NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

DIAGNOSIS AND MANAGEMENT OF URINARY TRACT INFECTION

Guidelines

1. **Institute for Clinical Systems Improvement (ICSI)**. Uncomplicated urinary tract infection in women. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Jul. 21 p. [34 references]
2. **Scottish Intercollegiate Guidelines Network (SIGN)**. Management of suspected bacterial urinary tract infection in adults. A national clinical guideline. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2006 Jul. 40 p. (SIGN publication; no. 88). [143 references]
3. **University of Michigan Health System**. Urinary tract infection. Ann Arbor (MI): University of Michigan Health System; 2005 May. 9 p. [10 references]

INTRODUCTION

A direct comparison of the Institute for Clinical Systems Improvement (ICSI), Scottish Intercollegiate Guidelines Network (SIGN), and University of Michigan Health System (UMHS) recommendations for the diagnosis and treatment of urinary tract infection (UTI) is provided in the tables below.

The three guidelines differ somewhat in scope. All three guidelines address lower UTI in adult non-pregnant women. In addition, the UMHS and SIGN guidelines address UTI in pregnant women. The SIGN guideline also considers UTI in adult men and patients with indwelling urinary catheters. The three guidelines focus primarily on uncomplicated lower UTI (LUTI), although UMHS provides recommendations for acute uncomplicated pyelonephritis and SIGN provides recommendations for upper UTI (UUTI). This synthesis only considers recommendations for the diagnosis and treatment of lower UTI in non-pregnant and pregnant adult women.

The tables below provide a side-by-side comparison of key attributes of each guideline, including specific interventions and practices that are addressed. The language used in these tables, particularly that which is used in Tables 4, 5 and 6, is in most cases taken verbatim from the original guidelines:

- Table 1 provides a quick-view glance at the primary interventions considered by each group.
- Table 2 provides a comparison of the overall scope of both guidelines.
- Table 3 provides a comparison of the methodology employed and documented by both groups in developing their guidelines.

- Table 4 provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis, including:
  - Diagnosis
    - History and Clinical Presentation
    - Laboratory Testing
  - Treatment
    - Antibiotic Treatment
    - Other Treatment
  - Referral and Follow-Up
  - Education
  - Supporting References
- Table 5 lists the potential benefits and harms associated with the implementation of each guideline as stated in the original guidelines.
- Table 6 presents the rating schemes used by ICSI, SIGN and UMHS to rate the level of evidence and/or the strength of the recommendations.

A summary discussion of the areas of agreement and differences among the guidelines is presented following the content comparison tables.

Abbreviations

- ASB, asymptomatic baceriuria
- ICSI, Institute for Clinical Systems Improvement
- LUTI, lower urinary tract infection
- SIGN, Scottish Intercollegiate Guidelines Network
- SMX, sulfamethoxazole
- STD, Sexually transmitted disease
- STI, Sexually transmitted infection
- TMP, trimethoprim
- UA, urinalysis
- UC, urine culture
- UMHS, University of Michigan Health System
- UTI, urinary tract infection
- UUTI, upper urinary tract infection

TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED
("✓" indicates topic is addressed)

	ICSI (2006)	SIGN (2006)	UMHS (2005)
DIAGNOSIS OF LOWER URINARY TRACT INFECTION			
History and clinical presentation	✓	✓	✓
Urinalysis (Dipstick or	✓	✓	✓

microscopy)			
Urine culture	✓	✓	✓
Phone triage	✓	✓	✓
TREATMENT FOR LOWER URINARY TRACT INFECTION			
Phone triage/treatment	✓	✓	✓
Empirical treatment	✓	✓	✓
Antibiotic therapy	✓	✓	✓
Non-antibiotic therapies		✓	✓
Recurrent UTI	✓	✓	✓
REFERRAL AND FOLLOW-UP			
Follow-up after initial therapy	✓	✓	✓
PATIENT EDUCATION			
Patient education	✓	✓	✓

TABLE 2: COMPARISON OF GUIDELINE SCOPE	
Objective and Scope	
ICSI (2006)	• To decrease the use of urine culture as a guide in the therapy of uncomplicated urinary tract infection (UTI) • To increase the use of short course therapy in women with uncomplicated UTI • To increase patient satisfaction with management of uncomplicated UTI
SIGN (2006)	To provide recommendations based on current evidence for best practice in the management of adults with community acquired UTI
UMHS (2005)	To implement a cost-effective strategy for uncomplicated UTI in women
Target Population	

