- Are there genetic and biological differences in testicular cancer among different ethnic groups?
- Why do treatment patterns for testicular cancer appear to be different for Caucasian and non-Caucasian patients?
- Why is the treatment of minority children with testicular cancer more expensive than that of Caucasian children?
- Is there a racial disparity in the treatment of testicular cancer? If so, how do we rectify the situation?

REFERENCES

1. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ. Cancer statistics, 2005. CA Cancer J Clin 2005;55:10-30.
2. McGlynn KA, Devesa SS, Sigurdson AJ, Brown LM, Tsao L, Tarone RE. Trends in the incidence of testicular germ cell tumors in the United States. Cancer 2003;97:63-70.
3. Schned A. The pathology of germ-cell cancers of the testes. In: Testicular and Penile Cancer. Ernstork M, Heaney, JA, Peschel, RD, ed: Blackwell Science, 1998;11-28.
4. Jacobson AI LP. Tumor markers in germ cell tumors of the testis. BC Decker.
5. Richie JP. Neoplasms of the testis. In: Campbell's Urology. Walsh PC, Retik AB, Vaughn ED, Wein AJ, eds. WB Saunders, 1998;2411-52.
6. U.S. Preventive Services Task Force. Screening for Prostate Cancer, 2002. Available at: http://www.ahrq.gov/clinic/uspstf/uspsprca.htm#related.
7. Garner MJ, Turner MC, Ghadirian P, Krewski D. Epidemiology of testicular cancer: an overview. Int J Cancer 2005;116:331-9.
8. Paltoo DN, Chu KC. Patterns in cancer incidence among American Indians/Alaska Natives, United States, 1992-1999. Public Health Rep 2004;119:443-51.
9. Schmoll HJ, Souchon R, Krege S, Albers P, Beyer J, Kollmannsberger C, Fossa SD, Skakkebaek NE, de Wit R, Fizazi K, et al. European consensus on diagnosis and treatment of germ cell cancer: a report of the European Germ Cell Cancer Consensus Group (EGCCCG). Ann Oncol 2004;15:1377-99.
10. Stephenson AJ, Sheinfeld J. The role of retroperitoneal lymph node dissection in the management of testicular cancer. Urol Oncol 2004;22:225-33; discussion 234-5.
11. Steele GS, Richie JP, Stewart AK, Menck HR. The National Cancer Data Base report on patterns of care for testicular carcinoma, 1985-1996. Cancer 1999;86:2171-83.
12. McKiernan JM, Goluboff ET, Liberson GL, Golden R, Fisch H. Rising risk of testicular cancer by birth cohort in the United States from 1973 to 1995. J Urol 1999;162:361-3.
13. Biggs ML, Schwartz SM. Differences in testis cancer survival by race and ethnicity: a population-based study, 1973-1999 (United States). Cancer Causes Control 2004;15:437-44.
14. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Public-Use, Nov 2004 Sub (1973-2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.
15. Hardell L, Van Bavel B, Lindstrom G, Carlberg M, Eriksson M, Dreifaldt AC, Wijkstrom H, Starkhammar H, Hallquist A, Kolmert T. Concentrations of polychlorinated biphenyls in blood and the risk for testicular cancer. Int J Androl 2004;27:282-90.

CHAPTER 18

Urinary Tract Infection in Women

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Urinary Tract Infection in Women

Tomas L. Griebling, MD

INTRODUCTION

Urinary tract infection is an extremely common condition that occurs in both males and females of all ages. The prevalence and incidence of urinary tract infection is higher in women than in men, which is likely the result of several clinical factors including anatomic differences, hormonal effects, and behavior patterns.

DEFINITION AND DIAGNOSIS

Urinary tract infection (UTI) is caused by pathogenic invasion of the urinary tract, which leads to an inflammatory response of the urothelium. Infections may be acute or chronic. The clinical manifestations of UTI depend on the portion of the urinary tract involved, the etiologic organism(s), the severity of the infection, and the patient's ability to mount an immune response to it. Signs and symptoms may include fever, chills, dysuria, urinary urgency, frequency, and cloudy or malodorous urine.

Bacteriuria refers to the presence of bacteria in the urine, but this is not equivalent to UTI. A UTI includes the inflammatory response and the associated signs and symptoms that result from the presence of the bacteria. Bacteriuria may be asymptomatic, particularly in elderly adults. *Pyuria* refers to the presence of white blood cells in the urine. It is a marker of inflammation in response to bacterial infection.

Infections in the urinary system are often classified by the anatomic site or organ involved, although the entire urinary tract may be affected. *Pyelonephritis* refers to a urinary tract infection involving the kidney. This may be an acute or chronic process. Acute pyelonephritis is characterized by fever, chills, and flank pain. Patients may also experience nausea and vomiting, depending on the severity of the infection and whether there is any obstruction to the flow of urine out of the renal collecting system. The risk of renal damage in most patients with uncomplicated UTI is low, even in those with uncomplicated acute pyelonephritis. Chronic pyelonephritis implies recurrent renal infections and may be associated with the development of renal scarring and impaired function if obstruction is present. A perinephric abscess may develop in severe cases of pyelonephritis. The clinical distinction between upper and lower UTI may be difficult, particularly in women.

Cystitis is an inflammatory process of the urinary bladder, typically caused by bacterial infection. It may be acute or chronic in nature. *Urethritis* refers to an inflammation or infection of the urethra. This often occurs in combination with cystitis and may be difficult to differentiate. Isolated bacterial urethritis is rare in women. Vaginitis and cervicitis, often related to sexually transmitted organisms, may also cause symptoms attributed to cystitis or urethritis.

Recurrent UTIs involve reinfection from a source outside the urinary tract or from bacterial persistence within it. In each case, the infections may be caused by the same or different organisms. The vast majority of recurrent UTIs in women are due to reinfection.

The standard ICD-9 diagnostic codes for UTI (Table 1) were used for the analyses presented in this chapter. These codes are categorized primarily on the

Table 1. Codes used in the diagnosis and management of female urinary tract infection

Females 18 years or older with one of the following ICD-9 diagnosis codes:	
Cystitis	
112.2	Candidiasis of other urogenital sites
120.9	Schistosomiasis, unspecified
595.0	Acute cystitis
595.1	Chronic interstitial cystitis
595.2	Other chronic cystitis
595.3	Trigonitis
595.89	Other specified types of cystitis
595.9	Cystitis, unspecified
646.6	Infections of genitourinary tract in pregnancy
760.1	Maternal renal and urinary tract diseases affecting fetus or newborn
Pyelonephritis	
590.0	Chronic pyelonephritis
590.00	Chronic pyelonephritis without lesion of renal medullary necrosis
590.01	Chronic pyelonephritis with lesion of renal medullary necrosis
590.1	Acute pyelonephritis
590.10	Acute pyelonephritis without lesion of medullary necrosis
590.11	Acute pyelonephritis with lesion of renal medullary necrosis
590.2	Renal and perinephric abscess
590.3	Pyeloureteritis cystica
590.8	Other pyelonephritis or pyonephrosis, not specified as acute or chronic
590.9	Infection of kidney, unspecified
593.89	Other specified disorders of kidney and ureter
Other	
597.89	Other urethritis
599.0	Urinary tract infection site not specified
646.5	Asymptomatic bacteriuria in pregnancy

basis of the site and type of infection involved. The primary categories include cystitis, pyelonephritis, and other infections. Common definitions are used here to permit comparisons among datasets.

The diagnosis of UTI may be made presumptively on the basis of clinical signs and symptoms in combination with urinalysis results. A urinalysis that reveals both bacteriuria and pyuria is considered clinically diagnostic of UTI. Traditionally, confirmatory cultures have been obtained to verify the infection and identify the specific organism(s) involved; however, this standard is evolving. If a culture is obtained, the presence of at least 10^5 colony-forming units (CFU) of bacteria on a voided specimen has classically been used as the culture-based definition of UTI. Lower colony counts (100 CFU) may be used to establish a clinical diagnosis in catheterized or aspirated specimens from symptomatic patients. Bacterial colonization of indwelling catheters is common, and it may be difficult to distinguish between this phenomenon and symptomatic UTI requiring therapy. Drug susceptibility data are typically obtained to verify that appropriate therapy has been selected. The increased prevalence of drug-resistant bacteria has made susceptibility testing particularly important.

RISK FACTORS

Research has identified a number of risk factors for UTI in women. Women are at greater risk for UTI than men, partly because of the relatively short, straight anatomy of the urethra. Retrograde ascent of bacteria from the perineum is the most common cause of acute cystitis in women. Host factors such as changes in normal vaginal flora may also affect the risk of UTI. Genetic factors, including expression of HLA-A3 and Lewis blood group Le(a-b-) or Le(a+b-), may also put women at higher risk for recurrent UTI. Sexually active women are at greater risk for UTI than women who do not engage in sexual intercourse. Simple hygiene habits, including voiding before and after sexual intercourse and wiping from anterior to posterior, are often advocated to decrease the risk of UTI; however, a recent review found no advantage to these behavioral techniques (1). Contraceptive use may affect the rate of UTI, which appears to be greater in women who use certain types of spermicides. Hematogenous and lymphatic spread of bacteria to the urinary tract is uncommon in healthy patients.

Vesicoureteral reflux has been identified as a risk factor for the development of pyelonephritis. This is most commonly diagnosed in children, but it may also be identified in adults. Patients with recurrent pyelonephritis warrant anatomic evaluation, usually with a voiding cystourethrogram to identify evidence of reflux.

A foreign body in the urinary system may act as a nidus for infection and may be associated with recurrent infections. Common examples include urinary calculi and indwelling catheters. Indwelling urinary catheters are associated with chronic bacterial colonization, which occurs in almost all patients after five to seven days. This colonization significantly increases the risk for symptomatic UTI. Catheter modifications with antibiotic and silver impregnation have been developed in an effort to decrease the rate of infection in patients with indwelling catheters (2). Urea-splitting organisms are often associated with UTI in the presence of stones.

Post-menopausal women are at higher risk for UTI than younger women are, because they lack estrogen, which is essential to maintain the normal acidity of vaginal fluid. This acidity is critical to permit the growth of *Lactobacillus* in the normal vaginal flora, which acts as a natural host defense mechanism against symptomatic UTI. Restoration of the normal hormonal milieu in the vagina is not effective treatment for active urinary tract infections, but it may be useful for prevention. Other urologic factors potentially associated with an increased risk of UTI in post-menopausal women include urinary incontinence, cystocele, and elevated volumes of post-void residual urine.

Urinary tract infections are often characterized as *uncomplicated* if they involve only the bladder and are not associated with the presence of foreign bodies or anatomic abnormalities. *Complicated* UTIs may include pyelonephritis, urosepsis and the presence of foreign bodies or anatomic disorders. Significant UTIs in elderly patients are often classified as *complicated* due to the increased risk of associated morbidity and mortality in this population.

Urinary tract infections may be caused by a variety of different organisms, most commonly bacteria. The most frequent bacterial cause of UTI in adult women is *Escherichia coli*, which is part of the normal gut flora. This organism accounts for approximately 85% of community-acquired UTIs and 50% of hospital-acquired UTIs. Other common organisms include *Enterococcus faecalis, Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*. Nosocomial infections and those associated with foreign bodies may involve more aggressive organisms such as *Pseudomonas aeruginosa, Serratia, Enterobacter, and Citrobacter species*.

Nonbacterial infections are less common and tend to occur more often in immunosuppressed individuals or those with diabetes mellitus. Fungal infections with *Candida spp* are the most common nonbacterial infections. Other less common urinary tract pathogens include *Mycobacterium tuberculosis* and a variety of anaerobic organisms. The overall role of anaerobic urinary infections is controversial; however, anaerobes may be especially dangerous in immunocompromised patients due to an increased risk of severe infections such as emphysematous pyelonephritis or cystitis. Bilharzial cystitis is uncommon in the United States but may be seen in patients who have recently immigrated or traveled to areas of the world where schistosomes are endemic.

Research on the physiology and microbiology of urinary tract infections has identified a number of organism and host factors that may increase the risk for UTI. Disruption of the urothelium due to trauma or other irritation may increase the ability of organisms to adhere to tissue and cause infection. Bacteria may develop a number of mechanisms such as pili, fimbriae, and chemical adhesins that increase their ability to adhere to host tissues.

PREVALENCE AND INCIDENCE

Urinary tract infection is an extremely common diagnosis in women, and treatment incurs substantial costs. It is estimated that at least one-third of all women in the United States are diagnosed with a UTI by the time they reach 24 years of age (3). In a random-digit-dialing telephone survey of 2,000 women, Foxman and colleagues found that 10.8% of women 18 years of age or older self-reported at least one UTI in the previous 12 months (95% CI, 9.4–12.1) (Figure

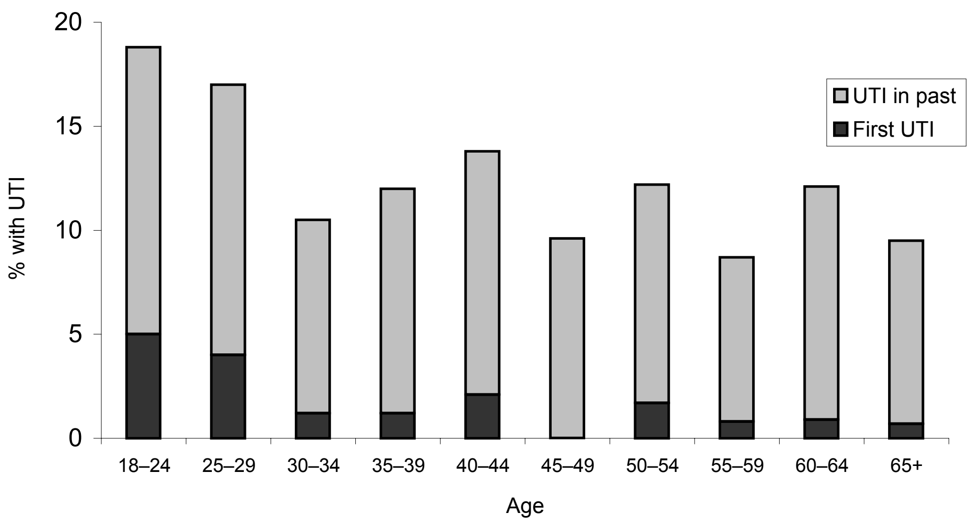

Figure 1. Self-reported incidence of physician-diagnosed urinary tract infection during the previous 12 months by age and history of urinary tract infection among 2000 United States women participating in a random digit dialing survey. The average standard error for the total incidences in each of the age groups is 2.3%.

SOURCE: Adapted from Annals of Epidemiology, 10, Foxman B, Barlow R, D'Arcy H, Gillespie B, and Sobel JD, Urinary tract infection: self-reported incidence and associated costs, 509–515, Copyright 2000, with permission from Elsevier Science.

Table 2. Female lifetime prevalence of urinary tract infections, by sociodemographic group, count, rate[a]

	Incidence	
	Count	Rate
Total count[b]	50,810,018	53,067
1–2 bladder infections ever	26,871,194	28,065
3+ bladder infections ever	23,938,824	25,002
Mean number of infections in the last 12 months of those ever having UTI	0.40	...
Race/ethnicity		
White non-Hispanic	41,641,569	55,937
Black non-Hispanic	5,129,383	45,976
Hispanic	3,195,829	45,550
Other	843,238	26,937
Region		
Midwest	12,081,920	52,335
Northeast	9,508,670	47,039
South	18,116,413	54,924
West	11,103,015	57,048
Urban/rural		
MSA	24,236,785	34,135
Non-MSA	26,573,233	107,393

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1991 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]The data in this table are based on the weighted number of persons who responded “1 or more” to question HAK4: “How many times have you had a bladder infection, also called urinary tract infection, UTI or cystitis?”

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Health and Nutrition Examination Survey III, 1988–1994.

Table 3. Female incidence of UTIs in past 12 months, by sociodemographic group, count, rate[a]

	Incidence	
	Count	Rate
Total count[b]	12,753,035	13,320
1 or more bladder infections in the last 12 months	12,753,035	13,320
Mean number of infections in the last 12 months	1.7	...
Age		
18–24	2,741,548	21,732
25–34	3,274,713	15,196
35–44	2,338,316	11,925
45–54	1,531,348	11,550
55–64	1,129,215	10,105
65–74	930,627	9,225
75–84	619,903	10,577
85+	187,365	11,770
Race/ethnicity		
White non-Hispanic	9,949,997	13,366
Black non-Hispanic	1,572,606	14,096
Hispanic	1,017,401	14,501
Other	213,032	6,805
Region		
Midwest	2,518,030	10,907
Northeast	2,346,347	11,607
South	5,037,597	15,273
West	2,851,061	14,649
Urban/rural		
MSA	6,425,838	9,050
Non-MSA	6,327,198	25,571

...data not available.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1991 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]The data in this table are based on the weighted number of persons who responded “1 or more” to question HAK5: “How many of these infections did you have during the past 12 months?”

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Health and Nutrition Examination Survey III, 1988–1994.

Table 4. Frequency of urinary tract infection (including cystitis, pyelonephritis, orchitis, and other) as a diagnosis in VA patients seeking outpatient care, rate[a]

	1999		2000		2001	
Sub-Conditions	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis
Male UTI[b]	2,082	2,705	1,963	2,591	1,719	2,334
Cystitis	136	177	131	175	111	161
Pyelonephritis	48	65	41	57	40	60
Orchitis	314	378	297	360	99	334
Other	1,649	2,187	1,555	2,097	1,351	1,868
Female UTI[b]	4,793	6,015	4,589	5,904	4,265	5,552
Cystitis	512	670	517	684	469	626
Pyelonephritis	72	81	55	71	64	78
Other	4,378	5,521	4,187	5,409	3,883	5,075

[a]Rate is defined as the number of unique patients with each condition (unweighted frequency or # of cases) divided by the base population in the same fiscal year (# unique SSNs per strata) x 100,000 to calculate the rate per 100,000 (# cases per 100,000 unique outpatients).

[b]Represents unique cases of UTI (i.e., patients with more than one UTI subtype are counted only once).

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

1). Using this information, the authors calculated the lifetime risk for UTI in their sample to be 60.4% (95% CI, 55.1–65.8). Using these data, the authors estimated that at least 11.3 million women in the United States had at least one UTI in 1995, and the overall cost of prescriptions to treat UTIs that year was more than $218 million.

Similarly, between 1988 and 1994, the overall lifetime prevalence of UTI was estimated to be 53,067 cases per 100,000 adult women, based on the National Health and Nutrition Examination Survey (NHANES-III) (Table 2). The prevalence in women was significantly higher than that estimated in men (13,689 cases per 100,000) in this study (Chapter 7, Table 2). Data from NHANES-III also shows the incidence of UTI in the past 12 months to be 13,320 per 100,000 adult women (Table 3).

Data from US Veterans Health Administration (VA) facilities revealed a similar disparity in the numbers of women and men seeking care for UTIs (Table 4). In 2001, the rate of women seeking outpatient care for cystitis was 626 cases per 100,000 (with 469 as the primary diagnosis), compared with 161 cases per 100,000 (111 as the primary diagnosis) in men. In contrast to cystitis, the overall prevalence of women seeking outpatient care for pyelonephritis was only slightly higher in women than in men: 78 cases per 100,000 (64 as the primary diagnosis) vs 60 cases per 100,000 (40 as the primary diagnosis). In the three years for which data are available (1999 to 2001), the overall frequency of an outpatient primary diagnosis of UTI in US female VA outpatient clinic patients gradually declined, from 4,793 per 100,000 to 4,265 per 100,000 (Table 5). Also, note that the prevalence rates in the VA data are much lower than those in NHANES because the VA identifies only UTIs for which patients sought medical attention in one year, whereas NHANES relies on self-reported UTI over a lifetime and hence presents a true population prevalence.

MORBIDITY AND MORTALITY

Urinary tract infections may be associated with significant morbidity and even mortality. This is particularly true in the frail elderly and in those with associated urinary incontinence, where UTI may be related to skin breakdown and ulceration. Complicated UTIs may lead to urosepsis and death; however, the risk of UTI-related mortality in the elderly and comorbid population is unknown. It is generally believed that asymptomatic bacteriuria in elderly patients does not need to be treated, although this issue is controversial (4). More commonly, UTI is associated with bothersome urinary symptoms that

Table 5. Frequency of urinary tract infection[a] as a diagnosis in female VA patients seeking outpatient care, rate[b]

	1999		2000		2001	
	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis
Total	4,793	6,015	4,589	5,904	4,265	5,552
Age						
18–25	4,396	5,154	4,852	5,878	4,431	5,325
25–34	4,969	5,840	4,726	5,705	5,051	6,063
35–44	4,547	5,634	4,370	5,525	3,909	5,087
45–54	4,624	5,841	4,451	5,717	4,127	5,366
55–64	4,543	6,081	4,645	6,320	4,273	5,729
65–74	5,097	6,843	4,887	6,677	4,040	5,681
75–84	5,546	7,395	4,818	6,598	4,229	5,979
85+	5,484	6,567	5,269	7,446	5,088	6,416
Race/ethnicity						
White	6,094	7,697	5,764	7,484	5,322	6,937
Black	5,735	7,182	5,280	6,664	4,942	6,403
Hispanic	6,672	8,556	5,801	7,605	5,666	6,922
Other	4,787	6,080	6,722	7,665	3,630	13,299
Unknown	3,255	4,038	3,209	4,111	3,048	3,976
Region						
Eastern	4,008	4,965	3,781	4,823	3,623	4,591
Central	4,640	5,871	4,696	5,939	4,195	5,456
Southern	5,313	6,747	4,888	6,489	4,482	6,002
Western	4,778	5,887	4,720	5,865	4,512	5,707
Insurance status						
No insurance/self-pay	4,792	5,957	4,658	5,928	4,375	5,576
Medicare/Medicare supplemental	6,064	7,828	5,308	7,192	4,791	6,692
Medicaid	5,229	6,536	5,482	6,360	5,915	6,839
Private insurance/HMO/PPO	4,001	5,146	3,829	4,914	3,428	4,559
Other insurance	4,174	4,973	3,697	4,736	3,512	4,484
Unknown	5,594	6,993	1,493	1,493	1,914	1,914

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for female urinary tract infections (including cystitis, pyelonephritis, and other UTIs).

[b]Rate is defined as the number of unique patients with each condition (unweighted frequency or # of cases) divided by the base population in the same fiscal year (# unique SSNs per strata) x 100,000 to calculate the rate per 100,000 (# cases per 100,000 unique outpatients).

NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 6. Prescribing trends from 1989 through 1998[a]

Antibiotic Prescribed	1989–1990	1991–1992	1993–1994	1995–1996	1997–1998	Adjusted Odds Ratio (95% Confidence Interval) for Predictor, Year (per decade)[b]
Trimethoprim-sulfamethoxazole	48	35	30	45	24	0.32 (0.20–0.51)
Recommended fluoroquinolones[c]	19	16	33	24	29	2.12 (1.26–3.56)
Nitrofurantoin	14	25	24	20	30	2.55 (1.50–4.31)
Overall non-recommended antibiotics[d]	33	49	36	32	46	1.57 (1.00–2.44)
No. of visits per 2-year period	208	178	181	192	227	n/a

[a]Unless otherwise indicated, data are percentages of patients.

[b]In all models, antibiotic prescribing was the dependent variable. All trends adjusted for age younger than 45 years and history of urinary tract infection.

[c]Recommended fluoroquinolones were defined as ciprofloxacin, ofloxacin, lomefloxacin, enoxacin, and fleroxacin.

[d]Non-recommended antibiotics were defined as all antibiotics other than trimethoprim or trimethoprim-sulfamethoxazole or recommended fluoroquinolones.

SOURCE: Reprinted from Huang ES, Stafford RS, National patterns in the treatment of urinary tract infections in women by ambulatory care physicians, Archives Internal Medicine, 162, 41–47, *Copyright © 2002, with permission from the American Medical Association*. All rights reserved.

can lead to work absence and decreased ability to engage in activities of daily living.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Medications

Antimicrobial therapy remains the mainstay of treatment for patients with UTIs. Bacterial urine cultures with appropriate drug susceptibility data should guide the selection of antimicrobials. However, most symptomatic patients require selection of therapy prior to the identification of the etiologic organism. Initial therapy is usually empiric, with subsequent modifications made on the basis of urine culture and susceptibility results as necessary. The need for urine culture is also an area of debate. Many experts advocate empiric therapy for most patients, with urine cultures reserved for those who fail to respond to treatment or have recurrent infections. The Infectious Disease Society of America published guidelines in 1999 that recommended the use of trimethoprim-sulfamethoxazole (TMP-SMX) as first-line therapy for patients without an allergy to this compound (5). Specific fluoroquinolones were recommended as second-line agents. In geographic

Table 7. Expenditures for female urinary tract infection and share of costs, by site of service (% of total)

Site of Service	1994	1996	1998	2000
Total[a]	$1,885,000,000	$1,944,300,000	$2,211,900,000	$2,474,000,000
Inpatient	$1,168,700,000 (62.0%)	$1,254,100,000 (64.5%)	$1,322,700,000 (59.8%)	$1,360,700,000 (55.0%)
Physician Office	$309,100,000 (16.4%)	$295,500,000 (15.2%)	$404,800,000 (18.3%)	$536,800,000 (21.7%)
Hospital Outpatient	$126,300,000 (6.7%)	$105,000,000 (5.4%)	$165,900,000 (7.5%)	$163,300,000 (6.6%)
Emergency Room	$280,900,000 (14.9%)	$289,700,000 (14.9%)	$318,500,000 (14.4%)	$413,200,000 (16.7%)

[a]Total unadjusted expenditures exclude spending on outpatient prescription drugs for the treatment of urinary tract infection. Average drug spending for UTI-related conditions (both male and female) is estimated at $96 million to $146 million annually for the period 1996 to 1998.

SOURCES: National Ambulatory Medical Care Survey, National Hospital Ambulatory Medical Care Survey, Healthcare Cost and Utilization Project, and Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

Table 8. Inpatient stays by female Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	114,640	579 (575–582)	127,460	632 (628–635)	128,380	674 (670–677)
Total < 65	8,480	355 (347–363)	9,400	350 (343–357)	11,200	403 (396–411)
Total 65+	106,160	609 (606–613)	118,060	675 (671–679)	117,180	720 (716–724)
Age						
65–74	27,880	303 (300–307)	27,300	303 (300–307)	24,760	313 (309–317)
75–84	42,180	715 (708–722)	46,980	785 (778–792)	46,480	796 (788–803)
85–94	31,700	1,527 (1,510–1,544)	37,660	1,694 (1,677–1,711)	39,460	1,774 (1,756–1,791)
95+	4,400	1,706 (1,656–1,757)	6,120	2,161 (2,108–2,215)	6,480	2,088 (2,038–2,139)
Race/ethnicity						
White	94,780	565 (561–568)	105,120	606 (602–609)	104,420	645 (642–649)
Black	13,540	803 (790–816)	17,280	939 (925–953)	17,180	974 (959–988)
Asian	…	…	300	318 (282–354)	740	418 (388–448)
Hispanic	…	…	1,660	826 (786–866)	3,040	827 (798–857)
N. American Native	…	…	200	1,238 (1,064–1,411)	380	1,457 (1,311–1,603)
Region						
Midwest	28,800	574 (567–580)	31,040	602 (595–609)	31,040	629 (622–636)
Northeast	21,000	463 (457–470)	23,980	534 (527–540)	23,660	604 (596–612)
South	50,760	726 (720–733)	56,420	781 (774–787)	57,940	826 (819–832)
West	12,780	448 (440–456)	14,420	504 (495–512)	14,040	517 (508–525)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

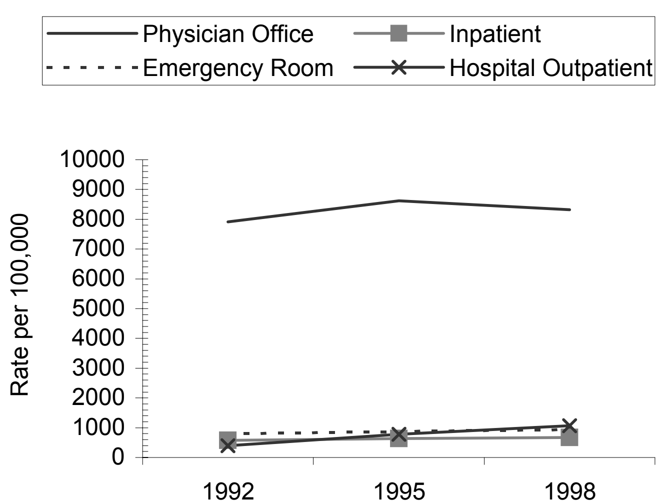

Figure 2. Trends in visits by females with urinary tract infection listed as primary diagnosis, by site of service and year.

SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

areas where resistance to TMP-SMX is high (>20%), fluoroquinolones are recommended as first-line therapy.

The recommendation to use older agents such as TMP-SMX as initial therapy has strong merit. These medications cost less than newer antimicrobials such as fluoroquinolones. In addition, reserving fluoroquinolones and broad-spectrum antimicrobials for complicated infections or cases with documented resistance to first-line therapy may help reduce the incidence of bacterial resistance. However, a recent study on the national trends in prescribing patterns for UTI in women among ambulatory care physicians revealed that the use of TMP-SMX is decreasing and the use of fluoroquinolones is increasing (6). The proportion of TMP-SMX use dropped from 48% in 1989–1990 to 24% in 1997–1998 (adjusted OR, 0.33; 95% CI, 0.21–0.52 per decade). At the same time, fluoroquinolone use increased from 19% to 29% (adjusted OR, 2.28; 95% CI, 1.35–3.83 per decade) (Table 6). This indicates that there is a trend toward using more-expensive antimicrobials such as fluoroquinolones as initial therapy. This trend may be due in part to increased rates of outpatient care and increased availability and marketing of these products. However, it has the potential to increase both overall costs and antimicrobial resistance.

Inpatient Care

Severe UTIs, particularly those associated with acute pyelonephritis, may require inpatient hospitalization for treatment with intravenous antimicrobials. In 2000, inpatient services constituted 55% of all expenditures for the treatment of UTI (Table 7). According to data from the Centers for Medicare and Medicaid Services (CMS), there was a gradual overall increase in the age-unadjusted rate of inpatient hospitalization for treatment of UTI in adult women between 1992 (579 per 100,000) and 1998 (674 per 100,000) (Table 8 and Figure 2). While the overall rate of inpatient stays for women 84 years of age and younger has remained relatively constant, there has been a dramatic increase in the rate of inpatient hospital stays for very elderly women. The rate for women 85 to 94 years of age increased from 1,527 per 100,000 in 1992 (95% CI, 1,510–1,544) to 1,774 per 100,000 in 1998 (95% CI, 1,756–1,791). The rate was even higher for women over 95, increasing from 1,706 per 100,000 in 1992 to 2,088 in 1998. Urinary tract infections may be more severe in frail elderly women due to additional comorbidity, and this may necessitate more aggressive treatment with inpatient hospitalization and intravenous antimicrobial therapy. African American women had higher rates of inpatient treatment than did other ethnic groups (1.1 to 2.95 times higher). Patients living in the South had higher rates of inpatient care than did women living in other regions.

Data from the Healthcare Cost and Utilization Project (HCUP) for the years from 1994 to 2000 indicate that the rate of inpatient hospitalization for a primary diagnosis of UTI has been generally decreasing for young and middle-aged women (18 to 54 years of age) and has been relatively stable overall for those aged 55 to 74 (Table 9). In addition, the overall rate of inpatient hospitalization is relatively low for young women, increasing approximately twofold when women reach the 65 to 74 age group. However, these data also demonstrate that there has been a gradual increase in the rate of inpatient hospitalizations for women 75 to 84 years of age when UTI is the primary admitting diagnosis. The most striking finding in the data is that women 85 and older had inpatient hospitalization rates 2.82 to 3.27 times higher than those of women in the 75 to 84 age range. This may be a reflection of the degree of associated morbidity and potential health impairment caused by UTI in elderly women. Nosocomial infections may also influence the rates of hospitalization in this patient group. It is unclear why estimated inpatient utilization rates are lower in HCUP data than in CMS data.

Acute pyelonephritis is a serious UTI often treated with intravenous antimicrobials, historically requiring inpatient care, although newer approaches include primary management with oral antimicrobials. Analysis of HCUP data for women admitted to the hospital for a primary diagnosis of pyelonephritis indicates that there was a gradual decline in the rate of admissions between 1994 and 2000 (Table 10). Pyelonephritis accounted for 28% of the female UTI hospitalizations in 1994 and 21% in 2000. The overall rate of admissions for pyelonephritis among women gradually declined from 65 per 100,000 (95% CI, 62–68) in 1994 to 49 per 100,000 (95% CI, 46–51) in 2000. This trend is reflected across essentially all age strata analyzed. It likely reflects increased use of oral

Table 9. Inpatient hospital stays by adult females with urinary tract infection (any anatomic location) listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	223,256	232 (223–240)	235,055	234 (226–243)	243,584	238 (230–246)	245,879	235 (227–242)
Age								
18–24	16,748	135 (126–144)	15,205	122 (114–130)	13,496	108 (101–115)	12,300	93 (87–99)
25–34	21,873	106 (99–113)	20,183	98 (92–105)	17,495	88 (83–94)	15,629	82 (76–87)
35–44	17,367	85 (80–90)	18,445	85 (80–89)	17,842	80 (75–84)	17,009	75 (71–79)
45–54	14,592	99 (93–105)	15,324	94 (88–100)	15,630	90 (85–94)	16,633	89 (85–93)
55–64	16,336	154 (145–163)	17,036	155 (146–164)	17,263	149 (142–156)	18,375	150 (144–157)
65–74	33,529	339 (324–355)	34,216	340 (324–356)	36,552	370 (353–387)	34,686	356 (342–370)
75–84	53,966	920 (881–960)	59,660	931 (892–970)	64,687	957 (922–992)	66,664	968 (935–1001)
85+	48,844	2,593 (2,477–2,709)	54,984	2,844 (2,725–2,962)	60,618	3,162 (3,038–3,286)	64,584	3,078 (2,975–3,182)
Race/ethnicity								
White	131,419	180 (172–187)	139,026	185 (177–193)	136,003	180 (173–187)	137,718	180 (174–187)
Black	26,970	234 (214–253)	28,841	239 (221–258)	24,887	200 (187–213)	23,177	180 (169–191)
Asian/Pacific Islander	1,856	68 (55–80)	1,914	56 (48–64)	2,423	64 (48–80)	3,351	83 (73–92)
Hispanic	12,829	156 (140–172)	14,359	159 (135–183)	15,865	162 (142–183)	16,430	154 (138–170)
Region								
Midwest	48,859	213 (197–228)	51,308	218 (204–233)	54,813	231 (215–247)	52,991	222 (209–236)
Northeast	47,668	235 (217–253)	44,923	223 (205–242)	47,095	232 (216–249)	47,204	229 (213–244)
South	92,109	281 (263–299)	98,838	277 (260–294)	101,638	280 (265–295)	103,304	278 (263–294)
West	34,620	170 (155–186)	39,986	189 (173–206)	40,038	182 (168–196)	42,380	183 (170–195)
MSA								
Rural	52,366	216 (200–232)	55,871	248 (230–265)	55,038	240 (225–255)	57,804	251 (236–265)
Urban	170,356	236 (226–246)	178,730	230 (220–239)	187,699	237 (227–246)	187,848	230 (221–238)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 10. Inpatient hospital stays by adult females with pyelonephritis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	62,223	65 (62–68)	61,949	62 (59–65)	54,933	54 (51–56)	50,881	49 (46–51)
Age								
18–24	12,008	97 (90–104)	11,075	89 (83–95)	9,607	77 (71–82)	8,645	65 (60–70)
25–34	14,709	72 (67–76)	13,483	66 (61–70)	11,131	56 (52–60)	9,613	50 (46–54)
35–44	9,765	48 (45–51)	10,267	47 (44–50)	9,364	42 (39–45)	8,664	38 (36–41)
45–54	6,656	45 (41–49)	7,075	44 (40–47)	6,339	36 (34–39)	6,380	34 (32–36)
55–64	5,045	48 (44–52)	5,328	48 (44–53)	4,686	40 (38–43)	4,870	40 (37–43)
65–74	6,420	65 (59–71)	6,348	63 (58–69)	5,694	58 (53–62)	5,220	54 (49–58)
75–84	5,078	87 (79–94)	5,661	88 (80–96)	5,433	80 (74–87)	4,999	73 (66–79)
85+	2,541	135 (118–151)	2,712	140 (124–157)	2,679	140 (123–156)	2,490	119 (106–132)
Race/ethnicity								
White	34,772	48 (45–51)	33,882	45 (43–47)	28,732	38 (36–40)	25,448	33 (32–35)
Black	7,718	67 (60–74)	7,792	65 (59–70)	5,493	44 (40–48)	4,712	37 (33–40)
Asian/Pacific Islander	754	28 (22–33)	636	19 (15–22)	824	22 (15–29)	918	23 (18–28)
Hispanic	4,711	57 (50–64)	5,374	60 (47–72)	5,151	53 (44–61)	5,206	49 (42–55)
Region								
Midwest	14,047	61 (56–66)	13,962	59 (54–65)	11,931	50 (46–55)	11,378	48 (44–52)
Northeast	11,335	56 (51–61)	10,185	51 (46–56)	9,490	47 (41–53)	8,246	40 (36–43)
South	24,287	74 (67–81)	24,009	67 (62–73)	21,362	59 (55–63)	19,969	54 (50–58)
West	12,554	62 (55–68)	13,793	65 (57–74)	12,150	55 (50–60)	11,288	49 (44–54)
MSA								
Rural	15,155	63 (56–70)	14,555	64 (58–71)	13,410	58 (54–63)	12,252	53 (49–57)
Urban	46,844	65 (62–68)	47,282	61 (57–64)	41,186	52 (49–55)	38,552	47 (45–50)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 11. Trends in mean inpatient length of stay (days) for adult females hospitalized with urinary tract infection listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	6.2	5.3	4.9	4.9
Age				
18–24	3.4	3.0	3.0	2.8
25–34	3.9	3.3	3.2	3.2
35–44	4.4	3.9	3.7	3.5
45–54	5.0	4.4	4.4	4.1
55–64	6.1	5.0	4.8	4.8
65–74	6.5	5.6	5.2	5.1
75–84	7.3	6.0	5.6	5.4
85+	7.7	6.3	5.7	5.5
Race/ethnicity				
White	6.2	5.3	5.0	4.9
Black	6.9	5.9	5.6	5.7
Asian/Pacific Islander	5.1	4.9	4.6	5.3
Hispanic	5.9	4.7	4.9	4.4
Other	6.6	5.7	4.4	5.2
Region				
Midwest	5.5	4.8	4.8	4.4
Northeast	8.4	6.9	6.0	5.6
South	5.8	5.0	4.8	4.9
West	5.2	4.7	4.4	4.4
MSA				
Rural	5.5	4.8	4.3	4.4
Urban	6.4	5.4	5.1	5.0
Primary payor				
Medicare	7.1	6.0	5.5	5.4
Medicaid	5.7	4.8	4.6	4.4
Private insurance/HMO	4.2	3.8	3.7	3.6
Self-pay	4.6	3.8	3.5	3.3
No charge	*	3.7	3.7	4.5
Other	5.2	3.8	4.1	3.6

*Figure does not meet standard for reliability or precision.
MSA, metropolitan statistical area; HMO, health maintenance organization.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

antimicrobials and home-based intravenous therapy in the treatment of women with pyelonephritis. The decline in age-unadjusted rates of hospitalization for women with pyelonephritis was most noticeable in African American and Caucasian women. Rates were relatively stable in Hispanic and Asian women. Rates of hospitalization declined in all geographic areas, and no distinct regional differences were noted.

The overall length of hospital stay of women who require inpatient hospitalization for the management of UTI has decreased, consistent with the general trend toward decreased length of stay (LOS) for all conditions (Table 11). Nationwide HCUP data reveal that the mean LOS for women with UTI decreased from 6.2 days in 1994 to 4.9 days in 2000. This trend was seen across all age groups, although elderly women continued to have a somewhat greater LOS than younger women, probably due to the more-severe infections or associated comorbidity in older adults. The decrease in LOS was more pronounced for women who have Medicare or Medicaid as their primary insurer than it was for women with either private insurance or HMO coverage.

Outpatient Care

Outpatient care for UTI is provided in a variety of settings, which are analyzed separately below.

Hospital Outpatient Care

The overall rate of hospital outpatient visits for women with UTI generally increased from 1994 to 2000, according to data from the National Hospital Ambulatory Medical Care Survey (NHAMCS), both when UTI was listed as the primary diagnosis (Table 12) and when UTI was listed as one of any diagnoses at the time of visit (Table 13). The most striking increases were observed in young women 18 to 34 years of age. Overall rates of hospital outpatient visits by young women for any reason were 1.64 times greater in 2000 than they were in 1994. Race/ethnicity appears to play some role in the rate of outpatient visits for UTI: Hispanic and African American women had higher age-unadjusted visit rates where reliable estimates are available. Some regional fluctuations were noted, but no consistent trends were observed. Rates of outpatient hospital visits for female UTI have been generally stable in metropolitan statistical areas (MSAs), that is, urban settings, but have been

Table 12. Hospital outpatient visits by adult females with urinary tract infection listed as primary reason for visit, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	432,626	449 (339–559)	358,850	357 (247–468)	563,504	551 (440–661)	559,406	534 (414–653)
Age								
18–34	178,349	542 (327–757)	135,538	411 (233–590)	181,772	562 (384–741)	233,033	719 (485–952)
35–64	167,763	366 (236–497)	128,161	261 (168–355)	228,773	445 (297–593)	212,682	397 (243–550)
65+	*	*	*	517 (73–961)	152,959	824 (497–1,152)	113,691	607 (305–909)
Race/ethnicity								
White	279,795	382 (282–482)	250,135	333 (199–466)	420,367	556 (427–685)	445,892	584 (434–734)
Black	*	*	*	386 (123–649)	*	*	*	*
Hispanic	*	*	60,153	667 (294–1,041)	62,288	638 (269–1,006)	*	*
Region								
Midwest	181,728	791 (403–1,180)	*	*	*	*	194,503	816 (494–1,139)
Northeast	52,869	261 (153–369)	69,047	343 (192–495)	160,350	791 (488–1,094)	102,854	498 (244–752)
South	147,905	451 (310–592)	69,346	194 (122–267)	252,082	695 (484–906)	181,573	489 (309–669)
West	50,124	247 (120–373)	64,839	307 (135–479)	*	*	*	*
MSA								
MSA	318,193	441 (329–553)	293,441	377 (246–508)	372,958	470 (349–591)	309,400	379 (274–483)
Non-MSA	*	*	*	*	190,546	830 (568–1,092)	250,006	1,084 (690–1,479)

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Hospital Ambulatory Medical Care Survey — Outpatient, 1994, 1996, 1998, 2000.

Table 13. Hospital outpatient visits by adult females with urinary tract infection listed as any reason for visit, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	568,202	590 (469–711)	566,676	565 (436–693)	784,752	767 (634–900)	816,459	779 (627–932)
Age								
18–34	216,162	656 (428–885)	215,041	653 (445–861)	296,592	917 (673–1,161)	349,866	1,079 (776–1,382)
35–64	233,678	510 (357–664)	213,031	434 (302–567)	281,648	548 (388–708)	282,465	527 (351–703)
65+	118,362	671 (359–984)	*	*	206,512	1,113 (714–1,512)	184,128	983 (537–1,428)
Race/ethnicity								
White	375,156	513 (396–629)	361,243	481 (332–629)	564,054	746 (591–901)	613,429	804 (622–985)
Black	75,811	658 (322–994)	92,769	769 (425–1,114)	92,170	740 (371–1,108)	110,994	861 (377–1,345)
Hispanic	*	*	103,775	1,151 (614–1,687)	115,176	1,179 (664–1,694)	85,076	797 (330–1,264)
Region								
Midwest	236,759	1,031 (610–1,452)	245,751	1,045 (571–1,520)	128,220	540 (301–778)	281,994	1,183 (787–1,580)
Northeast	80,917	399 (269–529)	133,440	664 (464–864)	233,853	1,154 (787–1,521)	177,027	858 (467–1,248)
South	195,507	596 (434–759)	104,439	293 (202–384)	313,752	864 (623–1,106)	238,542	643 (432–854)
West	55,019	271 (142–400)	83,046	393 (209–578)	108,927	495 (287–704)	118,896	513 (240–786)
MSA								
MSA	432,852	600 (471–728)	470,464	605 (454–756)	566,770	714 (563–865)	496,653	608 (456–759)
Non-MSA	135,350	560 (267–852)	*	*	217,982	950 (669–1,230)	319,806	1,387 (950–1,824)

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races are included in the totals.

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Hospital Ambulatory Medical Care Survey — Outpatient, 1994, 1996, 1998, 2000.

Table 14. Outpatient hospital visits by female Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total	78,180	395 (392–397)	157,420	780 (776–784)	204,360	1,072 (1,068–1,077)
Total < 65	8,960	375 (367–383)	21,980	818 (807–829)	28,620	1,030 (1,019–1,042)
Total 65+	69,220	397 (394–400)	135,440	774 (770–778)	175,740	1,080 (1075–1,085)
Age						
65–74	31,200	339 (336–343)	64,600	718 (712–723)	74,920	948 (941–955)
75–84	28,360	481 (475–486)	50,480	843 (836–851)	70,680	1,210 (1,201–1,219)
85–94	8,740	421 (412–430)	18,940	852 (840–864)	28,000	1,259 (1,244–1,273)
95+	920	357 (334–380)	1,420	501 (475–528)	2,140	690 (661–719)
Race/ethnicity						
White	60,120	358 (355–361)	126,480	729 (725–733)	169,320	1,047 (1,042–1,052)
Black	11,000	652 (640–665)	20,240	1,100 (1,085–1,115)	20,080	1,138 (1,123–1,154)
Asian	…	…	240	254 (222–286)	860	486 (454–518)
Hispanic	…	…	2,760	1,374 (1,323–1,424)	6,240	1,698 (1,656–1,740)
N. American Native	…	…	1,360	8,416 (7,989–8,843)	2,320	8,896 (8,551–9,241)
Region						
Midwest	23,000	458 (452–464)	42,500	824 (816–832)	59,980	1,216 (1,206–1,226)
Northeast	15,080	333 (327–338)	20,280	451 (445–457)	25,660	655 (647–663)
South	27,440	393 (388–397)	72,820	1,008 (1,001–1,015)	90,520	1,290 (1,282–1,298)
West	11,960	419 (412–427)	21,020	734 (724–744)	27,640	1,017 (1,005–1,029)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

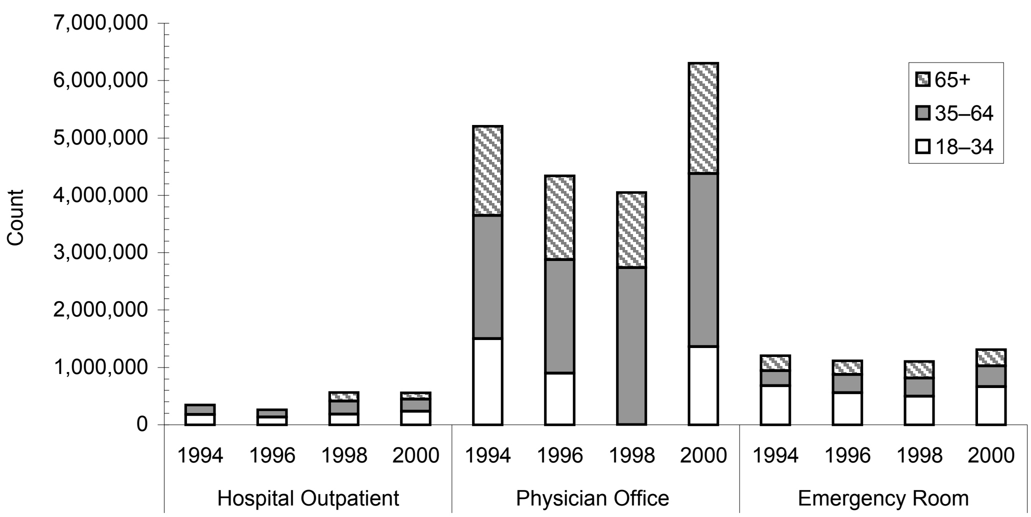

Figure 3. Trends in visits by females for urinary tract infection by patient age and site of service.

SOURCE: National Hospital Ambulatory Medical Care Survey (hospital outpatient and emergency room); National Ambulatory Medical Care Survey (physician office).

