CHAPTER 4

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.

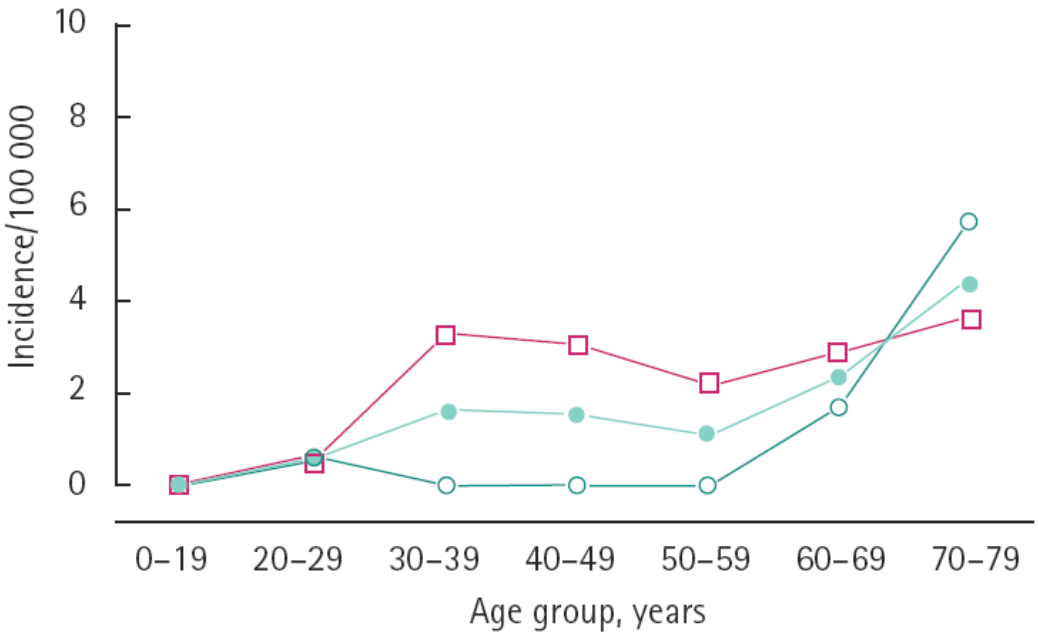

Figure 1. Age specific incidence rates for males (open circles), females (squares), and all patients (closed circles) with interstitial cystitis[a] in Olmsted County, MN 1976–1996.
[a]Interstitial cystitis, ICD-9 code 595.1.

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,

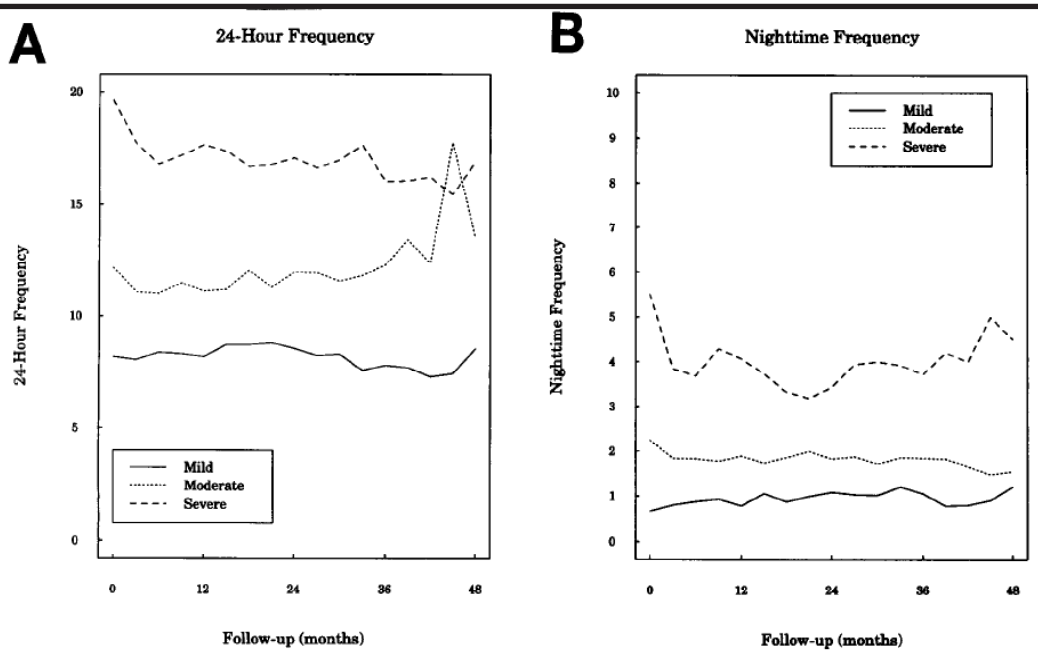

Figure 2. Mean urinary frequency measured from voiding log, by baseline severity of symptoms.