ICSI (2006)	Women age 18 to 65 with uncomplicated UTI
SIGN (2006)	Adult women (including pregnant women) and men and patients with urinary catheters *This guideline is not intended for use in the following populations:* • Children • Patients with hospital-acquired infection
UMHS (2005)	Adult women with uncomplicated urinary tract infection
Intended Users	
ICSI (2006)	Advanced Practice Nurses Allied Health Personnel Health Care Providers Health Plans Hospitals Nurses Physician Assistants Physicians
SIGN (2006)	Advanced Practice Nurses Health Care Providers Nurses Patients Physician Assistants
UMHS (2005)	Advanced Practice Nurses Nurses

	Physician Assistants Physicians

TABLE 3: COMPARISON OF METHODOLOGY	
Methods Used to Collect/Select the Evidence	
ICSI (2006)	*Searches of Electronic Databases* *Described Process*: Not stated *Number of source documents*: Not stated *Number of references*: 34
SIGN (2006)	*Hand-searches of Published Literature (Primary Sources)* *Searches of Electronic Databases* *Described Process*: The evidence base for this guideline was synthesized in accordance with the Scottish Intercollegiate Guidelines Network (SIGN) methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group. Literature searches were initially conducted in Medline, Embase, Cinahl, and the Cochrane Library using the year range 1994-2002. The literature search was extended from 1966-2003 for randomized clinical trials (RCTs) and diagnostic studies. The National Economic Evaluation Database (NEED) was searched for economic studies to cover the period up to January 2004. Key websites on the Internet were also searched. These searches were supplemented by the reference lists of relevant papers and group members' own files. The Medline version of the main search strategies can be found on the SIGN website. *Number of Source Documents*: Not stated *Number of References*: 143
UMHS (2005)	*Hand-searches of Published Literature (Primary Sources)* *Hand-searches of Published Literature (Secondary Sources)*

	Searches of Electronic Databases *Described Process*: The literature search for this update began with the results of the literature search performed for the earlier version of this guideline. A search for literature published since that time was performed. The search was conducted prospectively on MEDLINE (U.S. National Library of Medicine) using the major keywords of: *urinary tract infections (including bacteriuria, pyuria, or schistosomiasis haematobia), guidelines, controlled trials, published from 7/1/98 to 8/31/04, and adult women. Specific searches were performed for: predictive value of tests, diagnosis (other than predictive value of tests), treatment, uncomplicated urinary tract infection (UTI) -- treatment, pregnancy, postmenopausal women -- treatment, recurrent UTI, self initiated therapy, group B strep and non-pregnant women, telephone triage -- nursing protocol, other treatment, other references to UTI.* The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle. *Number of source documents*: Not stated *Number of references*: 10
Methods Used to Assess the Quality and Strength of the Evidence	
ICSI (2006)	Not stated
SIGN (2006)	Weighting According to a Rating Scheme (Scheme Given - Refer to Table 6)
UMHS (2005)	Weighting According to a Rating Scheme (Scheme Given - Refer to Table 6)
Methods Used to Analyze the Evidence	
ICSI (2006)	*Systematic Review* *(Process not described)*
SIGN (2006)	*Review of Published Meta-Analyses* *Systematic Review with Evidence Tables* *Described Process*: Once papers have been selected as potential

sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgment. The extent to which a study meets a particular criterion (e.g., an acceptable level of loss to follow up) and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN executive staff will arbitrate to reach an agreed quality assessment.

Evidence Tables

Evidence tables are compiled by SIGN executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the SIGN Web site.

UMHS (2005)	*Systematic Review* *Described Process:* Conclusions were based on prospective randomized clinical trials (RCTs) if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.
Methods Used to Formulate the Recommendations	
ICSI (2006)	Not stated
SIGN (2006)	*Expert Consensus* *Described Process*: **Synthesizing the Evidence** Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgment is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgment on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable. It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved. **Considered Judgment** It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of considered judgment. Under the heading of considered judgment, guideline development groups summarise their view of the total body of evidence covered

	by each evidence table. This summary view is expected to cover the following aspects: • Quantity, quality, and consistency of evidence • Generalisability of study findings • Directness of application to the target population for the guideline • Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them) • Implementability (i.e., how practical it would be for the NHS in Scotland to implement the recommendation) Guideline development groups are provided with a pro forma in which to record the main points from their considered judgment. Once they have considered these issues, the group is asked to summarise their view of the evidence and assign a level of evidence to it, before going on to derive a graded recommendation. Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN Web site.
UMHS (2005)	*Expert Consensus* *Described Process*: Consideration of benefits, harms, costs, and patient preferences
Outcomes	
ICSI (2006)	• Performance and results of laboratory tests, such as urinalysis and urine culture, including sensitivity, specificity, and predictive value • Effectiveness of treatment according to drug and treatment duration • Antibiotic resistance
SIGN (2006)	• Symptoms from UTI • Adverse treatments effects • Recurrence of symptoms • Development of symptoms in asymptomatic UTI patients
UMHS (2005)	• Assessment of diagnostic tests (sensitivity, specificity, predictive value, validity) • Response to treatment (cure rate, symptom relief) • Drug side effects