Table 15. Physician office visits by adult females with urinary tract infection listed as primary reason for visit, count, rate[a] (95% CI)

	Count	Rate	Count	Rate	Count	Rate
	1992		1994		1996	
Total	5,665,211	5,867 (4,766–6,968)	5,205,024	5,403 (4,513–6,292)	4,340,795	4,324 (3,493–5,156)
Age						
18–34	2,167,103	6,431 (4,314–8,549)	1,502,309	4,562 (3,255–5,869)	895,243	2,718 (1,749–3,687)
35–64	2,171,942	4,819 (3,391–6,248)	2,147,659	4,691 (3,413–5,969)	1,983,960	4,045 (2,874–5,217)
65+	1,326,166	7,454 (4,906–10,001)	1,555,056	8,819 (6,236–11,403)	1,461,592	7,943 (5,146–10,741)
Region						
Midwest	1,200,957	5,206 (3,157–7,255)	841,952	3,667 (2,385–4,948)	1,013,390	4,310 (2,460–6,159)
Northeast	864,968	4,280 (2,362–6,199)	981,042	4,838 (2,927–6,750)	769,391	3,827 (2,271–5,383)
South	2,437,343	7,295 (5,264–9,326)	2,042,634	6,231 (4,656–7,806)	1,386,711	3,889 (2,626–5,152)
West	1,161,943	5,848 (3,112–8,584)	1,339,396	6,590 (4,227–8,953)	1,171,303	5,550 (3,392–7,707)
MSA						
MSA	3,985,675	5,535 (4,377–6,694)	4,447,400	6,164 (5,074–7,253)	3,340,574	4,293 (3,351–5,235)
Non-MSA	1,679,536	6,841 (4,157–9,525)	*	*	1,000,221	4,432 (2,662–6,202)
Specialty						
Urology	1,103,291	1,143 (929–1,356)	731,871	760 (617–902)	780,023	777 (588–966)
GFP	2,357,447	2,441 (1,599–3,284)	2,277,566	2,364 (1,702–3,026)	1,861,398	1,854 (1,261–2,447)
All others	2,204,473	2,283 (1,623–2,943)	2,195,587	2,279 (1,711–2,847)	1,699,374	1,693 (1,151–2,234)
	1998		2000			
Total	5,288,958	5,169 (4,050–6,288)	6,300,754	6,013 (4,840–7,186)		
Age						
18–34	*	*	1,361,644	4,200 (2,479–5,921)		
35–64	2,738,069	5,325 (3,672–6,978)	3,015,698	5,624 (4,046–7,201)		
65+	1,313,974	7,081 (4,056–10,105)	1,923,412	10,265 (6,551–13,979)		
Region						
Midwest	*	*	1,377,591	5,781 (3,377–8,186)		
Northeast	*	*	1,344,803	6,514 (3,837–9,192)		
South	2,158,702	5,948 (4,030–7,865)	1,963,660	5,290 (3,449–7,131)		
West	*	*	1,614,700	6,963 (4,202–9,724)		
MSA						
MSA	3,879,002	4,888 (3,640–6,136)	4,630,497	5,666 (4,388–6,944)		
Non-MSA	1,409,956	6,143 (3,642–8,645)	1,670,257	7,245 (4,437–10,053)		
Specialty						
Urology	547,954	536 (363–708)	783,389	748 (553–942)		
GFP	2,388,058	2,334 (1,569–3,099)	2,821,067	2,692 (1,815–3,569)		
All others	2,352,946	2,300 (1,505–3,094)	2,696,298	2,573 (1,826–3,320)		

GFP, general and family practice; MSA, metropolitan statistical area.
*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 16. Physician office visits by adult females with urinary tract infection listed as any reason for visit, count, rate[a] (95% CI)

	1992		1994		1996	
	Count	Rate	Count	Rate	Count	Rate
Total	7,302,802	7,563 (6,307–8,819)	6,505,167	6,752 (5,757–7,747)	6,295,860	6,272 (5,276–7,268)
Age						
18–34	2,564,452	7,610 (5,280–9,941)	1,800,179	5,466 (3,963–6,970)	1,737,586	5,275 (3,765–6,786)
35–64	2,775,830	6,159 (4,523–7,795)	2,591,923	5,662 (4,286–7,037)	2,509,412	5,117 (3,817–6,417)
65+	1,962,520	11,030 (7,900–14,161)	2,113,065	11,984 (8,999–14,969)	2,048,862	11,135 (7,941–14,329)
Region						
Midwest	1,462,687	6,341 (4,114–8,567)	1,264,608	5,507 (3,746–7,269)	1,562,287	6,644 (4,413–8,876)
Northeast	1,232,828	6,101 (3,698–8,503)	1,247,926	6,155 (3,936–8,373)	939,584	4,673 (2,873–6,473)
South	2,909,465	8,708 (6,485–10,931)	2,357,740	7,193 (5,516–8,869)	2,301,628	6,455 (4,806–8,104)
West	1,697,822	8,545 (5,284–11,805)	1,634,893	8,044 (5,583–10,504)	1,492,361	7,071 (4,715–9,427)
MSA						
MSA	5,010,454	6,958 (5,651–8,266)	5,526,106	7,659 (6,438–8,880)	4,828,440	6,205 (5,086–7,325)
Non-MSA	2,292,348	9,337 (6,223–12,451)	979,061	4,047 (2,488–5,607)	1,467,420	6,502 (4,329–8,675)
Specialty						
Urology	1,280,128	1,326 (1,104–1,547)	849,076	881 (731–1,031)	895,705	892 (696–1,089)
GFP	3,022,128	3,130 (2,185–4,075)	2,840,667	2,948 (2,210–3,686)	2,629,808	2,620 (1,915–3,324)
Intern. Med.	1,208,039	1,251 (720–1,782)	1,442,635	1,497 (986–2,009)	1,344,616	1,340 (842–1,837)
All other	1,792,507	1,856 (1,286–2,427)	1,372,789	1,425 (1,046–1,804)	1,425,731	1,420 (981–1,859)

	1998		2000	
	Count	Rate	Count	Rate
Total	7,645,826	7,473 (6,146–8,800)	8,150,279	7,778 (6,464–9,093)
Age				
18–34	2,025,391	6,263 (4,184–8,342)	1,875,092	5,784 (3,776–7,792)
35–64	3,431,071	6,673 (4,874–8,472)	3,693,141	6,887 (5,146–8,628)
65+	2,189,364	11,798 (7,849–15,747)	2,582,046	13,780 (9,635–17,925)
Region				
Midwest	1,689,897	7,111 (4,244–9,979)	1,572,822	6,601 (4,145–9,057)
Northeast	*	*	1,615,468	7,826 (4,949–10,702)
South	3,401,109	9,371 (6,980–11,762)	2,486,626	6,699 (4,670–8,728)
West	1,812,256	8,241 (5,090–11,391)	2,475,363	10,674 (7,242–14,106)
MSA				
MSA	6,001,991	7,563 (6,033–9,092)	6,242,476	7,638 (6,116– 9,113)
Non-MSA	1,643,835	7,162 (4,509–9,816)	1,907,803	8,275 (5,380–11,170)
Specialty				
Urology	704,268	688 (498–879)	1,077,581	1,028 (785–1,272)
GFP	3,377,733	3,301 (2,396–4,207)	3,569,977	3,407 (2,437–4,377)
Intern. Med.	2,335,343	2,283 (1,494–3,071)	1,914,448	1,827 (1,171–2,483)
All other	*	*	1,588,273	1,516 (1,001–2,031)

GFP, general and family practice; MSA, metropolitan statistical area.

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey, 1992, 1994, 1996, 1998, 2000.

Table 17. Physician office visits by female Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	1,568,800	7,918 (7,907–7,930)	1,740,660	8,625 (8,613–8,638)	1,585,360	8,319 (8,307–8,332)
Total < 65	102,780	4,303 (4,277–4,329)	145,780	5,425 (5,398–5,453)	144,520	5,204 (5,177–5,230)
Total 65+	1,466,020	8,414 (8,401–8,427)	1,594,880	9,117 (9,103–9,130)	1,440,840	8,851 (8,837–8,865)
Age						
65–74	720,880	7,843 (7,826–7,861)	767,800	8,530 (8,512–8,548)	641,100	8,113 (8,094–8,132)
75–84	571,020	9,681 (9,657–9,705)	619,480	10,348 (10,324–10,373)	599,440	10,261 (10,236–10,285)
85–94	165,460	7,970 (7,933–8,007)	197,260	8,871 (8,834–8,909)	189,900	8,536 (8,499–8,573)
95+	8,660	3,359 (3,289–3,428)	10,340	3,652 (3,582–3,721)	10,400	3,352 (3,288–3,415)
Race/ethnicity						
White	1,403,820	8,363 (8,350–8,377)	1,555,680	8,965 (8,952–8,979)	1,403,340	8,674 (8,660–8,688)
Black	95,360	5,655 (5,621–5,690)	102,840	5,590 (5,557–5,624)	91,440	5,183 (5,150–5,216)
Asian	…	…	8,480	8,983 (8,801–9,165)	12,740	7,200 (7,080–7,321)
Hispanic	…	…	26,300	13,090 (12,942–13,237)	42,340	11,520 (11,417–11,623)
N. American Native	…	…	1,080	6,683 (6,300–7,067)	1,400	5,368 (5,096–5,640)
Region						
Midwest	364,120	7,255 (7,232–7,278)	394,540	7,652 (7,629–7,675)	358,200	7,261 (7,238–7,284)
Northeast	250,720	5,532 (5,511–5,553)	270,300	6,015 (5,993–6,037)	244,060	6,230 (6,206–6,253)
South	710,660	10,170 (10,148–10,193)	782,420	10,829 (10,807–10,852)	717,800	10,229 (10,206–10,251)
West	218,240	7,654 (7,623–7,685)	257,100	8,979 (8,946–9,012)	228,500	8,407 (8,374–8,440)

… data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

increasing acutely in non-MSA, or rural, settings. This may reflect increased availability of hospital-based outpatient services in nonmetropolitan areas.

An analysis of Medicare data for the years 1992, 1995, and 1998 also reflects the trend toward increased hospital outpatient utilization for the management of female UTIs (Table 14). The overall utilization rate across all ages was 395 per 100,000 (95% CI, 392–397) in 1992. It rose to 780 per 100,000 (95% CI, 776–784) in 1995, and to 1,072 per 100,000 (95% CI, 1,068–1,077) in 1998. These trends were similar when stratified by age (< 65 or ≥ 65 years). Very elderly women (≥ 95 years) had the smallest overall increase in hospital outpatient utilization, which corresponds to the larger increase in inpatient hospitalization previously described for this age group.

Physician Office Care

The outpatient physician office is the most widely utilized site of service for the treatment of female UTIs (Figure 3). According to data from the National Ambulatory Medical Care Survey (NAMCS), there were more than 6,300,000 physician office visits for a primary diagnosis of female UTI in the United States in 2000 (Table 15). The rates of utilization have remained relatively stable for all patients when UTI is among any of the reasons listed for the visit (Table 16), but they increased between 1996 and 2000 when UTI was the primary diagnosis (Table 15). These increases in physician outpatient services occurred in the 35 to 64 and ≥ 65 year old age groups, but not in 18- to 34-year-old groups. Regional variations were observed during the years analyzed, with a generally higher

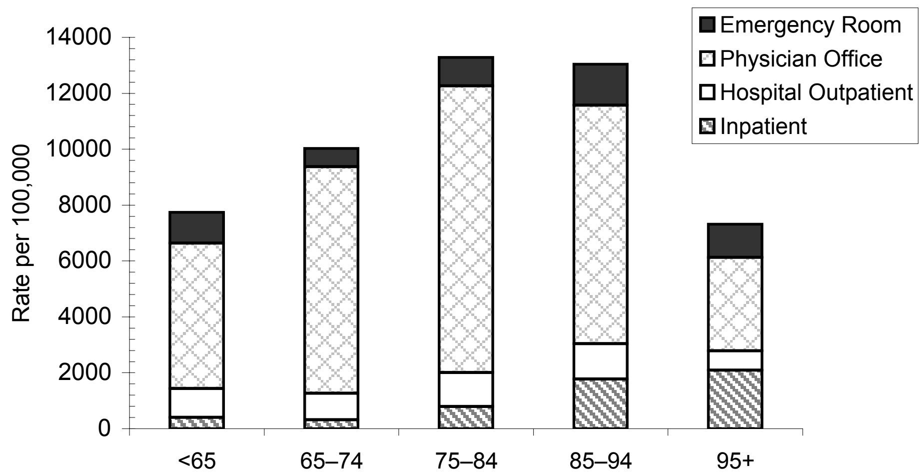

Figure 4. Distribution of urinary tract infection by site of visit, by age, 1998.

SOURCE: Centers for Medicare and Medicaid Services, 1998.

rate of physician office visits for UTI in the South and the West.

When physician outpatient services are stratified by provider specialty, some interesting trends emerge. The overall rates of visits to urologists are consistently lower than those for visits to family practitioners and general practitioners. This indicates that the majority of women with UTI are being treated by their primary care providers. The patients seen by urologists may be those with more complex or severe infections, recurrent UTI, acute pyelonephritis, or other concomitant urologic diagnoses. There was a larger growth in physician office visits for a primary diagnosis of UTI in nonmetropolitan service areas than in metropolitan areas. The significance of this is unclear, but the trend may reflect increased access to providers in less urban areas.

An analysis of CMS data for outpatient physician office visits for the treatment of UTI in women reveals a general increase in utilization between 1992 and 1995, which remained relatively stable in 1998 (Table 17). The most striking observation in this analysis is the peak in utilization among women between 75 and 84 years of age (Figure 4). Rates of utilization in this age group have been consistently higher than those in either older or younger patient populations. The reason for the spike in this age group is not immediately apparent. Most studies demonstrate a continued increase in the overall incidence and prevalence of UTI with increasing age. However, this likely represents the segment of the community-dwelling 75- to 84-year-old population who are treated as outpatients. Patients in the oldest age groups may be more likely to require inpatient treatment, but this accounts for only part of their lower rates of ambulatory care visits for which UTI is listed as the primary diagnosis (Tables 8–11). Outpatient visits by elderly women are likely to be for multiple conditions, any of which may be listed as the primary diagnosis.

An additional observation is the sizable geographic disparity between the South and other regions in the rate of physician office visits for UTI among female Medicare beneficiaries. Although this trend has been observed in some of the other analyses, it is most pronounced in this comparison. This difference appears to have been stable between 1992 and 1998. The reason for the sharply greater utilization in the South is unclear but may be associated with a higher prevalence of UTI in this region.

Ambulatory Surgery Care

Some women with UTIs may be treated in the ambulatory surgery setting. Data from Medicare beneficiaries treated for a diagnosis of UTI in

Table 18. Visits to ambulatory surgery centers by female Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	21,420	108 (107–110)	20,080	100 (98–101)	18,240	96 (94–97)
Total < 65	1,540	64 (61–68)	2,040	76 (73–79)	2,040	73 (70–77)
Total 65+	19,880	114 (113–116)	18,040	103 (102–105)	16,200	100 (98–101)
Age						
65–74	10,920	119 (117–121)	9,620	107 (105–109)	8,020	101 (99–104)
75–84	7,120	121 (118–124)	6,440	108 (105–110)	6,540	112 (109–115)
85–94	1,700	82 (78–86)	1,880	85 (81–88)	1,580	71 (68–75)
95+	140	54 (45–63)	100	35 (28–42)	60	19 (15–24)
Race/ethnicity						
White	18,860	112 (111–114)	17,820	103 (101–104)	16,080	99 (98–101)
Black	1,480	88 (83–92)	1,580	86 (82–90)	1,400	79 (75–83)
Asian	…	…	…	…	…	…
Hispanic	…	…	180	90 (77–103)	320	87 (78–97)
N. American Native	…	…	0	0	20	77 (42–111)
Region						
Midwest	7,300	145 (142–149)	6,260	121 (118–124)	6,140	124 (121–128)
Northeast	4,600	101 (99–104)	4,020	89 (87–92)	3,900	100 (96–103)
South	7,880	113 (110–115)	8,780	122 (119–124)	6,700	95 (93–98)
West	1,640	58 (55–60)	980	34 (32–36)	1,480	54 (52–57)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

ambulatory surgery centers (Table 18) revealed that the overall rate of utilization of this service site for a primary diagnosis of UTI was quite low, ranging from 108 cases per 100,000 (95% CI, 107–110) in 1992 to 96 cases per 100,000 (95% CI, 94–97) in 1998 (Figure 2). This most likely reflects the fact that UTI is not generally a primary surgical diagnosis. Many of these patients may have been scheduled for other operations and were subsequently found to have a UTI at the time of their presentation for surgery or were identified as having a UTI at the time of their pre- or post-operative visit. Utilization rates were generally low regardless of age, geographic region, or patient race/ethnicity. These data indicate that ambulatory surgery centers are not significant service sites for the treatment of UTI in women.

Emergency Room Care

The emergency room (ER) represents a significant site of care for many women with a primary diagnosis of UTI. According to NHAMCS data, approximately 1.3 million ER visits were made by women in the United States for evaluation and treatment of UTI in 2000 (Table 19). This represents a utilization rate of 1,252 visits per 100,000 adult women (95% CI, 1,077–1,426). Rates of use were highest for women 18 to 34 years of age (Figure 3). This trend was apparent in almost all the years analyzed (1994–2000). Utilization rates for young women ranged from 2.5 to 3.6 times those for 35- to 64-year-old women. Women 65 and over had higher utilization rates, but they were still lower than those of the youngest stratum. There was a slight decrease in the rate of ER utilization in all age groups between 1994 and 1998; however, the rates increased again for all patients in 2000.

Table 19. Emergency room visits by adult females with urinary tract infection listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	1,205,099	1,251 (1,086–1,415)	1,114,941	1,111 (951–1,270)	1,106,420	1,081 (916–1,247)	1,311,359	1,252 (1,077–1,426)
Age								
18–34	679,567	2,064 (1,697–2,430)	557,447	1,692 (1,351–2,034)	498,278	1,541 (1,192–1,890)	665,796	2,054 (1,655–2,452)
35–64	262,839	574 (430–718)	317,112	647 (473–820)	316,118	615 (425–804)	362,324	676 (502–849)
65+	262,693	1,490 (1,049–1,931)	240,382	1,306 (893–1,719)	292,024	1,574 (1,143–2,004)	283,239	1,512 (1,038–1,985)
Race/ethnicity								
White	817,265	1,117 (932–1,301)	732,145	974 (795–1,153)	772,815	1,022 (831–1,213)	879,708	1,152 (951–1,354)
Black	244,538	2,121 (1,531–2,711)	264,662	2,195 (1,576–2,815)	239,602	1,923 (1,304–2,542)	322,515	2,501 (1,833–3,170)
Region								
Midwest	265,481	1,156 (826–1,487)	241,660	1,028 (688–1,367)	277,562	1,168 (770–1,566)	410,628	1,723 (1,284–2,162)
Northeast	309,787	1,528 (1,113–1,943)	254,887	1,268 (927–1,608)	208,294	1,028 (756–1,300)	150,389	729 (500–957)
South	451,722	1,378 (1,088–1,668)	451,731	1,267 (963–1,571)	476,927	1,314 (991–1,637)	535,863	1,444 (1,112–1,775)
West	178,109	876 (597–1,156)	166,663	790 (535–1,044)	143,637	653 (409–897)	214,479	925 (622–1,228)
MSA								
MSA	950,511	1,317 (1,127–1,507)	758,101	974 (817–1,132)	779,686	982 (809–1,156)	968,197	1,185 (1,003–1,367)
Non-MSA	254,588	1,052 (724–1,381)	356,840	1,581 (1,124–2,038)	326,734	1,424 (995–1,852)	343,162	1,488 (1,030–1,947)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

[b]Persons of other races are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

Source: National Hospital Ambulatory Medical Care Survey — ER, 1994, 1996, 1998, 2000.

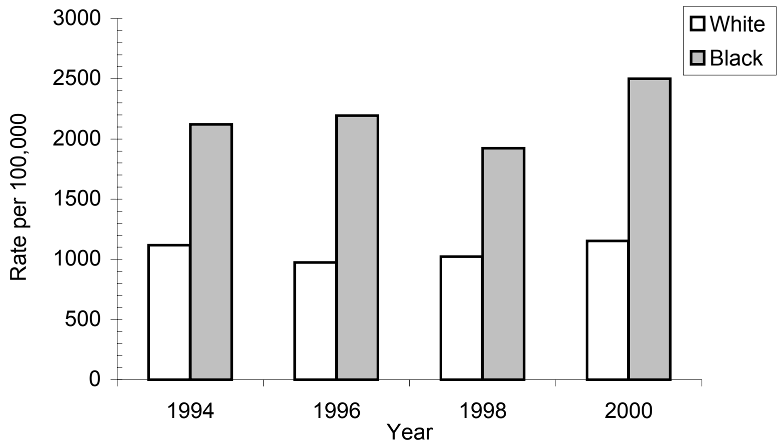

Figure 5. Rate of emergency room visits by females with urinary tract infection listed as primary diagnosis, by patient race and year.

SOURCE: Healthcare Cost and Utilization Project, 1994, 1996, 1998, 2000.

Table 20. Emergency room visits by female Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	157,180	793 (789–797)	177,700	881 (876–885)	177,780	933 (929–937)
Total < 65	21,620	905 (893–917)	28,180	1,049 (1,037–1,061)	30,840	1,110 (1,098–1,123)
Total 65+	135,560	778 (774–782)	149,520	855 (850–859)	146,940	903 (898–907)
Age						
65–74	53,720	584 (580–589)	56,500	628 (623–633)	51,080	646 (641–652)
75–84	53,300	904 (896–911)	56,760	948 (940–956)	59,480	1,018 (1,010–1,026)
85–94	25,640	1,235 (1,220–1,250)	32,120	1,445 (1,429–1,460)	32,680	1,469 (1,453–1,485)
95+	2,900	1,125 (1,084–1,165)	4,140	1,462 (1,418–1,506)	3,700	1,192 (1,154–1,231)
Race/ethnicity						
White	125,180	746 (742–750)	141,780	817 (813–821)	141,220	873 (868–877)
Black	22,640	1,343 (1,325–1,360)	27,380	1,488 (1,471–1,506)	26,340	1,493 (1,475–1,511)
Asian	…	…	600	636 (585–686)	740	418 (388–448)
Hispanic	…	…	2,720	1,354 (1,303–1,405)	4,880	1,328 (1,291–1,365)
N. American Native	…	…	340	2,104 (1,881–2,327)	400	1,534 (1,384–1,683)
Region						
Midwest	35,540	708 (701–715)	42,220	819 (811–827)	43,360	879 (871–887)
Northeast	27,300	602 (595–609)	29,660	660 (653–668)	26,860	686 (677–694)
South	73,280	1,049 (1,041–1,056)	83,120	1,150 (1,143–1,158)	84,300	1,201 (1,193–1,209)
West	19,380	680 (670–689)	20,780	726 (716–736)	21,000	773 (762–783)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 21. Female nursing home residents with an admitting or current diagnosis of urinary tract infection, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Total[b]	104,100	9,252 (8,489–10,015)	95,302	8,243 (7,514–8,972)	83,208	7,111 (6,423–7,800)
Age						
18–74	13,280	7,800 (5,883–9,717)	17,136	9,492 (7,518–11,465)	10,454	5,529 (4,042–7,015)
75–84	35,213	9,580 (8,223–10,938)	30,158	8,109 (6,829–9,388)	24,555	6,671 (5,494–7,848)
85+	55,607	9,467 (8,415–10,520)	48,008	7,953 (6,962–8,943)	48,200	7,864 (6,857–8,872)
Race/ethnicity						
White	93,253	9,330 (8,515–10,144)	84,602	8,379 (7,591–9,166)	71,181	7,125 (6,375–7,874)
Other	10,847	8,820 (6,604–11,036)	10,700	7,752 (5,735–9,770)	11,793	7,230 (5,435–9,024)

[a]Rate per 100,000 nursing home residents in the same demographic stratum.

[b]Persons of unspecified race are included in the totals.

SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Race/ethnicity appears to be an important factor in the ER utilization rates for treatment of UTI in women. The age-unadjusted rate of ER use by African American women was approximately twice that for Caucasians or other ethnic groups in all the years analyzed (Figure 5). This may reflect the general propensity toward increased ER utilization among African Americans for most clinical problems. Less regional variation was observed, although the overall rates of ER use among nonmetropolitan areas were higher than those in urban areas.

Analysis of Medicare data for ER use reveals similar trends (Table 20). Overall ER visits for female Medicare patients with UTI increased gradually between 1992 and 1998. When patients are stratified by age, little variation in utilization rates is seen over this time period. However, women over age 85 had a consistently higher rate of ER use than did younger women. The rate of ER use for Medicare beneficiaries was higher in the South than in other regions of the country. Caucasian women had lower rates of ER utilization than did other ethnic groups.

The notably higher overall rates of ER use by young women with UTI may reflect the relative lack of insurance in this segment of the population. These women may use the ER because they lack resources or have not identified a primary care provider. This pattern of utilization unnecessarily drives up the overall cost of healthcare.

Nursing Home Care

Data from the National Nursing Home Survey (NNHS) indicate that UTI as either an admitting or current diagnosis among female nursing home residents declined from 9,252 per 100,000 in 1995 to 7,111 per 100,000 in 1999 (Table 21). No clear association with age was observed over this time period. The decline in the identification of asymptomatic UTI in this population may result from the fact that screening for bacteriuria in nursing home residents is no longer widely practiced. Nursing home residents with UTI had higher rates of urinary incontinence than did women in the general nursing home population (Tables 22 and 23). As expected, the proportion of women with indwelling foley catheters or ostomies nearly double in women with UTI than it was in the female nursing home population in general.

Overall trends in nursing home patients indicate that 56 to 58% of female residents have problems with urinary incontinence (Table 23). At least half of these residents also require some form of assistance to use the toilet, usually from another person. The overall rate of indwelling catheter use in nursing homes appears low (7.9% to 9.1%), according to these data. This reflects a widespread trend toward minimizing the use of indwelling catheters in nursing home residents to help minimize the risk of UTI.

Table 22. Special needs of female nursing home residents with urinary tract infection, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Has indwelling foley catheter or ostomy						
Yes	17,818	17,116 (13,818–20,415)	13,302	13,958 (10,735–17,180)	14,210	17,077 (13,211–20,943)
No	85,707	82,331 (78,993–85,669)	81,772	85,803 (82,556–89,050)	68,998	82,923 (79,057–86,789)
Question left blank	575	553 (0–1,183)	228	240 (0–711)	0	0
Requires assistance using the toilet						
Yes	62,124	59,677 (55,411–63,943)	57,710	60,555 (56,034–65,076)	42,226	50,748 (45,705–55,791)
No	16,430	15,783 (12,601–18,966)	13,238	13,890 (10,729–17,052)	14,070	16,909 (13,018–20,800)
Question skipped for allowed reason	25,329	24,331 (20,585–28,078)	23,883	25,060 (21,041–29,079)	26,212	31,501 (26,771–36,231)
Question left blank	217	208 (0–617)	471	495 (0–1,181)	700	842 (0–1,716)
Requires assistance from equipment when using the toilet						
Yes	17,219	16,541 (13,311–19,770)	15,682	16,456 (13,032–19,879)	15,008	18,037 (14,290–21,784)
No	43,542	41,827 (37,564–46,089)	40,082	42,058 (37,479–46,637)	25,973	31,215 (26,578–35,852)
Question skipped for allowed reason	41,759	40,114 (35,852–44,377)	37,121	38,951 (34,441–43,460)	40,281	48,410 (43,365–53,456)
Question left blank	1,580	1,518 (465–2,571)	2,417	2,536 (1,093–3,979)	1,945	2,338 (865–3,810)
Requires assistance from another person when using the toilet						
Yes	62,124	59,677 (55,411–63,943)	57,119	59,935 (55,403–64,468)	42,695	51,311 (46,267–56,356)
No	0	0	214	225 (0–667)	156	188 (0–557)
Question skipped for allowed reason	41,759	40,114 (35,852–44,377)	37,121	38,951 (34,441–43,460)	40,281	48,410 (43,365–53,456)
Question left blank	217	208 (0–617)	847	889 (12–1,767)	76	91 (0–269)
Has difficulty controlling urine						
Yes	65,954	63,356 (59,162–67,550)	62,266	65,336 (60,922–69,749)	54,497	65,495 (60,622–70,369)
No	25,656	24,645 (20,917–28,373)	24,155	25,345 (21,327–29,363)	19,204	23,079 (18,709–27,450)
Question skipped for allowed reason	11,767	11,303 (8,485–14,121)	8,484	8,903 (6,208–11,597)	9,354	11,242 (7,983–14,501)
Question left blank	724	696 (0–1,501)	397	416 (0–996)	153	184 (0–546)

[a]Rate per 100,000 adult female nursing home residents with urinary tract infection in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 23. Special needs of female nursing home residents regardless of urinary tract infection diagnosis, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Has indwelling foley catheter or ostomy						
Yes	101,827	9,050 (8,281–9,819)	90,855	7,859 (7,151–8,566)	96,151	8,218 (7,484–8,951)
No	1,020,886	90,732 (89,954–91,510)	1,061,282	91,796 (91,072–92,520)	1,064,024	90,937 (90,162–91,712)
Question left blank	2,450	218 (89–347)	3,997	346 (182–510)	9,890	845 (571–1,120)
Requires assistance using the toilet						
Yes	659,035	58,572 (57,256–59,888)	652,615	56,448 (55,131–57,765)	670,006	57,262 (55,935–58,590)
No	286,946	25,503 (24,334–26,671)	280,242	24,240 (23,104–25,375)	273,104	23,341 (22,202–24,480)
Question skipped for allowed reason	173,839	15,450 (14,484–16,417)	216,408	18,718 (17,680–19,756)	218,971	18,714 (17,670–19,759)
Question left blank	5,343	475 (297–652)	6,870	594 (394–794)	7,983	682 (430–935)
Requires assistance from equipment when using the toilet						
Yes	182,812	16,248 (15,274–17,221)	180,518	15,614 (14,659–16,569)	178,305	15,239 (14,293–16,185)
No	460,230	40,903 (39,592–42,215)	433,640	37,508 (36,220–38,795)	467,351	39,942 (38,631–41,254)
Question skipped for allowed reason	460,785	40,953 (39,639–42,267)	496,649	42,958 (41,643–44,272)	492,075	42,055 (40,732–43,379)
Question left blank	21,336	1,896 (1,536–2,257)	45,327	3,921 (3,391–4,450)	32,334	2,763 (2,303–3,224)
Requires assistance from another person when using the toilet						
Yes	652,088	57,955 (56,636–59,274)	640,137	55,369 (54,048–56,689)	661,927	56,572 (55,242–57,901)
No	6,109	543 (345–741)	8,603	744 (511–977)	6,800	581 (384–779)
Question skipped for allowed reason	460,785	40,953 (39,639–42,267)	496,649	42,958 (41,643–44,272)	492,075	42,055 (40,732–43,379)
Question left blank	6,180	549 (357–741)	10,745	929 (681–1,178)	9,263	792 (527–1,056)
Has difficulty controlling urine						
Yes	633,123	56,269 (54,943–57,596)	672,699	58,185 (56,875–59,496)	685,747	58,608 (57,288–59,927)
No	424,287	37,709 (36,411–39,006)	422,839	36,574 (35,293–37,854)	422,162	36,080 (34,793–37,367)
Question skipped for allowed reason	64,822	5,761 (5,124–6,398)	57,080	4,937 (4,370–5,504)	55,713	4,761 (4,201–5,322)
Question left blank	2,931	260 (114–407)	3,517	304 (154–454)	6,444	551 (323–778)

[a]Rate per 100,000 adult female nursing home residents in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 24. Expenditures for female Medicare beneficiaries for treatment of urinary tract infection by site of service, 1998

	Total Annual Expenditures	
Service Type	**Age < 65**	**Age 65+**
Inpatient	$71,600,000	$687,600,000
Outpatient		
Physician Office	$17,200,000	$171,000,000
Hospital Outpatient	$2,900,000	$15,500,000
Ambulatory Surgery	$3,400,000	$24,000,000
Emergency Room	$9,800,000	$58,400,000
Total	$104,900,000	$956500,000

SOURCE: Centers for Medicare and Medicaid Services, 1998.

ECONOMIC IMPACT

The economic burden of UTIs in adult women is significant. A substantial number of inpatient hospitalizations, outpatient hospital and clinic visits, and ER visits for the diagnosis and management of female UTI occur each year. The associated direct and indirect costs are also large and include substantial out-of-pocket expenses for the patients. Composite data suggest that the overall expenditures for treatment of UTIs among women in the United States were approximately $2.47 billion in 2000, excluding spending on outpatient prescription drugs (Table 7). Inpatient services accounted for the majority of treatment costs, although the fraction of expenditures devoted to inpatient care declined over time. Total spending on UTIs for women, after adjustment for inflation, increased about 1% per year between 1994 and 2000. The biggest percentage increases in spending were for services provided in physician offices and ERs. Most of the UTI-related expenditures in Medicare beneficiaries were for inpatient services (Table 24). The bulk of this spending was for women over 65, although UTI-related expenditures exceeded $100 million in 1998 among Medicare enrollees under 65, primarily the disabled. This does not include expenditures for complementary and alternative

Table 25. Estimated annual expenditures of privately insured employees with and without a medical claim for a urinary tract infection in 1999[a]

	Annual Expenditures (per person)			
	Persons without UTI (N=267,520)	Persons with UTI (N=11,430)		
	Total	**Total**	**Medical**	**Rx Drugs**
Total	$3,099	$5,470	$4,414	$1,056
Age				
18–34	$2,685	$5,067	$4,333	$734
35–44	$2,861	$5,327	$4,398	$929
45–54	$3,173	$5,752	$4,565	$1,187
55–64	$3,279	$5,515	$4,342	$1,173
Gender				
Male	$2,715	$5,544	$4,528	$1,016
Female	$3,833	$5,407	$4,325	$1,082
Region				
Midwest	$2,988	$5,423	$4,367	$1,057
Northeast	$2,981	$5,197	$4,157	$1,040
South	$3,310	$5,838	$4,757	$1,080
West	$3,137	$5,762	$4,716	$1,046

Rx, prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.

SOURCE: Ingenix, 1999.

Table 26. Average annual spending and use of outpatient prescription drugs for treatment of urinary tract infection (male and female), 1996–1998[a]

Drug Name	Number of Rx Claims	Mean Price	Total Expenditures
Cipro™	774,067	$60.27	$46,652,998
Macrobid™	477,050	$26.80	$12,784,949
Triple antibiotic	329,253	$8.44	$2,778,898
Floxin™	279,564	$54.10	$15,124,394
Phenazopyridine	245,275	$5.50	$1,349,013
Amoxicillin	183,244	$8.46	$1,550,247
TMP/SMX	162,216	$6.23	$1,010,606
Bactrim	145,898	$13.62	$1,987,126
Nitrofurantoin	137,353	$38.22	$5,249,632
TMP-SMX ds	129,853	$5.48	$711,594
Oxybutynin	123,631	$28.87	$3,569,227
Cephalexin	118,985	$19.06	$2,267,854
Sulfacetamide	103,917	$6.17	$641,168
Sulfisoxazole	96,253	$7.82	$752,701
Total	3,306,559		$96,430,407

Rx, prescription.

[a]Estimates include prescription drug claims with a corresponding diagnosis for urinary tract infection (both males and females) and exclude drug claims for which there was insufficient data to produce reliable estimates. Including expenditures on these excluded medications would increase total outpatient drug spending for urinary tract infections by approximately 52%, to $146 million.

SOURCE: Medical Expenditure Panel Survey, 1996–1998.

Table 27. Annual cost of female urinary tract infection, 1995

	Cost
Direct costs	
Medical expenses	
Clinic charges	$385,000,000
Prescriptions	$89,000,000
Nonmedical expenses	
Travel and childcare for visits	$77,000,000
Output lost due to time spent for visits	$108,000,000
Total direct costs	$659,000,000
Indirect costs	
Output lost due to disability	
During bed days	$300,000,000
During other days of restricted activity	$300,000,000
During other days with symptoms	$336 000,000
Total indirect costs	$936 000,000
Total costs	$1,594 000,000

SOURCE: Reprinted from Annals of Epidemiology, 10, Foxman B, Barlow R, D'Arcy, H, Gillespie B, Sobel JD, Urinary tract infection: self-reported incidence and associated costs, 509–515, Copyright 2000, with permission from Elsevier Science.

therapies, which may be substantial, given widespread beliefs in such remedies as cranberry juice (7).

The mean annual healthcare expenditures for privately insured women with a diagnosis of UTI in 1999 were approximately 1.4 times higher than those for women without UTI ($5,407 vs $3,833) (Table 25). Although similar across regions, the estimated overall costs in the South were the highest in the United States. Patient age did not appear to be a significant factor in healthcare expenditures in 1999.

An analysis of prescribing costs reflects a propensity to prescribe expensive medications such as the fluoroquinolones disproportionately, rather than TMP-SMX or other less expensive agents (Table 26). The average cost for a course of a fluoroquinolone is more than six times that for a course of TMP-SMX. This finding is consistent with the well-documented increases in healthcare costs driven by prescription drug utilization. This is also of concern because of the increased risk of drug resistance. Conversely, fluoroquinolone use may be warranted in areas where bacterial resistance to less-expensive agents already exceeds 20% of cases. These data do not reflect the success of treatment or whether prescriptions were based on culture and susceptibility results. Nor does this analysis account for any subsequent savings that may occur incident to the use of fluoroquinolones. Use of the basic therapeutic guidelines discussed earlier might alleviate some of these risks and costs. The estimated direct costs for female UTI are substantially lower in other studies (Table 27).

In addition to the direct medical costs of treatment, UTIs can affect labor market factors such as absenteeism and work limitations (Tables 28 and 29). Although cystitis is more common among women, pyelonephritis is associated with the greatest burden of work loss. Data from Medstat's 1999 Health and Productivity Management survey suggest that 24% of women with a medical claim for pyelonephritis missed some work time related to treatment of the condition, the average being 7.7 hours lost per year.

SPECIAL CONSIDERATIONS

HCUP data on women hospitalized for UTI suggest that diabetes may be a risk factor for the development of infection (Table 30). This may be due to changes in voiding physiology in diabetic patients

Table 28. Average annual work loss of persons treated for urinary tract infection (95% CI)

Condition	Number of Persons[a]	% Missing Work	Average Work Absence (hrs) Inpatient	Outpatient	Total
Cystitis					
Males	116	18%	0.1 (0–0.4)	10.3 (0–24.5)	10.5 (0–24.7)
Females	426	16%	0	4.8 (3.0–6.6)	4.8 (3.0–6.6)
Pyelonephritis					
Males	71	21%	1.6 (0–4.7)	9.4 (2.6–16.2)	11.0 (3.6–18.4)
Females	79	24%	2.1 (0–4.2)	5.6 (2.0–9.1)	7.7 (3.7–11.7)
Other UTIs					
Males	779	15%	0.9 (0–2.6)	5.5 (3.7–7.3)	6.5 (4.0–8.9)
Females	1,846	17%	0	7.4 (5.5–9.3)	7.5 (5.6–9.3)
Orchitis	398	14%	1.5 (0.7–3.7)	6.1 (1.3–10.9)	7.6 (2.3–12.9)

[a]Individuals with an inpatient or outpatient claim for a urinary tract infection and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.
SOURCE: MarketScan, 1999.

that lead to an increase in urinary retention, which in turn provides a nidus for infection. In addition, there may be alterations in the overall immune status of diabetic patients that predispose them to UTI. Assuming a prevalence of diabetes in the 40- to 70-year-old general population of 12.9% (8), the observed UTI rate of approximately 26% (63,662 per 245,879 in 2000) in this population suggests a relationship between the two disorders. Other data from the National Health Interview Survey also support this observation (9). However, the role of diabetes in the risk of UTI development remains controversial, and additional research is needed to clarify the associations.

CONCLUSIONS

Urinary tract infection remains one of the most common urologic diseases of women in the United States. The overall lifetime risk of developing a UTI is high (> 50% of all adult women), and appropriate diagnosis and treatment are essential to quality care. This analysis has revealed several interesting trends. There appears to have been some decrease in the use of inpatient hospitalization for the treatment of UTI in younger women, although it is still a significant source of healthcare expenditures for elderly women with this diagnosis. There has been an overall trend toward increased use of outpatient care in a variety of settings for acute pyelonephritis and selected cases of complicated infections. Analysis of prescribing patterns reveals great reliance on fluoroquinolones over more traditional first-line antimicrobials. This could have a variety of significant impacts in terms of both cost and biology. Efforts to slow the development of drug-resistant pathogens will depend heavily on future prescribing patterns.

RECOMMENDATIONS

This analysis raises a number of significant research questions regarding the evaluation and treatment of UTI in women. To what degree should prevention be emphasized in UTI care? What are the best recommendations for prevention? What is the role of the environment in the development of UTI in women, given the general observation that the rates of infection are higher in the South than in other regions?

Economic research related to female UTI will also be important in the future. The costs of caring for women with UTI are high, and methods to reduce costs while maintaining high-quality care are needed. The role of innovative methods for prevention and treatment will be important. For example, self-start therapy, in which a woman keeps a supply of antimicrobials for use when she develops symptoms of a UTI, has been proposed for women with recurrent UTI. Additional studies will be needed to identify

Table 29. Average work loss associated with a hospitalization or an ambulatory care visit for treatment of urinary tract infection (95% CI)

Condition	Inpatient Care: Number of Hospitalizations[a]	Inpatient Care: Average Work Absence (hrs)	Outpatient Care: Number of Outpatient Visits	Outpatient Care: Average Work Absence (hrs)
Cystitis				
Males	*	*	157	7.6 (0–18.1)
Females	*	*	629	3.2 (2.2–4.3)
Pyelonephritis				
Males	*	*	87	7.7 (2.1–13.2)
Females	*	*	105	4.2 (2.0–6.4)
Other UTIs				
Males	*	*	1,047	4.1 (2.8–5.4)
Females	*	*	2,669	5.1 (3.9–6.4)
Orchitis	*	*	633	3.8 (1.2–6.5)

*Figure does not meet standard for reliability or precision.

[a]Unit of observation is an episode of treatment. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

SOURCE: MarketScan, 1999.

Table 30. Diabetes diagnosis as a comorbidity in adult females hospitalized for urinary tract infection, count (% of total), rate[a]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	223,256	232	235,055	234	243,584	238	245,879	235
Without diabetes as listed diagnosis	176,150 (79%)	183	179,391 (76%)	179	182,659 (75%)	179	182,217 (74%)	174
With diabetes as listed diagnosis	47,105 (21%)	49	55,663 (24%)	56	60,925 (25%)	60	63,662 (26%)	61

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US female adult civilian non-institutionalized population.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

the clinical efficacy and cost-utility of this approach. Additional research is also needed on the debate over definitions of UTI vs pyuria, the role of empirical therapy, and the need for routine urine culture and susceptibility testing, given the current controversies in the field. In addition, issues related to access to care will need to be explored. There has been a sharp rise in ER visits for UTI, particularly among young women. The cause of this utilization pattern needs to be identified and addressed. Answers to these research questions and others will contribute to the continued improvement of healthcare for women with UTI.

REFERENCES

1. Beisel B, Hale W, Graves RS, Moreland J. Does postcoital voiding prevent urinary tract infections in young women? J Fam Pract 2002;51:977.
2. Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. Emerg Infect Dis 2001;7:342-7.
3. Foxman B, Barlow R, D'Arcy H, Gillespie B, Sobel JD. Urinary tract infection: self-reported incidence and associated costs. Ann Epidemiol 2000;10:509-15.
4. Nicolle LE. Urinary infections in the elderly: symptomatic of asymptomatic? Int J Antimicrob Agents 1999;11:265-8.
5. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999;29:745-58.
6. Huang ES, Stafford RS. National patterns in the treatment of urinary tract infections in women by ambulatory care physicians. Arch Intern Med 2002;162:41-7.
7. Henig YS, Leahy MM. Cranberry juice and urinary-tract health: science supports folklore. Nutrition 2000;16:684-7.
8. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-24.
9. Boyko EJ, Lipsky BA, eds. Infection and Diabetes. Maryland: National Institute of Diabetes and Digestive and Kidney Diseases, 1995.

CHAPTER 19

Urinary Tract Infection in Men

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Urinary Tract Infection in Men

Tomas L. Griebling, MD

INTRODUCTION

Although urinary tract infections (UTI) occur in both men and women, clinical studies suggest that the overall prevalence of UTI is higher in women. Basic concepts related to the definition and diagnosis of UTI, associated risks of morbidity and mortality, and general treatment principles are reviewed in the introduction to the chapter on UTI in Women. This chapter addresses resource utilization, epidemiology, and costs of UTI in adult men.

DEFINITION AND DIAGNOSIS

Clinical

The clinical definitions of general UTI, including bacteriuria, cystitis, and pyelonephritis, are reviewed in the introduction to the chapter on UTI in women. As described above, male anatomic structures that may be involved with infectious processes include the prostate, testis, scrotum, and epididymis.

Analytic

Analyses presented in this chapter used ICD-9 diagnostic codes for UTI (Table 1). These codes are based primarily on the site and type of infection involved.

RISK FACTORS

Unlike the epidemiology of UTI in females, rates are much lower in young adults and rise dramatically in older men. Indeed, several potential risk factors for the development of UTI are unique to men. Bladder outlet obstruction due to benign prostatic hyperplasia (BPH) may be associated with urinary stasis. Even though a causal relationship has been difficult to prove, chronic prostatic obstruction is thought to increase the risk of UTI in older men with BPH. Instrumentation of the urinary tract may lead to iatrogenic UTI, either from cystoscopy or catheterization, both of which are common in the evaluation of men with obstructive voiding symptoms. UTI is an uncommon complication of transrectal prostate biopsy. Complications may range from acute prostatitis and cystitis to more complex infections, including pyelonephritis, osteomyelitis, and systemic urosepsis. The most common associated organisms are gastrointestinal flora, including anaerobes. Most clinicians utilize antimicrobial prophylaxis around the time of the procedure. Fluoroquinolones are particularly effective for this condition.

Bacterial prostatitis, which may be acute or chronic, is an uncommon clinical problem. Several forms of prostatitis are recognized in the National Institutes of Health (NIH) classification system (1). Acute bacterial prostatitis (Type I) is characterized by rapid onset of symptoms, including fever and associated constitutional signs and symptoms. Urine cultures are typically positive, and intravenous antimicrobial therapy is often indicated. In contrast, chronic bacterial prostatitis (Type II) tends to be less pronounced in onset, with patients remaining asymptomatic between recurrent episodes. Recurrent cystitis is common. This is most likely due to persistence of pathogenic organisms in the prostatic

Table 1. Codes used in the diagnosis and management of male urinary tract infection

Males 18 years or older with one of the following ICD-9 codes:	
Orchitis	
016.5	Tuberculosis of other male genital organs
072.0	Mumps orchitis
603.1	Infected hydrocele
604.0	Orchitis epididymitis and epididymo-orchitis with abscess
604.9	Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess
604.90	Orchitis and epididymitis, unspecified
604.99	Other orichitis epididymitis and epididymo-orchitis without abscess
608.4	Other inflammatory disorders of male genital organs
608.0	Seminal vesiculitis
Cystitis	
112.2	Candidiasis of other urogenital sites
120.9	Schistosomiasis, unspecified
595.0	Acute cystitis
595.1	Chronic interstitial cystitis
595.2	Other chronic cystitis
595.3	Trigonitis
595.89	Other specified types of cystitis
595.9	Cystitis, unspecified
Pyelonephritis	
590.0	Chronic pyelonephritis
590.00	Chronic pyelonephritis without lesion of renal medullary necrosis
590.01	Chronic pyelonephritis with lesion of renal medullary necrosis
590.1	Acute pyelonephritis
590.10	Acute pyelonephritis without lesion of renal medullary necrosis
590.11	Acute pyelonephritis with lesion of renal medullary necrosis
590.2	Renal and perinephric abscess
590.3	Pyeloureteritis cystica
590.8	Other pyelonephritis or pyonephrosis, not specified as acute or chronic
590.9	Infection of kidney, unspecified
593.89	Other specified disorders of kidney and ureter
Other	
597.8	Other urethritis
599.0	Urinary tract infection site not specified
607.2	Other inflammatory disorders of penis
607.1	Balanoposthitis

secretory system. Coliform bacterial species, particularly *Enterococcus fecalis* and *Escherichia coli*, are the most common organisms in cases of chronic bacterial prostatitis. Nonbacterial prostatitis (Type III), also known as chronic pelvic pain syndrome, is a condition characterized by chronic pelvic pain that is attributed to the prostate. Patients may also complain of obstructive and irritative urinary symptoms, sexual dysfunction, and penile, testicular, or groin pain. Chronic pelvic pain syndrome may be associated with increased concentrations of inflammatory cells in prostatic secretions, despite the absence of documentable bacterial infection.

The pathogenesis of prostatitis may be multifactorial. Reflux of infected urine into the prostatic ducts in the posterior urethra occurs in some patients, while ascending urethral infection plays a role in others. Hematogenous and lymphatic spread have also been hypothesized as possible causes. Reflux of noninfected urine may be associated with cases of nonbacterial prostatitis. It is hypothesized that this intraprostatic reflux of urine may lead to histochemical inflammatory changes in the absence of bacteria.

Prostatic abscess is a localized infection in the prostate. Patients at increased risk for development of prostatic abscesses include diabetics and men who are immunocompromised. Urethral instrumentation and chronic indwelling catheters may also increase risk. Historically, prostatic abscesses were caused by *Neisseria gonorrhea*. Today, however, most cases are associated with coliform organisms, *Pseudomonas spp*., and anaerobic organisms.

Urethritis and epididymitis are generally painful conditions caused by bacterial infection of the urethra and epididymis, respectively. Both disorders may be acute or chronic. These are considered separately in the chapter on sexually transmitted diseases (STDs).

Orchitis is often associated with bacterial epididymitis. Isolated bacterial orchitis is less common. Mumps orchitis represents a specific form of the disease; it occurs in about 30% of mumps cases in postpubertal boys. The acute inflammation that occurs in these cases may lead to testicular atrophy and subsequent infertility. Other forms of orchitis include tuberculous orchitis, gangrenous orchitis, and testicular inflammation associated with infected hydroceles. In older men, most orchitis is probably related to bacterial UTI; however, in younger men, it usually represents a complication of sexually transmitted urethritis. These differences explain some of the demographic differences in hospitalization rates for orchitis noted later in this chapter. Orchitis is also addressed in the chapters on STDs and pediatric UTIs.