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.

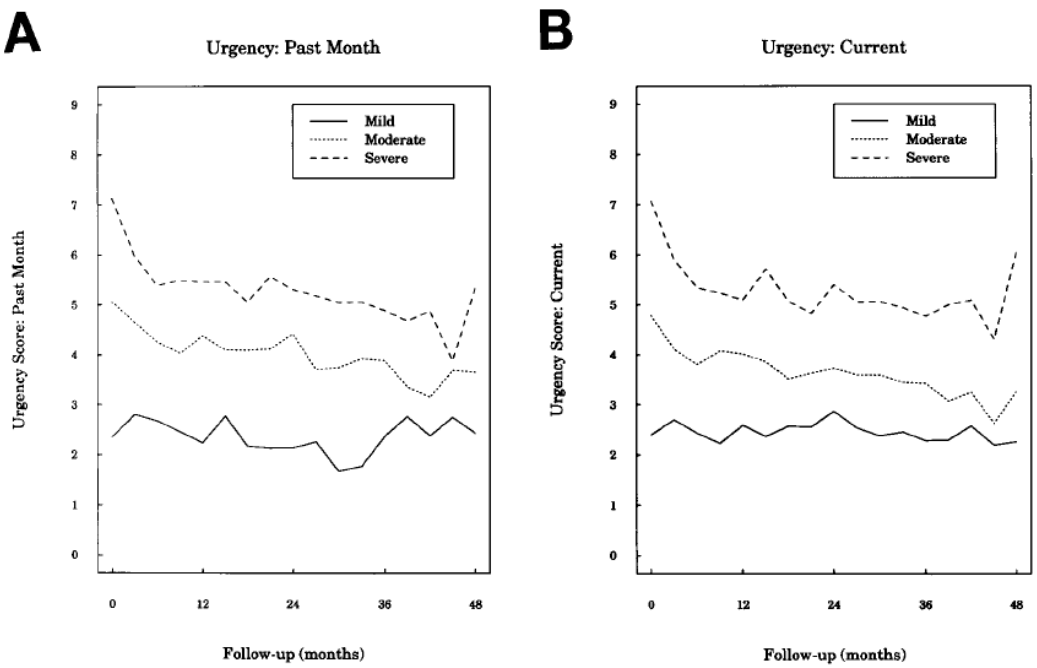

Figure 3. Mean urgency scores on 0 to 9 Likert scale with time by severity of urgency.

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.

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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

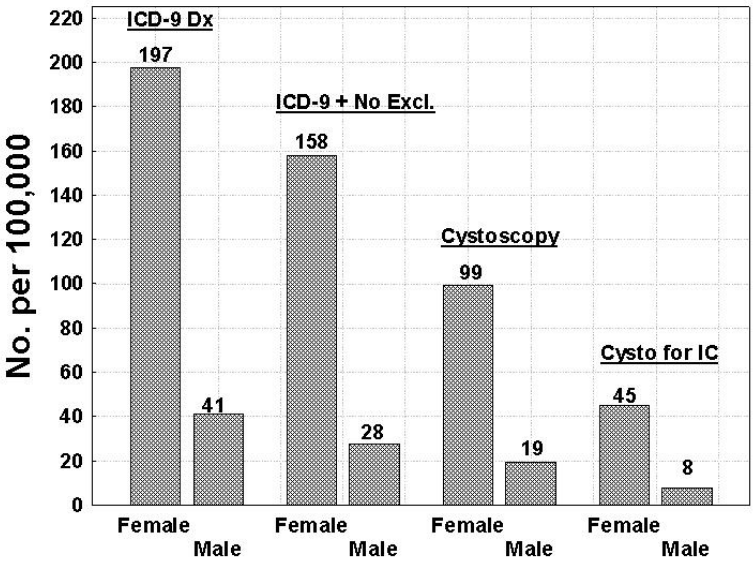

Figure 4. Gender specific prevalence of interstitial cystitis[a] in a managed care population.
[a]Interstitial cystitis, ICD-9 code 595.1.

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 $\geq$ 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

		IC/PBS		Interstitial Cystitis		Painful Bladder Syndrome	
	All People 18+	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.

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