Financial Disclosures/Conflicts of Interest	
ICSI (2006)	In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose. No work group members have potential conflicts of interest to disclose. ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.
SIGN (2006)	Declarations of interests were made by all members of the guideline development group. Further details are available from the Scottish Intercollegiate Guidelines Network (SIGN) Executive.
UMHS (2005)	The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

TABLE 4: COMPARISON OF RECOMMENDATIONS FOR THE DIAGNOSIS AND TREATMENT OF URINARY TRACT INFECTION	
DIAGNOSIS	
History and Clinical Presentation	
ICSI (2006)	An algorithm is provided for Uncomplicated Urinary Tract Infection in Women; clinical highlights and selected annotations (numbered to correspond with the algorithms) follow. **Clinical Highlights** • Assess all women ages 18 to 65 with symptoms of UTI for the

presence of complicating factors. The presence of complicating factors warrants provider evaluation and may require additional diagnostic work-up. *(Annotations #2, 4)*

Uncomplicated Urinary Tract Infection in Women Algorithm Annotations

Adult Female Presents or Calls with One or More of the Following Symptoms: Dysuria, Frequency, Urgency

The classic symptoms of UTI in women are dysuria, frequency, and urgency. One or more of these symptoms can trigger the initiation of the UTI guideline. Hematuria alone is not a classic uncomplicated UTI symptom. There is concern the presence of hematuria may be a sign of more significant disease. Patients whose symptoms do not subside should return to the clinic for a full examination.

Complicating Factors Present?

History-taking is essential in differentiating uncomplicated from complicated urinary infection. Women should be screened for the presence of complicating factors when presenting or calling with symptoms of UTI. Depending upon which complicating factor is present, short course therapy may or may not be appropriate.

Symptoms for which short course therapy with trimethoprim/sulfamethoxazole (TMP/SMX) is not appropriate:

1. Symptoms suggest pyelonephritis or other more severe infection: long duration, rigors, flank pain, or temperature greater than 101 degrees F.
2. Patient's medical history suggests likelihood of complicated urinary tract infection, or need for different investigation or therapy: diabetes, pregnancy, immunosuppression, underlying urinary tract disease or renal calculi, recent medical intervention (hospitalization or catheterization), or recurrent UTIs or failure of therapy.
3. Resident of an extended care facility

Factors for which short course therapy may be appropriate at physician discretion:

4. Potential sexually transmitted infection (STI): an infected partner, other genitourinary symptoms. The patient should be seen and STIs ruled out.
5. Younger or older patients (less than 18 or greater than 65). There is little literature documentation of efficacy of short course therapy in these age groups.
6. Recent pyelonephritis or failure of antibiotic treatment. These

patients may be at higher risk of complicated infection.

Evidence supporting this recommendation is of classes: B, R

Provider Evaluation

Symptomatic women with complicating factors may have a more extensive infection and/or a UTI with lower colony counts. Sensitivities should be obtained; hospitalization and/or urological evaluation may be indicated.

Women with a complicated history should be evaluated by a health care provider. The provider (physician or paraprofessional) will determine if a urine culture is necessary.

Complicating factors are listed in detail on the algorithm page (floating box 2 of the original guideline document), and include the following categories:

- Those that would preclude use of short course therapy
- Those that would allow for discretionary use of short course therapy
- Those that would necessitate a pelvic exam to rule out genitourinary disease

Evidence supporting this recommendation is of class: R

Symptoms of or Risk for Other Genitourinary Diseases?

Genitourinary disease symptoms may include a recent onset or change in vaginal discharge, odor, itching, or dyspareunia in women.

Women with the following characteristics are at greater risk of an STI:

Chlamydia Risk Factors

- Contact with a partner who is infected with an STI

  or

- New sexual partner within the last 3 months and no barrier contraception.