Scrotal infections may involve only the scrotal skin or may also include deeper structures. Fournier's gangrene is a severe form of scrotal infection associated with necrotizing fasciitis. Predisposing risk factors include diabetes, immunosuppression, poor perineal hygiene, and perirectal or perianal infections. Cultures typically yield mixed flora with both aerobic and anaerobic species. The risk of mortality with Fournier's gangrene is high because the infection can spread quickly along the layers of the abdominal wall that are contiguous with the scrotum. Aggressive surgical debridement and intravenous antimicrobial therapy are indicated.

PREVALENCE AND INCIDENCE

Approximately 20% of all UTIs occur in men. Between 1988 and 1994, the overall lifetime prevalence of UTI in men was estimated to be 13,689 cases per 100,000 adult men, based on the National Health and Nutrition Examination Survey (NHANES-III) (Tables 2 and 3). In comparison, the estimate for women was 53,067 cases per 100,000 adult women during the same time period (Chapter 6, Table 2).

Data from US Veterans Health Administration (VA) facilities supports the higher prevalence of UTI in women compared to men (Chapter 6, Figure 1 and Table 4). Between 1999 and 2001, the overall prevalence of UTI as a primary diagnosis in veterans seeking outpatient care was 2.3 to 2.48 times greater in women than it was in men. Rates of orchitis were generally higher than either cystitis or pyelonephritis when considered as either the primary or any diagnosis. Rates of UTI increased with age in this cohort and were higher in African American men than in other racial/ethnic groups (Table 4). The VA data show that overall rates of outpatient visits associated with a primary diagnosis of UTI among adult male veterans dropped steadily between 1999 and 2001; this trend was most pronounced for older

Table 2. Male lifetime prevalence of urinary tract infections, by socio-demographic group, count, rate[a]

	Count	Rate
Total count[b]	11,892,613	13,689
1–2 Bladder infections ever	8,983,769	10,341
3+ Bladder infections ever	2,908,845	3,348
Mean number of infections in the last 12 months of those ever having UTI	0.26	...
Race/ethnicity		
White non-Hispanic	9,864,439	14,458
Black non-Hispanic	932,376	10,326
Hispanic	909,324	13,229
Other	186,474	6,782
Region		
Midwest	3,327,654	15,899
Northeast	2,379,704	13,285
South	4,319,184	14,625
West	1,866,072	10,085
Urban/rural		
MSA	5,585,151	8,688
Non-MSA	6,307,463	27,919

...data not available.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1991 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

[b]The data in this table are based on the weighted number of persons who responded “1 or more” to question HAK4: “How many times have you had a bladder infection, also called urinary tract infection, UTI or cystitis?”

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Health and Nutrition Examination Survey III, 1988–1994.

Table 3. Male incidence of UTI in past 12 months, by socio-demographic group, count, rate[a]

	Count	Rate
Total count[b]	2,013,448	2,318
1 or more bladder infections in the last 12 months	2,013,448	2,318
Mean number of infections in the last 12 months	1.5	0
Age		
18–24	111,205	920
25–34	374,050	1,789
35–44	251,245	1,336
45–54	302,969	2,419
55–64	239,659	2,394
65–74	432,123	5,303
75–84	242,354	6,693
85+	59,842	7,754
Race/ethnicity		
White non-Hispanic	1,505,602	2,207
Black non-Hispanic	209,061	2,315
Hispanic	180,689	2,629
Other	118,096	4,295
Region		
Midwest	495,025	2,365
Northeast	334,275	1,866
South	846,422	2,866
West	337,725	1,825
Urban/rural		
MSA	837,678	1,303
Non-MSA	1,175,769	5,204

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1991 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

[b]The data in this table are based on the weighted number of persons who responded “1 or more” to question HAK5: “How many of these infections did you have during the past 12 months?”

NOTE: Counts may not sum to total due to rounding.

SOURCE: National Health and Nutrition Examination Survey III, 1988–1994.

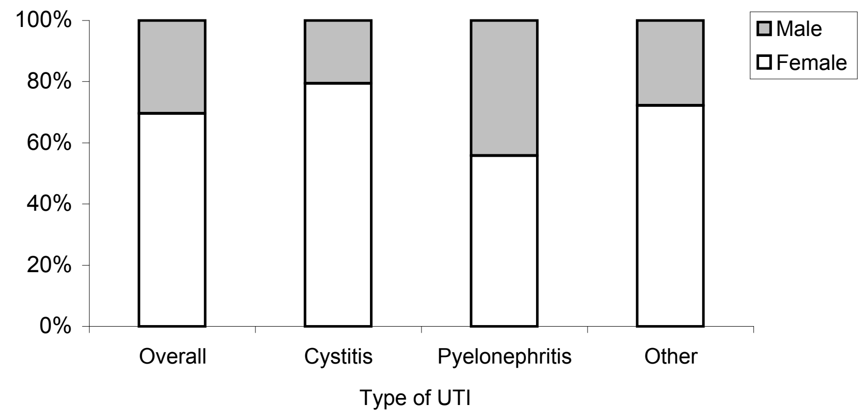

Figure 1. Percent contribution of males and females to types of urinary tract infections, 1999–2001.

SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

men and occurred across all racial/ethnic groups and geographic regions.

TRENDS IN HEALTHCARE RESOURCE UTILIZATION

Antimicrobial therapy is the primary mode of treatment for most patients with UTI. Antimicrobial selection is tailored on the basis of culture and susceptibility data following the initiation of empiric therapy. Selection of antimicrobials is guided by the severity and location of the individual infection and by consideration of regional and local epidemiological data on bacterial resistance.

Healthcare providers treat patients with UTI in a variety of clinical settings. This section examines trends in treatment patterns for male UTI at different sites of service.

Inpatient Care

Inpatient care with administration of intravenous antimicrobials may be required to treat men with severe UTI. Increased patient age appears to be associated with an increased rate of inpatient treatment for UTI in men. Data from the Centers for Medicare and Medicaid Services (CMS) from 1992 to 1998 reveal that across all years of study, the rates of inpatient care for men 65 years of age and older are approximately 1.7 times those of men younger than 65 (Table 5). The younger group comprises primarily those who qualified for Medicare because of disability or end-stage renal disease. The risk appears to increase significantly with age; rates more than double in men aged 85 and older. For example, the rate of inpatient care in 1992 for men 85 to 94 years of age was 1,678 per 100,000 (95% CI, 1649–1706) compared with 777 per 100,000 (95% CI, 768–786) for men aged 75 to 84, and 308 per 100,000 (95% CI, 304–312) for men 65 to 74. This trend was similar in 1995 and 1998. Increased use of inpatient care may be associated with more severe infections in older men due to increased comorbidity and changes in immune response associated with increased age. In the time period covered by the Medicare data, rates of inpatient hospitalization for male UTI care were about 1.5 times higher in African Americans than in Caucasians or Hispanics (counts in Asians and North American Natives were too low to produce reliable estimates of rates). The rate of inpatient utilization was somewhat higher in the South than in other regions.

Data for 1994 to 2000 from the Healthcare Cost and Utilization Project (HCUP) reveal that the rates of inpatient hospital care for men with a primary diagnosis of UTI at any anatomic location have been relatively stable for young and middle-aged men (18 to 64 years) and for men between ages 65 and 74 (Table 6). In contrast, the rates of hospitalization for men in the 75- to 84-year age group have slowly declined, while the rates for men over 85 have gradually increased over time. The rates of inpatient care increase steadily with

Table 4. Frequency of urinary tract infection[a] as a diagnosis in male VA patients seeking outpatient care, rate[b]

	1999		2000		2001	
	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis	Primary Diagnosis	Any Diagnosis
Total	2,082	2,705	1,963	2,591	1,719	2,334
Age						
18–24	1,351	1,475	1,429	1,620	1,586	1,731
25–34	1,524	1,803	1,545	1,796	1,415	1,673
35–44	1,663	2,022	1,634	1,995	1,492	1,867
45–54	1,725	2,179	1,707	2,184	1,538	2,017
55–64	2,013	2,623	1,894	2,499	1,695	2,267
65–74	2,172	2,901	1,986	2,698	1,654	2,308
75–84	2,695	3,581	2,361	3,211	1,979	2,786
85+	3,983	5,317	3,540	4,733	2,975	4,321
Race/ethnicity						
White	2,553	3,311	2,411	3,167	2,139	2,881
Black	3,313	4,287	3,172	4,077	2,912	3,841
Hispanic	3,111	4,118	2,935	3,989	2,888	4,052
Other	2,088	2,642	1,763	2,351	1,764	2,338
Unknown	1,101	1,438	1,058	1,430	925	1,295
Region						
Midwest	1,989	2,606	1,892	2,503	1,578	2,132
Northeast	1,784	2,304	1,646	2,128	1,449	1,910
South	2,349	3,104	2,188	2,966	1,918	2,681
West	2,103	2,640	2,043	2,608	1,861	2,471
Insurance status						
No insurance/self-pay	1,994	2,552	1,929	2,486	1,716	2,271
Medicare/Medicare supplemental	2,560	3,412	2,254	3,087	1,928	2,702
Medicaid	2,455	2,972	2,188	2,846	2,287	2,998
Private insurance/HMO/PPO	1,700	2,234	1,534	2,036	1,280	1,760
Other insurance	1,830	2,338	1,868	2,361	1,519	2,039
Unknown	5,540	7,405	4,692	5,768	1,168	1,550

HMO, health maintenance organization; PPO, preferred provider organization.
[a]Represents diagnosis codes for male UTIs (including cystitis, pyelonephritis, orchitis, and other UTIs).
[b]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.
NOTE: Race/ethnicity data from clinical observation only, not self-report; note large number of unknown values.
SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 5. Inpatient stays by male Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	74,320	505 (501–508)	72,820	478 (475–482)	70,480	487 (483–490)
Total < 65	9,960	322 (316–329)	10,940	318 (312–323)	10,840	315 (310–321)
Total 65+	64,360	553 (549–557)	61,880	526 (521–530)	59,640	540 (536–544)
Age						
65–74	22,300	308 (304–312)	19,980	278 (274–282)	17,320	269 (265–274)
75–84	27,440	777 (768–786)	26,180	716 (707–724)	26,180	715 (706–724)
85–94	13,260	1,678 (1,649–1,706)	14,560	1,716 (1,689–1,744)	14,760	1,705 (1,678–1,732)
95+	1,360	1,752 (1,659–1,844)	1,160	1,415 (1,334–1,495)	1,380	1,579 (1,496–1,661)
Race/ethnicity						
White	60,820	490 (486–494)	59,680	459 (455–463)	57,180	468 (464–471)
Black	9,780	768 (752–783)	10,100	729 (715–744)	9,800	734 (720–749)
Asian	…	…	180	247 (211–283)	380	277 (249–305)
Hispanic	…	…	1,000	504 (472–535)	1,560	465 (442–488)
N. American Native	…	…	140	696 (582–810)	340	1,216 (1,087–1,345)
Region						
Midwest	18,200	491 (484–498)	18,720	486 (479–493)	18,480	500 (493–507)
Northeast	15,460	488 (480–495)	13,900	437 (430–444)	13,820	497 (489–506)
South	31,620	604 (597–610)	30,720	560 (554–566)	28,500	531 (525–537)
West	8,260	368 (360–376)	8,340	360 (352–367)	8,260	369 (361–377)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, MedPAR and 5% Carrier File, 1992, 1995, 1998.

age, more than doubling with each decade beyond age 55. In this analysis, Asian men had the lowest rates of inpatient hospitalization for UTI care, followed by Hispanics and Caucasians. African American men had the highest rates of inpatient utilization. When analyzed by region, the lowest rates of inpatient care were seen in the West, while rates were similar in other geographic regions. Rates of inpatient care were similar in urban and rural settings. It is unclear why estimated inpatient utilization rates are lower in HCUP data than in CMS data.

Data from HCUP also reveal that approximately 10% of all inpatient care for UTI in men is for the treatment of orchitis (Table 7). Between 1994 and 2000, the overall rate of inpatient care for the treatment of orchitis was relatively stable, ranging from 12 to 14 per 100,000 population. Rates appear to rise gradually with age, the most significant increases occurring between 65 and 85 years of age. Inpatient utilization rates for elderly men decreased somewhat in 2000 compared to prior years. African American men had the highest rates of inpatient utilization for treatment of orchitis, and Asian men had the lowest rates. Inpatient utilization rates were slightly lower in the West than in other regions, and there was no significant difference between rates in urban and rural locations. The mean length of stay for inpatient hospitalizations in men with a primary diagnosis of UTI decreased from 6.5 days in 1994 to 5.1 days in 2000 (Table 8). Consistent with the general trend toward decreased use of inpatient care, this observation in men with UTI was noted across all age groups and

Table 6. Inpatient hospital stays by adult males with urinary tract infection (any anatomic location) listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	115,258	131 (126–135)	111,680	121 (117–126)	118,193	125 (121–130)	121,367	126 (122–130)
Age								
18–24	2,475	20 (18–23)	2,129	17 (15–20)	2,139	17 (15–19)	1,983	15 (13–17)
25–34	6,670	33 (31–36)	6,124	31 (28–33)	5,344	28 (26–30)	5,045	28 (25–30)
35–44	8,525	43 (40–46)	9,114	43 (40–46)	8,956	41 (39–43)	8,764	40 (38–42)
45–54	9,830	70 (66–74)	9,748	63 (59–67)	10,324	62 (59–66)	11,165	63 (59–66)
55–64	12,394	129 (121–137)	11,840	119 (112–126)	13,327	126 (119–133)	13,360	120 (113–126)
65–74	25,188	320 (304–336)	23,215	284 (269–299)	24,256	301 (286–317)	24,374	303 (289–318)
75–84	32,866	867 (828–905)	32,246	765 (729–800)	33,885	747 (717–777)	35,667	738 (709–767)
85+	17,309	1,931 (1,830–2,031)	17,265	1,996 (1,890–2,101)	19,962	2,025 (1,932–2,119)	21,010	2,054 (1,968–2,140)
Race/ethnicity								
White	68,442	101 (97–105)	68,319	98 (94–102)	68,032	97 (93–101)	68,899	97 (93–100)
Black	13,583	147 (136–158)	13,334	138 (128–148)	12,935	130 (121–139)	12,488	122 (113–131)
Asian/Pacific Islander	813	33 (26–40)	919	29 (24–34)	1,153	34 (29–39)	1,629	46 (40–52)
Hispanic	5,699	69 (61–78)	6,067	67 (58–77)	6,947	69 (61–77)	7,982	77 (71–83)
Region								
Midwest	25,498	122 (112–132)	25,542	119 (111–126)	26,933	124 (114–133)	26,666	119 (111–127)
Northeast	24,955	138 (128–148)	23,501	130 (119–141)	23,233	128 (119–137)	24,625	136 (127–145)
South	47,476	160 (151–168)	44,858	141 (133–149)	48,656	147 (140–154)	49,021	144 (137–151)
West	17,329	88 (80–97)	17,779	87 (79–94)	19,371	91 (82–100)	21,055	98 (90–105)
MSA								
Rural	26,408	118 (109–127)	26,148	126 (117–135)	25,469	121 (113–129)	26,675	125 (117–133)
Urban	88,714	135 (129–140)	85,413	120 (115–125)	92,416	126 (121–131)	94,578	126 (122–131)

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 7. Inpatient hospital stays by adult males with orchitis listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	12,322	14 (13–15)	11,363	12 (12–13)	11,941	13 (12–13)	12,174	13 (12–13)
Age								
18–24	614	5.0 (4.0–6.1)	454	3.7 (2.8–4.6)	584	4.7 (3.8–5.6)	532	4.1 (3.2–4.9)
25–34	2,058	10 (9.0–11)	1,548	7.8 (6.7–8.8)	1,428	7.4 (6.4–8.4)	1,312	7.2 (6.2–8.2)
35–44	2,207	11 (10–12)	2,390	11 (10–13)	2,481	11 (10–13)	2,469	11 (10–12)
45–54	1,848	13 (11–15)	1,928	12 (11–14)	2,100	13 (11–14)	2,446	14 (12–15)
55–64	1,610	17 (14–19)	1,431	14 (13–16)	1,710	16 (14–18)	1,786	16 (14–18)
65–74	1,964	25 (22–28)	1,896	23 (21–26)	1,674	21 (18–23)	1,865	23 (20–26)
75–84	1,570	41 (36–47)	1,305	31 (27–35)	1,509	33 (29–38)	1,384	29 (25–33)
85+	451	50 (37–64)	411	47 (36–59)	454	46 (36–57)	379	37 (28–46)
Race/ethnicity								
White	6,545	10 (8.9–10)	6,333	9.1 (8.5–9.8)	6,437	9.2 (8.5–9.8)	6,216	8.7 (8.0–9.4)
Black	1,896	21 (18–23)	1,647	17 (15–20)	1,571	16 (14–18)	1,613	16 (14–18)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	773	9.4 (7.1–12)	788	8.7 (7.3–10)	910	9.0 (7.0–11)	1,241	12 (10–14)
Region								
Midwest	2,720	13 (12–15)	2,874	13 (12–15)	2,752	13 (11–14)	2,650	12 (10–13)
Northeast	3,297	18 (16–20)	2,714	15 (13–17)	2,536	14 (12–16)	2,543	14 (12–16)
South	4,456	15 (13–17)	4,226	13 (12–14)	4,796	14 (13–16)	4,920	14 (13–16)
West	1,850	9.4 (8.1–11)	1,549	7.6 (6.5–8.6)	1,858	8.7 (7.1–10)	2,061	10 (8.1–11)
MSA								
Rural	2,686	12 (10–14)	2,527	12 (11–14)	2,551	12 (11–14)	2,397	11 (10–13)
Urban	9,589	15 (14–16)	8,829	12 (12–13)	9,340	13 (12–14)	9,759	13 (12–14)

*Figure does not meet standard of reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

[b]Persons of other races, missing or unavailable race and ethnicity, and missing MSA are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 8. Trends in mean inpatient length of stay (days) for adult males hospitalized with urinary tract infection listed as primary diagnosis

	Length of Stay			
	1994	1996	1998	2000
Total	6.5	5.4	5.1	5.1
Age				
18–24	4.4	3.9	3.6	3.4
25–34	4.9	4.2	4.0	4.2
35–44	5.2	4.6	4.1	4.4
45–54	5.4	4.8	4.5	4.8
55–64	5.9	4.9	4.8	4.8
65–74	6.3	5.3	5.0	5.1
75–84	7.2	6.0	5.5	5.4
85+	7.8	6.3	5.8	5.6
Race/ethnicity				
White	6.3	5.4	5.0	5.1
Black	7.5	6.3	5.9	5.7
Asian/Pacific Islander	7.1	5.5	5.6	5.4
Hispanic	6.1	5.3	5.2	5.0
Other	5.9	6.5	4.7	5.4
Region				
Midwest	6.0	5.1	4.9	4.8
Northeast	8.2	7.0	5.9	5.7
South	6.0	5.1	4.9	5.2
West	5.9	4.8	4.6	4.5
MSA				
Rural	5.7	5.0	4.6	4.6
Urban	6.7	5.6	5.2	5.2

MSA, metropolitan statistical area.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

geographic regions, and in both rural and urban hospitals.

Outpatient Care

Outpatient care for UTI in men is administered in a variety of clinical settings, including hospital outpatient clinics, physician offices, ambulatory surgery centers, and emergency rooms. Each of these settings was analyzed separately.

Hospital Care

Data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 1994 to 2000 reveal that hospital outpatient visits by men with UTI listed as any of the reasons for the visit have been variable (Table 9), ranging from 91 to 175 per 100,000. When UTI was listed as the primary reason for the hospital patient visit, the rates increased from 80 per 100,000 (95% CI, 33–127) in 1996 to 136 per 100,000 (95% CI, 80–193) in 1998. The rate in 2000 dropped slightly, to 124 per 100,000 (95% CI, 62–186). These data suggest that there has been a general trend toward increased outpatient care for UTI in men. This complements the observed decreases in inpatient care noted above.

Table 9. Hospital outpatient visits by adult males with urinary tract infection, count, rate[a] (95% CI)

	Primary Reason		Any Reason	
	Count	Rate	Count	Rate
1994	73,571	83 (44–122)	154,900	175 (92–259)
1996	73,508	80 (33–127)	83,579	91 (44–138)
1998	128,629	136 (80–193)	163,573	173 (110–237)
2000	119,557	124 (62–186)	152,422	159 (91–226)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

SOURCE: National Hospital Ambulatory Medical Care Survey—Outpatient, 1994, 1996, 1998, 2000.

Hospital outpatient visit data from CMS reveal a similar increase in utilization during the past decade (Table 10). Among Medicare beneficiaries at least 65 years old, rates of hospital outpatient visits for men with UTI rose from 191 per 100,000 (95% CI, 189–194) in 1992 to 301 per 100,000 (95% CI, 298–304) in 1995, and 362 per 100,000 (95% CI, 358–365) in 1998. The most dramatic increases were observed in the oldest elderly men. In those 95 years of age and older, the rates of hospital outpatient visits more than doubled between 1992 and 1995 and doubled again between 1995 and 1998. Rates of hospital outpatient visits for UTI care in men were highest in the Midwest and South, and the rates in both regions have increased over time. In the years for which complete data regarding racial/ethnic differences in outpatient hospital utilization were available (1995 and 1998), Hispanic men had the highest rates of utilization, followed by African American men. In 1998, the rates for Hispanic men were 1.23 and 1.80 times higher than those for African Americans and Caucasians, respectively (counts in

Table 10. Hospital outpatient visits by male Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	28,580	194 (192–196)	46,020	302 (300–305)	51,720	357 (354–360)
Total < 65	6,300	204 (199–209)	10,560	307 (301–312)	11,760	342 (336–348)
Total 65+	22,280	191 (189–194)	35,460	301 (298–304)	39,960	362 (358–365)
Age						
65–74	10,080	139 (137–142)	14,920	208 (204–211)	16,920	263 (259–267)
75–84	9,340	264 (259–270)	14,020	383 (377–390)	15,800	432 (425–438)
85–94	2,700	342 (329–355)	6,160	726 (708–744)	6,460	746 (728–764)
95+	160	206 (174–238)	360	439 (394–484)	780	892 (830–954)
Race/ethnicity						
White	18,540	149 (147–152)	33,160	255 (252–258)	40,560	332 (328–335)
Black	6,280	493 (481–505)	9,060	654 (641–668)	6,460	484 (472–496)
Asian	…	…	160	220 (185–254)	480	350 (319–381)
Hispanic	…	…	1,520	766 (727–804)	2,000	596 (570–622)
N. American Native	…	…	580	2,883 (2,649–3,116)	700	2,504 (2,321–2,686)
Region						
Midwest	8,460	228 (223–233)	12,780	332 (326–337)	15,160	410 (403–416)
Northeast	6,860	216 (211–221)	6,780	213 (208–218)	7,680	276 (270–283)
South	8,400	160 (157–164)	19,580	357 (352–362)	21,440	399 (394–405)
West	3,960	176 (171–182)	6,240	269 (262–276)	7,240	324 (316–331)

…data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Asians were too low to produce reliable estimates of rates). The reason for this observed difference is unclear.

Physician Offices

The majority of UTIs in both men and women are treated in physicians' offices. According to data from the National Ambulatory Medical Care Survey (NAMCS), more than 1,896,000 physician office visits that included a diagnosis of UTI were made in 2000 by men in the United States (Table 11). Of these visits, more than 1,290,000 were for a primary diagnosis of UTI. Fluctuations in rates of utilization have been observed over time, with peaks occurring in 1992 and 1996. In these years, the observed rates of physician office visits for UTI in men aged 55 and older were significantly higher than those for younger men. This likely reflects the higher incidence and prevalence of UTI in older men. The reasons for the dramatic increases in 1992 and 1996 are unclear but may be related to coding anomalies.

Medicare data for outpatient physician office visits for men with UTI indicate that rates of utilization remained relatively stable throughout the 1990s (Table 12). Rates were consistently highest in men in the 85- to 94-year age group, followed by those aged 75 to 84 (Figure 2). Rates in the most elderly cohort (95 and older) were similar to the overall mean. Regional variations in Medicare physician outpatient visits for men with UTI appear to have diminished over time and were least pronounced in 1998. As in the NHAMCS data, Hispanic men had the highest rates

Table 11. Physician office visits by adult males with urinary tract infection, count, rate[a] (95% CI)

	1992		1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
					Primary Reason for Visit					
Total	1,992,546	2,268 (1,598–2,938)	1,111,037	1,259 (889–1,629)	2,163,849	2,353 (1,601–3,105)	1,664,141	1,765 (1,060–2,470)	1,290,406	1,342 (854–1,830)
Age										
18–54	1,067,943	1,642 (964–2,320)	682,612	1,033 (652–1,414)	1,147,995	1,669 (913–2,425)	845,264	1,205 (582–1,828)	819,947	1,153 (568–1,738)
55+	924,603	4,050 (2,340–5,760)	428,425	1,932 (993–2,872)	1,015,854	4,379 (2,412–6,346)	*	*	470,459	1,879 (1,013–2,745)
					Any Reason for Visit					
Total	2,372,185	2,700 (1,997–3,402)	1,594,515	1,807 (1,368–2,245)	2,652,548	2,884 (2,093–3,675)	2,105,332	2,232 (1,447–3,018)	1,896,810	1,973 (1,377–2,568)
Age										
18–54	1,203,792	1,851 (1,149–2,553)	831,728	1,258 (843–1,674)	1,243,005	1,807 (1,041–2,574)	971,180	1,384 (731–2,038)	1,153,805	1,623 (915–2,330)
55+	1,168,393	5,118 (3,297–6,939)	762,787	3,441 (2,209–4,673)	1,409,543	6,076 (3,910–8,241)	*	*	743,005	2,967 (1,876–4,058)

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on 1992, 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: National Ambulatory Medical Care Survey—Outpatient, 1992, 1994, 1996, 1998, 2000.

Table 12. Physician office visits by male Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	524,880	3,564 (3,555–3,574)	540,200	3,549 (3,540–3,559)	498,620	3,444 (3,435–3,453)
Total < 65	62,880	2,035 (2,019–2,051)	75,040	2,178 (2,163–2,193)	71,420	2,078 (2,063–2,093)
Total 65+	462,000	3,970 (3,959–3,981)	465,160	3,951 (3,939–3,962)	427,200	3,869 (3,858–3,880)
Age						
65–74	231,780	3,202 (3,190–3,215)	231,720	3,224 (3,211–3,237)	197,840	3,078 (3,065–3,092)
75–84	177,880	5,037 (5,014–5,060)	180,140	4,925 (4,903–4,947)	173,720	4,744 (4,723–4,766)
85–94	49,700	6,289 (6,235–6,342)	50,300	5,929 (5,879–5,980)	52,980	6,119 (6,069–6,170)
95+	2,640	3,400 (3,273–3,528)	3,000	3,659 (3,530–3,787)	2,660	3,043 (2,928–3,157)
Race/ethnicity						
White	446,400	3,599 (3,589–3,610)	464,380	3,572 (3,562–3,582)	425,500	3,480 (3,469–3,490)
Black	47,140	3,700 (3,667–3,733)	48,560	3,507 (3,476–3,538)	40,760	3,054 (3,025–3,083)
Asian	…	…	2,400	3,293 (3,164–3,422)	4,700	3,427 (3,331–3,523)
Hispanic	…	…	9,740	4,906 (4,811–5,001)	14,980	4,463 (4,393–4,533)
N. American Native	…	…	520	2,584 (2,366–2,803)	440	1,574 (1,427–1,720)
Region						
Midwest	126,780	3,418 (3,399–3,436)	125,900	3,266 (3,248–3,284)	113,680	3,074 (3,056–3,092)
Northeast	86,280	2,721 (2,703–2,739)	93,300	2,934 (2,915–2,952)	83,440	3,002 (2,982–3,022)
South	223,640	4,270 (4,252–4,287)	220,600	4,021 (4,005–4,038)	210,400	3,920 (3,904–3,937)
West	76,500	3,405 (3,381–3,429)	83,260	3,590 (3,567–3,614)	76,820	3,435 (3,411–3,459)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

of physician office utilization among the racial/ethnic groups analyzed.

Ambulatory Surgery

Visits to ambulatory surgery centers represent a small percentage of Medicare visits for men with UTI (Table 13). Among Medicare beneficiaries at least 65 years old, rates ranged from 83 per 100,000 in 1992 (95% CI, 82–85) to 93 per 100,000 in 1995 (95% CI, 92–95) and 95 per 100,000 in 1998 (95% CI, 93–97). Rates were lower and more stable among younger Medicare beneficiaries who qualified because of disability or end-stage renal disease. As with Medicare physician office visits, the highest rates were observed in men 75 to 94 years of age. Rates were highest in the Midwest and Northeast and lowest in the South and West. The reasons for these geographic differences are unclear. No clear racial/ethnic differences were observed in this analysis. The low rates of utilization for ambulatory surgery centers indicate that this is not a primary site of service for men with UTI. The cases identified likely represent perioperative UTI in men scheduled for outpatient surgery.

Emergency Room

Patients with UTI may present to an emergency room (ER) for initial evaluation and management. Data from NHAMCS indicate approximately 424,700 ER visits by men with a primary diagnosis of UTI in 2000 (Table 14). The overall rate of utilization in 2000 was 442 per 100,000, which is similar to the rate of 420 per 100,000 observed in 1994. Lower rates of ER utilization in this population were observed in 1996 and 1998. The rates of ER utilization by male Medicare

Table 13. Visits to ambulatory surgery centers by male Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	11,120	76 (74–77)	12,860	84 (83–86)	12,200	84 (83–86)
Total < 65	1,420	46 (44–48)	1,860	54 (52–56)	1,720	50 (48–52)
Total 65+	9,700	83 (82–85)	11,000	93 (92–95)	10,480	95 (93–97)
Age						
65–74	5,400	75 (73–77)	5,880	82 (80–84)	4,940	77 (75–79)
75–84	3,500	99 (96–102)	4,200	115 (111–118)	4,460	122 (118–125)
85–94	780	99 (92–106)	860	101 (95–108)	1,040	120 (113–127)
95+	20	26 (14–37)	60	73 (55–91)	40	46 (32–59)
Race/ethnicity						
White	9,680	78 (76–80)	11,280	87 (85–88)	10,820	88 (87–90)
Black	780	61 (57–66)	1,100	79 (75–84)	940	70 (66–75)
Asian	…	…	100	137 (110–165)	20	15 (8.0–21)
Hispanic	…	…	100	50 (40–60)	240	72 (63–80)
N. American Native	…	…	…	…	20	72 (39–104)
Region						
Midwest	3,420	92 (89–95)	3,960	103 (100–106)	3,880	105 (102–108)
Northeast	2,940	93 (89–96)	3,000	94 (91–98)	3,000	108 (104–112)
South	3,840	73 (71–76)	4,540	83 (80–85)	3,960	74 (71–76)
West	880	39 (37–42)	1,240	53 (50–56)	1,260	56 (53–59)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

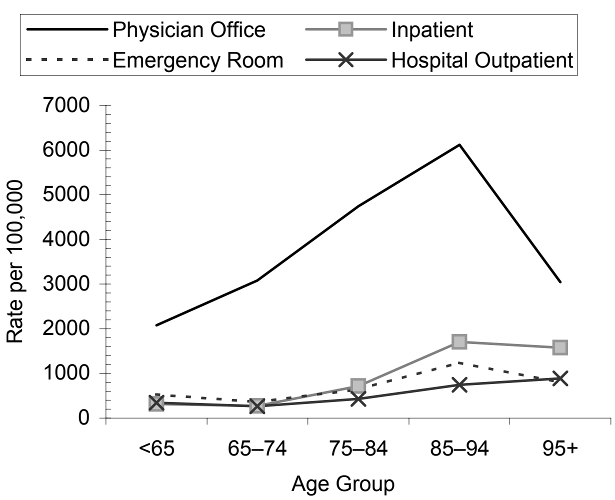

Figure 2. Trends in visits by males with urinary tract infection listed as primary diagnosis by patient age and site of service, 1998.

SOURCE: Centers for Medicare and Medicaid Services, 1998.

Table 14. Emergency room visits by adult males with urinary tract infection listed as primary diagnosis, count, rate[a] (95% CI)

	Count	Rate
1994	370,637	420 (320–520)
1996	296,377	322 (232–412)
1998	322,937	342 (245–440)
2000	424,705	442 (325–559)

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.

SOURCE: National Hospital Ambulatory Medical Care Survey—ER, 1994, 1996, 1998, 2000.

Table 15. Emergency room visits by male Medicare beneficiaries with urinary tract infection listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	74,500	506 (502–510)	78,220	514 (510–518)	76,280	527 (523–531)
Total < 65	15,100	489 (481–496)	17,680	513 (506–521)	18,320	533 (525–541)
Total 65+	59,400	510 (506–515)	60,540	514 (510–518)	57,960	525 (521–529)
Age						
65–74	26,440	365 (361–370)	24,200	337 (333–341)	23,000	358 (353–362)
75–84	22,960	650 (642–659)	25,040	685 (676–693)	23,540	643 (635–651)
85–94	9,140	1,156 (1,133–1,180)	10,360	1,221 (1,198–1,245)	10,720	1,238 (1,215–1,262)
95+	860	1,108 (1,034–1,181)	940	1,146 (1,073–1,220)	700	801 (741–860)
Race/ethnicity						
White	58,080	468 (464–472)	60,220	463 (460–467)	58,820	481 (477–485)
Black	12,200	958 (941–974)	14,820	1,070 (1,053–1,087)	13,040	977 (960–994)
Asian	…	…	140	192 (161–224)	300	219 (194–244)
Hispanic	…	…	1,300	655 (620–690)	2,240	667 (640–695)
N. American Native	…	…	120	596 (492–701)	300	1,073 (951–1,195)
Region						
Midwest	17,820	480 (473–487)	18,140	471 (464–477)	19,600	530 (523–537)
Northeast	12,720	401 (394–408)	13,660	430 (422–437)	12,140	437 (429–445)
South	33,080	632 (625–638)	36,740	670 (663–677)	34,240	638 (631–645)
West	9,680	431 (422–439)	8,500	367 (359–374)	8,980	402 (393–410)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

beneficiaries were somewhat higher, ranging from 506 per 100,000 (95% CI, 502–510) in 1992 to 527 per 100,000 (95% CI, 523–531) in 1998 (Table 15). In this analysis, utilization rates were consistently highest in the next-to-oldest cohort (85 to 94 years of age), followed closely by the oldest men (those 95 and older). Rates of ER utilization by older men were nearly twice those of men younger than 85 years of age. This may represent increased severity of infection in elderly men prompting evaluation in the ER. Rates of ER utilization in this cohort were consistently highest in the South. Again, the reason for the geographic variation is unclear. African American men had rates of ER utilization twice as high as those of Caucasians in this analysis (Figure 3). The lowest rates were observed in Asian men.

Nursing Homes

Information regarding UTI in men living in nursing home facilities was obtained from the National Nursing Home Survey of 1995, 1997, and 1999 (Tables 16–18). The overall rates for men with either an admitting or current diagnosis of UTI in this sample appear stable over time, ranging from 5,642 per 100,000 in 1997 (95% CI, 4,641–6,642) to 5,803 per 100,000 in 1995 (95% CI, 4,794–6,812). It is interesting to note that the rates of UTI for men living in nursing homes are closer to those for women than are the rates for the community-dwelling cohorts, as discussed in the chapter on UTI in Women (see Chapter 6 , Tables 21–23). No clear trends were observed over time with regard to age in male nursing home residents. In all years studied, about half of male nursing home residents required special assistance using the toilet,

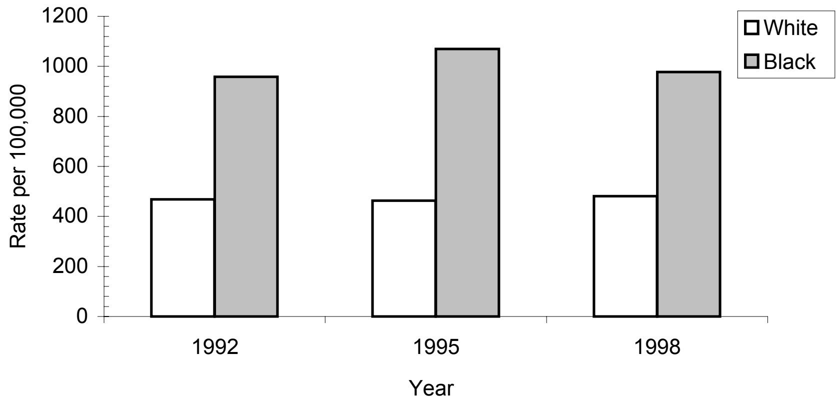

Figure 3. **Rate of emergency room visits for males with urinary tract infection listed as primary diagnosis by patient race and year.**

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

regardless of whether they had a UTI (Table 18). In 1997, only 39% of men with UTI required special assistance using the toilet, but this survey item was skipped at a much higher rate that year, making its results difficult to interpret (Table 17). Men with UTI had higher rates of incontinence than did the general cohort of male nursing home residents. It is not clear whether UTI or urinary incontinence is the causal factor.

The rates of indwelling catheter and ostomy use in male nursing home residents have remained stable at 11.9% in 1995 and 11.3% in 1999 (Table 18). This is of concern because of the well-established association between indwelling catheter use and urinary tract colonization and infection. Although these rates of catheter and ostomy use are not dramatic, they are higher than the 7.9 to 9.1% range observed in female nursing home residents. (see Chapter 6, Table 23).

ECONOMIC IMPACT

Direct Costs

Urinary tract infections in men are associated with a significant economic cost. Adjusted mean

Table 16. Male nursing home residents with an admitting or current diagnosis of urinary tract infection, count, rate[a] (95% CI)

	1995		1997		1999	
	Count	Rate	Count	Rate	Count	Rate
Total[b]	24,404	5,803 (4,794–6,812)	25,063	5,642 (4,641–6,642)	26,229	5,743 (4,761–6,724)
Age						
18–74	8,223	5,746 (4,046–7,445)	9,158	6,011 (4,302–7,720)	9,552	5,860 (4,266–7,455)
75–84	8,017	5,554 (3,886–7,223)	7,082	4,408 (2,956–5,859)	9,438	6,311 (4,397–8,225)
85+	8,164	6,135 (4,244–8,026)	8,822	6,723 (4,629–8,817)	7,239	5,020 (3,440–6,600)
Race						
White	18,678	5,500 (4,403–6,597)	19,029	5,364 (4,258–6,470)	18,455	5,070 (4,052–6,087)
Other	5,508	6,973 (4,453–9,493)	5,704	6,637 (4,252–9,021)	7,558	8,349 (5,608–11,089)

[a]Rate per 100,000 male nursing home residents in the same demographic stratum.
[b]Persons of unspecified race are included in the total.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 17. Special needs of male nursing home residents with urinary tract infection, count, rate[a] (95% CI)

Category	1995 Count	1995 Rate	1997 Count	1997 Rate	1999 Count	1999 Rate
Has indwelling foley catheter or ostomy						
Yes	6,925	28,375 (20,204–36,546)	8,960	357,50 (26,693–44,806)	6,880	26,229 (18,779–33,680)
No	17,479	71,625 (63,454–79,796)	16,103	64,250 (55,194–73,307)	19,349	73,771 (66,320–81,221)
Question left blank	0	0	0	0	0	0
Requires assistance using the toilet						
Yes	12,388	50,761 (41,692–59,830)	9,869	39,377 (30,473–48,280)	14,214	54,192 (45,293–63,092)
No	4,465	18,295 (11,292–25,297)	5,885	23,483 (15,212–31,754)	4,151	15,828 (9,343–22,312)
Question skipped for allowed reason	7,329	30,032 (21,702–38,363)	9,068	36,183 (27,302–45,064)	7,513	28,643 (20,417–36,869)
Question left blank	223	912 (0–2,715)	240	957 (0–2,850)	351	1,337 (0–3,204)
Requires assistance from equipment when using the toilet						
Yes	2,546	10,433 (4,740–16,126)	2,749	10,970 (54,89–16,452)	3,038	11,581 (5,996–17,166)
No	9,629	39,458 (30,628–48,288)	6,303	25,149 (17,344–32,954)	10,352	39,467 (30,808–48,125)
Question skipped for allowed reason	11,794	48,327 (39,262–57,392)	14,954	59,666 (50,709–68,623)	11,664	44,470 (35,581–53,360)
Question left blank	435	1,782 (0–4,262)	1,056	4,215 (504–7,925)	1,176	4,482 (911–8,053)
Requires assistance from another person when using the toilet						
Yes	12,388	50,761 (41,692–59,830)	9,637	38,450 (29,602–47,298)	14,214	54,192 (45,293–63,092)
No	0	0	0	0	0	0
Question skipped for allowed reason	11,794	48,327 (39,262–57,392)	14,954	59,666 (50,709–68,623)	11,664	44,470 (35,581–53,360)
Question left blank	223	912 (0–2,715)	472	1,884 (0–4,505)	351	1,337 (0–3,204)
Has difficulty controlling urine						
Yes	14,667	60,102 (51,208–68,997)	14,705	58,673 (49,604–67,743)	14,550	55,472 (46,703–64,240)
No	5,311	21,762 (14,269–29,256)	4,728	18,865 (11,759–25,972)	6,723	25,631 (17,996–33,265)
Question skipped for allowed reason	4,210	17,250 (10,366–24,135)	5,629	22,461 (14,800–30,122)	4,957	18,898 (12,329–25,467)
Question left blank	216	885 (0–2,635)	0	0	0	0

[a]Rate per 100,000 male nursing home residents with urinary tract infection in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 18. Special needs of male nursing home residents regardless of urinary tract infection diagnosis, count, rate[a] (95% CI)

Category	1995 Count	1995 Rate	1997 Count	1997 Rate	1999 Count	1999 Rate
Has indwelling foley catheter or ostomy						
Yes	50,298	11,961 (10,569–13,352)	53,938	12,141 (10,731–13,552)	51,457	11,266 (9,941–12,591)
No	369,452	87,854 (86,453–89,254)	389,880	87,762 (86,348–89,176)	401,402	87,884 (86,497–89,271)
Question left blank	781	186 (3–368)	430	97 (0–210)	3,883	850 (385–1,315)
Requires assistance using the toilet						
Yes	207,587	49,363 (47,203–51,523)	221,599	49,882 (47,736–52,028)	241,558	52,887 (50,755–55,020)
No	141,870	33,736 (31,689–35,783)	133,378	30,023 (28,069–31,977)	128,251	28,080 (26,154–30,005)
Question skipped for allowed reason	69,267	16,471 (14,863–18,080)	86,814	19,542 (17,809–21,275)	81,977	17,948 (16,308–19,588)
Question left blank	1,807	430 (146–714)	2,459	553 (238–869)	4,956	1,085 (571–1,599)
Requires assistance from equipment when using the toilet						
Yes	57,463	13,664 (12,183–15,145)	59,329	13,355 (11,901–14,809)	67,782	14,840 (13,323–16,357)
No	143,213	34,055 (32,011–36,100)	149,218	33,589 (31,564–35,614)	162,895	35,665 (33,630–37,699)
Question skipped for allowed reason	211,137	50,207 (48,047–52,368)	220,191	49,565 (47,419–51,711)	210,228	46,028 (43,899–48,156)
Question left blank	8,719	2,073 (1,466–2,680)	15,510	3,491 (2,702–4,281)	15,837	3,467 (2,650–4,285)
Requires assistance from another person when using the toilet						
Yes	203,490	48,389 (46,230–50,548)	217,556	48,972 (46,827–51,117)	238,252	52,163 (50,029–54,297)
No	2,350	559 (237–881)	2,571	579 (234–924)	2,690	589 (237–941)
Question skipped for allowed reason	211,137	50,207 (48,047–52,368)	220,191	49,565 (47,419–51,711)	210,228	46,028 (43,899–48,156)
Question left blank	3,554	845 (451–1,239)	3,930	885 (482–1,287)	5,573	1,220 (681–1,759)
Has difficulty controlling urine						
Yes	218,491	51,956 (49,797–54,115)	232,536	52,344 (50,203–54,485)	242,189	53,025 (50,898–55,153)
No	170,988	40,660 (38,537–42,783)	175,090	39,413 (37,325–41,500)	177,128	38,781 (36,709–40,852)
Question skipped for allowed reason	29,338	6,976 (5,881–8,072)	36,416	8,197 (7,028–9,366)	34,206	7,489 (6,406–8,572)
Question left blank	1,715	408 (110–705)	207	47 (0–138)	3,220	705 (255–1,155)

[a]Rate per 100,000 adult male nursing home residents in the NNHS for that year.
SOURCE: National Nursing Home Survey, 1995, 1997, 1999.

Table 19. Estimated annual expenditures of privately insured employees with and without a medical claim for a UTI in 1999[a]

	Annual Expenditures (per person)			
	Persons without UTI (N=267,520)	Persons with UTI (N=11,430)		
	Total	Total	Medical	Rx Drugs
Total	$3,099	$5,470	$4,414	$1,056
Age				
18–34	$2,685	$5,067	$4,333	$734
35–44	$2,861	$5,327	$4,398	$929
45–54	$3,173	$5,752	$4,565	$1,187
55–64	$3,279	$5,515	$4,342	$1,173
Gender				
Male	$2,715	$5,544	$4,528	$1,016
Female	$3,833	$5,407	$4,325	$1,082
Region				
Midwest	$2,988	$5,423	$4,367	$1,057
Northeast	$2,981	$5,197	$4,157	$1,040
South	$3,310	$5,838	$4,757	$1,080
West	$3,137	$5,762	$4,716	$1,046

Rx, prescription.

[a]The sample consists of primary beneficiaries ages 18 to 64 having employer-provided insurance who were continuously enrolled in 1999. Estimated annual expenditures were derived from multivariate models that control for age, gender, work status (active/retired), median household income (based on zip code), urban/rural residence, medical and drug plan characteristics (managed care, deductible, co-insurance/co-payments), and 26 disease conditions.

SOURCE: Ingenix, 1999.

healthcare expenditures for privately insured men diagnosed with a UTI was $5,544 in 1999, while the expenditure was $2,715 for men who did not experience a UTI (Table 19). In adults without a UTI, annual healthcare expenditures were lower for men than for women ($2,715 versus $3,833, respectively). However, there was little difference in total annual healthcare expenditures for men and women with UTI ($5,544 vs $5,407).

The total annual estimated expenditures for outpatient prescription medication for the treatment of UTI in both men and women between 1996 and 1998 were estimated to exceed $96.4 million (Table 20). Fluoroquinolones accounted for a large portion of these expenditures, in terms of both costs and numbers of claims. This may reflect a growing trend toward the use of fluoroquinolones rather than other types of antimicrobials for the treatment of UTI. The extent to which fluoroquinolones were prescribed as first-line therapy for prostatitis and other appropriate indications could not be determined from this dataset.

Indirect Costs

Overall time lost from work due to UTI was similar in men and women. Although men had only slightly higher rates of work loss due to cystitis (18% of men vs 16% of women), men tended to miss more than twice as much work time (10.5 hours vs 4.8 hours) (Table 21). Men with pyelonephritis also missed more total time from work than did women (11.0 hours vs 7.7 hours), although the percentage of men missing work was slightly lower than the percentage of women (21% vs 24%). Of men diagnosed with orchitis in this sample, 14% reported missing work, for a mean total of 7.6 hours (95% CI, 2.3–12.9). For each ambulatory care visit or hospitalization for orchitis, men missed an average of 3.8 hours of work (95% CI, 1.2–6.5) (Table 22).

Based on composite data, the overall medical expenditures for men with UTI in the United States were estimated to be approximately $1.028 billion in 2000 (Table 23). This is approximately 2.4 times lower than the overall amount spent to care for women with UTI during the same time period (see UTI in Women,

Table 20. Average annual spending and use of outpatient prescription drugs for treatment of urinary tract infection (male and female), 1996–1998[a]

Drug Name	Number of Rx Claims	Mean Price	Total Expenditures
Cipro™	774,067	$60.27	$46,652,998
Macrobid™	477,050	$26.80	$12,784,949
Triple antibiotic	329,253	$8.44	$2,778,898
Floxin™	279,564	$54.10	$15,124,394
Phenazopyridine	245,275	$5.50	$1,349,013
Amoxicillin	183,244	$8.46	$1,550,247
TMP/SMX	162,216	$6.23	$1,010,606
Bactrim	145,898	$13.62	$1,987,126
Nitrofurantoin	137,353	$38.22	$5,249,632
TMP-SMX ds	129,853	$5.48	$711,594
Oxybutynin	123,631	$28.87	$3,569,227
Cephalexin	118,985	$19.06	$2,267,854
Sulfacetamide	103,917	$6.17	$641,168
Sulfisoxazole	96,253	$7.82	$752,701
Total	3,306,559		$96,430,407

Rx, prescription.

[a]Estimates include prescription drug claims with a corresponding diagnosis for urinary tract infection (both males and females) and exclude drug claims for which there was insufficient data to produce reliable estimates. Including expenditures on these excluded medications would increase total outpatient drug spending for urinary tract infections by approximately 52%, to $146 million.

SOURCE: Medical Expenditure Panel Survey, 1996–1998.

Table 7). The costs of care for UTI in men appear to be increasing, as is the case with women (Table 23 and UTI in Women, Table 7). Inpatient care accounts for the largest portion of these expenditures, followed by physician office care and ER care. The total annual expenditures for male Medicare beneficiaries with UTI were approximately $480.2 million in 1998 (Table 24). This is significantly higher than the expenditures for younger male Medicare beneficiaries (total $91.1 million) but comparable on a per-person basis. Inpatient expenditures of older Medicare beneficiaries have remained constant over time after accounting for inflation (Table 25). However, spending on ambulatory services and emergency care has increased significantly in real terms between 1992 and 1998.

SPECIAL CONSIDERATIONS

Diabetes has been identified as a comorbid condition that may increase the risk of UTI. Some patients with diabetes develop voiding dysfunction, which predisposes them to an increased risk of UTI. Diabetes may also be associated with a component of immunosuppression. HCUP data from 1994 to 2000 indicate that the rates of diabetes as a comorbid condition in men hospitalized for UTI increased through the 1990s (Table 26). It is notable that diabetes is approximately twice as common among men hospitalized for UTI as it is in the general population (2).

Table 21. Average annual work loss of persons treated for urinary tract infection (95% CI)

Condition	Number of Persons[a]	% Missing Work	Average Work Absence (hr)		
			Inpatient	Outpatient	Total
Cystitis					
Males	116	18%	0.1 (0–0.4)	10.3 (0–24.5)	10.5 (0–24.7)
Females	426	16%	0	4.8 (3.0–6.6)	4.8 (3.0–6.6)
Pyelonephritis					
Males	71	21%	1.6 (0–4.7)	9.4 (2.6–16.2)	11.0 (3.6–18.4)
Females	79	24%	2.1 (0–4.2)	5.6 (2.0–9.1)	7.7 (3.7–11.7)
Other UTIs					
Males	779	15%	0.9 (0–2.6)	5.5 (3.7–7.3)	6.5 (4.0–8.9)
Females	1,846	17%	0	7.4 (5.5–9.3)	7.5 (5.6–9.3)
Orchitis	398	14%	1.5 (0.7–3.7)	6.1 (1.3–10.9)	7.6 (2.3–12.9)

[a]Individuals with an inpatient or outpatient claim for a UTI and for whom absence data were collected. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.
SOURCE: MarketScan, 1999.

Table 22. Average work loss associated with a hospitalization or an ambulatory care visit for treatment of urinary tract infection (95% CI)

	Inpatient Care		Outpatient Care	
Condition	Number of Hospitalizations[a]	Average Work Absence (hr)	Number of Outpatient Visits	Average Work Absence (hr)
Cystitis				
Males	*	*	157	7.6 (0–18)
Females	*	*	629	3.2 (2.2–4.3)
Pyelonephritis				
Males	*	*	87	7.7 (2.1–13)
Females	*	*	105	4.2 (2.0–6.4)
Other UTIs				
Males	*	*	1,047	4.1 (2.8–5.4)
Females	*	*	2,669	5.1 (3.9–6.4)
Orchitis	*	*	633	3.8 (1.2–6.5)

*Figure does not meet standard for reliability or precision.

[a]Unit of observation is an episode of treatment. Work loss is based on reported absences contiguous to the admission and discharge dates of each hospitalization or the date of the outpatient visit.

SOURCE: MarketScan, 1999.

Table 23. Expenditures for male urinary tract infection and share of costs, by site of service (% of total)

	Year			
Service Type	1994	1996	1998	2000
Total[a]	$811,500,000	$903,800,000	$969,300,000	$1,027,900,000
Inpatient	$626,500,000 (77.2%)	$629,900,000 (69.7%)	$691,100,000 (71.3%)	$733,900,000 (71.4%)
Physician Office	$81,200,000 (10.0%)	$179,900,000 (19.9%)	$157,000,000 (16.2%)	$135,700,000 (13.2%)
Hospital Outpatient	$18,700,000 (2.3%)	$18,100,000 (2.0%)	$31,000,000 (3.2%)	$28,800,000 (2.8%)
Emergency Room	$85,200,000 (10.5%)	$75,900,000 (8.4%)	$90,100,000 (9.3%)	$129,500,000 (12.6%)

[a]Total unadjusted expenditures exclude spending on outpatient prescription drugs for the treatment of UTI. Average drug spending for UTI-related conditions (both male and female) is estimated at $96 million to $146 million annually for the period 1996 to 1998.

SOURCES: National Ambulatory Medical Care Survey, National Hospital Ambulatory Mecial Care Survey, Healthcare Cost and Utilization Project, Medical Expenditure Panel Survey, 1994, 1996, 1998, 2000.

CONCLUSIONS

Urinary tract infections are among the most common urological disorders in both men and women. A variety of forms of UTI are recognized, and they may differ significantly, by location and severity. Overall, approximately 20% of all UTIs occur in men. These infections result in significant financial and personal costs for both individual patients and the healthcare system.

The data analyses presented here reveal several specific trends in men diagnosed with UTI. The overall rates of UTI in men appear to have remained stable during the 1990s. Although inpatient care still accounts for a significant portion of medical care for male UTI, there has been a general trend toward greater utilization of outpatient care in various settings for treatment of UTI-related disorders. Per capita financial expenditures for UTI in men appear similar to those for UTI in women. However, the mean time lost from work by men is somewhat greater.

Table 24. Expenditures for male Medicare beneficiaries for the treatment of urinary tract infection, by site of service, 1998

Site of Service	Total Annual Expenditures	
	Age < 65	Age 65+
Inpatient	$70,900,000	$376,400,000
Outpatient		
Physician Office	$9,800,000	$59,000,000
Hospital Outpatient	$1,300,000	$4,700,000
Ambulatory Surgery	$2,800,000	$17,700,000
Emergency Room	$6,400,000	$22,400,000
Total	$91,100,000	$480,200,000

SOURCE: Centers for Medicare and Medicaid Services, 1998.

Table 25. Expenditures for male Medicare beneficiaries age 65 and over for treatment of urinary tract infection

	Year		
Site of Service	1992	1995	1998
Total	$436,900,000	$452,800,000	$480,200,000
Inpatient	$363,600,000 (83.2%)	$364,200,000 (80.4%)	$376,400,000 (78.4%)
Outpatient			
Physician office	$41,400,000 (9.5%)	$46,900,000 (10.4%)	$59,000,000 (12.3%)
Hospital outpatient	$2,800,000 (0.6%)	$3,800,000 (0.8%)	$4,700,000 (1.0%)
Ambulatory surgery	$12,300,000 (2.8%)	$17,400,000 (3.8%)	$17,700,000 (3.7%)
Emergency room	$16,800,000 (3.8%)	$20,600,000 (4.5%)	$22,400,000 (4.7%)

NOTE: Percentages may not add to 100% because of rounding.
SOURCE: Centers for Medicare and Medicaid Services, 1992, 1995, 1998.

Table 26. Diabetes diagnosis as a comorbidity in adult males hospitalized for urinary tract infection, count (% of total), rate[a]

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	115,258	131	111,680	121	118,193	125	121,367	126
Without diabetes as listed diagnosis	92,853 (81%)	105	87,403 (78%)	95	90,294 (76%)	96	91,046 (75%)	95
With diabetes as listed diagnosis	22,405 (19%)	25	24,277 (22%)	26	27,899 (24%)	30	30,321 (25%)	32

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US male adult civilian non-institutionalized population.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

RECOMMENDATIONS

Analysis of these data raises several important research questions related to UTI in adult men. What is the relationship between comorbid urologic conditions such as benign prostatic hyperplasia, urinary incontinence, and urinary tract infection? What is the role of preventive care in men at risk for the development of UTI? How can the diagnosis and treatment of men with UTI be improved to minimize time lost from work and decrease overall medical expenditures? What roles do demographic factors, including race/ethnicity and geography, play in the risk for developing UTI? How can healthcare delivery be optimized to provide high-quality care while simultaneously decreasing costs and complications?

Many of these questions apply to both men and women with UTI. Additional research on health services, outcomes, economic impacts, and epidemiological factors is needed to answer these challenging questions.

REFERENCES

1. Krieger JN, Nyberg L, Jr., Nickel JC. NIH consensus definition and classification of prostatitis. JAMA 1999;282:236-7.
2. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-24.

CHAPTER 20

Sexually Transmitted Diseases

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Sexually Transmitted Diseases

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INTRODUCTION

This chapter focuses on the epidemiology and cost of sexually transmitted diseases (STDs) commonly seen in urologic practice in the United States. STDs generally comprise acute and/or chronic conditions attributed to acquisition of infectious agents during penile, anal, vaginal, and/or oral sex, but the emphasis in this chapter is on the urologic burden of these diseases.

The immediate and long-term disease burden and costs of STDs in the United States are immense, with severe and costly consequences for adolescents, adults, and their offspring. Infection with a bacterial STD may cause painful acute symptoms of urethritis, vaginitis, cervicitis, dysuria, or skin manifestations that require healthcare. If undetected and untreated, some bacterial STD infections may lead to serious and costly long-term consequences. For example, untreated bacterial STD in men may ascend to the upper genital tract, causing epididymitis, orchitis, or prostatitis. In women, untreated lower genital tract infection may lead to salpingitis or pelvic inflammatory disease (PID) that may result in infertility, life-threatening ectopic pregnancy, or chronic pelvic pain. Infection with a viral STD may become chronic, with single or relapsing episodes of painful or problematic symptoms and signs, as seen with genital herpes caused by herpes simplex virus (HSV) and genital warts and anogenital neoplasia caused by human papillomavirus (HPV). HSV infection also complicates the course and management of human immunodeficiency virus (HIV) infection. Infection by STDs during gestation or birth can result in eye infections (due to *Chlamydia trachomatis* or *Neisseriae gonorrhoeae*); pneumonia (from *C. trachomatis*); recurrent respiratory papillomatosis (from HPV); lifelong disability, including blindness, bone deformities, mental retardation (due to syphilis); or death (from syphilis or HSV).

The burden of disease and the trends for specific STDs vary considerably, but together these infections constitute a significant public health problem. The number of cases in the United States has been estimated to be in the tens of millions (Table 2), and as many as 15 million new (incident) STDs occur each year, of which 3 million are among teenagers (1).

GENERAL NOTES ON ANALYTIC APPROACH

In keeping with the goals and scope of this compendium, this assessment focused on the acute and chronic STD infections and clinical manifestations that are encountered commonly by urologists. Unlike patients with many other conditions associated with urinary tract pathology or dysfunction, those with STDs are not primarily referred to urologists for diagnosis and treatment. Accordingly, we quantified the burden of selected STDs that most commonly present with symptoms of the penis, urethra, bladder, and external genitalia. We focused on the numbers of cases of medical visits of inpatient and outpatient services for four pathogen-specific STDs (herpes, chlamydia, gonorrhea, and syphilis), genital warts (a presentation in which HPV is always implicated), and two syndromic presentations commonly due to STD infection (epididymitis/orchitis and urethritis).

Table 1. ICD-9 codes used in the diagnosis of sexually transmitted diseases[a]

Genital Herpes	
054.1	Genital herpes
054.10	Genital herpes unspecified
054.13	Herpetic infection of penis
054.19	Other genital herpes
Genital Warts	
078.11	Condyloma acuminatum
Chlamydia	
078.88	Other specified diseases due to Chlamydiae
079.88	Other specified chlamydial infection
079.98	Unspecified chlamydial infection
099.41	Other nongonococcal urethritis *Chlamydia trachomatis*
099.53	Other venereal diseases due to *Chlamydia trachomatis* lower genitourinary sites
099.54	Other venereal diseases due to *Chlamydia trachomatis* other genitourinary sites
099.55	Other venereal diseases due to *Chlamydia trachomatis* unspecified genitourinary site
Gonorrhea	
098.0	Gonococcal infection (acute) of lower genitourinary tract
098.1	Gonococcal infection (acute) of upper genitourinary tract
098.10	Gonococcal infection (acute) of upper genitourinary tract site unspecified
098.11	Gonococcal cystitis (acute)
098.12	Gonococcal prostatitis (acute)
098.13	Gonococcal epididymo-orchitis (acute)
098.14	Gonococcal seminal vesiculitis (acute)
098.15	Gonococcal cervicitis (acute)
098.16	Gonococcal endometritis (acute)
098.17	Gonococcal salpingitis specified as acute
098.19	Other gonococcal infection (acute) of upper genitourinary tract
098.2	Gonococcal infection (chronic) of lower genitourinary tract
098.30	Chronic gonococcal infection of upper genitourinary tract site unspecified
098.31	Gonococcal cystitis chronic
098.32	Gonococcal prostatitis chronic
098.33	Gonococcal epididymo-orchitis chronic
098.34	Gonococcal seminal vesiculitis chronic
Syphilis	
091.0	Genital syphilis (primary)
095.4	Syphilis of kidney
095.8	Other specified forms of late symptomatic syphilis
Epididymitis/orchitis not designated as due to Chlamydia or Gonococcus	
604	Orchitis and epididymitis
604.0	Orchitis, epididymitis, and epididymo-orchitis, with abscess
604.9	Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess [excludes gonococcal (098.13 and 098.33), mumps (072.0), tuberculous (016.4 and 016.50)]

Continued on next page

Table 1 (continued). ICD-9 codes used in the diagnosis of sexually transmitted diseases[a]

Epididymitis/orchitis (all codes)	
604	Orchitis and epididymitis
604.0	Orchitis, epididymitis, and epididymo-orchitis, with abscess
604.9	Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess [excludes gonococcal (098.13 and 098.33) (which is included below), mumps (072.0), tuberculous (016.4 and 016.50)]
098.13	Gonococcal epididymo-orchitis (acute)
098.33	Gonococcal epididymo-orchitis (chronic)
Urethritis not designated as due to Chlamydia trachomatis or gonococcus	
099.4	Other non-gonococcal urethritis (including 099.40 Unspecified, and 099.49 Other specified organism) but excluding 099.41 Urethritis due to *Chlamydia trachomatis*
Urethritis (all codes)	
098.0	Gonococcal infection (acute) of lower genitourinary tract
098.2	Gonococcal infection (chronic) of lower genitourinary tract
099.4	Other nongonococcal urethritis (including 099.40 Unspecified, and 099.49 Other specified organism) but excluding 099.41 Urethritis due to *Chlamydia trachomatis* (which is included below)
099.41	Other nongonococcal urethritis *Chlamydia trachomatis*

[a]Codes limited to acute manifestations of the lower genitourinary tract or external genitalia, or to sequelae due to ascension to the male upper genitourinary tract.

Epididymitis/orchitis and urethritis were included because of the likelihood of presentation to a urologist and the fact that STD pathogens are common etiologies. Sexually transmitted organisms are the most common cause of epididymitis in heterosexual men under 35 years of age (2); approximately two-thirds of the patients in this age group with acute epididymitis have epididymitis secondary to *N. gonorrhoeae* or *C. trachomatis* (3). Most urethritis is also the result of infection with a sexually transmitted organism (4). However, we excluded cases and visits for urethritis for Reiter Syndrome, urethritis designated as "not sexually transmitted," and urethral syndrome because their association with STDs is only partial. We also excluded acute or chronic prostatitis (unless there was a diagnosis code specifically linked to gonococcus in the data we examined) because the vast majority of prostatitis cases are not associated with an STD (5). We did not include proctocolitis, which may be due to sexual transmission of enteric pathogens, because this condition is rarely managed by urologists. Finally, we excluded common urinary tract infections (UTIs) of men or women that may be associated with sexual transmission, as these are addressed in another chapter.

Because of the limitations of the datasets used to quantify much of the burden of other diseases in this compendium, we relied heavily on the peer-reviewed literature for most of the summary statements about incidence and prevalence of the STDs and syndromic presentations. Several of these datasets are valuable for quantifying the overall healthcare burden for STDs, changes in demographic characteristics of persons with STDs, and the impact of STDs on minority populations. However, they do not readily allow for analyses restricted to cases seen exclusively by urologists.

We briefly discuss available data on the burden of other STDs that are rarely managed by urologists or are rare in general; these include HIV infection or its clinical manifestations, infection with HPV types associated with anogenital dysplasia and cancer, and hepatitis B. We also briefly discuss trichomoniasis, which was not included in the list of STDs fully investigated for burden of illness because of resource limitations. Although *Trichomonas vaginalis* infection commonly presents as a vaginitis, it is a frequent cause of lower urogenital tract infection that urologists may see and should think of when evaluating the etiology of urethritis in men or women. We briefly discuss

Table 2. Estimated incidence and prevalence of sexually transmitted diseases in the United States, 1996, by strength of evidence[a]

STD	Incidence[b]	Prevalence[c]
Chlamydia	3 million -II	2 million - II
Gonorrhea	650,000 - II	
Syphilis	70,000 - II	
Herpes	1 million - II	45 million - I
Human papilloma virus	5.5 million - III	20 million - III
Hepatitis B	77,000 - II	750,000 -I
Trichomoniasis	5 million - III	
Bacterial vaginosis	No estimates	
HIV	20,000 - II	560,000 - II
Total	15.3 million	

[a]Level I (good) surveillance data come from either representative national surveys or from national reporting systems with nearly complete counts. Level II (fair) surveillance data are derived from composite prevalence figures obtained from multiple populations over time or from less complete national reporting systems. Level III (poor) surveillance data are based on even weaker evidence and rough extrapolations.

[b]Incidence is the number of new cases in a given time period.

[c]Prevalence is the total number of cases in the population.

SOURCE: Adapted from ASHA Panel to Estimate STD Incidence, Prevalence, and Cost. Available at: http://www.kff.org/womenshealth/1445-std_rep2.cfm.

chancroid, but because they occur rarely, we excluded lymphogranuloma venereum and granuloma inguinale. We excluded pediculosis pubis, scabies, hepatitis A virus (HAV) infection, bacterial vaginosis, and vulvovaginal candidiasis because these conditions are not necessarily the result of sexual exposure and are not usually associated with long-term sequelae managed by urologists. Finally, we excluded infection with hepatitis C virus (HCV) because it is rarely acquired through sexual exposure.

We used many claims databases to estimate aspects of the burden of STDs. Surveillance systems that capture national STD incidence data rely on cases, not medical visits; however, an episode of infection may result in more than one visit or claim. In interpreting analyses with various datasets, one must keep in mind that counts of medical visits are not the same as case counts, and that counts of both cases and office visits can reflect incident cases, prevalent cases, or a combination of the two. Given the nature of the datasets on which we performed primary analyses and given the reliance on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) coding in these datasets, the summary statements they permit concern relative burden of disease referent to office visits rather than to case counts or numbers of infected persons. Using claims data, we counted medical visit claims as a measure of burden, since they, in association with drug claims and procedure claims, constitute a large part of the economic burden of STDs.

Databases we used include hospital claims data for all inpatient care in many states, analysis and review data for Medicare patients, VA data, and inpatient and outpatient claims data for privately insured patients. Because most of those databases included only ICD-9 diagnostic codes, not procedure codes or drug codes, we used ICD-9 codes to capture the burden of STDs for three pathogen-specific STDs (herpes, chlamydia, and gonorrhea), genital warts, and two syndromic presentations of STD infection (epididymitis/orchitis and urethritis) measured by patient visits. There were too few visits for syphilis in these datasets to allow for reliable estimates. The following are brief descriptions of the databases used in the analyses discussed here.

DEFINITION AND DIAGNOSIS

To capture aspects of the burden of various STDs, we applied selected ICD-9 codes to datasets reflecting inpatient and outpatient visits to healthcare providers; these datasets and the methods of analysis are described in the methods chapter of this compendium. Our analyses of all datasets included visits associated with diagnostic codes for acute manifestations of the lower genitourinary tract or external genitalia and for selected sequelae due to ascension to the male upper genitourinary tract. Table 1 lists the codes used in the diagnosis of STDs. Except in the case of syphilis, we excluded visits associated with non-genitorurinary tract diagnostic codes or procedures, herpetic infections of the oropharynx, herpetic vulvovaginitis, herpetic ulceration of the vulva, herpetic infection without specification of anatomic site, gonoccoccal arthritis, neurosyphilis, salpingitis, oophoritis, endometritis, and pelvic inflammatory disease (PID) (unless specifically associated with gonococcal or chlamydial infection). We included ICD-9 codes for chlamydial infection of other and unspecified genitourinary sites and for gonococcal infection of the *upper genital tract* in order to include infections of the male genitourinary tract that urologists would be likely to manage. There are specific ICD-9 codes for cervicitis, endometritis, and salpingitis associated with gonorrheal infection but none for chlamydial infections specific to the cervix, endometrium, or Fallopian tubes. Because we wanted to address gonorrhea and chlamydial infections of the upper genital tract as consistently as possible, and because we did not restrict our analysis to male patients, the ICD-9 codes we included may have represented cases of cervicitis, endometritis, salpingitis, and oophoritis that urologists are unlikely to manage. However, a review of data from MarketScan show that patient visits associated with ICD-9 codes for chlamydial infection of *other* and *unspecified* anatomic sites and gonorrheal cervicitis, endometritis, and salpingitis are quite rare (Table 3). Therefore, our estimates of chlamydial and gonorrheal infection should largely represent lower urogenital tract infections that urologists may encounter.

In addition, the following three points should be noted:

1. We used the National Electronic Telecommunications Surveillance System (NETSS) as the sole data source for primary and secondary cases of syphilis in adolescents and adults in this project. None of the other available datasets contained sufficient numbers of syphilis cases to describe with any confidence the demographic and geographic distribution of the disease in the population. Because many cases of primary and secondary syphilis are diagnosed only with a serologic test and because the anatomic site of signs or symptoms is not reported, we were unable to exclude from NETSS data the cases of primary and secondary syphilis that lacked genitourinary symptoms and signs (e.g., palmar rash) and that urologists would, therefore, be unlikely to encounter.

2. Some patients have multiple diagnoses and could potentially have diagnoses of both the syndromic presentation of epididymitis/orchitis and an STD (e.g., a chlamydial or gonococcal infection). Therefore, we chose to analyze the available data in a way that enabled us to evaluate both aggregate data restricted to ICD-9 codes for epididymitis/orchitis not designated as due to chlamydia or gonococcus and aggregate data for all ICD-9 codes for epididymitis/orchitis. (If one were doing a straight addition, codes not designated as due to chlamydia or gonococcus would not be included in the numbers of visits for infection with chlamydia or gonococcus in which one of these organisms was likely the etiology of the patient's disease.) Accordingly, we used two different schemes for including visits for epididymitis/orchitis, according to ICD-9 codes, as indicated in Table 1.

3. Because urethritis is often observed in association with cystitis and pyelonephritis in acute, community-acquired urinary tract infections (UTIs), most clinicians commonly code urethritis as cystitis. Some patients with urethritis of probable STD etiology have multiple diagnoses and in the datasets examined could have both a diagnosis of the syndromic presentation of urethritis and a diagnosis of an STD (e.g., herpetic, chlamydial, or gonococcal infection). We chose to analyze the available data in such a way that one could evaluate both aggregate data restricted to both ICD-9 codes for urethritis not designated as due to chlamydia or gonococcus and aggregate data for all ICD-9 codes for urethritis. No specific ICD-9 code exists for urethritis secondary to herpetic infection. Accordingly, we used two different schemes for including visits for urethritis according to ICD-9 codes, as indicated in Table 1.

Unfortunately, the use of ICD-9 coding to assess the urologic burden of disease is limited because STD pathogens can cause pathology of multiple organ systems, and diagnoses linked with specific syndromes may or may not be related to infection with an STD pathogen. Linking ICD-9 codes with Current Procedural Terminology (CPT) codes for STD tests or surgical treatments, or with National Drug Codes (NDCs) for anti-infective treatment, can help identify diagnoses more likely to be related to an STD pathogen. However, CPT codes and NDCs were analyzed in only one of the datasets examined, MarketScan. Even in MarketScan, linking CPT codes or NDCs to establish a more specific definition of a visit is problematic because the dates associated with these codes may not always coincide with those of the ICD-9 codes, raising questions about the actual clinical association of the diagnostic and procedure codes. In analyzing MarketScan data, we made assumptions about time periods of infection and constructed dates around which overlap of ICD-9 codes, CPT codes,

Table 3. The numbers of inpatient and outpatient visits identified by ICD-9 codes for genital herpes, genital warts, chlamydial infection, gonorrhea, epididymitis/orchitis, and urethritis[a]

ICD-9 codes	Number of Inpatient Visits	Number of Outpatient Visits
Genital herpes		
054.1Genital herpes (total)	33	1,505
054.10 Genital herpes, unspecified	33	1,369
054.13 Herpetic infection of penis	0	93
054.19 Other	0	43
Genital warts		
078.11 Condyloma acuminatum	18	3,813
Chlamydia		
079.98 Chlamydia	11	373
099.53 Chlamydial cystitis, lower genitourinary sites	0	91
099.54 Other genitourinary sites	0	9
099.55 Unspecified genitourinary site	0	5
099.41 *Chlamydia trachomatis*	0	45
078.88 Other specified disease due to chlamydia	9	148
079.88 Other specified chlamydia infection	1	75
Gonorrhea		
098.0 Gonococcal infection (acute) of lower genitourinary tract	7	420
098.1 Gonococcal infection (acute) of upper genitourinary tract		
098.10 Gonococcal infection (acute) of upper genitourinary tract site unspecified	0	7
098.11 Gonococcal cystitis (acute)	0	6
098.12 Gonococcal prostatitis (acute)	0	10
098.13 Gonococcal epididymo-orchitis (acute)	0	2
098.14 Gonococcal seminal vesiculitis (acute)	0	0
098.15 Gonococcal cervicitis (acute)	1	42
098.16 Gonococcal endometritis (acute)	0	1
098.17 Gonococcal salpingitis specified as acute	0	8
098.19 Other gonococcal infection (acute) of upper genitourinary tract	2	5
098.2 Gonococcal infection (chronic) of lower genitourinary tract	0	85
098.33 Gonococcal epididymo-orchitis chronic	0	3
098.31 Gonococcal cystitis chronic	0	0
098.30 Chronic gonococcal infection of upper genitourinary tract site unspecified	0	0
098.32 Gonococcal prostatitis chronic	0	3
098.34 Gonococcal seminal vesiculitis chronic	0	0
Epididymitis/orchitis not designated as due to Chlamydia or gonococcus		
604 Orchitis and epididymitis		
604.0 Orchitis, epididymitis, and epididymo-orchitis, with abscess of epididymis or testis		
604.9 Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess	0	28

Continued on next page

Table 3 (continued). The numbers of inpatient and outpatient visits identified by ICD-9 codes for genital herpes, genital warts, chlamydial infection, gonorrhea, epididymitis/orchitis, and urethritis[a]

ICD-9 Codes	Number of Inpatient Visits	Number of Outpatient Visits
Epididymitis/orchitis regardless of whether or not due to Chlamydia or gonococcus		
604 Orchitis and epididymitis		
604.0 Orchitis, epididymitis, and epididymo-orchitis, with abscess of epididymis or testis		
604.9 Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess	0	28
098.13 Gonococcal orchitis	14	1,552
098.33 Chronic gonococcal orchitis	0	1
Urethritis not designated as due to Chlamydia or gonococcus:		
099.40 Unspecified	0	355
099.49 Other specified organism	0	7
Urethritis regardless of whether or not due to Chlamydia or gonococcus:		
099.40 Unspecified	0	354
099.49 Other specified organism	0	7
099.41 Urethritis due to *Chlamydia trachomatis*	0	45
098.0 Acute gonococcal infection of the lower genitourinary tract	7	419
098.2 Chronic gonococcal infection of the lower genitourinary tract	0	85

[a]Numbers limited to enrollees who were continuously enrolled in a health plan throughout 1999.
[b]Males ages 16-35 years only.
SOURCE: MarketScan, 1999.

and/or NDCs could reasonably reflect a clinical association.

Finally, in interpreting the various claims and office visit datasets, it is important to keep in mind that ICD-9 codes for bacterial STDs tend to reflect incident cases that are treatable, whereas ICD-9 codes for viral STDs such as HPV and HSV tend to reflect prevalent cases with chronic manifestations that may involve extended therapy.

INCIDENCE, PREVALENCE, AND RISK FACTORS

Herpes Simplex

Background

An estimated 1 million people in the United States are newly infected each year with herpes simplex virus type two (HSV-2), the most common genital type. Since the late 1970s, the prevalence of HSV-2 infection has increased by 30%, and HSV-2 is now detectable in roughly one of every five persons over 11 years of age nationwide (6). The National Health and Nutrition Examination Surveys (1988–1994) (NHANES-III) reported that more than 25% of adults between 30 and 39 years of age were positive on serology for HSV-2 in those years (6). NHANES-III indicates that HSV-2 infection is more common in women than in men, affecting approximately one out of every four women, in contrast to fewer than one out of every five men (6). This may reflect differences in sexual behavior or more efficient transmission from male to females than from females to males (6).

HSV-2 infection increased fivefold among Caucasian teens (aged 12 to 19 years) between the 1970s and the 1990s, faster than among any other age or racial/ethnic group (6). Among Caucasians 20 to 29 years of age, the prevalence of HSV-2 infection increased twofold over that period. The percentage of people infected with either HSV-1 or HSV-2 increases with age, because people remain infected throughout their lives (7). Among persons 15 to 39 years of age, annual incidence of HSV-2 infection has been projected to increase steadily between 2000 and 2025, from 9 to 26 infections per 1,000 men and from 12 to 32 infections per 1,000 women; prevalence is projected to increase to 39% among men and 49% among women (8).

HSV-2 infection continues to spread across all social, economic, racial, and ethnic groups and is common in both urban and rural areas. There are no significant differences in prevalence among geographic regions of the United States. Although HSV-2 infection is increasing among young Caucasians, who have a seroprevalence of approximately 17%, infection is more common among African-Americans, who have a seroprevalence of 45% (6).

The principal symptoms of herpes—recurrent painful ulcers of the genitalia, perineum, and perianal area—can be treated, but the infection cannot be eliminated. However, most people with positive HSV serology do not have symptomatic infection that results in medical visits or in costs to the healthcare system (9). In NHANES-III, fewer than 10% who tested positive for HSV-2 had been symptomatic with genital herpes and knew they were infected (6); these numbers do not take into account the sizable percentage of genital herpes cases caused by HSV-1. With or without recognizable symptoms, HSV infection can be transmitted between sex partners and from mothers to newborns, and it is potentially fatal in infants born to infected women (6). Genital herpes can be particularly severe in people with HIV infection; it may cause genital ulcers and may increase HIV viral load, which increases the risk of HIV transmission (10).

The cost of incident herpes infections in the United States in 2000 was estimated to be $1.8 billion, but because of the increasing incidence, this cost has been predicted to rise to $2.5 billion by 2015 and $2.7 billion by 2025 (8).

In the National Disease and Therapeutic Index (NDTI), the number of initial visits to clinicians' offices per year for genital herpes rose from fewer than 10,000 in 1966–1970 to more than 150,000 in 1995–2001. In the NDTI and in the other datasets we analyzed, the unit of analysis is healthcare system contacts, not the actual numbers of genital herpes cases; the exception to this is the Veterans Health Administration (VA) claims data in which the unit of analysis is the individual patient. Patients with genital herpes may seek care in public healthcare facilities or from private ambulatory care providers and, as a consequence, may not be captured in certain datasets. However, the datasets we analyzed are useful for describing trends in care-seeking behavior for genital herpes. For any population in a given dataset, the total numbers of patient visits for genital herpes are minimum estimates of contacts with healthcare providers; thus, patient visits for initial episodes do not necessarily reflect incident cases.

The Data

Healthcare Cost and Utilization Project (HCUP) data indicate that hospitalization for genital herpes is a rare event that has decreased in frequency over time, possibly due to the increased availability of outpatient medication that reduces the severity and duration of symptoms (Table 4). In 1994, 930 patients were hospitalized with a primary diagnosis of genital herpes, of whom 716 (77%) were 18 to 44 years of age. Hospitalizations decreased progressively after 1994, declining to 388 in 2000, of which 295 (76%) were women, 161 (42%) resided in the South, and 339 (87%) resided in urban areas.

Hospital outpatient and inpatient data generated by the Centers for Medicare and Medicaid Services (CMS) from 1992 through 1998 contained too few claims for genital herpes to permit detailed interpretation. According to the Medicare outpatient files, physician office visit rates increased from 12 visits per 100,000 beneficiaries in 1992 to 17 per 100,000 in 1998 (Table 5). It is likely that this increase reflects the greater use of outpatient management of genital herpes with drugs that reduce the severity and duration of symptoms. In 1998, the rates seen among male and female Medicare beneficiaries were identical (17 per 100,000); the highest rates were seen among persons under 65 years of age (42 per 100,000), those residing in the West (23 per 100,000), and Hispanics (40 per 100,000). Note that Medicare beneficiaries under age 65 include the disabled and persons with end-stage renal disease and are distinct from Medicare beneficiaries 65 and older.

Genital herpes was the most common pathogen-specific STD presentation in 2001 VA data, with a total of 118 cases per 100,000 unique outpatients (Table 6). The highest rates were seen among women (426 per 100,000), persons 25 to 34 years of age (543 per 100,000), African Americans (214 per 100,000), and those residing in the West (176 per 100,000) (Table 7). Progressive increases were noted in the counts and

Table 4. Inpatient hospital stays by individuals with genital herpes listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	930	0.4 (0.3–0.4)	441	0.2 (0.1–0.2)	517	0.2 (0.1–0.2)	388	0.1 (0.1–0.2)
Age								
< 14	*	*	*	*	*	*	*	*
14–17	*	*	*	*	*	*	*	*
18–24	188	0.8 (0.5–1.0)	*	*	*	*	*	*
25–34	314	0.8 (0.5–1.0)	*	*	*	*	*	*
35–44	214	0.5 (0.3–0.7)	*	*	*	*	*	*
45–54	*	*	*	*	*	*	*	*
55–64	*	*	*	*	*	*	*	*
65–74	*	*	*	*	*	*	*	*
75–84	*	*	*	*	*	*	*	*
85+	*	*	*	*	*	*	*	*
Race/ethnicity								
White	359	0.2 (0.1–0.2)	220	0.1 (0.1–0.2)	151	0.1 (0–0.1)	*	*
Black	318	1.0 (0.6–1.4)	*	*	156	0.5 (0.3–0.7)	*	*
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	*	*	*	*	*	*	*	*
Gender								
Male	401	0.3 (0.2–0.4)	164	0.1 (0.1–0.2)	*	*	*	*
Female	529	0.4 (0.3–0.5)	277	0.2 (0.2–0.3)	400	0.3 (0.2–0.4)	295	0.2 (0.2–0.3)
Region								
Midwest	173	0.3 (0.2–0.4)	*	*	*	*	*	*
Northeast	196	0.4 (0.2–0.5)	*	*	*	*	*	*
South	494	0.6 (0.4–0.8)	*	*	234	0.2 (0.1–0.4)	161	0.2 (0.1–0.2)
West	*	*	*	*	*	*	*	*
MSA								
Rural	*	*	*	*	*	*	*	*
Urban	807	0.4 (0.3–0.5)	411	0.2 (0.2–0.2)	449	0.2 (0.2–0.3)	339	0.2 (0.1–0.2)

*Figure does not meet standard for reliability or precision; MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of other race/ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

rates of patients diagnosed with genital herpes from 1999 through 2001 in most strata (age, gender, race/ethnicity, insurance status, and region).

The 1999 MarketScan data reported 1,505 outpatient visits and 33 inpatient visits accompanied by a claim for services associated with one of the ICD-9 codes listed in Table 3. A much higher rate of visits was observed among women enrollees (88 per 100,000) than among men (50 per 100,000) (Table 8). The highest rates were seen among persons aged 25 to 29 years of age (182 per 100,000). This is consistent with the serologic findings discussed below and may reflect additional diagnoses made through screening of pregnant women by medical history or HSV serologic testing. It should be noted that initial episodes of genital herpes, which tend to be most symptomatic, are more likely to prompt medical care and to represent incident infections. Later episodes are less likely to have severe symptoms, and patients with recurrent episodes who are aware of genital herpes

Table 5. Physician office visits by Medicare beneficiaries with genital herpes listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	4,200	12 (12–13)	5,980	17 (16–17)	5,720	17 (17–17)
Total < 65	1,280	23 (22–25)	2,220	36 (35–38)	2,580	42 (40–43)
Total 65+	2,920	10 (9.7–10)	3,760	13 (12–13)	3,140	11 (11–12)
Age						
65–74	1,980	12 (12–13)	2,440	15 (14–16)	1,820	13 (12–13)
75–84	880	9.3 (8.7–9.9)	1,180	12 (12–13)	1,180	12 (12–13)
85–94	60	2.1 (1.6–2.6)	140	4.6 (3.8–5.3)	140	4.5 (3.8–5.3)
95+	0	0	0	0	0	0
Race/ethnicity						
White	3,320	11 (11–12)	4,540	15 (15–15)	4,000	14 (14–15)
Black	520	18 (16–19)	1,000	31 (29–33)	1,100	35 (33–38)
Asian	…	…	40	24 (17–31)	100	32 (25–38)
Hispanic	…	…	160	40 (34–46)	280	40 (35–45)
N. American Native	…	…	…	…	…	…
Gender						
Male	2,220	15 (14–16)	2,440	16 (15–17)	2,460	17 (16–18)
Female	1,980	10 (9.6–10)	3,540	18 (17–18)	3,260	17 (17–18)
Region						
Midwest	620	7.1 (6.5–7.7)	980	11 (10–12)	820	9.5 (8.9–10)
Northeast	580	7.5 (6.9–8.1)	1,160	15 (14–16)	1,120	17 (16–18)
South	1,860	15 (15–16)	2,240	18 (17–18)	2,500	20 (19–21)
West	1,100	22 (20–23)	1,400	27 (26–28)	1,160	23 (22–25)

…data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 6. Frequency of sexually transmitted diseases as a diagnosis in VA patients seeking outpatient care, 2001, count[a], rate[b]

	Primary Diagnosis		*Any Diagnosis*	
Sexually Transmitted Disease	**Count**	**Rate**	**Count**	**Rate**
Genital herpes	2,324	63	4,357	118
Genital warts	2,224	60	2,846	77
Chlamydia	380	10	515	14
Gonorrhea	473	13	634	17
Syphilis	71	2	100	3
Epididymitis (organism unspecified)[c]	1,519	41	1,833	50
Epididymitis (all cases)[c]	1,557	42	1,889	51
Urethritis (organism unspecified)	185	5	233	6
Urethritis (all cases)	590	16	771	21

[a]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.
[b]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.
[c]Includes males only.
SOURCE: Outpatient Clinic File (OPC), VA Austin Automation Center, 2001.

Table 7. Frequency of genital herpes[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	2,918	96	3,433	105	4,357	118
Age						
18–24	89	351	103	438	116	504
25–34	576	382	621	437	738	543
35–44	724	219	823	264	943	315
45–54	865	126	956	133	1,262	168
55–64	340	68	491	89	693	107
65–74	245	32	309	37	445	47
75–84	73	14	124	19	148	18
85+	6	12	6	10	12	15
Race/ethnicity						
White	1,122	82	1,321	90	1,587	99
Black	598	179	649	189	758	214
Hispanic	128	112	150	122	212	164
Other	11	57	16	79	23	105
Unknown	1,059	88	1,297	98	1,777	113
Gender						
Male	2,439	84	2,844	91	3,655	104
Female	479	339	589	390	702	426
Region						
Midwest	587	85	629	84	708	85
Northeast	550	75	576	74	701	81
South	1037	102	1,326	119	1,717	133
West	744	124	902	142	1,231	176
Insurance status						
No insurance/self-pay	2,241	123	2,521	139	3,114	164
Medicare/Medicare supplemental	256	37	350	38	478	40
Medicaid	6	121	8	101	18	200
Private insurance/HMO/PPO	377	78	495	97	675	122
Other insurance	38	150	57	198	66	198
Unknown	0	0	2	81	6	66

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for genital erpes.

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from observation only; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 8. Medical visits[a] for genital herpes in 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	8	3 (1–6)
10–14	8	5 (1-8)
15–19	106	57 (46–67)
20–24	162	141 (119–163)
25–29	179	182 (156–209)
30–34	244	171 (150–192)
35–39	238	125 (110–141)
40–44	198	92 (79–104)
45–54	287	61 (54–68)
55–64	105	29 (24–35)
65+	3	32 (0–69)
Gender		
Male	529	50 (46–54)
Female	1,009	88 (82–93)
Region		
Midwest	352	68 (61–75)
Northeast	271	72 (64–81)
South	644	69 (63–74)
West	111	100 (82–119)
Unknown	160	61 (51–70)
Urban/rural		
MSA	1,152	79 (74–83)
Non-MSA	226	47 (41–54)
Unknown	160	61 (51–70)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.

[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.

SOURCE: MarketScan, 1999.

symptoms may be less likely to seek care. Recurrent episodes of genital herpes also tend to become less frequent over time. This may explain why claims and visits for symptomatic genital herpes tend to peak in the younger age groups, as visits are generated for incident cases soon after infection, while HSV infection is more prevalent in older ages, as noted above. In MarketScan data, rates of inpatient and outpatient visits for genital herpes varied by geographical region, ranging from 100 per 100,000 enrollees in the West to 61 to 72 per 100,000 in the other regions. A marked difference in rates was also seen between urban areas (79 per 100,000) and rural areas (47 per 100,000).

For the 1,505 outpatient visits for genital herpes reported in the 1999 MarketScan data, 537 drug claims were filed for acyclovir, famcyclovir, or valacyclovir on the same date as an outpatient medical claim for genital herpes, and a total of 1,025 drug claims were filed for one of these drugs within 30 days after the outpatient visit. Drug claims were not analyzed for the small number of inpatient visits ICD-9 coded for genital herpes. In addition, 87,029 drug claims were filed for one of these three same drugs, regardless of ICD-9 codes for patient visits. Another recent study has underscored the difficulty of using drug claims for acyclovir as a way to estimate the burden of symptomatic genital herpes (11). Only 2% of the persons with acyclovir claims had ICD-9 codes for genital herpes, 9% had ICD-9 codes for herpes in nongenital sites (ICD-9 code 054 excluding 054.1), 6% had ICD-9 codes for herpes zoster (ICD-9 code 053), and 80% had ICD-9 codes for other medical care. Of those with ICD-9 codes for genital herpes, 27% did not have acyclovir claims.

Genital Warts

Background

Most genital warts are the result of infection with HPV type 6 or 11. Genital warts occur in sites on the external genitalia and can also occur in the vagina, urethra, and anus. Overall, the best estimates of the prevalence of genital warts are based on selected studies with extrapolations. Approximately 1% of sexually active adults in the United States are estimated to have genital warts. This estimate is based on levels of infection ranging from 1.5% among female college students treated in student health centers to 13% of patients in selected STD clinics (12, 13). A recent analysis of healthcare claims data from a private US health plan found that the prevalence of (and health plan costs associated with) genital warts billed through the health plan were highest among women 20 to 24 years of age (6.2 cases and $1,692 in costs per 1,000 person-years) and men 25 to 29 years of age (5.0 cases and $1,717 in costs per 1,000 person-years) (14). Risk factors for developing genital warts have been difficult to assess because of the lack of a marketed diagnostic test specific for HPV types 6 and 11 or other types associated with warts. However, urologists and other clinicians who engage in procedures directed at

Table 9. Inpatient hospital stays by individuals with genital warts listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	562	0.2 (0.2–0.3)	337	0.1 (0.1–0.2)	296	0.1 (0.1–0.1)	315	0.1 (0.1–0.2)
Age								
< 14	*	*	*	*	*	*	*	*
14–17	*	*	*	*	*	*	*	*
18–24	*	*	*	*	*	*	*	*
25–34	173	0.4 (0.2–0.6)	*	*	*	*	*	*
35–44	*	*	*	*	*	*	*	*
45–54	*	*	*	*	*	*	*	*
55–64	*	*	*	*	*	*	*	*
65–74	*	*	*	*	*	*	*	*
75–84	*	*	*	*	*	*	*	*
85+	*	*	*	*	*	*	*	*
Race/ethnicity								
White	298	0.2 (0.1–0.2)	162	0.1 (0–0.1)	*	*	*	*
Black	*	*	*	*	*	*	*	*
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	*	*	*	*	*	*	*	*
Gender								
Male	325	0.3 (0.2–0.3)	167	0.1 (0.1–0.2)	171	0.1 (0.1–0.2)	207	0.2 (0.1–0.2)
Female	237	0.2 (0.1–0.2)	170	0.1 (0.1–0.2)	*	*	*	*
Region								
Midwest	*	*	*	*	*	*	*	*
Northeast	195	0.4 (0.2–0.6)	*	*	*	*	*	*
South	232	0.3 (0.2–0.4)	*	*	*	*	*	*
West	*	*	*	*	*	*	*	*
MSA								
Rural	*	*	*	*	*	*	*	*
Urban	515	0.3 (0.2–0.4)	310	0.2 (0.1–0.2)	268	0.1 (0.1–0.2)	280	0.1 (0.1–0.2)

MSA, metropolitan statistical area.
*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.
[b]Persons of other race/ethnicity are included in the totals.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

ameliorating genital warts lesions should note that the possibility exists for nosocomial disease transmission through exposure to an aerosolized plume from HPV-infected tissue when using a carbon-dioxide laser (15, 16).

The primary goal in the treatment of visible genital warts is the removal of those that obstruct the urethra, vagina, anus, or oral cavity; cause discomfort, pain, or bleeding in the anogenital areas; or cause cosmetic problems. In the National Disease and Therapeutic Index (NDTI), the number of initial visits to physicians' offices for genital warts has risen from about 80,000 per year in 1966–1969 to more than 150,000 in every year since 1972. As with genital herpes, data from the NDTI and the other datasets used in this analysis (with the exception of the VA claims data) reflect healthcare system contacts, not the actual numbers of cases. However, year-to-year NDTI data are useful for describing trends in care-seeking in private physician's offices, although not in public healthcare facilities or from other private ambulatory care providers. Therefore, for any population in a given dataset, the total numbers of patient visits for genital warts are minimum estimates of healthcare contacts.

The Data

According to HCUP data, hospitalization for genital warts (ICD-9 code 078.11 only) is a very rare event that has remained stable over time (Table 9). In 2000, there was a weighted frequency of 315 hospitalizations with a primary diagnosis of genital warts, of which 207 (66%) were men and 280 (89%) resided in urban areas.

In all CMS databases examined, the diagnosis of genital warts was too rare to permit statistically meaningful interpretation (Table 10). Hospital outpatient visit rates for genital warts increased from 1.5 per 100,000 beneficiaries in 1995 to 4.0 per 100,000 in 1998; of an estimated 1,340 visits in 1998, the highest rates were seen among men (5.7 per 100,000) and persons under 65 years of age (16 per 100,000). ICD-9 codes for genital warts were revised substantially after 1992, resulting in increased specificity.

Table 10. Hospital outpatient visits by Medicare beneficiaries with genital warts listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992[c]		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[d]	7,440	22 (21–22)	520	1.5 (1.3–1.6)	1,340	4.0 (3.8–4.2)
Total < 65	3,320	61 (59–63)	420	6.8 (6.2–7.5)	980	16 (15–17)
Total 65+	4,120	14 (14–15)	100	0.3 (0.3–0.4)	360	1.3 (1.2–1.5)
Age						
65–74	2,380	14 (14–15)	40	0.2 (0.2–0.3)	300	2.1 (1.9–2.3)
75–84	1,320	14 (13–15)	60	0.6 (0.5–0.8)	60	0.6 (0.5–0.8)
85–94	360	13 (11–14)	0	0	0	0
95+	60	18 (13–22)	0	0	0	0
Race/ethnicity						
White	5,460	19 (18–19)	400	1.3 (1.2–1.4)	900	3.2 (3.0–3.4)
Black	920	31 (29–33)	100	3.1 (2.5–3.7)	260	8.4 (7.4–9.4)
Asian	…	…	…	…	…	…
Hispanic	…	…	…	…	60	8.5 (6.4–11)
N. American Native	…	…	…	…	…	…
Gender						
Male	3,740	25 (25–26)	380	2.5 (2.2–2.7)	820	5.7 (5.3–6.1)
Female	3,700	19 (18–19)	140	0.7 (0.6–0.8)	520	2.7 (2.5–3.0)
Region						
Midwest	2,260	26 (25–27)	240	2.7 (2.3–3.0)	420	4.9 (4.4–5.3)
Northeast	2,000	26 (25–27)	140	1.8 (1.5–2.1)	280	4.2 (3.7–4.7)
South	1,080	8.8 (8.3–9.4)	60	0.5 (0.4–0.6)	420	3.4 (3.1–3.7)
West	2,080	41 (39–43)	80	1.5 (1.2–1.9)	220	4.4 (3.9–5.0)

… data not available.

[a]Unweighted counts multiplied by 20 to arrive at values in the table.

[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.

[c]ICD-9 codes for genital warts were revised substantially after 1992, resulting in increased specificity. Counts for 1992 reflect the relative lack of specificity in coding for that year as compared to subsequent years.

[d]Persons of other races, unknown race and ethnicity, and other region are included in the totals.

NOTE: Counts less than 600 should be interpreted with caution.

SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 11. Frequency of genital warts[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	2,673	88	2,809	86	2,846	77
Age						
18–24	71	280	64	272	62	269
25–34	434	288	421	296	409	301
35–44	647	196	657	210	622	207
45–54	829	120	939	131	938	125
55–64	369	74	402	73	465	72
65–74	231	30	223	27	253	27
75–84	87	16	96	15	86	11
85+	5	10	7	12	11	14
Race/ethnicity						
White	1,356	99	1,378	94	1,373	85
Black	480	144	502	147	500	141
Hispanic	59	52	76	62	81	63
Other	11	57	13	64	6	27
Unknown	767	64	840	64	886	56
Gender						
Male	2,522	87	2,635	84	2,697	76
Female	151	107	174	115	149	90
Region						
Midwest	647	94	701	94	673	81
Northeast	488	67	483	62	461	53
South	983	97	1,032	92	1,098	85
West	555	92	593	93	614	88
Insurance status						
No insurance/self-pay	2,037	112	2,139	118	2,142	113
Medicare/Medicare supplemental	315	45	324	35	359	30
Medicaid	12	242	12	152	13	145
Private insurance/HMO/PPO	278	57	302	59	304	55
Other insurance	29	115	31	108	28	84
Unknown	2	105	1	41	0	0

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for genital warts.