Chlamydia trachomatis is an important sexually transmitted pathogen. In a low prevalence population for chlamydia, patients with dysuria, frequency, and urgency probably have a UTI. In a high prevalence population, these symptoms associated with sterile pyuria may be caused by chlamydia trachomatis. Other symptoms of

	chlamydial infection may include mucopurulent discharge (mucopus from the cervical os) and cervical friability. Gross hematuria is not a symptom of chlamydia. ***Evidence supporting this recommendation is of classes: C, M, R*** **Provider Evaluation** Women with the symptoms and risk factors listed in Annotation #5, "Symptoms of or Risk for Other Genitourinary Disease," are at high risk for STIs and should receive closer evaluation. These patients should be scheduled for a provider (physician or paraprofessional) visit and should receive a pelvic exam. Finding an STI does not rule out concomitant UTI, which could be treated with short course therapy. ***Evidence supporting this recommendation is of class R*** Refer to the original guideline document for more information about the comparative effectiveness of treatment duration.
SIGN (2006)	**Management of Bacterial UTI in Adult Women** **Diagnosis** Symptoms suggestive of acute UTI are one of the most common reasons for women to visit healthcare professionals. Although the clinical encounter typically involves taking a history and performing a physical examination, the diagnostic accuracy of the clinical assessment for UTI remains uncertain. The prior probability of bacteriuria in otherwise healthy women who present to their general practitioner (GP) with symptoms of acute UTI is estimated at between 50-80%. If dysuria and frequency are both present, then the probability of UTI is increased to greater than 90% and empirical treatment with antibiotic is indicated. If vaginal discharge is present, the probability of bacteriuria falls. Alternative diagnoses such as STDs and vulvovaginitis, usually due to candida, are likely and pelvic examination is indicated. Rarer causes include local vaginal and cervical pathology including erosions and very rarely cancer. **C** - In otherwise healthy women presenting with symptoms or signs

	of UTI, empirical treatment with an antibiotic should be considered. **C** - In women with symptoms of vaginal itch or discharge, explore alternative diagnoses and consider pelvic examination. **Good Practice Point**: In patients presenting with symptoms or signs of UTI who have a history of fever or back pain the possibility of UUTI should be considered. Empirical treatment with an antibiotic should be started and urine culture performed to guide the choice of antibiotic. **Good Practice Point**: In elderly patients (over 65 years of age), diagnosis should be based on a full clinical assessment, including vital signs.
UMHS (2005)	**NGC Note**: An algorithm is provided in the original guideline document for the diagnosis and management of UTI. **Diagnosis** • **History**. Diagnosis is made primarily by history. In women with dysuria and frequency, in the absence of vaginitis, the diagnosis is UTI 80% of the time *[C]*. • **Phone triage**. In women with prior history of uncomplicated UTIs, consider phone triage *[C]*. **Summary of diagnostic approach**. The diagnostic evaluation for UTI therefore begins with an estimation of prior probability of UTI based on the patient's symptoms. From the preceding, it is clear that presence of vaginal symptoms necessitates pelvic examination; however, in the absence of vaginal symptoms, vaginitis is very uncommon and pelvic examination is unnecessary. One caveat: the physician, nurse practitioner or triage nurse should be wary of anything in the patient's history that would increase the risk for sexually transmitted infection, as this may call for pelvic examination as well. Beyond performing a pelvic examination in patients for whom it is indicated, no formal physical exam is needed, unless the patient has complaints suggestive of pyelonephritis (see that section of the original guideline document). With a number of "classic" UTI symptoms, the prior probability of UTI very likely exceeds 80% and may in fact exceed the predictive usefulness of either dipstick urinalysis or urine microscopy. Therefore, it may be appropriate to simply treat a patient with classic UTI symptoms without any diagnostic testing. **UTI in Pregnancy**

	Screening for asymptomatic bacteriuria is recommended for pregnant women at the first prenatal visit. Urine culture is an appropriate screening tool. Clean catch urine analysis is recognized as appropriate by the American College of Obstetricians and Gynecologists.
Laboratory Testing	
ICSI (2006)	**<u>Clinical Highlights</u>** If laboratory evaluation is preferred by the provider, symptomatic women without complicating factors can be appropriately evaluated by a urinalysis rather than a urine culture. *(Annotation #11)* **Urinalysis (UA)/Hold for Urine Culture (UC)/Patient Education** Instructions on collecting a clean-catch, midstream urine specimen should be given to the patient. A dipstick and microscopic urinalysis is performed and the specimen is saved for possible culture. Education should also be given to the patient regarding urinary tract infection. (Refer to Support for Implementation section, "Other Resources Available" in the original guideline document.) The laboratory should be instructed to perform a urinalysis with microscopy and hold for possible urine culture. Urine specimens that are marked "Hold for UC" should be refrigerated. The final decision about culturing should be left to the provider. **Pyuria or Dipstick Abnormal?** A growing body of literature supports the practice of presumptive treatment of UTI in women without complicating factors on the basis of symptoms alone. For clinicians more comfortable with laboratory evaluation as an aid to the diagnosis of UTI, the use of clean-catch urinalysis is recommended. A variety of criteria for positive urinalysis in acutely dysuric women is reported in the literature. While microscopy is strongly supported by the literature, a positive leukocyte esterase may also be acceptable. However, a dipstick leukocyte esterase may not be sensitive enough to detect the degree of pyuria often associated with UTI. One method for measuring pyuria, determining cells per microscopic high-power field in a centrifuged urine specimen, does not correlate well with either the leukocyte excretion rate or the hemocytometer chamber technique. However, most practices do not use a hemocytometer for measurement of white blood cells in urine; therefore, defining a level of white blood cells per high-power field (wbc/hpf) that is abnormal is a matter of sensitivity and specificity.