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from observation only; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 12. Medical visits[a] for genital warts in 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	61	25 (19–31)
10–14	92	53 (42–64)
15–19	390	209 (188–229)
20–24	597	520 (478–562)
25–29	458	466 (424–509)
30–34	498	349 (318–380)
35–39	445	235 (213–256)
40–44	374	173 (156–191)
45–54	601	127 (117–137)
55–64	309	87 (77–96)
65+	6	64 (13–116)
Gender		
Male	1,722	163 (156–171)
Female	2,109	183 (176–191)
Region		
Midwest	1,030	199 (187–211)
Northeast	756	201 (187–216)
South	1,475	158 (149–166)
West	141	127 (106–148)
Unknown	429	163 (147–178)
Urban/rural		
MSA	2,717	186 (179–192)
Non-MSA	685	144 (133–154)
Unknown	429	163 (147–178)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.

[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.

SOURCE: MarketScan, 1999.

In 2001 VA data, genital warts were the second most common pathogen-specific STD presentation, with a total of 77 cases per 100,000 unique outpatients (Table 6). As with genital herpes, the highest rates of genital warts in 2001 were seen among women (90 cases per 100,000 unique outpatients), persons 25 to 34 years of age (301 per 100,000), and African Americans (141 per 100,000) (Table 11). However, unlike genital herpes, no consistent trend was seen when comparing case counts and rates from 1999 through 2001 across age groups, gender, race/ethnicity, insurance status, and region (Table 11).

The 1999 data from MarketScan had 3,813 outpatient visits and 18 inpatient visits for genital warts accompanied by a claim for services associated with ICD-9 code 078.11 (Table 3). There were 2,109 medical visits for genital warts by women and 1,722 by men, the rates per 100,000 enrollees being 183 and 163, respectively (Table 12). The highest rates were seen among those 20 to 24 years of age (520 per 100,000). Rates varied by geographical region, from 127 per 100,000 in the West to 201 per 100,000 in the Northeast. A difference was also seen between urban (186 per 100,000) and rural (144 per 100,000) residents.

By defining an episode of genital warts with ICD-9 code 078.10 (wart–common, digitate, filiform, infectious, viral) or 078.19 (other specified viral warts–genital warts, verruca plana, verruca plantaris) linked with CPT procedure codes for the destruction or excision of a lesion of the anus, penis, vulva, perineum, vagina, or introitus, one might identify more patients with genital warts. Claims for drugs used principally to treat genital warts could also identify many patients with the condition: in the 1999 Marketscan data, there were 5,056 drug claims for imiquimod (where the prescription was obtained from a urologist or gynecologist), podofilox, or podophyllin, and 1,356 claims in which the visits included ICD-9 code 078.10 or 78.19 accompanied by CPT codes for procedures to destroy or excise a lesion of the anus, penis, vulva, perineum, vagina, or introitus.

Using National Ambulatory Medical Care Survey (NAMCS) data, we estimated that of the 4.5 million medical visits per year for genital warts, many more were for possible cases (4 million) than for definite cases (0.25 million) or probable cases (0.25 million). Please see the methods chapter for a detailed discussion of definite, probable, and possible cases. Further exploration of this dataset as a source of information on genital warts will require an in-depth understanding of the coding practices of office-based clinicians with respect to diagnoses and procedures.

In both the MarketScan and NAMCS datasets, women made the majority of outpatient visits for genital warts. Further exploration of the datasets will be necessary to determine if this preponderance represents a greater incidence or prevalence among women, or whether it merely reflects differences in care-seeking behavior. For example, genital warts in women are more likely to come to medical attention than genital warts in men, if only because women periodically seek Pap smears. In contrast, in the HCUP data, men made the majority of inpatient visits. One possible explanation for the difference in the sex distribution of inpatients and outpatients receiving wart care may be that ablative procedures for anogenital warts in men are more commonly performed by hospital-based surgeons, while anogenital warts in women are more commonly managed with ablative and nonablative procedures by office-based gynecologists.

Chlamydia

Background

Chlamydia trachomatis infection causes inflammation of the lower and upper genital tract and presents commonly as cervicitis, salpingitis, endometritis, and urethritis in women, and urethritis, epididymitis, orchitis, prostatitis, and proctitis in men. *C. trachomatis* also causes asymptomatic infection that can result in serious and costly sequelae if acute infection is not treated promptly and properly. Congenitally exposed infants may develop neonatal inclusion conjunctivitis and pneumonitis syndromes. Over the past two decades, there has been a dramatic increase in the use of various measures for diagnostic testing of symptomatic patients and screening of asymptomatic patients. Tests include rapid, nonculture monoclonal antibody-based tests, enzyme immunoassays (EIAs), nucleic acid probe tests, and nucleic acid amplification tests (NAATs). These tests may detect *C. trachomatis* in endocervical or urethral specimens or in urine (17).

Primarily because of increased efforts to screen and treat women for chlamydial infection, the incidence of chlamydia is estimated to have decreased from well over 4 million annual infections in the early 1980s to the current level of 3 million new cases annually, of which up to 75% are asymptomatic (1). The annual economic burden of sexually transmitted chlamydial infections and related sequelae, including PID, ectopic pregnancies, and tubal infertility, was estimated to exceed $2 billion in 1994 (18).

Of the reportable STDs in the United States, chlamydia is the most widespread. In 2001, a total of 783,242 cases (278 per 100,000 population) were reported to the Centers for Disease Control and Prevention (CDC). These included cases with and without symptoms or signs detected during medical examinations or routine screening. Forty percent of the cases of chlamydia were reported among persons 15 to 19 years of age. Reported prevalence among routinely screened, sexually active women is

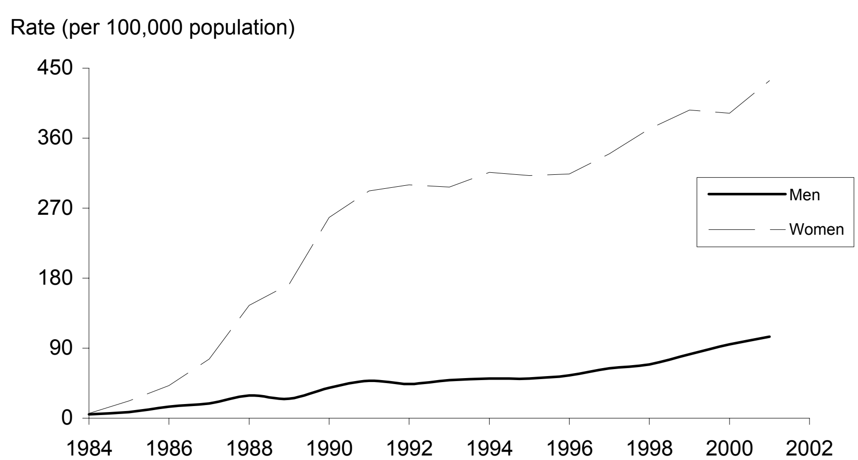

Figure 1. ***Chlamydia*** **– Rates by gender: United States, 1984–2001.**

SOURCE: Centers for Disease Control and Prevention. Adapted from Sexually Transmitted Disease Surveillance 2001 Supplement. Chlamydia Prevalence Monitoring Project - Annual Report 2001. Available at: http://www.cdc.gov/std/chlamydia2001/CT2001text.pdf.

consistently greater than 5%, and prevalence among teenage girls often exceeds 10%. In 1996–1999, 9.5% of the women 17 to 37 years of age routinely screened for STDs during their induction into the US Army tested positive for chlamydial infection (19). In addition, 15.6% of adolescent girls entering juvenile detention facilities where chlamydia screening was routine tested positive (20). Prevalence rates tend to be high in STD clinics or other settings where clients present with symptoms. Chlamydial infection is common among all races and ethnic groups, but prevalence is generally higher among women than among men (Figure 1). Using the LCx assay (Abbott Laboratories, Abbott Park, IL) for *C. trachomatis*, urine samples have been tested on a representative sample of participants 14 to 39 years of age in the 1999-2000 NHANES data (21). The prevalence of *C. trachomatis* infection was 2.6% with no significant difference between male and females. Routine screening in family planning clinics reveals that chlamydial infection is more prevalent in areas without long-standing screening and treatment programs; in 1999, 7 of the 10 states with the highest rates were in the South (13).

The advent of routine screening programs for female adolescents and young women has greatly influenced estimates of the distribution of infection. For example, there are more cases or visits based on positive laboratory tests in women than in men because of the large number of infections detected through female screening programs. Also, high rates of chlamydial infection in certain jurisdictions or among certain populations may indicate more effective screening programs and use of more sensitive tests, rather than a higher underlying incidence of disease. However, screening is not comprehensive. A Health Plan Employer Data and Information Set (HEDIS) report recently indicated that of women eligible for chlamydia screening under national screening guidelines (22), 19% of those 16 to 20 years of age and 16% of those 21 to 26 years of age received screening in managed care organizations that reported screening rates to the National Committee of Quality Assurance (NCQA) in 2000 (23). Selected public sector programs (STD clinics, prenatal clinics, and family planning clinics) screen higher percentages of women. Inclusion of screening costs for patients with positive test results must be considered in analyses of the overall economic burden of STDs.

The Data

HCUP data indicate that hospitalization for chlamydial infection is a rare event that has decreased over time (Table 13). In 1994, a total of 2,278 patients were hospitalized with a primary diagnosis of chlamydial infection; the number decreased to 183 in 2000.

Medicare data on hospital outpatient and inpatient visits for chlamydial infection from 1995 through 1998 were too sparse to permit meaningful interpretation (Table 14). For example, Medicare hospital outpatient visit rates decreased from 2.8 per 100,000 beneficiaries in 1995 to 1.4 per 100,000 in 1998.

In 2001 VA data, chlamydial infection was the fourth most common pathogen-specific STD presentation, with a total of 14 cases per 100,000 unique outpatients (Table 6). The highest rates were seen among women (76 per 100,000), persons under 25 years of age (226 per 100,000), African Americans (52 per 100,000), and persons residing in the West (16 per 100,000) (Table 15). The higher rates observed among women and persons under 25 years of age may be due in part to higher rates of screening of younger women who are asymptomatic, especially in family planning, prenatal, and STD clinics. No consistent trend was seen when comparing case counts and rates from 1999 through 2001 across age groups, gender, race/ethnicity, insurance status, and region.

The 1999 MarketScan data had 746 outpatient visits and 21 inpatient visits accompanied by a claim for services associated with one of the ICD-9 codes for chlamydial infection listed in Table 3. Of these 767 visits, 558 were by women and 209 were by men, the rates being 49 and 20 per 100,000 enrollees, respectively (Table 16). The highest rates of visits were by persons 20 to 24 years of age (105 per 100,000). The higher rates observed among women and persons under 25 years of age may be due in part to higher rates of screening of younger asymptomatic women during family planning and prenatal care. Rates did not vary greatly by geographical region, ranging from 31 per 100,000 in the Midwest to 39 per 100,000 in the Northeast. However, a marked difference was seen between urban (38 per 100,000) and rural (24 per 100,000) residents. The higher rates observed among urban residents may be due in part to higher rates

Table 13. Inpatient hospital stays by individuals with *Chlamydia* listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	2,278	0.9 (0.6–1.2)	684	0.3 (0.2–0.3)	272	0.1 (0.1–0.1)	183	0.1 (0–0.1)
Age								
< 14	1,548	2.9 (1.4–4.4)	268	0.5 (0.3–0.6)	*	*	*	*
14–17	*	*	*	*	*	*	*	*
18–24	172	0.7 (0.4–1.0)	*	*	*	*	*	*
25–34	*	*	*	*	*	*	*	*
35–44	*	*	*	*	*	*	*	*
45–54	*	*	*	*	*	*	*	*
55–64	*	*	*	*	*	*	*	*
65–74	*	*	*	*	*	*	*	*
75–84	*	*	*	*	*	*	*	*
85+	*	*	*	*	*	*	*	*
Race/ethnicity								
White	411	0.2 (0.2–0.3)	337	0.2 (0.1–0.2)	*	*	*	*
Black	434	1.4 (0.9–1.9)	154	0.5 (0.3–0.6)	*	*	*	*
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	*	*	*	*	*	*	*	*
Other	*	*	*	*	*	*	*	*
Gender								
Male	1,052	0.8 (0.4–1.3)	231	0.2 (0.1–0.2)	*	*	*	*
Female	1,226	1.0 (0.6–1.2)	453	0.3 (0.2–0.4)	224	0.2 (0.1–0.2)	164	0.1 (0.1–0.2)
Region								
Midwest	315	0.5 (0.3–0.7)	*	*	*	*	*	*
Northeast	1,364	2.7 (1.0–4.3)	317	0.6 (0.4–0.8)	*	*	*	*
South	430	0.5 (0.3–0.7)	*	*	*	*	*	*
West	169	0.3 (0.2–0.4)	*	*	*	*	*	*
MSA								
Rural	*	*	*	*	*	*	*	*
Urban	2,022	1.1 (0.6–0.5)	566	0.3 (0.2–0.3)	229	0.1 (0.1–0.2)	163	0.1 (0–0.1)

*Figure does not meet standard for reliability or precision.

MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of other race/ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 14. Hospital outpatient visits by Medicare beneficiaries with *Chlamydia* listed as primary diagnosis, count[a], rate[b] (95% CI)

	1995		1998	
	Count	Rate	Count	Rate
Total[c]	980	2.8 (2.6–2.9)	460	1.4 (1.2–1.5)
Total < 65	440	7.2 (6.5–7.8)	240	3.9 (3.4–4.3)
Total 65+	540	1.8 (1.7–2.0)	220	0.8 (0.7–0.9)
Age				
65–74	380	2.3 (2.1–2.6)	120	0.8 (0.7–1.0)
75–84	160	1.7 (1.4–1.9)	100	1.1 (0.8–1.3)
85–94	0	0	0	0
95+	0	0	0	0
Race/ethnicity				
White	540	1.8 (1.6–1.9)	280	1.0 (0.9–1.1)
Black	260	8.1 (7.1–9.1)	100	3.2 (2.6–3.9)
Asian	…	…	…	…
Hispanic	100	25 (20–30)	20	2.8 (1.6–4.1)
N. American Native	…	…	20	37 (20–54)
Gender				
Male	400	2.6 (2.4–2.9)	220	1.5 (1.3–1.7)
Female	580	2.9 (2.6–3.1)	240	1.3 (1.1–1.4)
Region				
Midwest	80	0.9 (0.7–1.1)	60	0.7 (0.5–0.9)
Northeast	460	6.0 (5.4–6.5)	180	2.7 (2.3–3.1)
South	240	1.9 (1.7–2.1)	120	1.0 (0.8–1.1)
West	180	3.5 (3.0–4.0)	80	1.6 (1.3–2.0)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTES: Counts less than 600 should be interpreted with caution. Coding changes make comparison with data from 1992 impossible.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Table 15. Frequency of *Chlamydia*[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	636	21	572	17	515	14
Age						
18–24	55	217	44	187	52	226
25–34	202	134	150	106	152	112
35–44	179	54	182	58	120	40
45–54	139	20	140	20	119	16
55–64	29	6	24	4	40	6
65–74	25	3	23	3	22	2
75–84	6	1	9	1	10	1
85+	1	2	0	0	0	0
Race/ethnicity						
White	145	11	122	8	110	7
Black	214	64	226	66	183	52
Hispanic	12	10	18	15	16	12
Other	2	10	0	0	3	14
Unknown	263	22	206	16	203	13
Gender						
Male	519	18	445	14	389	11
Female	117	83	127	84	126	76
Region						
Midwest	131	19	137	18	75	9
Northeast	185	25	134	17	134	15
South	183	18	191	17	197	15
West	137	23	110	17	109	16
Insurance status						
No insurance/self-pay	557	31	488	27	422	22
Medicare/Medicare supplemental	20	3	29	3	27	2
Medicaid	1	20	0	0	4	45
Private insurance/HMO/PPO	49	10	53	10	51	9
Other insurance	9	36	2	7	11	33
Unknown	0	0	0	0	0	0

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for chlamydia.

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from observation only; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 16. Medical visits[a] for chlamydial infection in 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	64	26 (20–33)
10–14	24	14 (8–19)
15–19	165	88 (75–102)
20–24	120	105 (86–123)
25–29	68	69 (53–86)
30–34	80	56 (44–68)
35–39	69	36 (28–45)
40–44	45	21 (15–27)
45–54	80	17 (13–21)
55–64	52	15 (11–19)
65+	0	0
Gender		
Male	209	20 (17–22)
Female	558	49 (44–53)
Region		
Midwest	163	31 (27–36)
Northeast	145	39 (32–45)
South	322	34 (31–38)
West	41	37 (26–48)
Unknown	96	36 (29–44)
Urban/Rural		
MSA	557	38 (35–41)
Non-MSA	114	24 (20–28)
Unknown	96	36 (29–44)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.

[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.

SOURCE: MarketScan, 1999.

of screening in urban areas, not greater incidence of infection.

In the 767 medical visits coded as being for chlamydial infection in the 1999 MarketScan data, 178 drug claims were filed for a recommended or alternate medication regimen from the CDC STD treatment guidelines (36 for amoxicillin, 73 for azithromycin, 46 for doxycycline, 14 for erythromycin, and 9 for ofloxacin) within 7 days before or 20 days after the date of the medical visit. Thus, in only 23% of the cases in which chlamydia was diagnosed was a drug prescribed that was consistent with CDC STD treatment guidelines. In the same dataset, an additional 3,654 medical claims were associated with ICD-9 codes, CPT codes, or NDCs for chlamydial infections. All those claims had at least one of the ICD-9 or CPT codes listed in Table 17 and a drug claim for amoxicillin, azithromycin, doxycycline, erythromycin, or ofloxacin within the 7 days before and 20 days after the date of the medical visit. This analysis indicates that the use of ICD-9 codes alone in the absence of CPT codes for *Chlamydia* testing and NDC codes for *Chlamydia* treatment in claims-based datasets substantially underestimates the numbers of provider visits for chlamydial infections. Because CPT codes for STDs are not available in HCUP or VA data and are presumably uncommon in Medicare data, they were not included in analyses for this chapter.

Gonorrhea

Background

Neisseriae gonorrhoeae is the cause of gonorrhea and its related clinical syndromes. Uncomplicated *N. gonorrhoeae* infection is usually confined to the mucosa of the cervix, urethra, rectum, and throat. The infection is often asymptomatic among females; untreated, it can lead to PID, tubal infertility, ectopic pregnancy, and chronic pelvic pain (24). *N. gonorrhoeae* usually causes symptomatic urethritis among males and occasionally results in epididymitis. Rarely, local infection disseminates to cause an acute dermatitis tenosynovitis syndrome, which can be complicated by arthritis, meningitis, or endocarditis (24).

In symptomatic patients, *N. gonorrhoeae* infection can be diagnosed presumptively using a gram stain of urethral or endocervical exudates if the smear contains typical gram-negative diplococci within polymorphonuclear leukocytes. However, other Neisseria species, including those normally in the flora of the oro- and nasopharynx, have a similar appearance. Culture testing has been the standard against which all other tests for *N. gonorrhoeae* have been compared. However, there are problems in maintaining the viability of organisms during transport and storage in the diverse settings in which culture testing is indicated. Nonculture tests are now available, including EIAs that detect specific gonococcal antigens, nucleic acid hybridization tests (NAATs) that detect *N. gonorrhoeae*-specific deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) sequences, and NAATs that amplify and detect *N. gonorrhoeae*-specific

Table 17. Codes used to identify additional medical visits for chlamydial infection[a] in MarketScan data

ICD-9 Codes	
V73.88	Screening for other specified chlamydial disease
V73.98	Screening, unspecified urethritis
099.40	Other nongonococcal urethritis, unspecified
099.49	Other nongonococcal urethritis, other specified organism
CPT codes	
86631	Chlamydia
86632	Chlamydia, IgM
87110	Chlamydia, culture
97270	*Chlamydia trachomatis*
87320	Infectious agent antigen detection by enzyme immunoassay technique, qualitiative or semiquantitative, multiple-step method; *Chlamydia trachomatis*
87490	Infectious agent detection by nucleic acid (DNA or RNA); *Chlamydia trachomatis*, direct probe technique
87491	Infectious agent detection by nucleic acid (DNA or RNA); *Chlamydia trachomatis*, amplified probe technique
87492	Infectious agent detection by nucleic acid (DNA or RNA); *Chlamydia trachomatis*, quantification
87810	Infectious agent detection by immunoassay with direct optical observation; *Chlamydia trachomatis*

[a]A medical visits was identified as an additional chlamydia visit if the date of a claim for amoxicillin, azithromycin, doxycyline, erythromycin, or ofloxacin was within the interval of 7 days before and 20 days after the date of the medical visit, and if the visit was associated with one of these ICD-9 or CPT codes.

DNA or RNA sequences. These tests are substantially more sensitive than the first-generation nonculture tests were (17, 24-29).

Of the reportable STDs, gonorrhea is second only to chlamydial infections in the number of cases reported annually to CDC; 361,705 cases were reported in 2001, with an age distribution similar to that for *C. trachomatis* infections (30). The number of reported cases of gonorrhea in the United States increased steadily from 1964 to 1977, fluctuated through the early 1980s, increased until 1987, decreased starting in 1987, and has leveled off since 1998. Antimicrobial resistance in *N. gonorrhoeae* contributed to the increase in cases in the 1970s and 1980s. The decline in prevalence that began in 1987 may be attributable to recommendations by CDC (31) that only highly effective antimicrobial agents be used to treat gonorrhea. Using the LCx assay for *N. gonorrhoeae*, urine specimens were tested on a representative sample of participants 14- to 39-years of age in the 1999 to 2000 NHANES data (32); the prevalence of *N. gonorrhoeae* was 0.25%. The prevlance of gonorrhea among non-Hispanic black (1.3%) was over 25 times that among non-Hispanic white (0.05%). Among those infected with *N. gonorrhoeae*, 57% were also infected with *C. trachomatis*.

The incidence of gonorrhea is highest in high-density urban areas among persons under 24 years of age who have more than one sex partner in a 6-month period and who engage in unprotected sexual intercourse. Increases in gonorrhea prevalence have been noted recently among men who have sex with men (MSM) (33). Up to 50% of infected men and women lack symptoms, and routine screening for gonococcal infection is not common except in public STD clinics. Thus, reported cases of gonorrhea substantially underestimate the true burden of the disease and may not accurately represent the true underlying trends over time or differences in disease rates by demographic characteristics. Because gonorrhea screening is more commonly offered in public STD clinics that are frequented by low-income men, gonorrhea rates may appear higher in these demographic groups merely as a result of the enhanced screening.

Infected women are more likely to be asymptomatic than infected men, and screening for gonococcal infection in asymptomatic women is uncommon; therefore, cases in women are less likely to be identified and reported. Reported gonorrhea rates have leveled off overall. From 1998 through

Figure 2. Gonorrhea – Reported rates: United States, 1970–2001.

SOURCE: Centers for Disease Control and Prevention. Adapted from Sexually Transmitted Disease Surveillance 2001 Supplement. Gonococcal Isolate Surveillance Project (GISP) - Annual Report 2001. Available at: http://www.cdc.gov/std/GISP2001/GISP2001Text&Fig.pdf.

2001, the gonorrhea rate in the United States persisted at around 129 cases per 100,000 population (Figure 2) (30). The South continues to have the highest rates of any region. Rates were highest among young women 15 to 19 years of age and men 20 to 24, regardless of race or ethnicity (13). Reported rates of gonorrhea among African Americans are more than 30 times higher than rates among Caucasians and more than 11 times higher than rates among Hispanics (13). As with chlamydia, high reported rates of gonorrhea in certain areas or among certain populations may indicate more effective screening programs and the use of more sensitive tests, rather than higher underlying rates of disease.

The annual economic burden of gonorrhea and related sequelae was estimated to exceed $1 billion in 1994 (18).

The Data

According to HCUP data, hospitalization for a primary diagnosis of gonorrhea is a rare event that decreased from 2,154 hospitalizations in 1994 to 969 in 2000 (Table 18). Although other data indicate that chlamydial infection is more common than gonorrhea (30), infection with *N. gonorrhoeae* is more likely to result in hospitalization because it tends to cause more severe symptoms and may require more sophisticated diagnostic assessment, intravenous antibiotics, or surgical intervention (e.g., abscess drainage).

Medicare data on hospital outpatient and inpatient visits for gonorrhea from 1992 through 1998 are too sparse to permit meaningful interpretation. Hospital outpatient visit rates of approximately 1 per 100,000 Medicare beneficiaries were observed in all three years of data.

In the 2001 VA data, gonorrhea was the third most common pathogen-specific STD clinical presentation, with a total of 17 cases per 100,000 unique outpatients (Table 6). As with chlamydia, the highest rates were seen among women (29 per 100,000), persons under 25 years of age (109 per 100,000), and African Americans (71 per 100,000); this may be due in part to higher rates of screening of younger asymptomatic women in family planning, prenatal, and STD clinics (Table 19). Geographic distribution throughout the country was relatively uniform (15 to 19 per 100,000). A generalized decreasing trend was noted when comparing case counts and rates from 1999 through 2001; this trend was most consistent among persons 25- to 54- years of age, among Caucasians and African Americans, and among persons living in the Northeastern, Southern, and Midwestern regions. In each year examined, the

Table 18. Inpatient hospital stays by individuals with gonorrhea listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	2,154	0.8 (0.7–1.0)	1,250	0.5 (0.4–0.6)	1,115	0.4 (0.3–0.5)	969	0.4 (0.3–0.4)
Age								
< 14	*	*	*	*	*	*	*	*
14–17	542	3.8 (2.8–4.8)	272	1.8 (1.2–2.3)	221	1.4 (1.0–1.8)	221	1.4 (0.9–1.8)
18–24	739	3.0 (2.3–3.7)	448	1.8 (1.4–2.3)	457	1.8 (1.4–2.2)	403	1.5 (1.2–1.9)
25–34	519	1.3 (1.0–1.6)	321	0.8 (0.6–1.0)	280	0.7 (0.5–0.9)	229	0.6 (0.4–0.8)
35–44	215	0.5 (0.4–0.7)	*	*	*	*	*	*
45–54	*	*	*	*	*	*	*	*
55–64	*	*	*	*	*	*	*	*
65–74	*	*	*	*	*	*	*	*
75–84	*	*	*	*	*	*	*	*
85+	*	*	*	*	*	*	*	*
Race/ethnicity								
White	381	0.2 (0.2–0.3)	258	0.1 (0.1–0.2)	195	0.1 (0.1–0.1)	193	0.1 (0.1–0.1)
Black	1,294	4.1 (3.2–5.0)	794	2.4 (1.9–2.9)	555	1.6 (1.3–2.0)	494	1.4 (1.1–1.8)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	*	*	*	*	*	*	*	*
Gender								
Male	173	0.1 (0.1–0.2)	*	*	*	*	*	*
Female	1,975	1.5 (1.2–1.8)	1,120	0.8 (0.7–1.0)	995	0.7 (0.6–0.9)	920	0.7 (0.5–0.8)
Region								
Midwest	539	0.9 (0.5–1.3)	254	0.4 (0.2–0.6)	279	0.4 (0.3–0.6)	295	0.5 (0.3–0.6)
Northeast	363	0.7 (0.5–1.0)	226	0.4 (0.2–0.6)	172	0.3 (0.2–0.5)	184	0.4 (0.2–0.5)
South	1,082	1.3 (0.9–1.6)	688	0.8 (0.5–1.0)	601	0.6 (0.5–0.8)	408	0.4 (0.3–0.5)
West	170	0.3 (0.1–0.5)	*	*	*	*	*	*
MSA								
Rural	*	*	*	*	*	*	*	*
Urban	1,865	1.0 (0.8–1.2)	1,066	0.5 (0.4–0.6)	978	0.5 (0.4–0.6)	882	0.4 (0.3–0.5)

MSA, metropolitan statistical area.

*Figure does not meet standard for reliability or precision.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of other race/ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 19. Frequency of gonorrhea[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	708	23	660	20	634	17
Age						
18–24	25	99	29	123	25	109
25–34	153	101	138	97	123	91
35–44	216	65	180	58	163	54
45–54	201	29	187	26	189	25
55–64	41	8	59	11	71	11
65–74	46	6	42	5	38	4
75–84	25	5	23	4	24	3
85+	1	2	2	3	1	1
Race/ethnicity						
White	144	11	130	9	127	8
Black	299	90	287	84	251	71
Hispanic	18	16	19	16	32	25
Other	1	5	2	10	2	9
Unknown	246	20	222	17	222	14
Gender						
Male	654	23	599	19	586	17
Female	54	38	61	40	48	29
Region						
Northeast	237	32	159	20	164	19
Midwest	125	18	139	19	128	15
South	250	25	234	21	232	18
West	96	16	128	20	110	16
Insurance status						
No insurance/self-pay	588	32	559	31	507	27
Medicare/Medicare supplemental	46	7	43	5	42	4
Medicaid	1	20	1	13	2	22
Private insurance/HMO/PPO	68	14	54	11	69	12
Other insurance	5	20	3	10	11	33
Unknown	0	0	0	0	3	33

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for gonorrhea.

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from observation only; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 20. Medical visits[a] for gonorrhea in 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	16	7 (3–10)
10–14	6	3 (1–6)
15–19	104	56 (45–66)
20–24	82	71 (56–87)
25–29	70	71 (55–88)
30–34	87	61 (48–74)
35–39	64	34 (25–42)
40–44	57	26 (20–33)
45–54	71	15 (12–18)
55–64	44	12 (9–16)
65+	1	11 (0–32)
Gender		
Male	203	19 (17–22)
Female	399	35 (31–38)
Region		
Midwest	159	31 (26–35)
Northeast	87	23 (18–28)
South	278	30 (26–33)
West	19	17 (9–25)
Unknown	59	22 (17–28)
Urban/rural		
MSA	430	29 (27–32)
Non-MSA	113	24 (19–28)
Unknown	59	22 (17–28)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.

[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.

SOURCE: MarketScan, 1999.

highest rates of gonorrhea occurred among those who had no insurance or were self-paying patients.

The 1999 MarketScan data had 592 outpatient visits and 10 inpatient visits which were accompanied by a claim for services associated with one of the ICD-9 codes listed in Table 1 for gonorrhea (Table 3). There were 399 medical visits for gonococcal infection by women and 203 by men, the rates being 35 and 19 per 100,000, respectively (Table 20). The highest rates were seen equally among those 20 to 24 years of age and those between 25 and 29 (71 per 100,000). Again, the higher rates of gonococcal infection observed among women and those under 25 may be due in part to higher rates of screening of younger asymptomatic women. Rates varied by geographical region, ranging from 17 per 100,000 enrollees in the West to 31 per 100,000 in the Midwest. A difference was also seen between urban (29 per 100,000) and rural (24 per 100,000) residents. The 602 medical visits that were ICD-coded as being for gonococcal infection resulted in 169 (28%) claims for one of the drugs recommended by CDC for treatment of uncomplicated, lower urinary tract gonococcal infection filed within 7 days before or 20 days after the date of the medical visit. However, in the same dataset, 2,530 visits resulted in drug claims for one of these same drugs filed within 7 days before or 20 days after the date of the medical visit and were *either* ICD-coded as being for gonorrhea *or* included a CPT code that referred to a test for gonorrhea. Thus, defining probable and possible visits for gonococcal infection based only on ICD-9 codes would substantially underestimate the number of visits for treatment of gonococcal infection. Clinicians tend not to use gonococcus-specific ICD-9 codes when simply ruling out gonococcal infection with a test; in the case of a test later found to be positive, the original ICD-9 code is not customarily altered to reflect gonococcal infection.

Syphilis

Background

Syphilis is a systemic disease caused by *Treponema pallidum*. Patients with syphilis may seek treatment for signs or symptoms of primary infection (i.e., ulcer or chancre at the infection site), secondary infection (e.g., skin rash, mucocutaneous lesions, or lymphadenopathy), or tertiary infection (e.g., cardiac, ophthalmic, or auditory abnormalities, or gummatous lesions) (31). Signs of primary and secondary syphilis that most commonly would be seen by a urologist include chancre and rash. Latent infections are detected by serologic testing. Latent syphilis acquired within the preceding year is referred to as early latent syphilis; all other cases of latent syphilis are classified as either late latent syphilis or latent syphilis of unknown duration. The latent stages of syphilis begin with disappearance of the secondary symptoms. Unless they have cause to screen patients, urologists rarely see latent syphilis or its manifestations that occur outside the genitourinary system.

The diagnosis of syphilis depends on clinical findings and directly visualizing *T. pallidum* organisms in secretions or tissue or on serology. Darkfield examinations and direct fluorescent antibody tests of lesion exudate or tissue are the definitive methods for diagnosing early syphilis, but such testing is rarely performed outside STD clinics. A presumptive diagnosis is possible with the use of two types of serologic tests for syphilis: nontreponemal tests (e.g., Venereal Disease Research Laboratory [VDRL] and Rapid Plasma Reagin [RPR]) and treponemal tests (e.g., fluorescent treponemal antibody absorbed [FTA-ABS] and *T. pallidum* particle agglutination [TP-PA]). The use of only one type of serologic test is insufficient for diagnosis because false-positive nontreponemal test results may occur secondary to various medical conditions. Routine serologic screening is done in only a few settings, including blood banks, prenatal care and STD clinics, and some HIV care clinics; it is also required in premarital testing in some states.

Staging of syphilis is based on serology results and relies on knowledge of past titers and treatment history. This can be challenging if no information on past titers or treatment is available, as is often the case when patients pursue care in more than one setting. Treatment with penicillin is often provided based on a single, isolated serologic result because such treatment is generally safe, effective, and inexpensive. If a patient is successfully treated, the titer of the nontreponemal serologic test will fall, usually within the 6 months following treatment. Primary, secondary, and early latent stages are all infectious stages; primary and secondary stages in adults and congenital syphilis are subject to national surveillance because their infectious nature or origin makes them important to public health. Other stages are not under national surveillance but add to the overall burden of disease.

In 1996, 11,400 new cases of primary and secondary syphilis and 53,000 new cases of all stages of syphilis were reported to CDC; if we assume 20% underreporting, approximately 70,000 total syphilis infections were diagnosed in that year (34). However, the rate of primary and secondary syphilis reported in the United States decreased 90% between 1990 and 2000, from 20.34 to 2.12 cases per 100,000 population (Figure 3). In 2001, the overall rate (2.17 per 100,000) represented a 2% increase over the 2000 rate, which was the lowest rate since reporting began in 1941 (35), and the first annual increase since 1990. In 1999, CDC estimated that the annual direct medical costs for adult and congenital syphilis were $213 million, with an additional cost of $752 million for syphilis-attributable HIV infection (36).

Figure 3. Primary and secondary syphilis – Reported rates: United States, 1970–2001.

SOURCE: Centers for Disease Control and Prevention. Adapted from Sexually Transmitted Disease Surveillance 2001 Supplement. Syphilis Surveillance Report - February 2003. Available at: http://www.cdc.gov/std/Syphilis2001/2001SyphSuppText.pdf.

The Data

During 2001, 6,103 primary and secondary syphilis cases were reported to state and local health departments in the United States. The highest rate of primary and secondary syphilis among women was seen in those 20 to 24 years of age (3.8 per 100,000 population); the highest rate among men was seen in those 35 to 39 years of age (7.2 per 100,000). The 2001 rate for men was 15.4% higher than the rate in 2000, and the rate for women was 17.7% lower. The male-to-female case ratio of primary and secondary syphilis rose from 1.1:1 in 1996 to 2.1:1 in 2001. Current efforts to eliminate syphilis in the United States are focused on communities in which relatively elevated rates of STDs are being observed among men who have sex with men (MSM) and on heterosexual communities with high prevalence, many of which are in the South. The recent increase in cases in men, the growing disparity in case numbers between men and women observed across all racial and ethnic groups, and reported outbreaks of syphilis among MSM in large urban areas all suggest that increases in syphilis are occurring among MSM. Rates have also remained disproportionately high in the South (3.4 per 100,000) and among non-Hispanic blacks (11 per 100,000) (37, 38). Urologists who care for MSM or work in communities with a high incidence of syphilis may diagnose and treat patients with primary or secondary stages of syphilis, especially when they present with genital ulcers.

Epididymitis/Orchitis

Background

Epididymitis, or inflammation of the epididymis, commonly occurs as a complication of urethral infection with *N. gonorrhoeae*, *C. trachomatis*, or *Pseudomonas aeruginosa*. It may also occur as a complication of systemic infection with *Mycobacterium tuberculosis*, *Brucella spp*., *Streptococcus pneumoniae*, *Neisseria meningiditis*, *Treponema pallidum*, and various fungi (3). Epididymitis causes considerable morbidity in terms of pain, suffering, and loss of productivity. The condition is common in the United States; in 1977, an estimated 634,000 patients sought treatment for it (39). Changes in the incidence of epididymitis have not been consistently monitored over time because the condition is not subject to national surveillance.

Orchitis is an inflammation of the testicles, which may be caused by any of several bacteria or viruses. Orchitis tends to occur in conjunction with infections of the prostate or epididymis and, like those conditions, may occur as a manifestation of STDs such as gonorrhea or chlamydial infection. The most common viral cause of orchitis is mumps, a non-sexually-transmissible virus (2). The incidence of orchitis is not subject to national surveillance. Because orchitis tends to occur commonly in conjunction with epididymitis, most ICD-9 codes do not distinguish between the two conditions. There are only two unique orchitis codes—one for gonococcal orchitis and one for chronic gonococcal orchitis; there is no unique code for gonococcal epididymitis (Table 1). Summary analyses of cases and visits in national datasets suggest that only about 60% of the cases of epididymitis and orchitis are attributable to STDs (3).

The Data

HCUP data indicate that since 1996 there has been little change over time in hospitalizations for both epididymitis/orchitis using all ICD-9 codes (Table 21) and epididymitis/orchitis not specified as due to Chlamydia or gonococcus (organism unspecified) (Table 22). In 1996, 8,954 hospitalizations had epididymitis/orchitis (all cases) listed as the primary diagnosis; there was a steady increase in rates of stays across all 10-year age categories from 25 to 34 through 85+ (Table 21). In 2000, there were 8,448 hospitalizations for epididymitis/orchitis, with increasing rates of stays across 10-year age categories from <14 through 85+ (Table 21). Over 99% of the cases were for epididymitis/orchitis not designated as due to Chlamydia or gonococcus (Table 22); it appears that clinicians rarely code patients specifically as having acute or chronic gonococcal orchitis (ICD codes 098.13 or 098.33).

Medicare hospital outpatient data indicate that rates of epididymitis/orchitis (organism unspecified) increased from 14 per 100,000 beneficiaries in 1992 to 26 per 100,000 in 1998 (Table 23). An inverse relationship was seen in the Medicare inpatient data, where hospitalizations for epididymitis/orchitis (organism unspecified) decreased from 26 per 100,000 beneficiaries in 1992, to 19 per 100,000 in 1995, to 14 per 100,000 in 1998 (Table 24).

Table 21. Inpatient hospital stays by individuals for epididymitis/orchitis (all cases) listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	10,235	8.3 (7.8–8.8)	8,954	7.0 (6.5–7.4)	8,954	6.8 (6.4–7.3)	8,448	6.3 (5.9–6.8)
Age								
< 14	657	2.4 (1.8–2.9)	526	1.8 (1.4–2.3)	396	1.4 (1.0–1.7)	435	1.5 (1.1–1.9)
14–17	423	5.8 (4.3–7.3)	277	3.5 (2.4–4.7)	208	2.6 (1.8–3.4)	182	2.2 (1.5–2.9)
18–24	586	4.8 (3.7–5.9)	385	3.1 (2.4–3.9)	428	3.4 (2.6–4.2)	420	3.2 (2.5–3.9)
25–34	1,660	8.3 (7.1–9.4)	1,161	5.8 (5.0–6.7)	1,072	5.6 (4.7–6.5)	872	4.8 (3.9–5.6)
35–44	1,586	8.0 (6.9–9.1)	1,565	7.4 (6.4–8.5)	1,668	7.6 (6.7–8.6)	1,490	6.8 (5.9–7.7)
45–54	1,223	8.7 (7.4–10)	1,251	8.1 (6.9–9.2)	1,336	8.1 (7.0–9.2)	1,354	7.6 (6.6–8.6)
55–64	1,205	12 (11–14)	1,029	10 (8.8–12)	1,159	11 (9.3–13)	1,042	9.3 (8.1–11)
65–74	1,507	19 (16–22)	1,427	18 (15–20)	1,171	15 (12–17)	1,324	16 (14–19)
75–84	1,098	29 (25–33)	1,059	25 (21–29)	1,205	27 (23–30)	1,079	22 (19–26)
85+	291	32 (21–44)	275	32 (22–41)	311	32 (23–40)	252	25 (17–32)
Race/ethnicity								
White	5,370	5.9 (5.4–6.4)	5,118	5.5 (5.1–5.9)	4,892	5.2 (4.8–5.7)	4,374	4.6 (4.2–5.0)
Black	1,568	11 (9.3–12)	1,102	7.2 (6.0–8.4)	1,070	6.8 (5.7–8.0)	1,054	6.6 (5.6–7.7)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	718	5.5 (4.2–6.8)	684	4.8 (3.8–5.7)	670	4.3 (3.2–5.3)	820	5.0 (4.1–6.0)
Region								
Midwest	2,310	7.9 (7.0–8.8)	2,280	7.6 (6.7–8.5)	2,133	7.0 (6.1–7.8)	2,010	6.4 (5.7–7.2)
Northeast	2,789	11 (10–13)	2,161	8.7 (7.5–9.9)	2,029	8.2 (6.9–9.5)	1,684	6.8 (5.8–7.8)
South	3,642	8.8 (7.8–9.8)	3,257	7.3 (6.6–8.1)	3,428	7.5 (6.8–8.3)	3,392	7.3 (6.4–8.1)
West	1,494	5.4 (4.5–6.3)	1,256	4.3 (3.7–4.9)	1,365	4.5 (3.7–5.4)	1,363	4.5 (3.7–5.3)
MSA								
Rural	2,351	7.5 (6.5–8.6)	2,035	7.0 (6.0–8.0)	2,052	7.0 (6.1–7.9)	1,763	6.0 (5.1–6.9)
Urban	7,812	8.5 (7.9–9.1)	6,919	7.0 (6.5–7.4)	6,865	6.8 (6.2–7.3)	6,676	6.4 (5.9–6.9)

MSA, metropolitan statistical area.
*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.
[b]Persons of other race/ethnicity are included in the totals.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 22. Inpatient hospital stays by individuals with epididymitis/orchitis not designated as due to *Chlamydia* or gonococcus listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	10,082	8.2 (7.7–8.7)	8,894	6.9 (6.5–7.4)	8,882	6.8 (6.3–7.2)	8,387	6.3 (5.9–6.7)
Age								
< 14	650	2.3 (1.8–2.9)	521	1.8 (1.3–2.3)	396	1.4 (1.0–1.7)	435	1.5 (1.1–1.9)
14–17	377	5.2 (3.7–6.7)	256	3.3 (2.1–4.4)	176	2.2 (1.5–2.9)	177	2.1 (1.4–2.9)
18–24	512	4.2 (3.2–5.2)	363	3.0 (2.3–3.7)	422	3.4 (2.6–4.2)	388	3.0 (2.3–3.7)
25–34	1,649	8.2 (7.0–9.4)	1,156	5.8 (5.0–6.7)	1,047	5.4 (4.6–6.3)	852	4.7 (3.8–5.5)
35–44	1,577	8.0 (6.9–9.0)	1,558	7.4 (6.3–8.4)	1,664	7.6 (6.7–8.6)	1,490	6.8 (5.9–7.7)
45–54	1,223	8.7 (7.4–10)	1,251	8.1 (6.9–9.2)	1,336	8.1 (7.0–9.2)	1,354	7.6 (6.6–8.6)
55–64	1,199	12 (10–14)	1,029	10 (8.8–12)	1,154	11 (9.3–12)	1,042	9.3 (8.1–11)
65–74	1,507	19 (16–22)	1,427	18 (15–20)	1,171	15 (12–17)	1,319	16 (14–19)
75–84	1,098	29 (25–33)	1,059	25 (21–29)	1,205	27 (23–30)	1,079	22 (19–26)
85+	291	32 (21–44)	275	32 (22–41)	311	32 (23–40)	252	25 (17–32)
Race/ethnicity								
White	5,323	5.8 (5.3–6.4)	5,099	5.5 (5.0–5.9)	4,887	5.2 (4.8–5.6)	4,374	4.6 (4.2–5.0)
Black	1,471	10 (8.7–11)	1,071	7.0 (5.8–8.2)	1,043	6.7 (5.6–7.8)	1,004	6.3 (5.3–7.3)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	718	5.5 (4.2–6.8)	679	4.7 (3.8–5.7)	654	4.2 (3.1–5.2)	820	5.0 (4.1–6.0)
Region								
Midwest	2,284	7.8 (6.9–8.7)	2,270	7.5 (6.6–8.4)	2,118	6.9 (6.0–7.8)	1,984	6.4 (5.6–7.1)
Northeast	2,743	11 (9.8–12)	2,137	8.6 (7.4–9.8)	2,001	8.1 (6.8–9.4)	1,679	6.8 (5.8–7.8)
South	3,569	8.6 (7.7–9.6)	3,240	7.3 (6.5–8.1)	3,408	7.5 (6.7–8.2)	3,371	7.2 (6.4–8.1)
West	1,485	5.3 (4.4–6.2)	1,247	4.3 (3.7–4.9)	1,355	4.5 (3.7–5.4)	1,354	4.4 (3.6–5.3)
MSA								
Rural	2,300	7.4 (6.3–8.4)	2,028	7.0 (6.0–8.0)	2,046	7.0 (6.1–7.9)	1,752	6.0 (5.1–6.9)
Urban	7,710	8.4 (7.8–9.0)	6,866	6.9 (6.4–7.4)	6,798	6.7 (6.2–7.2)	6,626	6.4 (5.9–6.9)

MSA, metropolitan statistical area.
*Figure does not meet standard for reliability or precision.
[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.
[b]Persons of other race/ethnicity are included in the totals.
NOTE: Counts may not sum to totals due to rounding.
SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 23. Outpatient hospital visits by Medicare beneficiaries with epididymitis/orchitis not designated as due to *Chlamydia* or gonococcus listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	2,100	14 (14–15)	3,320	22 (21–23)	3,740	26 (25–27)
Total < 65 yrs	320	10 (9.2–12)	1,060	31 (29–33)	1,060	31 (29–33)
Total 65+	1,780	15 (15–16)	2,260	19 (18–20)	2,680	24 (23–25)
Age						
65–74	940	13 (12–14)	1,380	19 (18–20)	1,740	27 (26–28)
75–84	660	19 (17–20)	600	16 (15–18)	820	22 (21–24)
85–94	180	23 (19–26)	240	28 (25–32)	100	12 (9.2–14)
95+	0	0	40	49 (34–63)	20	23 (13–33)
Race/ethnicity						
White	1,480	12 (11–13)	2,300	18 (17–18)	2,900	24 (23–25)
Black	440	35 (31–38)	740	53 (50–57)	460	34 (31–38)
Asian	…	…	…	…	80	58 (45–71)
Hispanic	…	…	140	71 (59–82)	80	24 (18–29)
N. American Native	…	…	…	…	80	286 (222–351)
Region						
Midwest	800	22 (20–23)	1,120	29 (27–31)	1,400	38 (36–40)
Northeast	240	7.6 (6.6–8.5)	640	20 (19–22)	480	17 (16–19)
South	680	13 (12–14)	1,140	21 (20–22)	1,200	22 (21–24)
West	320	14 (13–16)	420	18 (16–20)	660	30 (27–32)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

VA data for 2001 report 50 cases of epididymitis/orchitis (organism unspecified) per 100,000 unique outpatients (Table 25). Comparably high rates were seen in all 10-year age categories from 25 to 34 through 55 to 64 (61 per 100,000 to 73 per 100,000). The highest rates were seen among African Americans (87 per 100,000) and persons residing in the West (57 per 100,000). When the definition of epididymitis/orchitis was expanded to include all cases (organism both specified and unspecified), there were 51 cases per 100,000 unique outpatients, similar to the incidence of epididymitis/orchitis (organism unspecified alone).

The 1999 MarketScan data report that 1,580 outpatient visits and 14 inpatient visits were accompanied by a claim for services associated with one of the ICD-9 codes listed in Table 1 for epididymitis and/or orchitis not designated as due to chlamydia or gonococcus (Table 3); among males 16- to 35- years of age, rates of epididymitis/orchitis varied by region, from 556 per 100,000 enrollees in the Midwest to 715 per 100,000 enrollees in the Northeast (Table 26). A small difference was also seen between urban (617 per 100,000) and rural (670 per 100,000) residents. While 1,594 visits were identified as epididymitis/orchitis not designated as due to chlamydia or gonococcus (organism unspecified), only one visit for gonococcal orchitis was identified; as in the HCUP data, it appears that clinicians rarely code patients specifically as having acute or chronic gonococcal orchitis (ICD-9 code 098.13 or 098.33). This may be due to a low underlying prevalence of gonococcal orchitis or to the use of other ICD-9 codes to capture gonococcal orchitis (604, 604.0, 098.1, 098.10, or 098.30).