	There is agreement that greater than or equal to 6 wbc/hpf demonstrates a reasonable predictive value for UTI, but it is also known that UTIs can occur in symptomatic women with less than or equal to 6 wbc/hpf. The presence of pyuria on urinalysis has high sensitivity (95%) but a relatively low specificity (71%) for infection. The presence of visible bacteria on microscopical examination is less sensitive but more specific (40 to 70% and 85 to 95%, respectively, depending on number of bacteria observed). Urinary dipstick testing has largely supplanted microscopy and urine-culture analysis, because the dipstick method is cheaper, faster, and more convenient. Dipsticks are most accurate when the presence of either nitrite or leukocyte esterase is positive, yielding a sensitivity of 75% and a specificity of 82%. ***Evidence supporting this recommendation is of classes: C, R***
SIGN (2006)	**Near Patient Testing** *Urine Microscopy* There is wide variation in sensitivity (60 to 100%) of urine microscopy to predict significant bacteriuria in symptomatic and ambulatory women. Near patient testing by microscopy raises concerns about health and safety at work, maintenance of equipment and training of staff which does not justify its use. **Good Practice Point**: Urine microscopy should not be undertaken in clinical settings in primary or secondary care. *Dipstick Tests* **B** - Dipstick tests should only be used to diagnose bacteriuria in women with limited symptoms and signs *(no more than two symptoms)*. • Women with limited symptoms of UTI who have negative dipstick urinalysis *(leucocyte esterase or nitrite)* should be offered empirical antibiotic treatment. • The risks and benefits of empirical treatment should be discussed with the patient and managed accordingly. • If a woman remains symptomatic after a single course of treatment, she should be investigated for other potential causes. **Good Practice Point**: In elderly patients (over 65 years of age), diagnosis should be based on a full clinical assessment, including

	vital signs. **Diagnosis of UTI in Pregnant Women** *Near Patient Testing* **A** - Standard quantitative urine culture should be performed routinely at first antenatal visit. **A** - The presence of bacteriuria in urine should be confirmed with a second urine culture. **A** - Dipstick testing should not be used to screen for bacterial UTI at first or subsequent antenatal visits. **Good Practice Point**: Dipsticks to test only for proteinuria and the presence of glucose in the urine should be used for screening at the first and subsequent antenatal visits as a more cost-effective alternative to multi-reagent dipsticks that detect the presence of nitrite, leukocyte esterase and blood in addition to protein and glucose. **Screening During Pregnancy** **C** - Women with bacteriuria confirmed by a second urine culture should be treated and have repeat urine culture at each antenatal visit until delivery. **Good Practice Point**: Women who do not have bacteriuria in the first trimester should not have repeat urine cultures.
UMHS (2005)	**Diagnosis** • **Urinalysis**. Urinalysis for detection of pyuria by dipstick or microscope has a sensitivity of 80 to 90% and a specificity of 50% for predicting UTI *[B]*. • **No urine culture**. Urine culture is NOT indicated in the vast majority of UTIs. UC has a sensitivity of 50% (if threshold for positive is $>10^5$ organisms); sensitivity can be increased to >90% if threshold is $>10^2$ organisms *[C]*. Consider urine culture only in recurrent UTI or in the presence of complicating factors. **<u>Uncomplicated UTI</u>** <u>Summary of diagnostic approach</u>. If diagnostic testing is desired, dipstick UA (the cheapest and quickest test) should be performed first. If this confirms a high likelihood of UTI, no further testing need be done, and treatment can

	be initiated. If dipstick UA is equivocal, possible next steps would be to perform a pelvic exam, perform urine microscopy, and/or defer treatment and send urine for culture. **UTI in Pregnancy** Screening for asymptomatic bacteriuria is recommended for pregnant women at the first prenatal visit. Urine culture is an appropriate screening tool. Clean catch urine analysis is recognized as appropriate by the American College of Obstetricians and Gynecologists.
TREATMENT	
Antibiotic Treatment	

ICSI (2006)	An algorithm is provided for Uncomplicated Urinary Tract Infection in Women; clinical highlights and selected annotations (numbered to correspond with the algorithms) follow.
	
	Clinical Highlights
	
	• Patients who have classic symptoms of UTI and no complicating factors can be offered the option of phone treatment, if preferred by both provider and patient. *(Annotation #8)*
	• Symptomatic women without complicating factors can be effectively treated with the following recommended therapy: *(Annotation #9)*
	  • Trimethoprim sulfamethoxazole double strength (D.S.) 1 twice a day (BID) x 3 days
	  • Trimethoprim 100 mg 1 twice daily x 3 days
	
	If allergic to sulfa or trimethoprim:
	
	  • Nitrofurantoin (Macrobid) 100 mg twice daily x 7 days
	  • Ciprofloxacin 250 mg BID x 3 days
	
	Sulfa and ciprofloxacin may cause an increase in international normalized ratio (INR) values for patients taking warfarin.
	
	• All patients should be provided patient education about the prescribed therapy and the need to return to clinic if the symptoms do not subside. *(Annotation #9, 13)*
	
	Complicating Factors Present?
	
	History-taking is essential in differentiating uncomplicated from complicated urinary infection. Women should be screened for the presence of complicating factors when presenting or calling with

symptoms of UTI. Depending upon which complicating factor is present, short course therapy may or may not be appropriate.

Symptoms for which short course therapy with trimethoprim/sulfamethoxazole (TMP/SMX) is not appropriate:

1. Symptoms suggest pyelonephritis or other more severe infection: long duration, rigors, flank pain, or temperature greater than 101 degrees F.
2. Patient's medical history suggests likelihood of complicated urinary tract infection, or need for different investigation or therapy: diabetes, pregnancy, immunosuppression, underlying urinary tract disease or renal calculi, recent medical intervention (hospitalization or catheterization), or recurrent UTIs or failure of therapy.
3. Resident of an extended care facility

Factors for which short course therapy may be appropriate at physician discretion:

4. Potential sexually transmitted infection (STI): an infected partner, other genitourinary symptoms. The patient should be seen and STIs ruled out.
5. Younger or older patients (less than 18 or greater than 65). There is little literature documentation of efficacy of short course therapy in these age groups.
6. Recent pyelonephritis or failure of antibiotic treatment. These patients may be at higher risk of complicated infection.

Evidence supporting this recommendation is of classes: B, R

Patient/Provider Preference for Phone Treatment Without UA?

Treatment of uncomplicated UTI over the phone (using a well developed protocol) for women between the ages of 18 and 65 is a reasonable practice. Patient education should be provided over the phone, handed out at the pharmacy, or mailed to the patient, and should include the following information:

- Prescribed therapy
- Prevention techniques
- **The need to return to the clinic if symptoms do not subside**

Of note, there is currently no data to suggest that risk of pregnancy increases with concomitant use of oral contraceptives and antibiotics recommended in this guideline.

Evidence supporting this recommendation is of classes: D, R

Short Course Therapy/Patient Education

Key Points:

- Short course therapy (3-day) with TMP/SMX is as effective as 10-day therapy with TMP/SMX with fewer side effects.

Short Course Therapy

Symptomatic adult female patients with uncomplicated UTIs and a positive UA should be treated with short course therapy. After telephone screening to assess the symptomatology and presence of risk factors, short course therapy may be prescribed over the phone by a physician or via a clinic visit with a medical or paramedical provider.

The drugs recommended for short course therapy are as follows:

- Trimethoprim-sulfamethoxazole 1 twice daily x 3 days
- Trimethoprim 100 mg 1 twice daily x 3 days (Trimethoprim may have lower side effect profile than Trimethoprim sulfamethoxazole)

If allergic to Sulfa or Trimethoprim:

- Nitrofurantoin (Macrobid) 100 mg twice daily x 7 days
- Ciprofloxacin 250 mg twice daily x 3 days

Sulfa and Ciprofloxacin may cause an increase in INR values for patients taking warfarin.

Provider Evaluation

Symptomatic women with a negative urinalysis should receive further evaluation as clinically indicated.

Within the population there may be some patients who do not appear to have a UTI by laboratory tests who will nonetheless respond to a trial of antibiotics. In addition, there may be patients who are well known to providers and who are known to be accurate historians who may not be able to come in for laboratory testing. In both cases, it may be reasonable to treat based on history without laboratory support.