Table 24. Inpatient stays by Medicare beneficiaries with epididymitis/orchitis not designated as due to *Chlamydia* or gonococcus listed as primary diagnosis, count[a], rate[b] (95% CI)

	1992		1995		1998	
	Count	Rate	Count	Rate	Count	Rate
Total[c]	3,760	26 (25–26)	2,840	19 (18–19)	2,020	14 (13–15)
Total < 65 yrs	540	17 (16–19)	680	20 (18–21)	500	15 (13–16)
Total 65+	3,220	28 (27–29)	2,160	18 (18–19)	1,520	14 (13–14)
Age						
65–74	1,680	23 (22–24)	1,200	17 (16–18)	640	10 (9.2–11)
75–84	1,200	34 (32–36)	780	21 (20–23)	620	17 (16–18)
85–94	320	40 (36–45)	160	19 (16–22)	240	28 (24–31)
95+	20	26 (14–37)	20	24 (13–35)	20	23 (13–33)
Race/ethnicity						
White	3,220	26 (25–27)	2,360	18 (17–19)	1,500	12 (12–13)
Black	320	25 (22–28)	360	26 (23–29)	400	30 (27–33)
Asian	…	…	40	55 (38–71)	0	0
Hispanic	…	…	40	20 (14–26)	40	12 (8.3–16)
N. American Native	…	…	20	99 (55–144)	0	0
Region						
Midwest	1,000	27 (25–29)	800	21 (19–22)	460	12 (11–14)
Northeast	660	21 (19–22)	440	14 (13–15)	460	17 (15–18)
South	1,380	26 (25–28)	1,160	21 (20–22)	780	15 (14–16)
West	580	26 (24–28)	420	18 (16–20)	280	13 (11–14)

… data not available.
[a]Unweighted counts multiplied by 20 to arrive at values in the table.
[b]Rate per 100,000 Medicare beneficiaries in the same demographic stratum.
[c]Persons of other races, unknown race and ethnicity, and other region are included in the totals.
NOTE: Counts less than 600 should be interpreted with caution.
SOURCE: Centers for Medicare and Medicaid Services, 5% Carrier and Outpatient Files, 1992, 1995, 1998.

Urethritis

Background

Urethritis, or urethral inflammation of any etiology, causes urethral discharge, dysuria, or pruritis at the end of the urethra (40). In heterosexual men, the most common causes of urethritis are gonococcal and chlamydial infections, and infection is limited to the distal urethra (41). In women, urethritis is often observed in association with cystitis and pyelonephritis. *Escherichia coli* remains the predominant uropathogen (80%) isolated in acute community-acquired uncomplicated UTIs, followed by *Staphylococcus saprophyticus* (10% to 15%) (42), but clinicians more commonly code such UTIs as cystitis, rather than as urethritis. Sexually transmitted infections that may result in urethritis include *N. gonorrhoeae* and *C. trachomatis*, but the resulting inflammation creates nonspecific symptoms and signs that cannot be used to identify the etiologic pathogen (2, 40, 41). As with epididymitis and orchitis, there are no systematic national surveillance systems for urethritis, so its incidence cannot be tracked over time. However, because reported cases of gonorrhea in men tend to be cases of urethritis (24, 43), trends in urethritis resemble those in the reporting of gonorrhea.

Urethritis causes considerable morbidity in terms of pain, suffering, and loss of productivity. In the United States, men and women with symptoms of lower UTIs account for an estimated 7 million office visits per year to physicians in office practice (44). In the NDTI, the number of initial visits to physicians' offices per year for nonspecific urethritis in men and women averaged about 250,000 in 1996–1997 and decreased to about 200,000 in 2001.

Table 25. Frequency of epididymitis/orchitis not designated as due to *Chlamydia* or gonococcus[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	1,853	61	1,921	59	1,833	50
Age						
18–24	19	75	17	72	15	65
25–34	122	81	110	77	99	73
35–44	277	84	257	82	198	66
45–54	515	75	568	79	540	72
55–64	330	66	350	63	394	61
65–74	258	34	377	46	357	38
75–84	213	40	216	34	211	26
85+	19	39	26	45	19	24
Race/ethnicity						
White	957	70	1,019	69	956	59
Black	315	94	342	100	309	87
Hispanic	88	77	91	74	100	78
Other	7	36	9	44	8	37
Unknown	486	40	460	35	460	29
Region						
Midwest	370	54	412	55	377	46
Northeast	421	57	415	53	377	43
South	674	66	704	63	681	53
West	388	65	390	61	398	57
Insurance status						
No insurance/self-pay	1,246	68	1,254	69	1,186	62
Medicare/Medicare supplemental	338	49	389	43	414	35
Medicaid	1	20	5	63	3	33
Private insurance/HMO/PPO	247	51	251	49	211	38
Other insurance	20	79	22	76	19	57
Unknown	1	52	0	0	0	0

HMO, health maintenance organization; PPO, preferred provider organization.
[a]Represents diagnosis codes for epididymitis (organism unspecified).
[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.
[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.
NOTE: Race/ethnicity data from observation only; note large number of unknown values.
Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 26. Medical visits[a] for epididymitis/orchitis not designated as due to *Chlamydia* or gonococcus, by males aged 16–35 years, 1999, count, rate[b] (95% CI)

	Count	Rate
Region		
Midwest	382	556 (500–611)
Northeast	291	715 (633–797)
South	691	654 (605–702)
West	84	567 (446–687)
Unknown	146	491 (412–571)
Urban/rural		
MSA	1,092	617 (581–654)
Non-MSA	356	670 (601–739)
Unknown	146	491 (412–571)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.
[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.
SOURCE: MarketScan, 1999.

The Data

The HCUP data report a small decrease in the number of hospitalizations for all urethritis (using all urethritis ICD-9 codes). In 1994, there were 1,313 hospitalizations with a urethritis diagnosis, and a progressive decrease in each year of data to 687 hospitalizations in 2000 (Table 27). Analysis of Medicare hospital outpatient data from 1992 to 1998 yielded counts for cases of urethritis that were too small to calculate meaningful rates.

VA data indicate that in 2001, urethritis (organism unspecified) was diagnosed in 6 cases per 100,000 unique outpatients (Table 28), with the highest rates seen among men (7 per 100,000), those under the age of 25 (39 per 100,000), and African Americans (20 per 100,000). There was a fairly even distribution of case rates across the country (6 to 7 per 100,000 in each region). Urethritis (using all urethritis ICD-9 codes) was diagnosed in 21 per 100,000 unique outpatients, with the highest rates seen among those under the age of 25 (135 per 100,000), women (35 per 100,000), and African Americans (85 per 100,000); there was a fairly even distribution across the country (19 to 24 per 100,000 in each region) (Table 29). Comparing the frequencies in Tables 28 and 29 indicates that in all three years of study approximately 70% of urethritis cases were classified as due to *Chlamydia* or gonococcus.

The 1999 MarketScan data reported 362 outpatient visits and no inpatient visits accompanied by a claim for services associated with one of the ICD-9 codes listed in Table 1 for nonchlamydial or nongonococcal urethritis (Table 3). Women made 74 medical visits for urethritis (organism unspecified), and men made 288, for rates of 6 and 27 per 100,000 enrollees, respectively (Table 30). The highest rate was seen among those 30 to 34 years of age (39 per 100,000). Rates varied greatly by geographical region, with the highest rate seen in the South (21 per 100,000). There was a minimal difference between the rates for urban (16 per 100,000) and rural (18 per 100,000) residents. In addition to the 362 visits for urethritis not due to chlamydia or gonococcus, 45 outpatient visits were reported for chlamydial urethritis, and 504 outpatient and 7 inpatient visits were reported for gonococcal urethritis. Combining these cases with cases of urethritis not specified as due to *Chlamydia* or gonococcus, a total of 425 women and 492 men made medical visits for all urethritis, yielding rates of 37 per 100,000 and 47 per 100,000, respectively (Table 31). The highest rate was seen among those 25 to 29 years of age (104 per 100,000). Rates varied greatly by geographical region, with the highest rate seen in the South (47 per 100,000). Again, there was a minimal difference between the rates for urban (43 per 100,000) and rural (41 per 100,000) populations.

THE BURDEN OF OTHER STDs NOT COMMONLY MANAGED BY UROLOGISTS

Several other presentations account for a large burden of STD (in terms of both morbidity and cost) that is not quantified in these analyses. These include the other manifestations of infection with HPV and infection with HIV/AIDS, hepatitis B virus (HBV), and *Haemophilus ducreyi*. Although we did not perform any new analyses of these diseases using the datasets described above, we provide here a brief overview of the overall burden of each of them from the published literature.

Human Papillomavirus (HPV) Infections Other Than Genital Warts

We discussed HPV infection in conjunction with genital warts (for which HPV types 6 and 11 are the principal causes) above. In addition, multiple types of

Table 27. Inpatient hospital stays by individuals with urethritis (all cases) listed as primary diagnosis, count, rate[a] (95% CI)

	1994		1996		1998		2000	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total[b]	1,313	0.5 (0.4–0.6)	778	0.3 (0.2–0.4)	752	0.3 (0.2–0.3)	687	0.2 (0.2–0.3)
Age								
< 14	*	*	*	*	*	*	*	*
14–17	321	2.3 (1.5–3.0)	184	1.2 (0.8–1.6)	*	1 (1–1)	163	1.0 (0.6–1.4)
18–24	352	1.4 (1.0–1.8)	260	1.0 (0.7–1.4)	314	1.2 (0.9–1.6)	286	1.1 (0.8–1.4)
25–34	345	0.8 (0.6–1.1)	220	0.5 (0.4–0.7)	160	0.4 (0.3–0.6)	161	0.4 (0.3–0.6)
35–44	171	0.4 (0.3–0.6)	*	*	*	*	*	*
45–54	*	*	*	*	*	*	*	*
55–64	*	*	*	*	*	*	*	*
65–74	*	*	*	*	*	*	*	*
75–84	*	*	*	*	*	*	*	*
85+	*	*	*	*	*	*	*	*
Race/ethnicity								
White	212	0.1 (0.1–0.2)	*	*	*	*	*	*
Black	788	2.5 (1.9–3.1)	473	1.4 (1.1–1.8)	347	1.0 (0.8–1.3)	365	1.1 (0.8–1.4)
Asian/Pacific Islander	*	*	*	*	*	*	*	*
Hispanic	*	*	*	*	*	*	*	*
Gender								
Male	185	0.2 (0.1–0.2)	*	*	*	*	*	*
Female	1,128	0.9 (0.7–1.1)	651	0.5 (0.4–0.6)	636	0.5 (0.4–0.6)	648	0.5 (0.4–0.6)
Region								
Midwest	341	0.6 (0.3–0.8)	165	0.3 (0.2–0.4)	190	0.3 (0.2–0.4)	189	0.3 (0.2–0.4)
Northeast	189	0.4 (0.2–0.5)	*	*	*	*	159	0.3 (0.1–0.5)
South	635	0.7 (0.5–1.1)	422	0.5 (0.3–0.6)	416	0.4 (0.3–0.6)	283	0.3 (0.2–0.4)
West	148	0.3 (0.1–0.4)	*	*	*	*	*	*
MSA								
Rural	*	*	*	*	*	*	*	*
Urban	1,156	0.6 (0.5–0.8)	664	0.3 (0.3–0.4)	656	0.3(0.2–0.4)	632	0.3 (0.2–0.4)

*Figure does not meet standard for reliability or precision; MSA, metropolitan statistical area.

[a]Rate per 100,000 based on 1994, 1996, 1998, 2000 population estimates from Current Population Survey (CPS), CPS Utilities, Unicon Research Corporation, for relevant demographic categories of US civilian non-institutionalized population.

[b]Persons of other race/ethnicity are included in the totals.

NOTE: Counts may not sum to totals due to rounding.

SOURCE: Healthcare Cost and Utilization Project Nationwide Inpatient Sample, 1994, 1996, 1998, 2000.

Table 28. Frequency of urethritis not designated as due to *Chlamydia* or gonococcus[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	275	9	230	7	233	6
Age						
18–24	11	43	8	34	9	39
25–34	52	34	40	28	30	22
35–44	73	22	59	19	62	21
45–54	66	10	74	10	63	8
55–64	29	6	20	4	32	5
65–74	26	3	16	2	19	2
75–84	16	3	12	2	17	2
85+	2	4	1	2	1	1
Race/ethnicity						
White	82	6	74	5	73	5
Black	90	27	74	22	72	20
Hispanic	9	8	5	4	5	4
Other	0	0	1	5	1	5
Unknown	94	8	76	6	82	5
Gender						
Male	268	9	227	7	230	7
Female	7	5	3	2	3	2
Region						
Midwest	85	12	85	11	49	6
Northeast	40	5	39	5	52	6
South	98	10	63	6	84	6
West	52	9	43	7	48	7
Insurance status						
No insurance/self-pay	208	11	176	10	169	9
Medicare/Medicare supplemental	32	5	26	3	27	2
Medicaid	0	0	2	25	1	11
Private insurance/HMO/PPO	35	7	25	5	35	6
Other insurance	0	0	1	3	1	3
Unknown	0	0	0	0	0	0

HMO, health maintenance organization; PPO, preferred provider organization.

[a]Represents diagnosis codes for urethritis (organism unspecified).

[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.

[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.

NOTE: Race/ethnicity data from observation only; note large number of unknown values.

Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 29. Frequency of urethritis (all cases)[a] listed as any diagnosis in VA patients seeking outpatient care, count[b], rate[c]

	1999		2000		2001	
	Count	Rate	Count	Rate	Count	Rate
Total	919	30	835	25	771	21
Age						
18–24	39	154	36	153	31	135
25–34	207	137	169	119	149	110
35–44	273	83	235	75	210	70
45–54	237	34	249	35	225	30
55–64	61	12	67	12	85	13
65–74	62	8	51	6	40	4
75–84	37	7	26	4	29	4
85+	3	6	2	3	2	3
Race/ethnicity						
White	205	15	179	12	167	10
Black	366	110	351	102	301	85
Hispanic	25	22	23	19	25	19
Other	1	5	2	10	3	14
Unknown	322	27	280	21	275	17
Gender						
Male	858	30	769	25	714	20
Female	61	43	66	44	57	35
Region						
Northeast	259	35	188	24	205	24
Midwest	188	27	214	29	159	19
South	323	32	271	24	268	21
West	149	25	162	25	139	20
Insurance status						
No insurance/self-pay	757	41	693	38	612	32
Medicare/Medicare supplemental	68	10	56	6	54	5
Medicaid	1	20	3	38	4	45
Private insurance/HMO/PPO	87	18	79	15	90	16
Other insurance	6	24	4	14	9	27
Unknown	0	0	0	0	2	22

[a]Represents diagnosis codes for urethritis (all urethritis codes).
[b]The term count is used to be consistent with other UDA tables; however, the VA tables represent the population of VA users and thus are not weighted to represent national population estimates.
[c]Rate is defined as the number of unique patients with each condition divided by the base population in the same fiscal year x 100,000 to calculate the rate per 100,000 unique outpatients.
NOTE: Race/ethnicity data from observation only; note large number of unknown values.
Source: Outpatient Clinic File (OPC), VA Austin Automation Center, 1999–2001.

Table 30. Medical visits[a] for urethritis not designated as due to *Chlamydia* or gonococcus in 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	11	5 (2–7)
10–14	6	3 (1–6)
15–19	23	12 (7–17)
20–24	30	26 (17–35)
25–29	35	36 (24–47)
30–34	55	39 (28–49)
35–39	66	35 (26–43)
40–44	34	16 (10–21)
45–54	66	14 (11–17)
55–64	36	10 (7–13)
65+	0	0
Gender		
Female	74	6 (5–8)
Male	288	27 (24–30)
Region		
Midwest	66	13 (10–16)
Northeast	44	12 (8–15)
South	193	21 (18–24)
West	21	19 (11–27)
Unknown	38	14 (10–19)
Urban/rural		
MSA	235	16 (14–18)
Non-MSA	88	18 (15–22)
Unknown	39	15 (10–19)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.
[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.
SOURCE: MarketScan, 1999.

Table 31. Medical visits[a] for urethritis (all cases), 1999, count, rate[b] (95% CI)

	Count	Rate
Age		
<10	27	11 (7–15)
10–14	10	6 (2–9)
15–19	110	59 (48–70)
20–24	111	97 (79–115)
25–29	102	104 (84–124)
30–34	139	97 (81–114)
35–39	127	67 (55–79)
40–44	88	41 (32–49)
45–54	133	28 (23–33)
55–64	69	19 (15–24)
65+	1	11 (0–32)
Gender		
Female	425	37 (33–40)
Male	492	47 (43–51)
Region		
Midwest	226	44 (38–49)
Northeast	112	30 (24–35)
South	441	47 (43–51)
West	41	37 (26–48)
Unknown	97	37 (29–44)
Urban/rural		
MSA	623	43 (39–46)
Non-MSA	196	41 (35–47)
Unknown	98	37 (30–45)

[a]The number of medical visits includes both inpatient visits and outpatient visits; however, most medical visits were outpatient visits.
[b]Rate per 100,000 enrollees who were continuously enrolled in a health plan throughout 1999.
SOURCE: MarketScan, 1999.

HPV are carcinogenic (high-risk). Using polymerase chain reaction (PCR), investigators report an overall prevalence of HPV-DNA of 42% in penile carcinomas and 50% in vulvar carcinomas (45). HPV is detectable in 80% to 100% of lesions in basaloid and warty penile cancers (of which Bowen's disease, erythroplasia of Queyrat, and bowenoid papulosis are precursor lesions), whereas it is detectable in only 33% of keratinizing and verrucous penile carcinomas (46).

Cervical cancer is the second most common female malignancy worldwide and the principal cause of cancer in women in most developing countries (47). Certain types of HPV have been identified as the principal causes of invasive cervical cancer and cervical intraepithelial neoplasia (48, 49). Despite the widespread implementation of cancer screening, 13,000 new cases of cervical cancer were diagnosed in the United States in 2002, and there were an estimated 4,100 associated deaths (50).

The major known risk factors for acquiring genital HPV infection include having multiple sex partners (51, 52) and having sex partners who have had multiple partners (51). The cumulative 3-year incidence of genital HPV infection of all types among college-age students has been found to be 43%, and the mean duration of new infections is 8 months (53). Extrapolating these data to the US population, we estimate that there are at least 5.5 million new genital HPV infections each year (34) and that approximately 20 million people have productive genital HPV (that is, active shedding of HPV DNA) (12). In 1994, the economic burden of genital HPV infection and related sequelae, including cervical cancer, in the United States was estimated to exceed $4.5 billion per year (18).

Human Immunodeficiency Virus (HIV)/AIDS

In all US states and territories, data on persons with AIDS are reported to state or local health departments, which forward the data, without personal identifiers, to CDC. Data concerning sex, race/ethnicity, behavioral risk, and state and county of residence are abstracted from medical records of persons who meet either the clinical (opportunistic illness) criteria or the immunologic AIDS-defining criteria that were added to the definition in 1993 (54).

As of the end of December 2001, more than 816,000 cases of AIDS had been reported to CDC. Adult and adolescent AIDS cases totaled 807,000, of which 666,000 were in men and 141,000 were in women. More than 9,000 of the reported AIDS cases were in children under 13 years of age. As of the same date, more than 467,000 persons reported to have AIDS had died—462,000 adults and adolescents and more than 5,000 children under 15 years of age. Current, detailed estimates of the numbers of persons in the United States living with AIDS, by region of residence and year, are available at http://www.cdc.gov/hiv/stats/htm.

The widespread use of highly active antiretroviral therapy (HAART) resulted in substantial decreases in AIDS deaths between 1995 and 1999 in all demographic and risk groups, as well as decreases in new AIDS diagnoses. Further decreases in AIDS diagnoses and deaths in the United States at this point will require better access to therapy, simpler drug regimens, and the continued development of effective drugs. Unfortunately, HIV continues to be transmitted among MSM, among intravenous drug users, and via heterosexual contact. Between 1990 and 1999, the number of living persons diagnosed with AIDS increased fourfold in the United States. The proportions of persons with AIDS are increasing among women, African Americans, Hispanics, intravenous drug users, heterosexuals, and residents of the South, reflecting earlier trends in HIV transmission, differences in testing behaviors, and differential effects of HAART. The poor are disproportionately affected, and HIV incidence rates remain especially high among African Americans with high-risk behaviors.

Hepatitis B

Hepatitis B is caused by infection with hepatitis B virus (HBV). In adults, only 50% of acute HBV infections are symptomatic, and about 1% of cases result in acute liver failure and death. Risk for chronic infection is associated with age at infection. About 90% of infected infants and 60% of infected children under the age of 5 become chronically infected, compared with 2% to 6% of adults. The risk of death from cirrhosis or hepatocellular carcinoma among persons with chronic HBV infection is 15% to 25%.

An estimated 181,000 persons in the United States were infected with HBV during 1998, and about 5,000 deaths occurred from HBV-related cirrhosis or hepatocellular carcinoma. According to NHANES-III data, an estimated 1.25 million people are chronically infected with HBV, serve as a reservoir for infection, and are at increased risk for death from chronic liver disease (31).

HBV is efficiently transmitted by percutaneous or mucous membrane exposure to infectious body fluids. Sexual transmission among adults accounts for about two-thirds of the incident HBV infections in the United States. In the 1990s, transmission among heterosexual partners accounted for about 40% of the infections, and transmission among MSM accounted for another 15%. The most common risk factors for heterosexual transmission include having more than one sex partner in a 6-month period and having a recent history of an STD.

Among MSM, risk factors for HBV infection include having more than one sex partner in a 6-month period, engaging in unprotected receptive anal intercourse, and having a history of other STDs. Changes in sexual practices among MSM to prevent HIV infection have resulted in a lower risk for HBV infection than was observed in the late 1970s, when studies found HBV markers among up to 70% of adult MSM. Recent surveys of young MSM (15 to 22 years of age) indicated that 11% had serologic evidence of past or current HBV infection (anti-HBc or HbsAg) and that 9% had evidence of having been immunized against HBV (anti-HBs alone among persons reporting having received one or more doses of hepatitis B vaccine) (55).

Up to 70% of persons with acute hepatitis B have previously received care in settings where they could have been vaccinated (e.g., STD clinics, drug treatment programs, and correctional facilities). A 1997 survey of STD clinics demonstrated that hepatitis B vaccine was routinely offered in only 5% of these settings (56).

Chancroid

Chancroid, caused by *Haemophilus ducreyi*, is one of the genital ulcerative STDs, along with syphilis and HSV. Chancroid is prevalent in Africa and Asia and has been shown to be a risk factor in the transmission of HIV. It is a reportable disease in some states and territories but tends to be underreported because laboratory diagnosis of chancroid is difficult, and most laboratories are incapable of culturing H. ducreyi (57). National surveillance data collated by CDC reveal that reported cases of chancroid in the United States rose from about 1,000 per year in 1981–1984 to 5,000 in 1987 but have decreased steadily since then to fewer than 100 cases in 2001 (30).

Trichomoniasis

Trichomonas vaginalis is another common cause of lower urogenital tract infection that urologists may see when evaluating the etiology of urethritis in men or women or urinary symptoms (with or without vaginitis and cervicitis) in women. *T. vaginalis* is a microscopic parasite found worldwide, and trichomoniasis is one of the most common STDs, affecting mainly 16- to 35-year-old women. Signs and symptoms of infection in women range from no symptoms to foul-smelling or frothy green discharge from the vagina, vaginal itching, and redness. Other symptoms can include painful sexual intercourse, lower abdominal discomfort, and the urge to urinate. Most men with this infection do not have symptoms, but those who are symptomatic most commonly have a discharge from the urethra, the urge to urinate, and a burning sensation with urination.

In the NDTI, the number of initial visits to physicians' offices per year for trichomonal vaginitis declined from more than 500,000 in 1966 to fewer than 100,000 in 2001. Vaginal infections caused by *T. vaginalis* are among the most common conditions found in women visiting reproductive health facilities. In 1996, between 3% and 48% of sexually active young women requesting routine care at prenatal, family planning, and college health clinics were diagnosed with trichomoniasis (58). Currently, there are no national surveillance data on this disease (13), but it has been estimated that 5 million persons in the United States become infected with *T. vaginalis* each year, with infection being more common in women who have had more than one sex partner in a 6-month period (1).

THE ADDITIONAL BURDEN OF STDs DUE TO SEQUELAE OF ACUTE INFECTIONS AND PERINATAL TRANSMISSION

Several bacterial and viral STDs can cause serious and costly complications if they are not detected and treated promptly. In women, sequelae of acute lower genital tract bacterial STDs that are not promptly treated include PID and its consequences of ectopic pregnancy, infertility, and chronic pelvic pain. Pregnant women can perinatally transmit several STDs, including syphilis resulting in congenital syphilis, gonorrhea resulting in ophthalmia neonatorum, chlamydial infection resulting in pneumonitis and conjunctivitis, HSV resulting in neonatal herpes, HIV resulting in neonatal infection, hepatitis B resulting in neonatal infection, and HPV resulting in respiratory papillomatosis. Bacterial vaginosis in women has been associated with preterm delivery. Infection with certain HPV types can result in dysplasia or cancer of the cervix, penis, vulva, vagina, and anus. Although these complications are far less common than acute cases of bacterial STD and cases of chronic viral STD, they tend to be more complicated and expensive to manage and therefore contribute substantially to the overall clinical and economic burden of STDs. (For details on the burden of these diverse sequelae, see references (59-66)).

MSM: A HIGH-RISK POPULATION FOR STD

Studies demonstrate that MSM with a large number of sexual partners are at higher risk of infection with STDs, including HIV, hepatitis A virus (HAV), and HBV, than are homosexual, bisexual, or heterosexual men who have fewer sexual partners. Although the frequency of unsafe sexual practices and reported rates of bacterial STDs and incident HIV infection have declined substantially in MSM during the past several decades, recent outbreaks of syphilis and gonorrhea have been observed among MSM in several US cities, contributing to increased rates among men (67). MSM, many of whom have been HIV-infected, accounted for most of the new syphilis cases in many urban areas in 2001. These trends threaten to reverse the marked declines in syphilis morbidity seen over the past decade.

Several factors may explain the recent increases in STD and HIV infection observed among MSM. Increases in unsafe sexual behavior by this population have been seen in several US cities, including those with recent outbreaks. Possible reasons for these relapses in safe behaviors include confidence in the effectiveness of antiretroviral therapy in reducing or eliminating transmission risk, "prevention fatigue," lack of awareness of how STDs increase HIV transmission, and increased use of the Internet to identify new sexual partners.

Inadequate provision of STD services to MSM may also play an important role in the recent increases in STD and HIV infection. Anecdotes suggest that many programs provide syphilis serology to MSM only at the initial patient visit because it can be performed readily using blood collected for HIV viral load tests. However, routine risk assessment of sexual risks, clinical assessment and screening for gonorrhea and chlamydial infection, and provision of hepatitis B vaccine at initial or follow-up visits appears to be less common. Thus, many clinicians are missing opportunities to assess risk, encourage risk reduction, educate patients about the risks of HIV transmission despite antiretroviral therapy, and treat STDs that could promote HIV transmission to others.

Urologists who care for MSM should be aware of common symptoms and signs of STDs, e.g., urethral discharge, dysuria, anorectal symptoms (such as pain, pruritis, discharge, and bleeding), genital or anorectal ulcers, other mucocutaneous lesions, lymphadenopathy, and skin rash. Urologists should consider the unique variations in signs that may be encountered in this population such as oral and perianal chancres in those who practice oral and anal sex. Urologists should also be aware of recent trends in STDs in MSM and recent guidelines for risk assessment, diagnosis, and treatment of HIV-uninfected and HIV-infected patients (31). Clinicians should assess sexual risk for all male patients, including routinely inquiring about the gender of patients' sex partners. MSM, including those with HIV infection, should routinely undergo straightforward, nonjudgmental STD/HIV risk assessment and client-centered prevention counseling to reduce the likelihood of acquisition or transmission of HIV and other STDs (31). In addition, screening for STDs and vaccination for HAV and HBV should be considered for MSM at risk for STDs (31, 68, 69).

ECONOMIC IMPACT

Patient visits, claims for testing, diagnostic procedures, drugs, and other treatment account for the majority of direct medical costs. Most published literature on the economic burden of STDs is based on cost per case, not cost per visit. To calculate the direct medical cost of STDs, one must consider unit costs of medical visits that may involve diagnoses, procedures, drugs, and other treatments. Such unit costs can be estimated from special cost studies or by using claims data (such as MarketScan data). Projections of the economic costs for selected populations could be made using some of the datasets that we examined, but with multiple caveats and assumptions. For example, assuming that Medicare and VA costs are lower than the commercial costs reflected in MarketScan data, one could apply a slightly lower average unit cost when estimating actual "costs" rather than "charges." All the visit/drug costs—weighted across the various datasets—could then be applied to the total number of visits to obtain a national estimate of direct medical costs.

The most recent aggregate estimates of the direct medical costs of STDs were published in 1998 (54). These estimates included the STDs examined in this report, as well as manifestations of STDs rarely managed by urologists (e.g., salpingitis) and other STDs not addressed here. Direct medical costs for STD treatment in the United States were estimated (adjusted to 1997 dollars) to be in excess of $8 billion per year (Tables 32 and 33). This figure does not include lost wages and productivity, out-of-pocket costs, costs related to STD screening programs, or costs resulting from perinatal transmission. Of all STDs other than HIV, HPV has the highest incidence and accounts for the highest direct medical costs (more than $1.6 billion annually), most or which are associated with treating precancerous and cancerous cervical lesions (34). Estimates of direct medical costs will vary over time as screening, diagnostic, treatment, and prevention practices change.

RECOMMENDATIONS

In the United States, estimates of incidence and prevalence of the more common STDs depend on convenience samples; incomplete national reporting (for chlamydial infection, HBV, syphilis, and gonorrhea); inconsistent, non-representative prevalence data; and rough extrapolations. None of the datasets we examined provides data for accurately estimating the incidence or prevalence of any STD. For example, if we use of only ICD-9 codes to define a case or visit, we substantially underestimate the costs of chronic STDs, such as genital herpes and genital warts, which commonly result in multiple claims for medical visits that may involve diagnoses, procedures, drugs, and surgical treatment. In addition, ICD-9 codes and CPT codes do not readily capture screening for the several STDs that may be asymptomatic and are commonly detected through screening. However, most of the available datasets do provide data that describe basic trends in incidence, populations at highest risk, types of clinicians who provide STD care, and care-seeking behavior for various STDs.

Table 32. Estimated annual medical costs of the major curable STDs in the United States adjusted to 1997 dollars

STD	Total Cost[a]
Chlamydia	$374,600,000
Gonorrhea	$56.000,000
Pelvic inflammatory disease	$1,125,200,000
Trichomoniasis	$375,000,000
Syphilis	$43,800,000
Total costs, bacterial STDs	$1,974,600,000

[a]All cost figures are adjusted to 1997 dollars using the Consumer Price Index, from the US Department of Labor's Bureau of Labor Statistics.

SOURCE: Adapted from ASHA Panel to Estimate STD Incidence, Prevalence and Cost. Available at: http://www.kff.org/womenshealth/1445-std_rep2.cfm.

Table 33. Estimated annual medical costs of the major viral STDs in the United States adjusted to 1997 dollars

STD	Total Cost[a]
Genital herpes	$208,000,000
HPV	$1,622,800,000
Hepatitis B	$51,400,000
HIV	$4,540,000,000
Total costs, viral STDs	$6,422.200,000

[a]All cost figures are adjusted to 1997 dollars using the Consumer Price Index, from the US Department of Labor's Bureau of Labor Statistics.

SOURCE: Adapted from ASHA Panel to Estimate STD Incidence, Prevalence and Cost. Available at: http://www.kff.org/womenshealth/1445-std_rep2.cfm.

Truly reliable estimates of prevalence based on representative national surveys are limited to HSV-2, C. trachomatis infection, and gonorrhea; similarly reliable estimates of incidence based on fairly complete national surveillance are limited to HIV. Estimates of the burden of HPV have tended to underestimate the oncogenic types of the disease and will change as new guidelines are implemented for Pap smears, with primary testing of women under the age of 30. Population-based serologic surveys, such as NHANES, appear to have the greatest potential for estimating the prevalence of viral STDs in various segments of the population. For estimating the incidence of bacterial STDs, extrapolations from passive surveillance data provide the most reliable data at a population level. Based on our review of the literature and the analyses of numerous datasets, the overall estimate of the STD burden of the early 21st century should approximate that of the late 1990s, with 15 million new cases of STDs occurring annually. The magnitude of this figure underscores the importance of understanding the burden of STDs—by clinicians, public health agencies, persons at risk for STDs, the general public, and persons with STDs (31).

Urologists and other clinicians who see persons at risk for or infected with STDs stand to profit by understanding the incidence, prevalence, subclinical shedding, and transmission modes and risks of STDs. They should also be aware of prevention measures, risk assessment, screening, diagnostic testing, treatment, diagnosis and management of complications, counseling, patient education, sex partner services, and reporting of cases mandated by public health law. As more urologists pursue specialization in gynecological urology, issues of the detection, management, and impact of STDs on upper genitourinary sites may become more central to urologic practice. For all sexually active adolescent and adult patients, urologists and other clinicians should consider STDs as an etiology of genitourinary symptoms and signs and should screen or diagnose and treat according to national guidelines (17, 31). Urologists and other clinicians should also provide appropriate counseling, patient education, follow-up, and medical referral for sex partners and should report cases of notifiable diseases. Fortunately, resources for improving knowledge and skills are available for the clinician through commercial continuing medical education programs and through government-supported training networks (including CDC-sponsored Prevention Training Centers in all regions), on-line training courses, and various clinical decision support tools (such as the STD treatment guidelines that are available online) (31). In addition, continued commitment and advocacy for resources are needed to reduce the burden of STDs and to provide access to high-quality prevention and treatment services in the United States. For additional resources, including recommendations, guidelines, and statistical reports, the reader is referred to the website of the Division of STD Prevention at CDC: http://www.cdc.gov/nchstp/dstd/dstp.html.

REFERENCES

1. Cates W, Jr. Estimates of the incidence and prevalence of sexually transmitted diseases in the United States. American Social Health Association Panel. Sex Transm Dis 1999;26:S2-7.
2. Krieger JN. Epididymitis, orchitis, and related conditions. Sex Transm Dis 1984;11:173-81.
3. Berger RE. Acute epididymitis. In: Holmes KK, Sparling PK, P-A. M, al. e, eds. Sexually Transmitted Diseases. New York: McGraw-Hill, 1999:847-858.
4. Bowie WR. Nongonococcal urethritis. Urol Clin North Am 1984;11:55-64.
5. Krieger JN, Riley DE. Prostatitis: what is the role of infection. Int J Antimicrob Agents 2002;19:475-9.
6. Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK, St Louis ME. Herpes simplex virus type 2 in the United States, 1976 to 1994. N Engl J Med 1997;337:1105-11.
7. Corey L, Wald A. Genital herpes. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:285-312.
8. Fisman DN, Lipsitch M, Hook EW, 3rd, Goldie SJ. Projection of the future dimensions and costs of the genital herpes simplex type 2 epidemic in the United States. Sex Transm Dis 2002;29:608-22.
9. Mertz GJ, Schmidt O, Jourden JL, Guinan ME, Remington ML, Fahnlander A, Winter C, Holmes KK, Corey L. Frequency of acquisition of first-episode genital infection with herpes simplex virus from symptomatic and asymptomatic source contacts. Sex Transm Dis 1985;12:33-9.
10. McClelland RS, Wang CC, Overbaugh J, Richardson BA, Corey L, Ashley RL, Mandaliya K, Ndinya-Achola J, Bwayo JJ, Kreiss JK. Association between cervical shedding of herpes simplex virus and HIV-1. AIDS 2002;16:2425-30.
11. Tao G, Kassler WJ, Rein DB. Medical care expenditures for genital herpes in the United States. Sex Transm Dis 2000;27:32-8.
12. Koutsky L. Epidemiology of genital human papillomavirus infection. Am J Med 1997;102:3-8.
13. Tracking the Hidden Epidemics 2000. Trends in STDs in the United States. 2000; Available at:http://www.cdc.gov/nchstp/od/news/RevBrochure1pdf.htm.
14. Insinga RP, Dasbach EJ, Myers ER. The health and economic burden of genital warts in a set of private health plans in the United States. Clin Infect Dis 2003;36:1397-403.
15. Garden JM, O'Banion MK, Bakus AD, Olson C. Viral disease transmitted by laser-generated plume (aerosol). Arch Dermatol 2002;138:1303-7.
16. Kashima HK, Kessis T, Mounts P, Shah K. Polymerase chain reaction identification of human papillomavirus DNA in CO2 laser plume from

recurrent respiratory papillomatosis. Otolaryngol Head Neck Surg 1991;104:191-5.
17. Johnson RE, Newhall WJ, Papp JR, Knapp JS, Black CM, Gift TL, Steece R, Markowitz LE, Devine OJ, Walsh CM, Wang S, Gunter DC, Irwin KL, DeLisle S, Berman SM. Screening tests to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections--2002. MMWR Recomm Rep 2002;51:1-38; quiz CE1-4.
18. Committee on Prevention and Control of Sexually Transmitted Diesases IoM. The neglected helath and economic impact of STDs. In: Eng TR, Butler WT, eds. The Hidden Epidemic. Washington, DC: National Academy Press, 1997:28-68.
19. Gaydos CA, Howell MR, Quinn TC, McKee KT, Jr., Gaydos JC. Sustained high prevalence of Chlamydia trachomatis infections in female army recruits. Sex Transm Dis 2003;30:539-44.
20. Mertz KJ, Voigt RA, Hutchins K, Levine WC. Findings from STD screening of adolescents and adults entering corrections facilities: implications for STD control strategies. Sex Transm Dis 2002;29:834-9.
21. Mertz KJ, McQuillan GM, Levine WC, Candal DH, Bullard JC, Johnson RE, St Louis ME, Black CM. A pilot study of the prevalence of chlamydial infection in a national household survey. Sex Transm Dis 1998;25:225-8.
22. Guide to preventitive services. Baltimore, MD. Williams & Wilkins.
23. Shih SC, Bost JE, Pawlson LG. Standardized health plan reporting in four areas of preventive health care. Am J Prev Med 2003;24:293-300.
24. Hook EW, 3rd, Handsfield HH. Gonococcal infections in the adult. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:451-466.
25. Rothenberg RB. Analysis of routine data describing morbidity from gonorrhea. Sex Transm Dis 1979;6:5-9.
26. Knapp JS, Koumans EH. *Neisseria* and *Branhamella.* In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of Clinical Microbiology. 7th ed. ed. Washington, DC: American Society of Microbiology, 1999:586-603.
27. Koumans EH, Johnson RE, Knapp JS, St Louis ME. Laboratory testing for *Neisseria gonorrhoeae* by recently introduced nonculture tests: a performance review with clinical and public health considerations. Clin Infect Dis 1998;27:1171-80.
28. Chernesky MA. Nucleic acid tests for the diagnosis of sexually transmitted diseases. FEMS Immunol Med Microbiol 1999;24:437-46.
29. Chernesky M, Morse S, Schachter J. Newly available and future laboratory tests for sexually transmitted diseases (STDs) other than HIV. Sex Transm Dis 1999;26:S8-11.
30. US Public Health Service. 2001 sexually transmitted diseases surveillance report. 2002; Available at: http: www.cdc.gov/std/stats.
31. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. MMWR Recomm Rep 2002;51(No. RR-6):1-78. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5106a1.htm.
32. International Society for Sexually Transmitted Diseases Research Congress. Prevalence of chlamydia and gonorrhea in the United States among persons aged 14-39 years, 1999-2000. Ottawa, Canada. July, 2003.
33. Geisler WM, Whittington WL, Suchland RJ, Stamm WE. Epidemiology of anorectal chlamydial and gonococcal infections among men having sex with men in Seattle: utilizing serovar and auxotype strain typing. Sex Transm Dis 2002;29:189-95.
34. Kaiser Family Foundation and American Social Health Association (ASHA). Sexually Transmitted Diseases in America: How Many and at What Cost? 1998; Available at: http://www.kff.org/womenshealth/1445-std_rep2.cfm.
35. Atlanta, GA. Sexually transmitted disease surveillance 2001. US Department of Health and Human Services, Public Health Service, 2001.
36. Centers for Disease Control and Prevention. The national plan to eliminate syphilis from the United States. 1999; Available at: http://www.cdc.gov/stopsyphilis/Plan.pdf.
37. CDC. Outbreak of syphilis among men who have sex with men--Southern California, 2000. MMWR Morb Mortal Wkly Rep 2001;50:117-20.
38. CDC. Primary and secondary syphilis--United States, 2000-2001. MMWR Morb Mortal Wkly Rep 2002;51:971-3.
39. Berger RE, Alexander ER, Harnisch JP, Paulsen CA, Monda GD, Ansell J, Holmes KK. Etiology, manifestations and therapy of acute epididymitis: prospective study of 50 cases. J Urol 1979;121:750-4.
40. Martin DH, Bowie WR. Urethritis in males. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:833-845.
41. Holmes KK, Stamm WE. Lower genital tract infection syndromes in women. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:761-781.
42. Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. Am J Med 2002;113 Suppl 1A:14S-19S.
43. Spence MR. Gonorrhea. Clin Obstet Gynecol 1983;26:111-24.

44. Schappert SM. Ambulatory care visits of physician offices, hospital outpatient departments, and emergency departments: United States, 1995. Vital Health Stat 13 1997:1-38.
45. Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla AL, Quint WG, Pirog EC. Detection and typing of human papillomavirus DNA in penile carcinoma: evidence for multiple independent pathways of penile carcinogenesis. Am J Pathol 2001;159:1211-8.
46. Gross G, Pfister H. Role of human papillomavirus in penile cancer, penile intraepithelial squamous cell neoplasias and in genital warts. Med Microbiol Immunol (Berl) 2003.
47. Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV, Snijders PJ, Meijer CJ. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med 2003;348:518-27.
48. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol 1999;189:12-9.
49. Bosch FX, Lorincz A, Munoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. J Clin Pathol 2002;55:244-65.
50. Centers for Disease Control and Prevention. Invasive cervical cancer among Hispanic and non-Hispanic women--United States, 1992-1999. MMWR Morb Mortal Wkly Rep 2002;51:1067-70. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12500902.
51. Burk RD, Ho GY, Beardsley L, Lempa M, Peters M, Bierman R. Sexual behavior and partner characteristics are the predominant risk factors for genital human papillomavirus infection in young women. J Infect Dis 1996;174:679-89.
52. Hippelainen M, Syrjanen S, Koskela H, Pulkkinen J, Saarikoski S, Syrjanen K. Prevalence and risk factors of genital human papillomavirus (HPV) infections in healthy males: a study on Finnish conscripts. Sex Transm Dis 1993;20:321-8.
53. Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. N Engl J Med 1998;338:423-8.
54. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep 1992;41(No. RR-17):1-19. Available at: http://www.ncbi.nlm.nih.gov/entrez.fcgi?cmd=Retrieve&cdb=PubMed&dopt=Citation&list_uids=1361652.
55. MacKellar DA, Valleroy LA, Secura GM, McFarland W, Shehan D, Ford W, LaLota M, Celentano DD, Koblin BA, Torian LV, Thiede H, Janssen RS. Two decades after vaccine license: hepatitis B immunization and infection among young men who have sex with men. Am J Public Health 2001;91:965-71.
56. Wilson BC, Moyer L, Schmid G, Mast E, Voigt R, Mahoney F, Margolis H. Hepatitis B vaccination in sexually transmitted disease (STD) clinics: a survey of STD programs. Sex Transm Dis 2001;28:148-52.
57. Beck-Sague CM, Cordts JR, Brown K, Larsen SA, Black CM, Knapp JS, Ridderhof JC, Barnes FG, Morse SA. Laboratory diagnosis of sexually transmitted diseases in facilities within the United States. Results of a national survey. Sex Transm Dis 1996;23:342-9.
58. Cotch MF, Pastorek JG, 2nd, Nugent RP, Hillier SL, Gibbs RS, Martin DH, Eschenbach DA, Edelman R, Carey JC, Regan JA, Krohn MA, Klebanoff MA, Rao AV, Rhoads GG. Trichomonas vaginalis associated with low birth weight and preterm delivery. The Vaginal Infections and Prematurity Study Group. Sex Transm Dis 1997;24:353-60.
59. Cates W, Jr., Brunham RC. Sexually transmitted disease and infertility. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1079-1087.
60. Watts DH, Brunham RC. Sexually transmitted diseases including HIV infection in pregnancy. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1089-1132.
61. Lim W, Rogers M. Pediatric HIV infection. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1133-1143.
62. Gutman LT. Gonococcal diseases in infants and children. In: Holmes KK, Sparling PK, Mardh P-A, al. e, eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1145-1153.
63. Hammerschlag MR. Chlamydial infections in infants and children. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1155-1164.
64. Radolf JD, Sanchez PJ, Schulz KF, Murphy FK. Congenital syphilis. In: Holmes KK, Sparling PK, Mardh P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1165-1189.
65. Stagno S, Whitley RJ. Herpes virus infections in neonates and children: cytomegalovirus and herpes simplex virus. In: Holmes KK, Sparling PK, Mardh

P-A, et al., eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1191-1212.

66. Kasima H, Shah K, Mounts P. Recurrent respiratory papillomatosis. In: Holmes KK, Sparling PK, Mardh P-A, al. e, eds. Sexually Transmitted Diseases. Third Ed. ed. New York: McGraw-Hill, 1999:1213-1218.
67. Ciesielski CA. Sexually transmitted diseases in men who have sex with men: an epidemiologic review. Curr Infect Dis Rep 2003;5:145-152.
68. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1999;48(No. RR-12):1-37. Available at: http://www.cdc.gov/mmwrpreview/mmwrhtml/rr4812a1.htm.
69. Centers for Disease Control and Prevention. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Recomm Rep 1991;40(No. RR-13):1-25. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtmla/00033405.htm.

CHAPTER 21

Methods

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Methods

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OVERVIEW

The purpose of the *Urologic Diseases in America* (UDA) project was to assess the burden of illness imposed upon the United States by the major urologic diseases. To accomplish this task, the UDA team reviewed a large number of existing public and private datasets. Component elements of these databases were evaluated to compare their specific characteristics, uses, benefits, and limitations. Criteria for selecting the preliminary set of databases included (a) availability of information on key features of the data collection process, e.g., the unit of observation, reliability of the data, etc.; (b) issues related to the study design, e.g., the target population selected, whether incidence or prevalence data were available, etc.; (c) analytic information, e.g., whether adjustment for sample design characteristics such as clustering was necessary, etc.; (d) the robustness of the dataset relative to others available to assess the same UDA condition; and (e) an estimate of the time required to procure and analyze the dataset. Ultimately, a complementary set of data sources was selected for this project, in coordination with approval from various experts in the field of urologic illnesses, as well as at the National Institute of Diabetes and Digestive and Kidney Diseases (see Appendix B). Together, these datasets allowed us to paint a broad picture of the burden of urologic diseases in America.

DATABASE SOURCES

Databases selected to study the UDA conditions included in this compendium fall into three categories. The first group describes the Medicare program's experience with the UDA conditions. The datasets were derived from Centers for Medicare and Medicaid Services (CMS) administrative records as either a complete or a 5% sample (which was then appropriately weighted to represent the national Medicare population). These datasets include the Medicare inpatient (MEDPAR) sample, the Medicare carrier file (previously referred to as the Physician/ Part B file), and the hospital outpatient file. Finally, the Medicare denominator file, which includes all Medicare beneficiaries enrolled in a given year, was used to supply denominator data for analysis. Medicare data is also available linked to information from the Surveillance Epidemiology and End Results (SEER) database.

The second group of datasets allows computation of national estimates of healthcare utilization, costs, and, for some conditions, prevalence. Data for inpatient utilization measures were obtained from the Healthcare Cost and Utilization Project–Nationwide Inpatient Sample (HCUP-NIS), conducted by the Agency for Healthcare Research and Quality. Data for pediatric inpatient stays were collected using the Kids' Inpatient Database (KID), conducted part of the HCUP. Data for physician office and hospital outpatient utilization measures were obtained from two surveys conducted by the National Center for Health Statistics: the National

Ambulatory Medical Care Survey (NAMCS) and the outpatient and emergency department components of the National Hospital Ambulatory Medical Care Survey (NHAMCS). Data on ambulatory surgery services were obtained from the National Survey of Ambulatory Surgery (NSAS). These databases contain data on national samples of visits to physician offices, outpatient hospital departments, and emergency departments, respectively, and yield a higher number of patients with diagnoses and procedures of interest than do population-based surveys. We supplemented our analyses of these databases with the household component of the Medical Expenditure Panel Survey (MEPS), a population-based survey. We used the MEPS data to create nationally representative estimates of expenditures on diseases of interest. Finally, we examined the National Health and Nutrition Examination Survey (NHANES), a population-based survey, for items that could be used to create estimates of true nationally representative disease prevalence.

The third group of datasets was selected to provide greater depth on special populations and topics of interest. This group included the National Association of Children's Hospitals and Related Institutions (NACHRI) dataset, the Kids' Inpatient Database (KID), the National Nursing Home Survey (NNHS), the Society of Assisted Reproductive Technology (SART) database, the Veterans Health Administration (VA) Outpatient Clinic (OPC)(dataset, The Veterans Health Administration National Surgical Quality Improvement Project (NSQIP) database, The Veterans Health Administration Pharmacy Benefits Management version 3.0 database, the urology subset of the MarketScan Health and Productivity Management (HPM) database, private claims data from the Center for Health Care Policy and Evaluation (CHCPE), and the Ingenix claims dataset. Data from CHCPE, KID, and NACHRI were used to enhance analysis of the burden of urologic illnesses on the pediatric population. The NNHS provided information on individuals residing in nursing homes. The SART database allowed assessment of male factor infertility as part of the burden of overall infertility. The VA databases allowed description of veterans' use of outpatient services for urologic care. Data from Ingenix were used to model costs of care for various urologic illnesses. Because some urologic conditions have costs that accrue to employers of affected individuals, we felt it important to measure indirect costs of illness as well. Data from MarketScan provided unique information on indirect costs, e.g., work absences associated with medical services for urologic conditions.