Short Course Therapy/Phone Contact or Clinic Visit with a Medical Provider

	Patients should be encouraged to contact provider if symptoms have not resolved. Patients and providers should also understand that treatment with nitrofurantoin may take longer than treatment with TMP. ***Evidence supporting this recommendation is of classes: A, C***
SIGN (2006)	**Antibiotic Treatment** *Symptomatic Bacteriuria, LUTI* **A** - Non-pregnant women with symptoms or signs of acute LUTI, and either high probability of or proven bacteriuria, should be treated with antibiotics. Three to six days of antibiotic treatment for uncomplicated LUTI in women aged 60 or over is as effective as treatment for 7 to 14 days. Guidelines from the Infectious Diseases Society of America (IDSA) and Health Protection Agency (HPA) recommend three days treatment with trimethoprim for LUTI. There is more direct evidence for three days treatment with co-trimoxazole but it is reasonable to infer that trimethoprim is equally effective as co-trimoxazole. Three days of treatment with nitrofurantoin has been shown to be effective in non-pregnant adult women with uncomplicated UTI. The IDSA recommends seven days treatment with nitrofurantoin. There is no direct evidence comparing three days nitrofurantoin with seven days nitrofurantoin. **B** - Non-pregnant women of any age with symptoms or signs of acute LUTI should be treated with trimethoprim or nitrofurantoin for three days. **Good Practice Point**: Women with renal impairment should not be treated with nitrofurantoin as: • An effective concentration of antibiotic in the urine is not achievable • A toxic concentration of antibiotic can occur in the plasma **D** - Women with LUTI, who are prescribed nitrofurantoin, should be advised not to take alkalinising agents (such as potassium citrate). Resistance is increasing to all of the antibiotics used to treat UTI and there is no clear first choice alternative to trimethoprim or nitrofurantoin. **B** - Patients who do not respond to trimethoprim or nitrofurantoin

should have urine taken for culture to guide change of antibiotic.

Good Practice Point: Quinolones should not be used for empirical treatment of LUTI.

Telephone Consultation

Although telephone consultation and antibiotic prescribing by nurse practitioners could be a cost-effective alternative to a general practitioner visit it goes against one of four key recommendations made to primary care by the Department of Health, Standing Medical Advisory Committee, which was to "limit antibiotic prescribing over the telephone". The available evidence also raises serious questions about the safety of telephone consultations for excluding STDs. Telephone consultation cannot be recommended as an alternative to a standard consultation.

Management of Bacterial UTI in Pregnant Women

Symptomatic Bacteriuria

B - Pregnant women with symptomatic UTI should be treated with an antibiotic.

Good Practice Points:

A single urine sample should be taken for culture before empiric antibiotic treatment is started.

Refer to local guidance for the safest, cheapest, effective antibiotic for pregnant women.

Given some antibiotics are toxic in pregnancy, refer to the British National Formulary (BNF) for contraindications.

Given the risks of symptomatic bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure.

Asymptomatic Bacteriuria

A - Asymptomatic bacteriuria detected during pregnancy should be treated with an antibiotic.

Good Practice Point: Refer to local guidance for the safest, cheapest, effective antibiotic for pregnant women.

Screening During Pregnancy

	C - Women with bacteriuria confirmed by a second urine culture should be treated and have repeat urine culture at each antenatal visit until delivery.

UMHS (2005)	**NGC Note:** An algorithm is provided in the original guideline document for the diagnosis and management of UTI.
	
	Treatment
	
	• **First line**: three days of trimethoprim/sulfa *[A]*.
	• **Second line**:
	  • three days of quinolone (contraindicated in pregnancy) *[A]*.
	  • seven days of nitrofurantoin, amoxicillin, first-generation cephalosporin *[A]*.
	
	Recurrent UTI's
	
	Treatment. Most women with recurrent UTI's respond to recommended antibiotics regimens (see Table 3 in the original guideline document). Persistent bacteriuria or early clinical reoccurrence should raise the possibility of relapse. These patients can be identified by early positive post therapy cultures with sensitivities showing "sensitive" to the agent used to treat them. Patients with documented relapse should be treated with prolonged courses of antibiotics (2 to 6 weeks) with follow-up urine cultures to document sterility. Consideration should then be made for prophylactic therapy. One should also have a somewhat lower threshold for urologic structural evaluation.
	