The combination of databases (Medicare, nationally representative datasets, and special populations and topics) allowed us to complete a comprehensive evaluation of the following primary service utilization categories: (1) inpatient stays, (2) physician office visits, (3) hospital outpatient visits, (4) emergency room visits, and (5) ambulatory surgery center visits for the UDA conditions in this compendium. The data also enabled us to derive estimates of disease prevalence for some conditions. Following is a detailed description of the databases analyzed in this compendium and an in-depth discussion of the analytic approach we used for each data source.

MEDICARE DATA

Description

Medicare enrollment and claims data are available from the Centers for Medicare and Medicaid Services (CMS). Data from 1992, 1995, 1998, and 2001 claims were used for the tables in this compendium. The enrollment file contains information on all Medicare beneficiaries enrolled or entitled in the year, and these data were used to generate counts for the denominator when calculating rates. The Medicare claims data consist of three separate files: MEDPAR, which contains records for Medicare beneficiaries who used hospital inpatient services during the given year, the carrier file (previously referred to as the Physician (Part B) claims file), and the outpatient claims file (which contains hospital outpatient, laboratory, radiology, nursing home, and various other facility charges). For our analyses, we used 5% random samples drawn from these files. Previous work using CMS data has found that this sample size is adequate to detect significant racial and ethnic differences in use of cardiac procedures and tests (7). The carrier and outpatient files contained individual claims for provider services, and the MEDPAR sample contained information on hospitalizations incurred by those same Medicare enrollees.

Analytic Approach

Data from the three Medicare files (MEDPAR, carrier, and outpatient) were linked to determine inpatient, ambulatory surgery center, hospital outpatient, physician office and emergency room (ER) utilization, as well as to calculate average payments for the various UDA conditions by place of service. The procedure we used is described below.

First, personal identifiers and dates from facility records in the inpatient and outpatient files were evaluated to ascertain the number of visits to inpatient hospitals, ERs, hospital outpatient departments, and ambulatory surgery centers. Next, person identifiers and dates of service for these visits were linked to the matching line items listing payment for those services recorded in the carrier file. An algorithm was developed to assign the remaining carrier file line items and outpatient file records to the appropriate place of service. Utilization of physician office visits was determined by examining line items in the carrier file for appropriate place-of-service and physician-evaluation-and-management billing codes.

Remaining unmatched line items and claims (primarily laboratory charges) from the outpatient file were totaled by disease entity and by place of service (physician office, hospital outpatient, hospital inpatient, ambulatory surgery, or ER). Total dollars of expenditure associated with these unmatched items were then added to the total expenditure calculation for each place of service, stratified by disease. Average cost per service unit was calculated by dividing this total by the number of disease-related visits to that place of service.

At the completion of the matching process, descriptive tables were generated using appropriate International Classification of Diseases, 9th ed. (ICD-9) diagnosis codes for the conditions of interest. Hospitalization or facility visit was used as the unit of analysis for the number of claims for each type of service. Denominators were derived using the CMS enrollment file. Because a 5% sample of Medicare records was utilized, national estimates of service use were obtained by multiplying counts by a constant weight of 20 to represent use in the entire Medicare-eligible population. The data were stratified by age, gender, and race variables. Confidence intervals were calculated using standard methods for proportions (1). In Medicare data analyses, 5% samples are considered adequate for meaningful comparisons among different minority, geographic, and age groups (2).

The analytic methodology is described in more detail in Appendix A, Technical Programming for Medicare Data.

NATIONALLY REPRESENTATIVE HEALTHCARE UTILIZATION AND COST DATA

Description

We used six datasets to derive nationally representative estimates of disease-specific service use, disease prevalence, and healthcare payments. These datasets include data for inpatient stays or hospitalizations (HCUP-NIS) and data for outpatient and ambulatory care utilization (NSAS, NAMCS and NHAMCS). In addition, MEPS, a population-based survey, was used to evaluate costs. Finally, NHANES was used to determine the prevalence of urinary incontinence and urinary tract infection.

The databases assessed had different designs, depending on the goals of the surveys they represented. The NAMCS and NHAMCS databases used a nationally representative multistage probability sample. The sample design consisted of a number of stages that subcategorized the sample into units. First, counties or groups of counties were selected. Next, a probability sample of hospitals and their associated clinics or physicians (depending on the database) was selected within each county. Finally, a systematic sampling of patient visits to those physicians or clinics was selected within a randomly assigned window of time during the year. The sample size for the years of data evaluated in these two databases ranged from approximately 22,000 to 35,000 patient visits per year, and the sample was used to describe utilization of physician office visit, hospital outpatient, and ER services in the United States. Similarly, the NSAS used a multistage probability sample, with the hospitals or freestanding ambulatory surgery centers sampled at the first stage or second stage and specific surgical procedures sampled at the final stage. The 'hospital' universe includes non-Federal general, short-stay and children's hospitals located in the 50 states and the District of Columbia. The universe of "freestanding ambulatory surgery centers" comprises facilities which are state-licensed or Medicare-certified or which provide ambulatory surgery as the primary business activity and operate independently as separate businesses. The HCUP database is also a nationally representative probability sample, but rather than using a multistage approach, the design is based on a sample stratified on five characteristics: geographic area (US Census Region), location (Metropolitan Statistical Area (MSA)), the teaching status of the hospital (teaching or non-teaching), the control of the hospital (public, voluntary, or proprietary), and size, by number of beds (small, medium, or large). This database is much larger than the NAMCS or NHAMCS; it contains from 6 million to 7.5 million discharge records from community hospitals for any given year of our analysis. HCUP data are thus adequate to describe utilization of hospital inpatient services in the United States.

The benefits of using this combination of data sources are numerous. First, the databases are nationally representative samples that allow for the evaluation of genitourinary conditions even within special subpopulations (e.g., pediatric or ER patients). Demographic information is also available to complement the clinical data provided. However, the datasets have some limitations; for example, they use an inpatient stay or clinic visit, not an individual patient, as the unit of analysis, thus making it impossible to follow patients over time. Also, some of the databases sample a small fraction of total service use, so rare or more-chronic conditions may be missed.

MEPS is a nationally representative survey of healthcare service use and expenditures conducted under the auspices of the Agency for Healthcare Research and Quality (AHRQ). MEPS relies on self-reports and medical record abstraction and describes utilization of all healthcare services, expenditures, sources of payment, and insurance coverage by individuals in the US civilian non-institutionalized population. The data are collected five times per year, the first collection having been made in 1996. The years evaluated for this compendium are 1996, 1997, and 1998. The sample includes approximately 10,000 families, or 24,000 individuals, per year. Medical expenditure data at both the person and the household level are continuously collected for the database, which has an overlapping panel design. Two calendar years of data are collected from each household in a series of five rounds. These data are then linked with additional information collected from the respondents' medical providers, employers, and insurance providers. The series of data collection activities is repeated each year on a new sample of households, resulting in overlapping panels of survey data from 195 communities across the nation.

The MEPS database is particularly valuable for the purposes of this compendium because it contains detailed information on utilization and payments across treatment settings. In addition, the medical provider component supplements and validates self-reported information in the household component. However, to preserve respondent confidentiality, nearly all of the condition codes in the MEPS file have been collapsed from fully specified (five-digit) ICD-9 codes into three-digit code categories. This limits the ability to examine certain conditions, such as urinary incontinence and urinary tract infection. Also, the sample sizes are relatively small, so unusual urologic conditions are not captured well in the data. Finally, there may be underreporting of some conditions because the data are obtained from self-reports of illness (though these reports are later followed up by abstraction of medical charts and financial data).

The NHANES, conducted by the National Center for Health Statistics (NCHS), collects data by household interview, supplemented by medical examination and laboratory testing in a mobile center. The sample design is a stratified, multistage, probability sample of clusters of persons representing the civilian non-institutionalized population; African-Americans and Mexican-Americans are oversampled. Data include medical histories in which specific queries are made regarding urological symptoms and conditions. These items were selected for analysis. NCHS releases public use data sets from the continuous NHANES in two-year cycles. In our analyses, we present data from NHANES III, 1988–1994 and NHANES data from 1999–2000.

The Surveillance, Epidemiology, and End Results (SEER) Program maintains several population-based registries in the United States and Puerto Rico and provide data on all residents diagnosed with cancer and follow up information on all previously diagnosed patients. A continuing project of the National Cancer Institute, the SEER Program collects cancer data twice a year from designated population-based cancer registries in various areas of the country. Data are compiled twice a year. SEER is a product of the National Cancer Act of 1971, which mandated the collection, analysis, and dissemination of all data useful in prevention, diagnosis, and treatment of cancer. Trends in cancer incidence, mortality and patient survival in the United States, as well as many other studies, are derived from this data bank. The geographic areas comprising the SEER Program's database represent an estimated 26% of the US population. SEER coverage includes 23 percent of African Americans, 40 percent of Hispanics, 42 percent of American Indians and Alaska Natives, 53 percent of Asians, and 70 percent of Hawaiian/Pacific Islanders. The database contains information on 6 million in situ and invasive cancers diagnosed between 1973 and 2003; approximately 350,000 new cases are accessioned yearly in 18 geographical areas in the United States including Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey, Rural Georgia, the Alaska Native Tumor Registry, Arizona Indians, Greater California, Kentucky, Louisiana, and New Jersey. Cancer mortality data are obtained from vital statistics for the entire US. SEER provides authoritative genitourinary cancer prevalence and incidence data which provide context for trends in expenditures and utilization documented in the other UDA datasets.

Analytic Approach

SEER-Medicare data

Thorough a collaborative effort between the National Cancer Institute and CMS, SEER data have been linked to Medicare claims in order to allow greater specificity when analyzing utilization of resources by older patients with cancers. SEER data, which are replete with clinical detail, are paired with related Medicare claims for covered healthcare services from the time of a person's Medicare eligibility until death. Linkage is accomplished by matching SEER identifiers with identifiers located in Medicare's master enrollment file. Linkages have been completed for years subsequent to 1991. Linkages are updated every 3 years. Data are currently available through 2002. SEER-Medicare data are requested as a series of files containing data on inpatient stays, outpatient claims, clinical cancer information, etc. Investigators may link individual patients across files using the unique SEER case ID number. Data are available for both subjects with cancer from SEER and a random sample of Medicare beneficiaries without cancer (for comparison purposes).

NAMCS, NHAMCS, HCUP, KID, MEPS, NHANES, NSAS

The years of NAMCS, NHAMCS and HCUP data analyzed are 1994, 1996, 1998, and 2000. In addition, the 1992 NAMCS data were reviewed. The MEPS data we evaluated were for 1996 through 1998. NSAS data were available from 1994 to 1996. KID data were available for 1997 and 2000.

First, we identified individuals with visits for specific urologic conditions, based on the ICD-9 diagnosis or procedure codes or SEER disease codes that defined each of the conditions and any age and gender specifications necessary to create subpopulations for the analyses (for MEPS data, three-digit ICD-9 diagnosis codes were used). Analytical files for outpatient visits included records of visits with a relevant diagnosis code listed as one of any reasons for the visit. Tables were produced reflecting service use both when the diagnosis codes in question were listed as any of the reasons for the visit and when they were listed as the primary reason for the visit. Analytical files for inpatient stays included only those records of inpatient hospitalizations for which a relevant diagnosis code was listed as the *primary diagnosis* during the hospitalization. The raw number of visits in each subset varied by condition and by year. Analyses were conducted at the visit level or the stay level, depending on which database was being analyzed. The MEPS database was used to calculate payments for all services, as well as to derive nationally representative estimates of outpatient prescription drug use.

For the NHANES, cases were identified on the basis of answers to specific questions asked in the survey. The frequency of individual "yes" answers and answers regarding the intensity of symptoms were tabulated by gender, age, and other demographic variables. Using the weights provided by the NCHS, raw counts were weighted to give nationally-representative estimates of disease prevalence.

National estimates of the annual frequency of visits for the demographic groups studied for each of the UDA conditions were calculated when the raw counts were deemed large enough to produce reliable estimates. Under NCHS guidelines, two conditions must be met for creation of reliable national estimates: (1) there must be at least 30 unweighted counts, and (2) estimates must have a relative standard error (RSE) of less than 30 percent[a]. When insufficient data were available, subgroups (e.g., age categories) were combined to create adequate unweighted counts. In some instances, unweighted corresponding counts for conditions in NHAMCS Outpatient (NHAMCS–OP) and NAMCS were combined to provide reliable estimates of overall outpatient service use. HCUP cell sizes were always large enough to produce reliable estimates ($N \geq 30$), and therefore no combining or regrouping of stratification variables was necessary.

Population weights were applied to unweighted counts, according to the methodology provided by each organization sponsoring a survey, to obtain national estimates of the frequency of visits in the entire population and in subpopulations of interest. SAS (3) was used to derive the standard errors and compute the 95% confidence intervals (CIs) for these estimates. The sample design of the database was taken into account when computing statistics to ensure the proper estimation of variance in each case.

To create an estimate of the burden of outpatient visits for urologic conditions in relation to the total burden of illness represented by outpatient visits, national estimates of visits for urologic conditions within various subpopulations were divided by national estimates of the total number of outpatient visits for the demographic groups of interest. This number was multiplied by 100 to generate a percentage. National annual outpatient visit rates were calculated using the US Census non-institutionalized civilian population estimates corresponding to demographic and visit-characteristic groupings for each survey year used. Population estimates were obtained from the Current Population Survey (CPS)[b] for select demographic categories of the US civilian non-institutionalized population.

Stratification variables evaluated for all databases include age, race/ethnicity, gender, region and/or MSA, and other variables selected as appropriate for the database of interest.

SPECIAL POPULATION DATA

Description

The data sources used for special-population analyses target an array of unique populations not completely captured in the databases described above. These include children, the elderly, veterans, and two populations that allow us to combine data to conduct a cost analysis—the privately insured and the employed. Together, these datasets, along with the others described in this compendium, provide a unique picture of the relationship between urologic diseases in America and their impact on healthcare utilization, services, and costs.

NACHRI

The National Association of Children's Hospitals and Related Institutions (NACHRI) maintains a dataset containing information on all inpatient stays at member hospitals, including approximately 2 million pediatric inpatient discharges. Data have been collected annually since 1999. Fifty hospitals located in 30 states participated in 1999, 55 participated in 2000, and 58 participated in 2001. Data include the age, race, sex, and ICD-9 code for the principal diagnosis of each pediatric inpatient cared for at participating facilities. Information on length of stay, total charges, and cost-to-charge ratio is also collected. Because it collects data from children's hospitals, the NACHRI dataset provides a unique opportunity to study the inpatient burden placed on the healthcare system by relatively uncommon pediatric urologic conditions. The dataset is rigorously edited and cleaned to ensure data quality. However, because NACHRI collects data from specialized facilities, its information on such topics as length of stay, patient demographics, and treatment costs may not be representative of the national experience.

NNHS

The National Nursing Home Survey (NNHS) is a series of national sample surveys of nursing homes, the providers of care, and their residents. The dataset contains information on a sample of approximately 1,500 facilities, 8,100 residents, and 6,800 discharge records. The data are collected using a nationally representative, stratified, two-stage probability sampling design. All nursing homes in this sample have at least three beds and are certified by Medicare or Medicaid or have a state license to operate as a nursing home. Characteristics of each facility, including size, ownership, occupancy rate, number of days of care provided, and expenses, are collected. Additionally, information is provided on the recipients of care, including demographics, health status, and services received. One of the unique aspects of using this database is that it provides information on nursing homes from two perspectives: that of the nursing home facility and that of the residents themselves. However, the survey does not provide detailed information on the health services provided. It indicates only whether the patient received a service from within a general service category. Also, the records for the survey years reviewed for this compendium do not contain facility numbers to allow linkage of the records to the facilities.

KID

The Kids' Inpatient Database (KID) was created as part of the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality. KID is the only all-payer inpatient care database for children in the United States. KID contains a sample of pediatric discharges from approximately 3,000 community hospitals nationwide; it contains data from 2 to 3 million pediatric hospital discharges. For this compendium, data were available for 1997 and 2000. KID provides information on primary and secondary diagnoses, admission and discharge status, patient demographics (e.g., gender, age, race, median income for ZIP code), expected payment source, total charges (regardless of payer), length of stay, and hospital characteristics (e.g., ownership, size, teaching status) related to pediatric inpatient stays. KID samples all pediatric discharges from all hospitals in its sampling frame, stratified as "uncomplicated in-hospital birth", "complicated in-hospital birth," and "other pediatric discharges." After sorting discharges by state, hospital, diagnosis related group, and a random number within the diagnosis related group, systematic random sampling was applied. While the NACHRI dataset may allow description of utilization for relatively uncommon pediatric conditions which may be referred to tertiary care centers, KIDs' sampling design allows nationally generalizable observations to be made about inpatient utilization for pediatric conditions.

SART database

The Society for Assisted Reproductive Technology (SART) database contains outcome information for approximately 350 fertility clinics nationwide. SART monitors fertility clinic outcomes, in concert with the Centers for Disease Control and Prevention (CDC) in compliance with the Fertility Clinic Success Rate and Certification Act of 1992 (Wyden Act). The database contains information from the large majority of fertility clinics operating nationally, and allows for uniform reporting of outcome variables of interest. Clinical information from each male involved in a fertility procedure is collected. Hence, SART data can be used to examine the burden of male factor infertility in terms of related use of fertility services, the costs of which are often borne by patients. It can also be used to examine the effect of male factor infertility on subsequent outcomes.

MarketScan HPM

The MarketScan Health and Productivity Management Database (HPM) is an integrated inpatient and outpatient medical claims database that provides information on productivity losses associated with medical services. The data contain key information on short-term disability, absence, and worker's compensation resulting from urologic conditions. Absence data are derived from employee time-reporting records collected through employer payroll systems and contain detailed information on when employees were out of work, the number of work hours missed, and the reasons for the absences. Information on work absence can be linked to eligibility files and medical claims data. The linked files allow users to examine medical treatment and its association with work loss and disability. Although the database includes employers from all areas of the country, the data are not nationally representative.

Ingenix

Data for individual-level analyses were obtained from Ingenix, Inc., a healthcare information company that provides cost management and benefit consulting services to employers, health plans, pharmaceutical manufacturers, and others. Data were obtained on insurance eligibility and medical claims for the employees of 25 large (Fortune 500) companies and their dependents. All individuals had private, employer-sponsored health insurance coverage, including prescription drug benefits. Out of concern that data on healthcare use and costs might be incomplete for the employees' dependents (e.g., in cases of dual coverage), we excluded dependents from the analysis. The sample we used consisted of 278,950 primary beneficiaries 18 to 64 years of age who were continuously enrolled for the entire 1999 calendar year.

The medical claims include detailed financial information, dates of service, diagnosis and procedure codes, types of facility, and providers. Drug claims include prescription fill date, patient and plan costs, and, in most cases, national drug codes (NDC), which were used to examine utilization of specific drugs and therapeutic classes. Claims data contain records only for those who used services. To identify those who may not have used services, enrollment data were also obtained. Enrollment files included each person's age, sex, plan type (FFS, PPO, POS, HMO), zip code of residence, and relationship to employee.

The claims data were linked with information about plan benefits. For each plan, photocopies of the summary of benefits provided by the companies to their employees were obtained, and the benefit information, including the salient features of each plan's covered benefits, was abstracted from its summary-plan design. Drug benefits typically included copayments or coinsurance rates for both retail and mail-order pharmacies; the data on drug benefits included generic substitution rules and a list of drugs or drug classes excluded from coverage. Characteristics of the medical benefit included plan deductibles and patient cost-sharing arrangements for inpatient and ambulatory settings.

Center for Health Care Policy and Evaluation

The Center for Health Care Policy and Evaluation (CHCPE) of UnitedHealth Group maintains a centralized research database (RDB) that contains current and historical medical and pharmaceutical claims and enrollment data for 27 geographically distinct health plans—more than 22 million member-years of data. The majority of UnitedHealthcare members are enrolled through employers (i.e., they are commercially insured), although membership also includes Medicaid and Medicare beneficiaries. The health plans contract with broad networks of physicians, pharmacies, and facilities to provide healthcare to enrollees. Most providers are reimbursed on a fee-for-service basis; pharmacies receive dispensing fees; and most facilities have contracted per diem rates or prospective payments (DRGs). Because information on pediatric urologic diseases in the nationally representative data sources was sometimes limited, data from CHCPE were used to enhance understanding of the burden of urologic disease on the pediatric population. One limitation of this data source is that it is drawn from an insured population, which may differ in important ways from the uninsured population. CHCPE does collect information on children with Medicaid, and these data were reported.

The RDB contains automated utilization data from all types of healthcare sites (e.g., hospital inpatient, hospital outpatient, physician office, emergency department, surgery center) and for all types of services, including care from out-of-network providers. CHCPE assembles enrollment and claims data generated by UnitedHealthcare operations into the RDB as four component files (enrollment, physician, facility, and pharmacy). Table 1 shows the total number of members enrolled in the 15 plans

Table 1. Health plan population and claims count, by year, region, and insurance type

	1994		1996		1998		2000	
Region	Commercial	Medicaid	Commercial	Medicaid	Commercial	Medicaid	Commercial	Medicaid
Midwest	637,093	46,009	887,957	39,192	1,186,702	274	1,350,819	442
Northeast	151,405	816	159,953	34,986	200,994	36,079	164,354	41,604
Southeast	205,934	11,590	471,528	59,600	976,050	46,452	1,099,531	8,266
West	76,084	563	90,689	13,318	109,654	20,599	134,537	29,451
Total	1,070,516	58,978	1,610,127	147,096	2,473,400	103,404	2,749,241	79,763

selected for this project, stratified by year, region, and type of insurance.

VA datasets

VA-OPC

The Department of Veterans Affairs (VA) delivers healthcare to eligible veterans through the Veterans Health Administration. The VA is the largest healthcare system in the United States, comprising more than 160 hospitals (>45,000 beds), more than 600 community-based outpatient clinics, and more than 100 nursing homes. The VA maintains a centralized data repository reflecting healthcare utilization by the population of veteran users. This repository, known as the Austin Automation Center, contains computerized utilization data on many types of health services, including outpatient visits. The SAS files created from this database allow for file linkages of patients.

The VA outpatient clinic (VA-OPC) files, on which the UDA analyses were performed, include demographics, visits, and clinic stops (i.e., different clinic appointments and services attended in a given visit day) and are available for 1980 to the present. Ambulatory procedures were added to the OPC in 1990, and outpatient diagnoses (ICD-9-CM) were added in FY1997. These datasets provide a rich resource for assessing the prevalence of disease among VA healthcare users. The ability to link files across VA healthcare facilities and across settings within facilities allows a relatively complete portrait of utilization and patterns of care to be obtained. However, the VA datasets do not provide comprehensive information about veterans' healthcare utilization *outside* the VA healthcare system.

The diagnosis codes were derived from outpatient visits from recent physician-patient encounters and thus *do not reflect all existing or historical cases among veteran users*; instead, they reflect the population for whom care was sought during the year being reviewed. Therefore, prevalence based on counts of cases in a given fiscal year of outpatient utilization data is likely to underestimate prevalence in the total population of users.

NSQIP

The VA National Surgical Quality Improvement Program (NSQIP) collects pre-operative risk factors, intra-operative variables, and 30-day post-operative mortality and morbidity outcomes on most major surgical operations performed in the VA healthcare system. An assessment is done on all patients undergoing a major operation under general, spinal, or epidural anesthesia. Some operations with known low mortality and morbidity are excluded. Also, certain common operations (transurethral prostatectomy, transurethral bladder tumor resection, inguinal hernia) are limited to the first 5 cases in an 8-day cycle. Most VA hospitals collect all of their major cases. A few high-volume hospitals are permitted to take a sample of cases (the first 36 consecutive cases in each 8-day cycle, with each cycle beginning on a different day of the week). NSQIP was initiated in 1991 at the 44 largest VA hospitals that perform both cardiac and non-cardiac surgery. In 1994, the Program was expanded to include all 132 VA medical centers that perform surgery. Each year, risk-adjustment models are created and risk-adjusted 30-day mortality and morbidity surgical outcomes are fed back to the medical centers, so that they can compare their results to other VA medical centers on a blinded basis. A dedicated NSQIP nurse, trained in the data collection procedures, collects the data at each VA medical center. Procedures for the Program are documented in an operations manual, including definitions of all variables. The database contains about 1 million operations, and about 100,000 cases are added each year.

The VA NSQIP is funded by the VA's Office of Patient Care Services in VA Central Office in Washington, D.C. The chairman's office is at the West Roxbury, MA VA medical center. The data coordinating center is located at the Denver VA medical center and the University of Colorado Health Outcomes Program under the direction of Dr. William Henderson, Co-chairman of the NSQIP.

PBM

Disease-specific medication data for veterans were obtained from the Pharmacy Benefits Management version 3.0 database (PBM v3.0). The PBM national database includes medication utilization information based on unique patients for every prescription filled in the VA. The database produces information on each occasion of drug dispensation, which helps to track total prescription usage on a gross or discrete level. Data originate from the VISTA pharmacy packages at each VA facility and are sent monthly via computer to the PBM office in Hines, IL. Upon receipt, the PBM collects, processes, and translates the information into the national database format. The database includes comparative data for all VA facilities nationwide and data can be aggregated nationally, by veteran integrated service network (VISN), which approximates geographic regions, or by facility. The database contains information from October 1, 1998 to the present. The information in the PBM uses patient-specific social security numbers so that other needed clinical data can be easily linked to the pharmacy data.

Analytic Approach

NACHRI

After obtaining a list of ICD-9 diagnosis codes used to define the pediatric UDA conditions of interest, researchers at NACHRI created an analytic file containing all inpatient discharges reported at member institutions for which a UDA diagnosis code appeared as a primary diagnosis for admission. Information was analyzed for FY 1999–2001. Data were imported into SPSS 4.0 (4), and available stratification variables were examined. Mean values and counts for these variables were compared with those provided by NACHRI to ensure data integrity after importation. One-way ANOVA was used to generate confidence intervals for frequencies and means of desired variables.

NNHS

The years of data evaluated for this dataset were 1995, 1997, and 1999, and the unit of analysis was the individual. The analytic approach follows that used for the nationally representative datasets, with the exception that urolithiasis, sexually transmitted diseases (STDs), and pediatric conditions were excluded due to small sample sizes.

KID

The KID database was evaluated using the approach described for the nationally representative datasets (described above).

CHCPE

Records from component files maintained by CHCPE were linked, using common fields such as member and physician identifiers and dates of service, as described below.

CHCPE enrollment records serve to track plan membership for billing premiums. The enrollment file includes date of birth, gender, and dates of enrollment and disenrollment. The physician file contains information submitted by physicians and other healthcare practitioners, using the CMS-1500 claim form. This file includes the member identifier, unique provider identifier, the service or procedure performed, up to four diagnosis codes, the place of service, billed amounts and payments, and the insurance product under which the service falls. Diagnoses are coded according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), and procedures are coded using the Current Procedural Terminology (CPT) coding system. The facility file contains information submitted by facilities using the CMS-145 claim form. This file includes the member identifier, unique facility identifier, facility type, revenue codes, up to nine diagnosis codes, the place of service (e.g., inpatient, outpatient, emergency room), DRG payments, and the insurance product under which the service falls. As with physician claims, diagnoses are coded using ICD-9-CM codes and procedures are coded using ICD-9-CM procedure codes or CPT-4 procedure codes. Claims from out-of-network facilities are included.

The period of analysis for this compendium included 1994, 1996, 1998, and 2000. Analyses were conducted on members of 15 commercial and Medicaid health plans located in four regions (Midwest, Northeast, Southeast, West) of the United States. Data on commercial and Medicaid health plan members were reported separately, as these populations tend to differ in socioeconomic status.

VA datasets

VA-OPC

The VA-OPC file was used to identify all unique cases of each urologic condition. The event (SE) files of the OPC, which combine the diagnostic and procedural information, were used for generating these data. Three consecutive years of data, 1999 through 2001, were examined. A unique count of cases was generated by identifying the cohort of veterans with each qualifying ICD-9 code within each UDA urologic condition under review. Redundant cases (i.e., individual patients with more than one qualifying diagnosis code) were then eliminated in order to generate a count of unique cases. Two cohort files were created: prevalence estimates (1) by f*irst (or primary) diagnosis* and (2) by *all diagnosis* codes (i.e., any mention of eligible diagnostic codes from our case definition).

Given the size of the national VA utilization datasets, all initial diagnosis groups and linkage procedures were pilot-tested on *local regional data* to examine preliminarily the prevalence of the selected conditions for one year of data. An initial set of tables was created showing the national prevalence of the first four UDA conditions (benign prostatic hyperplasia, urolithiasis, urinary tract infection, and urinary incontinence) *for all diagnoses*. Prevalence rates were presented in total and by selected demographic characteristics (e.g., age, gender, race/ethnicity) and geographic features (e.g., region) as unique cases per 100,000 population of veteran users served by VA in fiscal year 2001 (October 1, 2000, through September 30, 2001). These analyses were then expanded to the other data years. The unit of analysis in the Austin

Table 2. Base population of veteran users of VA healthcare and total veteran population by age, gender, and race/ethnicity

	Veteran Population			
	Veteran Users of VA Healthcare (VA Outpatient Clinic file)			Total Veteran Population (US Census, 2000)[a]
	1999	2000	2001	2000
Total	3,039,688	3,276,298	3,691,533	26,403,703[b]
Age				
18–24	25,328	23,526	23,033	16,740,194
25–34	150,809	142,082	135,854	
35–44	330,512	312,179	299,820	
45–54	689,196	716,638	753,251	
55-64	501,642	554,117	648,880	
65-74	758,809	825,990	950,660	9,663,506
75–84	536,269	643,466	801,677	
85+	49,123	58,305	78,358	
Gender				
Male	2,898,582	3,125,448	3,526,627	24,810,000
Female	141,106	150,850	164,906	1,593,000
Race/ethnicity				
White	1,366,295	1,472,022	1,610,947	21,888,669[c]
Black	333,719	342,547	354,807	2,561,159[c]
Hispanic	114,386	122,469	128,930	1,135,359[c]
Other	19,356	20,248	21,822	1,240,974[c]
Unknown	1,205,932	1,319,017	1,575,027	...

...data not available.

[a]SOURCE: US Census 2000, Veterans (May 2003). Questions on veteran status asked "Has this person ever served on active duty in the U.S. Armed Forces, military Reserves, or National Guard?" The question was followed by a note "Active duty does not include training for the Reserves or National Guard, but DOES include activation, for example, for the Persian Gulf War." Response categories included the following:

□ Yes, now on active duty

□ Yes, on active duty in past, but not now

□ No, training for Reserves or National Guard only → skip

□ No, never served in the military → skip

[b]Veterans comprised approximately 12.7% of 208.1 million civilians 18 years and older in the US in 2000.

[c]Derived from U.S. Census table as 82.9% White alone (not Hispanic or Latino), 9.7% (Black or African American alone), 4.3% (Hispanic or Latino, of any race), 4.7% other (combined American Indian and Alaskan Native alone, Asian alone, Native Hawaiian and Other Pacific Islander alone, some other race alone, or two or more races) as a percentage of total veteran population in 2000. Note that the percentage for Hispanic includes any race because the available veteran census breakdown did not cross-tabulate race and ethnicity, yielding an overcount in these cells.

Automation Center (AAC) SAS datasets is the patient. A patient who had more than one qualifying diagnosis code was counted as only a single case. Similarly, a patient with one or more of the qualifying diagnosis codes at more than one VA healthcare facility was counted only once. Prevalence rates were stratified by patient characteristics (i.e., age, gender, race/ethnicity, insurance status,[c] and region).

Where possible, the VA sociodemographic categories (e.g., 10-year age groups for adults, such as 25–34, 35–44, etc.) were made consistent with those applied to the CMS data. Categories were regrouped as necessary to maintain adequate cell sizes for analysis.

The VA data represent the population of all veteran users of VA healthcare services during the years under study (pediatric cases are excluded from the VA database). Therefore, confidence intervals were included for the calculated rates. Denominator data were obtained for all veteran outpatient users and then refined, based on age, gender, or other restrictions of the UDA conditions, to generate unadjusted prevalence rates for the number of cases per 100,000 population.

The VA data presented are unweighted frequencies representing population prevalence rates among all veteran users of VA healthcare in a given fiscal year. No effort was made to weight veteran users of VA healthcare services to the total US veteran population. Table 2 presents denominator data on this base population analyzed in VA tables that appear in this compendium.

NSQIP

Risk-adjustment models are created each year for all operations combined, and for 9 major subspecialties, including urology. Individual substudies using the database have created risk-adjustment models for some specific operations and for some specific post-operative complications. The post-operative complications that are collected include:

- Post-op wound complications—superficial infection, deep wound infection, dehiscence
- Respiratory complications—pneumonia, unplanned intubation for respiratory/cardiac failure, pulmonary embolism, failure to wean >48 hours
- Urinary tract complications—progressive renal insufficiency, acute renal failure, urinary tract infection
- Central nervous system complications—stroke, coma >24 hours, peripheral nerve injury
- Cardiac complications—cardiac arrest, myocardial infarction
- Other complications—bleeding >4 units, graft/prosthesis failure, deep vein thrombosis/ thrombophlebitis, systemic sepsis, other

PBM

The medications extracted from the PBM database for the current project included, LHRH agonists, antiandrogens, erectile dysfunction agents and combined LHRH and antiandrogen therapy (defined as >14 days of overlap). Total prescription data was obtained for each agent. Unique patient counts were then determined for each class and each individual agent within the class for fiscal years 1999 through 2003. Combined therapy was defined as an overlap of at least 14 days or greater of an LHRH agonist and an antiandrogen agent.

Data are presented as total number of unique patients on each class of agents, total unique number of patients on each individual agent nationally and per region. The four regions used are east, west, south, central and other. Data are also presented as total number of unique patients on each class of agent per VISN. A VISN is the unique way in which the Department of Veterans Affairs is divided into regions.

Rates per 100,000 are determined for national and VISN data for each class of agents. The unique rates are based on number of unique veterans in the prescription database nationwide and per VISN (Appendix B). The number of unique veterans per region is not available in the prescription database. Hence, regional data are presented as raw unique numbers per year only.

SPECIAL NOTES ON THE SEXUALLY TRANSMITTED DISEASES CHAPTER

The datasets used extensively for other urologic diseases throughout this compendium (HCUP, CMS, VA, and NAMCS) describe hospital discharge data, inpatient and outpatient medical claims data, and health survey data. For sexually transmitted diseases (STDs), these datasets provide sparse, incomplete, or non-representative data on numbers of cases and patient visits (Table 2) and on patient visit rates (Table 3). Several databases did not capture services rendered to many Medicaid patients, uninsured patients, or patients attending public STD, prenatal, family planning, military, or other clinics that provide a substantial amount of STD care. The inpatient datasets are limited because they enumerate hospitalizations for conditions that rarely require hospitalization. We therefore used additional data from three other databases and from the published literature to obtain more reliable estimates of the burden of the STDs discussed.

National Electronic Telecommunications Surveillance System (NETSS)

The NETSS includes reports of all cases of notifiable diseases, including STDs, sent to CDC by state health departments. After removing personal identifiers, US states and territories report cases of *C. trachomatis* or *N. gonorrhoeae* infection, primary and secondary syphilis, HIV, and hepatitis B virus (HBV). This passive surveillance system has notifiable-disease regulations and is limited by underreporting by clinicians and laboratories. Barriers to reporting include lack of awareness or priority given to public health reporting, patient or clinician concerns about violation of confidentiality for stigmatized diseases, lack of routine reporting systems, insufficient incentives, and administrative costs (5). Reporting by laboratories of cases confirmed by positive STD test results is far more complete than reporting of clinically diagnosed cases by clinicians. However, because of minimal variation in the level of completeness of such reporting from year to year, case reports provided to public health departments have historically been the best source of information about

Table 3. Codes used to identify additional medical visits for genital warts[a] in MarketScan data

Any persons having one of the following two ICD-9 Codes and at least one of the following CPT procedure codes:	
ICD-9 Codes:	
078.10	Viral warts unspecified
078.19	Other specified viral warts
and	
CPT Procedure Codes:	
00900	Anesthesia for procedures on perineal integumentary system
00902	Anesthesia for anorectal procedure
00910	Anesthesia for transurethral procedures
00920	Anesthesia for procedures on male genitalia
00940	Anesthesia for vaginal procedures
45100	Biopsy of anorectal wall, anal approach
45905	Dilation of anal sphincter under anesthesia other than local
45999	Unlisted procedure, rectum
46030-46999	Surgery of anus
52000-52318	Endoscopy-cystoscopy, urethroscopy, cystourethroscopy, transurethral surgery
53000-53899	Surgery for urethra
54000-55899	Surgery for male genital system
56350-56363	Hysteroscopy
56405-58285	Surgery for female genital system
74400-74485	Radiology, urinary tract
74710-74775	Radiology, gynecological and obstetrical

[a]A medical visit was identified as an additional visit for genital warts if the visit was associated with at least one of these ICD-9 codes and at least one of these CPT codes.

the temporal and geographic trends of STDs and the characteristics of infected persons (6, 7). Although a few states have had reporting requirements for herpes simplex infection, pelvic inflammatory disease (PID), and unspecified STDs (8), most states do not have reporting requirements for several STD pathogens, clinical manifestations, and syndromes for which etiologic causes or therapeutic interventions have only relatively recently been identified. These include HSV infections or genital herpes, HPV infections or their manifestations of genital warts and cervical dysplasia, and nonspecific urethritis, epididymitis/orchitis, prostatitis, cervicitis, vaginitis, salpingitis, and STD-related skin disorders. In the NETSS, pathogen-specific codes, not ICD-9 diagnostic codes, are used.

National Disease and Therapeutic Index (NDTI)

The NDTI is a private survey of a random sample of office visits to US physicians in office-based practices, using ICD-9 coding. It allows estimation of the burden and trends of diseases that are not reported by states to the national surveillance systems; these diseases include genital HSV, genital warts, nongonococcal urethritis, and trichomoniasis. However, because the NDTI does not include visits to public health, hospital outpatient, or military medical facilities, it does not permit accurate estimates of the total number of consultations in the United States for these conditions. With ICD-9 codes for abstraction, NDTI data can be used to estimate the diagnosis-specific volumes of office visits to private practitioners for various STDs (including those of reportable diseases such as syphilis, gonorrhea, and chlamydia). Because the NDTI is a national survey based on a sample rather than on the entire universe of patient visits to physician offices, patient visits must be weighted to produce unbiased national estimates.

VA-OPC

Regarding analyses of VA data, medical visits for two syndromic conditions, epididymitis/orchitis and urethritis, were classified according to whether an STD pathogen was specified in any of the four listed ICD-9 codes. For example, the visit was classified as "epididymitis, organism specified" if the first four ICD-9 codes for a given outpatient visit included ICD-9 code 604 for orchitis or epididymitis as well as one of many ICD-9 codes for gonorrhea or chlamydia or if any of the first four ICD-9 codes were specific to gonoccocal epididymitis/orchitis (098.13 or 098.33). The medical visit was classified as "epididymitis, organism unspecified" if the first four ICD-9 codes for a given outpatient visit included ICD-9 code 604 for orchitis or epididymitis but did not include ICD-9 codes for gonorrhea or chlamydia or for gonoccocal epididymitis/orchitis (098.13 or 098.33).

In addition, to capture aspects of the burden of various STDs, we applied the ICD-9 codes in Table 3 to data from HCUP, MarketScan, Medicare (MEDPAR, Outpatient, and Physician-Supplier), and the VA (Inpatient and Outpatient). The burden of each STD examined (per 1,000 population) was stratified by demographic variables. The demographic variables considered in HCUP include sex, age, race/ethnicity, region, urban/rural, and expected primary source of payment. The demographic variables considered in Medicare include sex, age, race/ethnicity, region, and setting of care (inpatient, ambulatory). The demographic variables considered in MarketScan include sex, age, region, and urban/rural.

Additional analytic comments specific to each STD or condition evaluated are presented below.

Herpes

With MarketScan data, we evaluated the extent to which medical claims for genital herpes using ICD-9 codes can estimate the burden of the disease. Some care for genital herpes may not result in a diagnostic claim (ICD-9 code) for herpes but may result in a drug claim, e.g., to refill a prescription for a chronic condition. In addition, some clinicians may be reluctant to document a claim coded as genital herpes to protect the confidentiality of patient information. Therefore, we also analyzed claims for drugs (acyclovir, famcyclovir, and valacyclovir) used to treat genital herpes.

Genital Warts

Because MarketScan includes NDCs, we were able to evaluate the use of drugs for treating genital warts. We estimated claims for podofilox and podophyllin, two medications used almost exclusively to treat genital and perianal warts, regardless of ICD-9 codes assigned. We also estimated drug claims for imiquimod regardless of ICD-9 codes assigned, but only if the prescription was obtained from a urologist or gynecologist, since imiquimod is also commonly used for nongenital warts and other cutaneous lesions commonly managed by other clinical specialties.

A diagnosis of genital warts may be coded with ICD-9 code 078.11 (condyloma acuminata); this was the sole code used in routine analysis of data from HCUP, MarketScan, Medicare, and the VA. However, genital warts may also be coded with ICD-9 code 078.10 (wart—common, digitate, filiform, infectious, viral) or 078.19 (other specified viral warts—genital warts, verruca plana, verruca plantaris), two codes that are also used for nongenital warts. Using MarketScan data, we identified the proportion of those two codes that were likely to represent genital warts. We assumed that medical visits with ICD-9 code 078.10 or 078.19 were for genital warts if the CPT code (listed in Table 3) indicated that the patient had procedures related to destruction or excision of lesions of the anus, penis, vulva, perineum, vagina, or introitus. However, classifying only ICD-9 claims with these procedures as genital warts probably substantially underestimates the number of visits for genital warts; many warts do not require any medication or ablative procedures (and associated NDCs or CPT codes) because they do not create annoying symptoms or cosmetic problems. Restricting our analysis to warts that require ablative procedures may result in minimal estimates of the burden of warts that result in the highest healthcare costs.

Using NAMCS data from 1995–1996, we also estimated the burden of genital warts as follows. We classified medical visits that may or may not have been for genital warts into three groups: definite cases (having ICD-9 code 078.11); probable cases (having ICD-9 code 078.10 or 078.19 and having either NDCs for medication with podofilox, podophyllin, or imiquimod or CPT procedure codes for destruction or excision of lesions of the anus, penis, vulva, perineum, vagina, or introitus); and possible cases (having ICD-9 code 078.10 or 078.19 and no surgical procedure code).

Chlamydia

Using MarketScan data, which include NDCs and CPT codes, we estimated the chlamydia burden using information on drugs for treating chlamydial infection and tests used to identify symptomatic *C. trachomatis* infection or to screen for asymptomatic *C. trachomatis* infection. First, we selected medical visits with any of the codes listed in Table 17 for nongonococcal urethritis or tests used for *C. trachomatis*. Then, we defined the selected visits as being for *C. trachomatis* infection if the date of drug claims was within 7 days before or 20 days after the date of the medical visit. The drug claims included amoxicillin, azithromycin, doxycycline, erythromycin, and ofloxacin, the drugs recommended by CDC for treatment of uncomplicated, lower genital tract *C. trachomatis* infection in 1998 (9). Note that amoxicillin is a recommended regimen in CDC's guidelines when pregnancy is a consideration and that the recommended drugs are not necessarily the same ones recommended for upper-tract infections such as PID.

Gonorrhea

Using MarketScan data, which include NDCs and CPT codes, we estimated the gonorrhea burden using information on drugs for treating gonorrhea and tests used to identify symptomatic gonococcal infection or to screen for asymptomatic gonococcal infection. First, we selected medical visits with the following codes: ICD-9 code V02.7 (carrier or suspected carrier of gonorrhea) or CPT codes 87590 (gonorrhea, direct probe technique), 87591 (gonorrhea, amplified probe technique), 87592 (gonorrhea, quantification), or 87850 (*N. gonorrhoeae*). Then, we identified the selected visits having a specific drug claim within 7 days before or 20 days after the date of the medical service claims. The drug claims included cefixime, ceftriaxone, ciprofloxacin, ofloxacin, or levofloxacin, the drugs recommended by CDC for treatment of uncomplicated lower-tract gonococcal infection.

Syphilis

Data from HCUP, MarketScan, NAMCS, Medicare, and the VA were not useful for estimating the incidence of syphilis because the numbers of cases were too low to permit statistically reliable estimates. For example, in the VA data, an ICD-coded syphilis diagnosis was recorded for only 3 per 100,000 unique outpatients. Therefore, we used NETSS data, which include as variables sex, age, race/ethnicity, geographic region, and urban/rural, to estimate the incidence of primary and secondary syphilis. We included data only on individuals with primary and secondary syphilis because they are the most likely to be seen by urologists for genitourinary symptoms and signs. However, primary and secondary syphilis cases enumerated in national data include many symptomatic cases more commonly seen by family practitioners, internists, obstetrician/gynecologists, and dermatologists, as well as asymptomatic cases identified through routine serologic screening.

Epididymitis/Orchitis

To estimate the incidence of epididymitis/orchitis, we analyzed ICD-9 codes for epididymitis/orchitis not designated as due to chlamydia or gonococcus as well as all ICD-9 codes for epididymitis/orchitis associated with chlamydia or gonococcus. We took this approach because some patients could have both a diagnosis of the syndromic presentation of epididymitis/orchitis and a diagnosis of chlamydial or gonococcal epididymitis/orchitis. We applied the definitions to data from HCUP, MarketScan, and Medicare. Epididymitis/orchitis data from the VA were available in dichotomous categories of organism specified (e.g., chlamydia, gonorrhea, other) and organism unspecified; there is no ICD-9 code to describe orchitis without epididymitis in which the organism is not specified. With HCUP, MarketScan, Medicare, and VA data, the same variables were explored as those considered for genital herpes (see above).

Urethritis

To estimate the incidence of urethritis, we analyzed the available data for urethritis not designated as due to chlamydia or gonococcus as well as aggregate data for all ICD-9 codes for urethritis, including those for chlamydia or gonococcus, listed in Table 1 of the STD chapter. We took this approach because some patients could have both a diagnosis of the syndromic presentation of urethritis and a diagnosis of gonococcal or chlamydial urethritis. We applied the definitions to data from HCUP, MarketScan, and Medicare. Inpatient and outpatient VA data report urethritis in dichotomous categories of organism specified (e.g., gonococcal, chlamydial, other) and organism unspecified. With HCUP, Medicare, VA, and MarketScan data, the same variables were explored as were considered for genital herpes (see above).

ESTIMATING COSTS ASSOCIATED WITH UROLOGIC DISEASES

Marketscan and Ingenix Data

General Methodology for Estimating Costs

Most cost-of-illness studies distinguish between the direct costs of treating a medical condition and the indirect costs associated with lost work days, reduced quality of life, and premature mortality. Direct costs typically include expenditures for medical treatments, such as hospitalizations, emergency care, ambulatory visits, nursing home and home healthcare, medical supplies, prescription drugs, and other services provided by medical professionals. Indirect costs usually refer to disability days, work loss, and other labor-market consequences associated with medical illness.

In this analysis, we were interested in costs as a dollar-denominated measure of resource utilization. Costs are closely linked to other important financial concepts, including charges, out-of-pocket expenses, and payments. These other concepts are more easily measured and can be used to approximate costs, but they are not necessarily equivalent. Since the majority of the databases we examined lacked cost information, direct medical costs were imputed by assigning prices to a comprehensive list of utilization and services. Prices of medical services and pharmacy claims were estimated based on average payments made by the enrollee (copayments, deductibles, excluded expenses) and by all third-party payers (primary and secondary coverage, net of negotiated discounts). The sources of utilization data were national surveys and claims records.

Deriving reliable estimates of indirect costs requires detailed information rarely included in survey data or medical claims. Even when these data are available, converting outcomes such as premature mortality, disability days, and productivity losses into costs requires a set of assumptions about the causal effects of the illness, future wage rates and retirement decisions, and the value of time for heterogeneous patient populations. The available evidence suggests that these underlying assumptions have a considerable effect on the magnitude and reliability of the cost estimates. Because of these limitations, the indirect costs of urologic conditions were not estimated. Rather, administrative data from a large number of

Table 4. Primary Data Source for Medical Care Utilization (non-Medicare population)	
Type of Service	**Primary Data Source**
Hospital Inpatient	HCUP
Hospital Outpatient	NHAMCS
Emergency Room	NHAMCS
Physician Office	NAMCS
Outpatient Prescription Drugs	MEPS
Nursing Home	NNHS

employers were used to impute the average work loss associated with each condition.

A key issue in cost-of-illness studies is the determination of how to attribute costs to a specific condition in an appropriate and consistent way. Ideally, one would like to capture the costs of treating a urologic condition regardless of the primary diagnosis attached to the service. For estimation purposes, this means *excluding* treatment costs of other conditions incurred during a visit or hospitalization for a urologic illness and *including* urology-related costs that are secondary to the primary diagnosis. Medicare claims data permit this level of detail, reporting reimbursements associated with each unit of service, or "line-item." However, this level of specificity is not available in most claims-based datasets and surveys. Thus for the non-Medicare population, average expenses per unit of service were estimated solely on the basis of hospitalizations or visits with a primary diagnosis of a specific urologic condition. This approach overstates average expenditures by including treatment costs of nonurologic conditions. At the same time, it understates reimbursements by excluding costs of urologic conditions that are secondary to the principal diagnosis. The net effect of this measurement error is uncertain, but it is unlikely to constitute a large fraction of the total economic burden of each condition.

Measuring Direct Costs

Measuring resource costs depends on having appropriate measures of both utilization and unit cost. Medical expenditures were estimated by assigning prices to a comprehensive list of utilization and services. For the non-Medicare population, average prices of a hospitalization, an ER admission, a hospital outpatient visit, and a physician office visit were imputed, based on average payments reported in the 1996–1998 MEPS. In cases where MEPS lacked adequate statistical power to reliably estimate prices for specific services, average payments from a large administrative database of private employers or Medicare claims were imputed. Average prices for outpatient prescription drugs were based on published compilations from First Data Bank (10) and *RedBook* (11).

Medicare claims from 1992 through 1998 were used to impute average annual growth rates in expenditures over this period. These rates were then applied to 1996–1998 prices derived from MEPS. All expenditures for medical and pharmacy services were reported in nominal dollars.

National surveys and claims-based databases were relied upon for deriving estimates of medical service utilization by the non-Medicare population, where the data source depends on the type of service provided (Table 4).

Medicare claims were used to estimate utilization and average reimbursements for the Medicare population. Medicare does not provide full coverage for all services. Moreover, beneficiaries pay deductibles and coinsurance expenses under Part A and Part B, and these expenses are not included in the Medicare claims. In order to capture these costs, the recommendations of CMS' Office of the Actuary were followed: Part A payments were inflated by 8%, and Part B payments were inflated by 38% (12).

Computing Work Absences

The MarketScan Health and Productivity Management (HPM) database was used to derive the average work loss associated with each condition. The HPM data are collected through employer payroll systems and include detailed information on when employees are out of work, the number of hours missed, and the reasons for the absences. Reasons for absence include sickness, disability, vacation, and other types of leave. The absence data are linked to eligibility files and medical claims to estimate hours of work loss associated with each condition.

Assigning work absences to specific medical treatments required a complex algorithm using all three databases. In general, the dates of an ambulatory visit or an inpatient stay for a specific urologic condition were matched to the individual's absence data. Absences associated with a hospitalization included any work loss reported between the admission and discharge dates, including days contiguous to those dates. For example, if a person was admitted to the hospital on June 1 with a primary diagnosis of upper tract urolithiasis and was discharged on June 5, any sick time or short-term disability in that period, as well as on contiguous days prior to June 1 or after June 5, was counted. Any work loss on June 7 was not included, however, in the absence of work loss on June 6.

As underscored by this example, appropriately assigning absences to specific treatments is very difficult. Therefore, a set of decision rules and exclusion criteria were established for computing these estimates. The most important criteria were the following:

- To be included, persons had to be fully enrolled in the health plan throughout the year and had to have an inpatient or outpatient medical claim for a specific urologic condition.
- Individuals in the top 0.5% of total absences during the year and persons on long-term disability or COBRA were excluded.
- Work absences were capped at 12 hours if the beginning and end dates of the absence were the same.
- If two outpatient visits occurred in the span of one absence, then hours absent before the first visit counted toward the first visit, and hours absent after the second visit counted toward the second visit. The hours of work lost between the visits counted toward the closest visit. In the event of a tie, the hours were assigned to the first visit. For example, consider an employee absent from work due to sickness from January 1 to January 10, with physician office visits on January 3 and January 7. In this case, work hours missed between January 1 and January 5, were assigned to the first visit and hours missed between January 6 and January 10 were assigned to the second visit.
- Short-term disability hours for persons whose start date coincided with a hospital admission and for whom there was a return-to-work date were included.
- Work absences associated with outpatient visits were calculated in two ways. The first method included absences contiguous to the date of the visit. The second approach excluded contiguous dates. For example, the first method would count a work absence on Wednesday associated with a medical visit on Tuesday. The second approach would not count Wednesday's work loss unless there was also an absence on Tuesday.

Computing Costs at the Individual Level

The Ingenix data were used to estimate the incremental medical costs incurred by persons with urologic conditions. The data link medical and pharmacy claims to health plan benefits for more than 275,000 primary beneficiaries 18 to 64 years of age with employer-provided insurance. Individuals with an inpatient or outpatient claim for specific urologic conditions were identified. Multivariate regression models were used to predict medical and pharmacy spending in 1999 for persons with and without a particular condition, controlling for differences in patient demographics, health status, and insurance coverage.

The primary outcomes of interest included annual medical and pharmacy expenditures for each person. Expenditures consisted of total annual payments made by the enrollee (copayments, deductibles, excluded expenses) and by all third-party payers (primary and secondary coverage, net of negotiated discounts) for medical services and outpatient prescription drug claims.

The covariates included a set of variables to describe the medical and drug benefits, including individual plan deductibles, copayments or coinsurance rates, and a binary indicator for plan type (HMO, POS, PPO, FFS). Other covariates included age, sex, work status (active or retired), urban residence, and median household income in the zip code of residence. Observed differences in comorbid conditions were controlled for, based on ICD-9 diagnostic codes from the medical claims files. The medical claims were used to identify individuals treated for any of 26 chronic conditions, including hypertension, diabetes, congestive heart failure, asthma, and depression, and included a binary indicator for each condition.

The statistical analyses used a two-part model. The first part of the model used probit regression to estimate the probability that a member of the study sample had at least one medical or pharmacy claim. The second part of the model used a generalized linear model with a logarithmic link function to estimate the level of spending among members with at least one claim for the outcome of interest.

The two parts of the model were combined to predict average annual spending for persons with and without a urologic condition, controlling for other factors known to affect utilization. Specifically, estimates from the first part of the model were used to predict the probability of nonzero expenditures for persons with and without a specific urologic condition. Similarly, the second part of the model was used to predict expenditures, conditional upon having at least one claim, for each of the two groups. Total expenditures were calculated as the product of the two parts of the model and were averaged over all individuals in the sample, both those with and those without a urologic condition.

LIMITATIONS

We found that for many urologic conditions, population-based datasets contained limited information on true prevalence. Many conditions were not studied in prevalence surveys or were studied in a limited fashion. To buttress our analysis, we turned to published estimates of prevalence and incidence drawn from specific population-based studies focusing on various urologic conditions. For de novo analyses, we relied heavily on datasets that use administrative coding systems such as the ICD-9 CM to identify disease burden. Reliance on such administrative codes can result in both underestimation and overestimation of utilization, depending on the sensitivity and specificity of the disease code in question.

DATA QUALITY

A systematic approach was developed to evaluate the quality of the data generated for this project. A multi-tiered effort was made to ensure that the data met a high level of accuracy and consistency throughout. Data generated from each database were subjected to multiple levels of examination.

The first level of review required confirmation that the base populations used for each database were correct for each condition being evaluated (e.g., the population at risk for BPH included only males aged 40 years and older, whereas both sexes are at risk for STDs). Also, the total frequencies were checked to ensure that they were correctly reported (e.g., that there was no double counting of cases).

Next, individual frequencies were evaluated within patient subgroups to ensure that the counts were appropriate. Any numbers that appeared inconsistent were flagged for a programmer to recheck and review. For example, one would not expect to find greater incidence of a particular condition among divorced persons than among married persons, and this inconsistency might be identified for further review.

Third, the rates were compared over all years for which data were available. This allowed for an evaluation of whether any unusual rates were reported for a particular year or service. Any rates that appeared out of range were flagged for further review. To this end, a comprehensive literature review was performed using the relevant disease search terms. Rates generated from the datasets were compared with published estimates, and clinical experts adjudicated whether discrepancies signaled analysis errors. Also, confidence interval calculations were reviewed to ensure that they were within the appropriate range for all rates reported.

For the next level of verification, a mean-annual-payment summary table was produced to compare payments across years and services. Again, any payments that appeared out of range were flagged for further evaluation. In many cases, a small sample size explained a wide variation in reported payments

Finally, summary base population tables were generated for all conditions and years. These tables revealed cases where the sum of subpopulations did not total the base population for any given year, or where a base population was mistakenly used for the wrong year.

This systematic approach to reviewing data quality successfully uncovered issues that were later remedied at all levels of evaluation.

Table 5. Databases selected for analysis

Database	Acronym	Category	Purpose
Centers for Medicare and Medicaid Services-Medicare Provider Analysis and Review	CMS-MEDPAR	Medicare	Records of hospital inpatient services for Medicare beneficiaries
Centers for Medicare and Medicaid Services-Carrier File	CMS-Carrier	Medicare	Claims submitted by non-institutional providers for Medicare beneficiaries
Centers for Medicare and Medicaid Services-Outpatient File	CMS-Outpatient	Medicare	Claims submitted by institutional outpatient providers for Medicare beneficiaries
Centers for Medicare and Medicaid Services-Denominator File	CMS-Denominator	Medicare	Demographic and enrollment information on Medicare beneficiaries
Healthcare Cost and Utilzation Project–Nationwide Inpatient Sample	HCUP-NIS	Healthcare utilization and cost	National sample of inpatient stays and hospitalizations
Surveillance, Epidemiology, and End Results	SEER	Healthcare utilization and cost	Population-based, nationally representative tumor registry data
Surveillance, Epidemiology, and End Results linked with Medicare claims	SEER-Medicare	Healthcare utilization and cost	Claims submitted by inpatient and outpatient providers for Medicare beneficiaries who are tracked in SEER
National Ambulatory Medical Care Survey	NAMCS	Healthcare utilization and cost	National sample of ambulatory care utilization
National Hospital Ambulatory Medical Care Survey–Outpatient and Emergency Room Components	NHAMCS-OP NHAMCS-ER	Healthcare utilization and cost	National sample of ambulatory care services in hospital emergency and outpatient departments
Medical Expenditure Panel Survey	MEPS	Healthcare utilization and cost	National sample of healthcare use, expenditures, and sources of payment
National Association of Children's Hospitals and Related Institutions	NACHRI	Target populations	Pediatric inpatient stays at member hospitals only
National Nursing Home Survey	NNHS	Target populations	National sample of nursing homes, the providers of care, and their residents
Department of Veterans Affairs-Outpatient Clinic Files	VA-OPC	Target populations	National sample of VA outpatient services
MarketScan Health and Productivity Management Database	MarketScan	Cost of disease	Fortune 500 company inpatient and outpatient medical claims providing productivity and pharmacy data for employees and dependents
Ingenix Database	Ingenix	Cost of disease	Medical claims database providing utilization and cost data for 75 large employers
Society of Assisted Reproductive Technology Database	SART	Target Populations	Data regarding male and female factor infertility procedures from fertility clinics across the US
National Survey of Ambulatory Surgery	NSAS	Healthcare utilization and cost	National sample of ambulatory surgery performed in hospitals and freestanding ambulatory surgery centers
HCUP Kids' Inpatient Database	KID	Healthcare utilization and cost	Database of hospital inpatient stays for children to examine a broad range of conditions and procedures related to child health issues.
National Health and Nutrition Examination Survey	NHANES	Healthcare utilization and cost	Continuing series of national surveys of households and household members to assess health and nutritional status of adults and children
VA Pharmacy Benefits Management version 3.0 Database	PBM v3.0	Target populations	VA entity responsible for managing the national VA drug formulary process
VA National Surgical Quality Improvement Program	NSQIP	Target populations	Collects pre-operative risk factors, intra-operative variables, and 30-day post-operative mortality and morbidity outcomes on most major surgical operations performed in the VA system

APPENDIX A: TECHNICAL PROGRAMMING FOR MEDICARE DATA

This appendix describes the process by which data from the Medicare MEDPAR, carrier, and outpatient files were combined to assign number of visits and costs to five separate types of service: inpatient stays, physician office visits, hospital outpatient visits, ambulatory surgery visits, and emergency room (ER) visits.

The MEDPAR files contain summary records for all stays. The carrier and outpatient files contain a 5% random sample of the Medicare population. The same 5% sample of stays was used in building the files for this research effort[d]. The carrier file contains detailed information at the line-item level, which provided information on payment and place of service by line item[e]. Therefore, the carrier records were processed by line item rather than claim for this project. The outpatient file also contains detailed information, but not about payments or place of service[f].

An iterative process was used to build the analysis files. First, inpatient stays were identified, using MEDPAR records. Next, ER, outpatient surgery, and ambulatory surgery visits shown in the outpatient file were defined and selected, using appropriate revenue center codes. Finally, the line items and outpatient records that were not facility charges were matched to these visits and inpatient stays, using the following procedure: (a) person and exact dates of service were matched; (b) unassigned line items and outpatient records were assigned, using place of service and date ranges; (c) remaining line items with place of service listed as *office* and procedure codes with a range of 99024-99058 or 99199-99999 became the physician office visit core records; payments from other line items with the same patient identifier, provider, and date of service were added to these physician office visit records; and (d) payments from any line item or facility records that had not yet been assigned were aggregated by place of service. These "orphan" payments were included only in the calculation of cost per visit.

CREATING THE FILES

The Inpatient Analysis File

Inpatient stays were identified in MEDPAR as those stays in which a UDA diagnosis was the primary diagnosis. This number is the count of inpatient stays for the UDA utilization tables. All other data added to the stay were used to track payments that were occasioned by the stay.

Assigning Payments from Carrier Line Items To Inpatient Stays

Line items were matched to stays, using person identifier and dates of service. Each stay had an admission date and a discharge date. Each line item also had a begin date and an end date (although for most line items they were equivalent). The rules for assigning line-item payments to stays varied by whether the line item matched the admission date, the discharge date, or a date in between (or an interim stay date).

Payments from any line item that matched a person and an admission or interim stay date were assigned to the stay. Payments from line items that matched a person and discharge date and had place of service equivalent to *inpatient* or *ambulance* were assigned to the stay. Payments from any line item with a place of service equivalent to *emergency room* that matched a stay on admission date or any interim dates were included with the stay. If the line item also matched an emergency room facility, the payments were included with the emergency room visit.

Matching Outpatient Files with Inpatient Stays

Outpatient claims were matched to inpatient stays using HICs,[g] inpatient admission and discharge dates, and outpatient begin and end dates. Outpatient dollars were added to the inpatient stay if at least one of the following rules was met:

- The outpatient claim began and ended between (or including) the inpatient admission and discharge dates.
- The outpatient claim began during an inpatient stay and ended after the stay.
- The outpatient claim began and ended on the inpatient admission date.
- The outpatient claim began and ended on the inpatient discharge date.

An outpatient claim with an ER revenue center "flag" that occurred on the same day as an admission date counted both as an ER visit in the ER facility of service and also had its associated dollars rolled into the inpatient stay. In other words, it was double-counted.

Facility claims matching the discharge date of one stay and the admission date of a second stay were assigned to the second stay. These were generally ambulance services related to hospital transfers.

Inpatient payments were inflated by 8% (12) to account for deductible expenses.

The Hospital Outpatient, Ambulatory Surgery, and ER Analysis Files

Each of these files was created using the revenue center codes found on the claims. The reason for the visit to one of these places of service was determined by the UDA condition found at the revenue center, not on the condition shown in data imported from the carrier file.

The revenue centers used to define *hospital outpatient* were:

- Clinic-general classification
- Clinic-chronic pain center
- Clinic-psychiatric
- Clinic-OB-GYN
- Clinic-pediatric
- Clinic-urgent care
- Clinic-family practice
- Clinic-other

- Free standing clinic-general classification
- Free standing clinic-rural health, clinic
- Free standing clinic-rural health, home
- Free standing clinic-family practice
- Free standing clinic-urgent care

The revenue centers used to define an *ambulatory surgery visit* were:

- Ambulatory surgical care-general
- Ambulatory surgical care-other
- Operating room services-general classification[h]
- Operating room services-minor surgery[h]
- Operating room services-other operating room services[h]

The revenue centers used to define an *emergency room visit* were:

- Emergency room-general classification
- Emergency room-EMTALA[i] emergency medical screening services
- Emergency room-emergency room beyond EMTALA screening
- Emergency room-urgent care (effective 10/96)
- Emergency room-other

If an individual had two ER visits on the same day, they were counted as separate encounters.

There could be up to 45 revenue centers on a single outpatient claim record. For some claims, the revenue center fell into more than one facility of service. They were then assigned to the appropriate facility of service based on their HCPCS[j] codes.

Physician services were next drawn from the line-item file (carrier), and the payments associated with these services were assigned to an emergency room visit, hospital outpatient visit, or ambulatory surgery visit, using place of service, HIC, and exact date matches, as follows.

Payments from line items that matched an ER visit by person and exact date and had a place of service that included ER, ambulance, or independent laboratory or had a CPT code ranging from 99281 to 99285 were assigned to the emergency room facility of service. Payments from line items that matched a hospital outpatient visit by person and exact date and had a place of service that included outpatient hospital, ambulatory surgery center, ambulance, or independent laboratory were assigned to the hospital outpatient facility of service. Similarly, payments from line items that matched an ambulatory surgery visit by person and exact date and had a place of service equivalent to outpatient hospital, ambulatory surgery center, ambulance, or independent laboratory were assigned to the ambulatory surgery facility of service.

The remaining line items on the carrier file that had a place of service that included inpatient, ER, outpatient, or ambulatory surgery were examined. The number of days between each line item and each visit for a person were reviewed, and payments for remaining line items (most of which were laboratory services) were matched to the payment total for the type of service encounter that occurred closest in time to the date of the line item[k]. For example, the payment for a line item with a place of service listed as hospital outpatient that occurred within seven days of a hospital outpatient visit was added to the grand total of all hospital outpatient payments, but was not assigned to the cost of that particular visit. The mean payment for a hospital outpatient visit would be calculated by dividing the grand total for all hospital outpatient payments by the total number of hospital outpatient visits. If the nearest date for a service encounter was more than seven days from the date of the line item, the line item was dropped from further analysis.

The Physician Office Analysis File

After the above steps were performed, the remaining line items, having procedure codes equivalent to 99024–99058 or 99199–99999, formed the core physician office visit file. Payments from any line items from the carrier file or remaining facility records from the outpatient file that matched by patient, provider, and exact date of service were added to this visit file.

Remaining Carrier and Outpatient Payment Items

Remaining facility records that were not matched in the steps outlined above were matched to ER visits, hospital outpatient visits, or ambulatory surgery visits based on exact date of service. Payments from these facility records were added to the payment total for the relevant visit. If a record matched more than one such place of service, its payment amount was split between them. All remaining ambulance service revenue center payments were added to the total payments for ER visits. All radiation therapy revenue center payments were added to the total for hospital outpatient visits.

The remaining facility records were those that did not match a place of service by exact date, and hence were coined "orphan" records. These records payments were added to the established total payments for physician office visits, ambulatory surgery visits, hospital outpatient visits, and ER visits by HIC to the nearest date of service, using the following rules:

- Any facility records more than seven days from an existing date of service were deleted.
- Matches were allowed to the ER only by plus or minus one day.
- Records that matched more than one place of service by the same number of days were assigned in the following order: physician office, hospital outpatient, ER, ambulatory surgery.

Counts—Units of Analysis

Counts presented in the tables of this compendium are claims for each type of service. An individual could be counted more than once in each table if he or she had multiple events during the year. Within each facility of service, group counts, as well as payments, were tabulated for all persons and were stratified by age group, gender, race, and region. Gender and race codes used were those found on the claims record. The age category was derived from the age recorded on the claim record. The region code used was the census region, with claims recoded to region, using the state of residence.

Calculation of Denominators

Denominators for tables were derived from the CMS denominator file. This file includes the entire Medicare-eligible population and contains one record for each individual. Data from the denominator file can be linked to all other CMS files, using a unique identifier (ID) common to all files. In addition to eligibility status, the denominator file contains information about HMO membership. Individuals who were members of an HMO at any time during a year were dropped from the analysis because HMO claim records contain no payment information.

Weighting

The carrier file and the outpatient file are simple 5% random samples of the Medicare-eligible population. The sample was drawn using the last two digits of enrollees' SSNs. Individuals were selected from the 100% MEDPAR and denominator files, using the same criteria. National estimates presented in the tables were obtained by multiplying counts by a constant weight of 20 to represent the entire Medicare-eligible population.

Computing Confidence Intervals for Proportions

Ninety-five percent confidence intervals were calculated using the normal approximation to the binomial distribution (1). The confidence interval is

$$(p - 1.96\ \mathrm{sqrt}(pq/n),\ p + 1.96\ \mathrm{sqrt}(pq/n))$$

where p is the estimated proportion of interest, q=1–p, n is the number of observations, and sqrt refers to the square-root function.

APPENDIX B: SUMMARY OF DATASETS

Centers for Medicare and Medicaid Services (CMS)

Sponsor:
Robyn Thomas, Director
Division of Quality Coordination and Data Distribution (DQCDD)
OIS/EDG/DQCDD N1-15-03
Centers for Medicare and Medicaid Services (CMS)
7500 Security Blvd.
Baltimore, MD 21244-1850

Design: The Medicare dataset contains a number of files, including the Medicare provider analysis and review (MEDPAR) file, the carrier file, the outpatient file, and the denominator file. The *MEDPAR file* contains records for Medicare beneficiaries who used hospital inpatient services during the given year. Each record summarizes a stay. The *carrier file* contains final action claims data submitted by non-institutional providers, such as physicians, physician assistants, nurse practitioners, and standalone ambulatory surgical centers. Each observation in this file is at the claim level. The *outpatient file* contains final action claims data submitted by institutional outpatient providers, such as hospital outpatient departments, rural health clinics, and outpatient rehabilitation facilities. The unit of observation is also at the claim level. Finally, the *denominator file* contains demographic and enrollment information about each beneficiary enrolled in Medicare during the calendar year.

Time Frame: Data are available for 1991 through 2000, except in the denominator file, which contains data for 1984 through 2000. The years of data used for the conditions evaluated in this compendium were 1992, 1995, and 1998.

Sample Size: The MEDPAR dataset contains 100% of the Medicare beneficiaries and contains approximately 11 million records annually. For our analyses, a 5% MEDPAR sample was used. The carrier and outpatient dataset samples we used were based on a 5% simple random sample of the HIC numbers from each database. The carrier file contains 30 million records, and the outpatient file contains 5 million records

Use: MEDPAR provides in-depth information on all Medicare beneficiaries, including information on their diagnoses and procedures, along with a breakdown of charges for the year.

Benefits: Longitudinal tracking is possible, given the continuous data collection and large sample size. The detailed breakdown of charges allows for calculation of expenditures over a given year. The database also includes multiple diagnosis/procedure codes, thereby allowing for a more detailed level of analysis of charges associated with the urologic conditions under review.

Limitations: These data contain limited demographic information. Most beneficiaries are at least 65 years of age.

Healthcare Cost and Utilization Project (HCUP)—Nationwide Inpatient Sample (NIS)

Sponsor:
Healthcare Cost and Utilization Project (HCUP) — Nationwide Inpatient Sample (NIS)
Agency for Healthcare Research and Quality
HCUP Central Distributor
Social and Scientific Systems
8757 Georgia Ave., 12th Floor
Silver Spring, MD 20910
(866) 556-4287

Design: The Nationwide Inpatient Sample (NIS) is a subsample of the State Inpatient Databases (SID). NIS represents a 20% sample of hospital discharges from SID that includes all ages. The database utilizes a nationally representative stratified sample of approximately 6 million to 7.5 million records for the time period analyzed in this study.

Time Frame: The database contains data for 1988 through 2000.

Sample Size: Initially, the database covered only eight states; it has since grown to 28 states. It contains discharge data from 994 hospitals, approximating a 20% stratified sample of US community hospitals. The 2000 sample of hospitals comprises about 80% of all hospital discharges in the United States.

Use: Data on hospital inpatient stays can be used to identify, track, and analyze national trends in access, charges, quality, and outcomes and is the only national hospital database with charge information on all patient stays, regardless of payer.

Benefits: This large, nationally representative sample allows for the evaluation of trends over time. It can also be used to evaluate rare conditions and special populations (e.g., pediatric), and it includes charge information on all patient stays.

Limitations: Only hospitalizations are included, thereby limiting the types of service that can be analyzed. However, it may be possible to document change from inpatient to outpatient care over the years if HCUP is combined appropriately with other databases.

Ingenix

Sponsor:
Ingenix Health Intelligence
Corporate Headquarters
2525 Lake Park Blvd.
Salt Lake City, UT 84120

Design:
This database contains a subset of claims, utilization, and cost data from 75 large employers.

Time Frame: The available data are for 1997 through 1999.

Sample Size: The dataset includes approximately 1.8 million enrolled employees and their dependents.

Use: The medical claims data provide detailed financial information, as well as dates of service, diagnosis and procedure codes, types of facility, and providers. Drug claims include prescription fill date, patient and plan costs, and, in most cases, national drug codes (NDCs). Claims data contain records for only those who used services.

Benefits: This claims-based dataset captures all healthcare claims and encounters for employees and their dependents and includes detailed information on both medical and prescription drug costs.

Limitations: The longitudinal data are available for only a subset of firms.

MarketScan

Sponsor:
Medstat
777 E. Eisenhower Parkway
Ann Arbor, MI 48108
(734) 913-3000

Design: The MarketScan dataset is a collection of integrated inpatient and outpatient medical claims data and encounters; prescription drug, enrollment, and eligibility information; and productivity data. Claims are collected from employers who record corresponding employee absenteeism data and disability claims. Age, gender, and regional distribution of patients are available.

Time Frame: Only one year of data, 1999, is presently available for analysis.

Sample Size: This is a proprietary dataset of claims data from 100 health plans serving Fortune 500 employers. It includes data on 800,000 covered lives and approximately 340,000 employees.

Use: This dataset enables the evaluation of productivity and pharmacy data and associated medical claims information.

Benefits: MarketScan is a unique source of information on the indirect costs of a variety of urologic illnesses. It contains productivity and pharmacy data as well, and cases may be followed longitudinally.

Limitations: MarketScan data are not nationally representative. The database covers a working population, which is not necessarily similar to other patient populations. Issues related to the "healthy worker effect" might also be present (i.e., a healthier subset of people in the general population are more likely to work).

Medical Expenditure Panel Survey (MEPS)—Household Component

Co-Sponsors:
Agency for Healthcare Research and Quality (AHRQ) and National Center for Health Statistics (NCHS):

Agency for Healthcare Research and Quality
8757 Georgia Ave.
Silver Spring, MD 20910
(866) 556-4287

National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
6525 Belcrest Rd.
Hyattsville, MD, 20782-2003
(301) 458-4636

Design: MEPS is a nationally representative survey of healthcare use, expenditures, sources of payment, and insurance coverage for the US civilian non-institutionalized population. It is designed to yield comprehensive data for estimating the level and distribution of healthcare use and expenditures, monitoring the dynamics of healthcare delivery and insurance systems, and assessing healthcare policy implications. The database continuously collects medical expenditure data at both the person and the household level, using an overlapping panel design. Two calendar years of data are collected from each household in a series of five rounds. These data are then linked with additional information collected from the respondents' medical providers, employers, and insurance providers. The series of data collection activities is repeated each year on a new sample of households, resulting in overlapping panels of survey data in 195 communities across the nation.

Time Frame: Data have been collected five times a year from 1996 to the present.

Sample Size: 10,000 families, or approximately 24,000 individuals.

Use: This national probability survey provides information on the financing and utilization of medical care in the United States. The household component collects information on demographics, health conditions, health status, payments, access to care, satisfaction with care, insurance, income, and employment. These data are collected at the person and the household level over two calendar years and are then linked with additional information collected from the respondents' medical providers, employers, and insurance providers.

Benefits: The database contains longitudinal data for the core survey components. The medical provider component supplements and validates self-reported information in the household component.

Limitations: Because it is a household sample, MEPS may include data on only a few urologic illnesses. In addition, conditions may be underreported if one household member responds for others in the household and is unaware of some illnesses.

National Association of Children's Hospitals and Related Institutions (NACHRI)

Sponsor:
National Association of Children's Hospitals and Related Institutions
401 Wythe Street
Alexandria VA 22314
(703) 684-1355

Design: This dataset records information on all pediatric inpatient stays at member hospitals.

Time Frame: Data have been collected annually since 1999.

Sample Size: The dataset contains information on approximately 2 million pediatric inpatient discharges. Fifty hospitals located in 30 states participated in 1999, 55 participated in 2000, and 58 participated in 2001.

Use: Data are collected on the age, race, sex, and ICD-9 principal diagnosis of each pediatric inpatient cared for at participating facilities. Additionally, information is collected on length of stay, total charges, and cost-to-charge ratio.
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Benefits: Because it collects data from children's hospitals, the NACHRI dataset provides a unique opportunity to study the inpatient burden placed on the healthcare system by relatively uncommon pediatric urologic conditions. The dataset is rigorously edited and cleaned to ensure data quality.

Limitations: Because NACHRI collects data from specialized facilities, information regarding such topics as length of stay, patient demographics, treatment, and costs may not be representative of the national experience.

Society of Assisted Reproductive Technology (SART) database

Co-Sponsors:
Society of Assisted Reproductive Technology
1209 Montgomery Highway
Birmingham, AL 35216
(205) 978-5000

Centers for Disease Control and Prevention
1600 Clifton Rd.
Atlanta, GA 30333
(404) 639-3311

Design: Prospective ongoing data collection from fertility clinics across the US as mandated by Federal law.

Time Frame: 1999

Sample Size: 347 fertility clinics throughout the US**.**

Use: This dataset allows description of impact of male infertility on use of fertility services, and can be used to examine the influence of male factor infertility on reproductive outcomes.

Benefits: Utilization for infertility services related to male factor infertility are usually born by the patient; this dataset provides a window into utilization that is not easily captured in claims-based datasets.

Limitations: Access to fertility clinics is not uniform and varies by socioeconomic status; these data are not representative of the national burden of male factor infertility. Low income men with male factor infertility may not have access to these services.

National Survey of Ambulatory Surgery (NSAS)

Sponsor:
National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
6525 Belcrest Road
Hyattsville, MD, 20782-2003
(301) 458-4636

Design: The NSAS is a multistage probability sample, with the hospitals or freestanding ambulatory surgery centers sampled at the first stage or second stage and specific surgical procedures sampled at the final stage. The "hospital" universe includes non-Federal general, short-stay and children's hospitals located in the 50 states and the District of Columbia. The universe of "freestanding ambulatory surgery centers" is comprised of facilities which are state licensed or Medicare certified or which provide ambulatory surgery as the primary business activity and operate independently as a separate business. Facilities specializing in dentistry, podiatry, abortion, family planning, or birthing were also excluded from NSAS.

Time Frame: 1994–1996

Sample Size: The 1996 NSAS abstracted data from 125,000 ambulatory surgery visits to 488 facilities.

Use: As surgical services migrate to outpatient settings, describing ambulatory surgery use is required to present a comprehensive portrait of disease burden. Specific trends within surgical diseases can be examined in relation to subject demographics.

Benefits: This unique dataset allows for national estimation of ambulatory surgery services and trends over a 3-year period.

Limitations: ICD-9 procedure codes are used, which are of limited specificity when compared with Common Procedural Terminology procedure codes. At the time of these analyses, only data from 1994–1996 were available. The National Center for Health Statistics is planning a NSAS data collection for 2006.

Kids' Inpatient Database (KID)

Sponsor:
Healthcare Cost and Utilization Project (HCUP)—Nationwide Inpatient Sample (NIS)
Agency for Healthcare Research and Quality
HCUP Central Distributor
Social and Scientific Systems
8757 Georgia Ave., 12th Floor
Silver Spring, MD 20910
(866) 556-4287

Design: US community hospitals (defined as short-term, non-Federal, general and specialty hospitals, excluding hospital units of other institutions).

Time Frame: 1997, 2000

Sample Size: The 2000 KID contains data drawn from 27 State Inpatient Databases on children 20 years of age and younger. The 1997 KID contains data drawn from 22 State Inpatient Databases on children 18 years of age and younger. KID includes a sample of pediatric discharges from over 2,500 to 3,500 US community hospitals (defined as short-term, non-Federal, general and specialty hospitals, excluding hospital units of other institutions).

Use: KID allows national estimates of pediatric inpatient utilization, including procedure use.

Benefits: This dataset allows national estimates of time trends, quality of care, and charges related to pediatric urologic conditions.

Limitations: Procedures are listed using ICD-9 coding, which limits specificity when compared with CPT coding. Despite the size of the dataset, some urologic conditions are incompletely described by the data. As the trend toward outpatient care in urology continues, this limitation may grow.

National Ambulatory Medical Care Survey (NAMCS)

Sponsor:
National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
6525 Belcrest Road
Hyattsville, MD, 20782-2003
(301) 458-4636

Design: Data are collected from non-federally-employed physicians engaged in direct patient care (this excludes anesthesiology, radiology, and pathology) during a randomly assigned one-week reporting period. The physicians are selected on the basis of a national probability sample of office-based physicians. During the reporting period, data are gathered on an encounter form that records a systematic random sample of visits per physician. Data collected include patients' symptoms, physicians' diagnoses, and medications either ordered or provided to the patient.

Time Frame: The survey was conducted annually from 1973 through 1981 and once in 1985; it has been conducted annually since 1989.

Sample Size: The sample size for the years of data evaluated in this compendium ranges from 1,200 to 1,700 physicians and 23,000 to 35,000 patient visits annually.

Use: The data provide information about the provision and use of ambulatory medical care in the United States.

Benefits: This database may be considered nationally representative, since it has a multistage probability design and captures the physician subspecialties that may encounter urologic conditions. Also, this database may identify a number of urologic conditions (e.g. UTI, BPH) that might otherwise go unreported because many of them are identified on the basis of office visits alone.

Limitations: There are no identifiers to track patients longitudinally. Also, some rare pediatric conditions may be missed because of the limited number of visits reported. The number of urologists sampled may be small for specific analyses. There are no cost data, and there may be more than one record per person because the data report number of *patient visits*, not *patients*.

National Health and Nutrition Examination Survey (NHANES)

Sponsor:
National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
3311 Toledo Road
Hyattsville, MD 20782
(301) 458-4636

Design: NHANES is a continuing series of national sample surveys of households and household members in 50 states.

Time Frame: NHANES 3 was conducted from 1988–1994. NHANES is currently a continuing survey, with the latest data release covering 1999–2000.

Sample Size: The sample for NHANES 3 includes approximately 33,994 respondents, age 2 months and older.

Use: The survey allows collection of data regarding urologic diseases and symptoms that can be used to generate true national prevalence for these diseases and symptoms during the time period covered in the survey.

Benefits: The data are unique in that they allow for nationally-representative estimates of the prevalence of certain urologic conditions.

Limitations: Relatively few urologic conditions are asked about in this survey. Subject self-report regarding medical history is subject to error.

National Hospital Ambulatory Medical Care Survey (NHAMCS)

Sponsor:

National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
6525 Belcrest Road
Hyattsville, MD, 20782-2003
(301) 458-4636

Design: These data are collected in order to provide a better understanding of the utilization and extent of ambulatory care services in hospital emergency and outpatient departments. Data are collected on a national sample of emergency department and outpatient visits, excluding federal, military, and VA hospitals. The database uses a four- stage probability design: First, a sample of geographic areas is defined. Next, a sample of hospitals is identified within these areas. Third, clinics are selected within these hospitals. And fourth, patients are selected on the basis of their visits to these clinics.
A patient record form is completed by hospital staff during a randomly assigned four-week period.

Time Frame: The data have been collected annually since 1992.

Sample Size: The sample size for the years of data evaluated in this compendium is in the range of 22,000 to 30,000 patient visits annually.

Use: The data describe utilization and provision of ambulatory care services in hospital emergency and outpatient departments (excluding federal, military, and VA hospitals).

Benefits: The survey covers a nationally representative multistage probability sample, which includes a pediatric population and contains data on genitourinary care in ERs. Other data reported include demographic characteristics of patients, expected source(s) of payment, diagnoses, medication, and certain characteristics of the hospital, such as type of ownership.

Limitations: There are no cost data and no identifiers to track patients longitudinally. An individual may have more than one record, since the data are based on number of *patient visits*, not *patients*. Because the number of visits is small, rare conditions and those that are chronic in nature may be missed.

National Nursing Home Survey (NNHS)

Sponsor:
National Center for Health Statistics
Centers for Disease Control and Prevention
Division of Data Services
3311 Toledo Road
Hyattsville, MD 20782
(301) 458-4636

Design: NNHS is a continuing series of national sample surveys of nursing homes, their residents and their staff.

Time Frame: These surveys were conducted in 1973–1974, 1977, 1985, 1995, 1997, and 1999. The years of data used for this compendium are 1995 through 1999.

Sample Size: The sample includes approximately 1,500 facilities, where interviews (occasionally via self-administered questionnaires) were conducted with administrators and staff.

Use: The survey provides information from the perspectives of both the providers of service and the recipients. Data collected include information about the size and ownership of the facility, Medicare/Medicaid certification, occupancy rate, number of days of care provided, and expenses. Recipient data collected include demographic characteristics, health status, and services received.

Benefits: The dataset is unique in that information is solicited from both the provider and the recipient of care. It also targets a specific, useful population for study.

Limitations: The surveys do not contain information on the health services provided; they report only whether a patient received service within general categories. The records do not contain a facility number that would allow linkage of records to the facility.

Veterans Affairs Outpatient Clinic Dataset (VA-OPC)

Sponsor:
Austin Automation Center (AAC) Enterprise Business Office
Austin, TX (http://www.aac.va.gov)
(512) 326-6005

Design: The Department of Veterans Health Administration maintains a centralized data repository that contains computerized utilization data for all outpatient visits and acute care hospital stays, as well as other utilization datasets on nursing home stays, contract services paid for by the VA, etc. These datasets are integral to the National Patient Care Database (NPCD) in the VA.

Time Frame: The computerized outpatient clinic files (OPC) contain data from 1980 to the present. Ambulatory procedures were added in 1990, and outpatient diagnoses (ICD-9-CM) were added in FY1997. Patient treatment files (PTF) contain data from 1970 to the present.

Sample Size: The VA is the largest healthcare system in the United States, comprising more than 160 hospitals (>45,000 beds), more than 600 community-based outpatient clinics, and more than 100 nursing homes. The VA serves more than 3 million veterans annually. Each dataset within the NPCD contains records for the population of patients seen in all VA healthcare facilities, representing a comprehensive national record of the delivery of VA healthcare services to veterans.

Use: The OPC files include demographics, visits, and clinic stops. The PTF contains demographics and admission and discharge data, as well as diagnoses, DRGs, length of stay, transfers, and hospital-based procedures.

Benefits: The datasets represent the population of veteran users of VA healthcare for whom utilization data were recorded. They provide a rich resource for assessing prevalence of disease among healthcare users, as well as for evaluating patterns of care. Encrypted SSNs permit file linkage across

VA healthcare facilities and across settings within facilities, providing a relatively complete portrait of healthcare utilization in VA sites of care.

Limitations: The VA datasets do not provide comprehensive information about healthcare utilization obtained by veterans *outside* the VA healthcare system. Also,

the diagnosis codes are derived from outpatient visits from physician/patient encounters and thus *do not reflect all existing cases among veteran users*, but instead reflect the population for whom care was sought during the year under review.

VA Pharmacy Benefits Management version 3.0 database (PBM v3.0).

Sponsor:
Pharmacy Benefits Management Strategic Healthcare Group
VA Central Office
810 Vermont Ave. NW
Washington, DC 20420

Design: The PBM national database includes medication utilization information based on unique patients for every prescription filled in the VA. The database produces information on each occasion of drug dispensation, which helps to track total prescription usage on a gross or discrete level

Time Frame: 1998 to 2003

Sample Size: The VA serves more than 3 million veterans annually.

Use: The PBM v. 3.0 can be used to examine time trends and overall utilization for various medications used to treat urologic conditions.

Benefits: This comprehensive database provides a portrait of oral medication utilization for urologic conditions that often effect Medicare aged individuals, for whom such information is generally unavailable.

Limitations: Certain medications which are ordered by clinics or hospital wards (e.g., intravesical agents) may not be captured if no prescription is created prior to dispensation.

VA National Surgical Quality Improvement Program (NSQIP)

Sponsor:
Office of Patient Care Services
VA Central Office
810 Vermont Ave. NW
Washington, DC 20420

Design: The Department of Veterans Health Administration NSQIP collects pre-operative risk factors, intra-operative variables, and 30-day post-operative mortality and morbidity outcomes on most major surgical operations performed in the VA healthcare system. Data for each operative case are abstracted. Each year, risk-adjustment models are created and risk-adjusted 30-day mortality and morbidity surgical outcomes are reported.

Time Frame: 1998 to 2003

Sample Size: Approximately 160 hospitals (>45,000 beds). The VA serves more than 3 million veterans annually.

Use: The NSQIP can be used to examine complication rates and mortality for common urologic procedures in the VA population

Benefits: Uniformity of data collection minimizes selection bias. The database contains a wide variety of pre-operative clinical variables which may influence the outcomes of urologic surgery.

Limitations: For some urologic conditions, outcomes of importance to the patient (e.g., quality of life outcomes) are not collected.

NOTES

[a] 2000 NAMCS Micro-data file documentation, Data Dissemination Branch, National Center for Health Statistics, 6525 Belcrest Road, Room 1064, Hyattsville, MD, 20782.

[b] CPS Utilities, Unicon Research Corporation, March, 1992–2000.

[c] The VA does not generate a claim or patient bill for eligible veteran users, with the exception of certain copayments or through medical care cost recovery of selected charges among coinsured veterans. As a result, the insurance categorization in the VA administrative databases may not be as accurate as those in private or other public sector healthcare organizations or systems for which financing is based entirely on reimbursement of charges. Prevalence estimates for private/HMO insurance may also be underestimates for these veterans, as the VA databases do not capture visits or diagnoses associated with visits to non-VA providers.

[d] These files excluded anyone with health maintenance organization (HMO) experience during any years of our analysis.

[e] Line items with place of service other than physician office, inpatient hospital, ER, ambulatory surgery, outpatient hospital, ambulance, or independent laboratory were excluded from the analysis.

[f] Outpatient claims with facility type listed as skilled nursing facilities (SNF) or home health agencies (HHA) were excluded from analysis.

[g] HIC is an acronym for Health Insurance Claim number. It is an 11-digit code made up of a nine-digit claim account number (CAN) (which is actually a social security number (SSN)) and a two-digit beneficiary identification code (BIC), which uniquely identifies multiple people claiming benefits under the same SSN.

[h] Operative procedures provided at these revenue centers were reviewed by clinical experts and were all considered to be appropriately categorized as ambulatory surgery.

[i] The Emergency Medical Treatment and Active Labor Act, a statute that governs when and how a patient may be (1) refused treatment or (2) transferred from one hospital to another when he or she is in an unstable medical condition.

[j] The HCFA Common Procedure Coding System.

[k] If matches of ER and ambulatory surgery were within one day of each other, then half the costs were assigned to each facility of service. Also, when the office visit line item was matched to a place of service, the non-office-visit line items that matched on HIC, provider, and date were also assigned to that place of service.

REFERENCES

1. Modern elementary statistics. Fifth ed. Englewood Cliffs, NJ: Prentice Hall, 1979.
2. Escarce JJ, McGuire TG. Methods for using Medicare data to compare procedure rates among Asians, blacks, Hispanics, Native Americans, and whites. Health Serv Res 2003;38:1303-17.
3. Statistical Analysis System, Release 8.2. SAS Institute; Cary, NC.
4. Statistical Package for the Social Sciences for Windows, Release 9.0, 1998. SPSS Inc; Chicago, IL.
5. Rothenberg R, Bross DC, Vernon TM. Reporting of gonorrhea by private physicians: a behavioral study. Am J Public Health 1980;70:983-6.
6. Rothenberg RB. Analysis of routine data describing morbidity from gonorrhea. Sex Transm Dis 1979;6:5-9.
7. Chorba TL. Disease surveillance. In: Thomas JC, Weber DJ, eds. Epidemiologic methods for the study of infectious diseases. New York: Oxford University Press, 2001:138-162.
8. Chorba TL, Berkelman RL, Safford SK, Gibbs NP, Hull HF. Mandatory reporting of infectious diseases by clinicians. Jama 1989;262:3018-26.
9. 1998 guidelines for treatment of sexually transmitted diseases. Centers for Disease Control and Prevention. MMWR Recomm Rep 1998;47:1-111.
10. National Drug Data File Plus Tm reference software. First Data Bank Inc; San Bruno, CA.
11. Drug Topics Redbook. 107th ed. Montvale, NJ: Medical Economics Co., 2003.
12. Brown ML, Riley GF, Schussler N, Etzioni R. Estimating health care costs related to cancer treatment from SEER-Medicare data. Med Care 2002;40:IV-104-17.

GLOSSARY OF SELECTED TERMS

Race **—**The concept of race reflects self-identification by people according to the race or races with which they most closely identify. These categories are sociopolitical constructs and should not be interpreted as being scientific or anthropological in nature. Furthermore, the race categories include both racial and national-origin groups. According to the Office of Management and Budget (OMB) standards, race is a considered a separate concept from Hispanic origin (ethnicity).

White — A person having origins in any of the original peoples of Europe, the Middle East, or North Africa. It includes people who indicate their race as "White" or report entries such as Irish, German, Italian, Lebanese, Near Easterner, Arab, or Polish.

Black or African American — A person having origins in any of the Black racial groups of Africa. It includes people who indicate their race as "Black, African Am., or Negro," or provide written entries such as African American, Afro American, Kenyan, Nigerian, or Haitian.

American Indian and Alaska Native (North American Native) — A person having origins in any of the original peoples of North and South America (including Central America) and who maintain tribal affiliation or community attachment.

Asian — A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. It includes "Asian Indian," "Chinese," "Filipino," "Korean," "Japanese," "Vietnamese," and "Other Asian."

Pacific Islander — A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands. It includes people who indicate their race as "Native Hawaiian," "Guamanian or Chamorro," "Samoan," and "Other Pacific Islander."

Other race — Includes all other responses not included in the "White", "Black or African American", "American Indian and Alaska Native", "Asian" and "Native Hawaiian and Other Pacific Islander" race categories described above. Respondents providing write-in entries such as multiracial, mixed, interracial, Wesort, or a Hispanic/Latino group (for example, Mexican, Puerto Rican, or Cuban) in the "Some other race" category are included here.

Ethnicity **—** The heritage, nationality group, lineage, or country of birth of the person or the person's parents or ancestors before their arrival in the United States.

Hispanic — Persons of Cuban, Mexican, Puerto Rican, South- or Central-American, or other Spanish culture or origin, regardless of race.

Region **—** The States are grouped into four regions corresponding to those used by the US Bureau of the Census:

Northeast	Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, and Pennsylvania
Midwest	Michigan, Ohio, Illinois, Indiana, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, and Kansas
South	Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma, and Texas
West	Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Hawaii, and Alaska

Metropolitan Statistical Area **—** An MSA consists of a large population nucleus of 50,000 population or greater, together with adjacent communities having a high degrees of social and economic integration with that core. Metropolitan areas comprise at least one county, except in New England, where cities and towns are the basic geographic unit.

Urban Area — Urban areas consist of urbanized areas and other urban entities. An urban area consists of densely settled territory with a population of 50,000 or more inhabitants. Other urban areas have from 2,500 to 49,999 population.

Rural — Territory, population, and housing units not classified as urban.

Source of Payment

Medicare — The health insurance program for the aged and disabled administered by the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration).

Medicaid — A jointly funded Federal-State health insurance program providing medical care to those unable to afford it.

Private insurance — A private insurance plan not specified as an HMO/PPO. This includes Blue Cross/Blue Shield plans, medical coverage provided by life insurance companies, casualty insurance companies, health insurance companies, and independent plans such as employer/union-sponsored plans and/or self-funded plans (partial or total).

HMO/PPO — Any Health Maintenance Organization (HMO) or Preferred Provider Organization (PPO) sponsored by consumers, communities, physicians, or hospitals.

Self pay — The majority of the costs for the visit were paid by the patient, spouse, family, or next-of-kin.

Other insurance — Includes any nonprofit source of payment (such as church welfare, United Way, or Shriner's Hospitals for Children).

Poverty Income Ratio — This is a calculated variable based on family income and family size using tables published each year by the Bureau of the Census in a series "Current Population Reports" on poverty in the United States. The primary reporting categories are:

0.00-0.999	(Below poverty)
1.000 and above	(At or above poverty)

or

0.000-1.850	(Low)
1.851-3.500	(Middle)
3.501 and above	(High)

Primary Diagnosis — The condition that is determined during the hospital stay to be the chief reason for causing the hospital admission.

Any Diagnosis — Includes primary diagnosis and additional conditions that coexist at the time of admission, or that develop during the stay, and which have an effect on the treatment or length of stay in the hospital.

Discharge Status: The disposition of a patient at the time of discharge from an inpatient facility.

Nursing Home: In the National Nursing Home Survey, nursing homes are defined as facilities that routinely provide nursing care services and have three or more beds set up for residents. Facilities may be certified by Medicare or Medicaid or not certified but licensed by the state as a nursing home. The facilities may be freestanding or a distinct unit of a larger facility

Intermediate Care Facility: Institutions certified by the Medicaid program to provide health-related services on a regular basis to Medicaid-eligible individuals who do not require hospital or skilled nursing facility care, but do require institutional care above the level of room and board.

Skilled Nursing Facility: An institution (or a distinct part of an institution) that is primarily engaged in providing skilled nursing care and related services for residents who require medical or nursing care, or rehabilitation services for the rehabilitation of injured, disabled, or sick persons, and is not primarily for the care and treatment of mental diseases.

Home Health: A collection of supportive care services focused on providing skilled nursing in the home, along with a range of the following services: personal care services; homemaker and companion services; physical therapy; medical social services; medical equipment and supplies; counseling; 24-hour home care; occupation and vocational therapy; dietary and nutritional services; speech therapy; audiology; and pharmacy care, such as intravenous

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