	The vast majority of women with uncomplicated recurrent UTI's experience reinfection. They will respond clinically and bacteriologically to three day courses of antibiotic therapy. These women rarely have any urologic structural abnormality causing the recurrent reinfections, and structural evaluation is therefore not indicated. Patients should be counseled about risk factors for UTI's (diaphragm use, spermicide use, atrophic vaginitis in postmenopausal women, not emptying the bladder after intercourse). Post therapy urine cultures should occasionally be checked in women with recurrent UTI's to differentiate relapse from reinfection, but in general are not necessary. In women with recurrent UTI's due to reinfection prophylactic or self-initiated therapy should be considered.
	
	Prophylaxis of Recurrent UTIs
	
	Prophylactic antibiotic use, either daily or used only postcoitally, has been shown to reduce frequency of UTI in sexually active women. The benefits accrue only during active prophylaxis. Once antibiotics are discontinued, UTIs occur at the same rate as in placebo-treated

	sexually active women. Adverse events from antibiotic use are generally mild, although women vary in their evaluation of the impact of various side effects (i.e., oral or vaginal candidiasis may be seen as a severe side effect by some, mild by others.) Commonly used prophylactic antibiotics include cotrimoxazole, nitrofurantoin, cephalexin, or a quinolone. Nitrofurantoin appears to have the highest withdrawal rate, followed by cephalexin. It appears that post-coital prophylaxis is as effective as daily intake. Quinolones should be avoided, given concerns about antibiotic resistance, as well as higher cost. When used, they may be considered for weekly dosing. They are contra-indicated in pregnancy. **UTI in Pregnancy** Treatment of asymptomatic bacteria can be accomplished with a variety of FDA category B drugs, including amoxicillin, cephalosporins, nitrofurantoin and trimethoprim/sulfa. Quinolones should generally not be used during pregnancy (FDA category C). A seven-day course is recommended with follow-up urine cultures to document sterile urine. Persistent bacteriuria requires retreatment guided by sensitivities and then consideration of suppressive therapy, usually with nitrofurantoin. Symptomatic cystitis in pregnancy, although rare, should be treated and followed-up similarly to asymptomatic bacteria.
Other Treatment	
ICSI (2006)	No recommendations offered
SIGN (2006)	**Non-Antibiotic Treatment** *Cranberry Products* **A** - Women with recurrent UTI should be advised to take cranberry products to reduce the frequency of recurrence. **Good Practice Point**: Women should be advised that cranberry capsules may be more convenient than juice and that high strength capsules may be most effective. There is no evidence to support the effectiveness of cranberry products for treating symptomatic episodes of UTI. **D** - Patients taking warfarin should avoid taking cranberry products unless the health benefits are considered to outweigh any risks.

	Good Practice Point: Increased medical supervision and INR monitoring should be considered for any patient taking warfarin with a regular intake of cranberry products. **Good Practice Point**: Women with recurrent UTI should be advised that cranberry products are not available on the National Health Service (NHS) but are readily available from pharmacies, health food shops, herbalists and supermarkets. *Methenamine Hippurate* **B** - Methenamine hippurate may be used to prevent symptomatic UTI in patients without known upper renal tract abnormalities. *Oestrogen* **A** - Oestrogens are not recommended for routine prevention of recurrent UTI in postmenopausal women. Treatment with oestrogens may be appropriate for some women. *Analgesia* **Good Practice Point:** Women with uncomplicated UTIs may wish to use over the counter remedies to try and relieve symptoms.
UMHS (2005)	**For recurrent UTIs**. In patients with recurrent UTIs (>3/year): • consider prophylaxis/self-initiated therapy *[A]* • urologic structural evaluation rarely indicated *[D]* **Prophylaxis of Recurrent UTIs** In regards to the use of other prophylactic measures, some studies have shown that cranberry juice or cranberry tablets can significantly reduce the annual incidence of UTIs in sexually active women with a history of recurrent UTIs. [A]. The best dose is unknown, but one trial suggests that tablets are equally as effective as juice, and cost less. No trials that suggest cranberry in any form is useful in the treatment of UTI. Only poor data are available regarding the use of vaginal estradiol for UTI prophylaxis in postmenopausal women.
FOLLOW-UP AND REFERRAL	
ICSI (2006)	**Short Course Therapy/Phone Contact or Clinic Visit With a Medical Provider**

	Patients should be encouraged to contact provider if symptoms have not resolved. Patients and providers should also understand that treatment with nitrofurantoin may take longer than treatment with TMP.
SIGN (2006)	**Near Patient Testing** **B**- If a woman remains symptomatic after a single course of treatment, she should be investigated for other potential causes. **Antibiotic Treatment** **B** - Patients who do not respond to trimethoprim or nitrofurantoin should have urine taken for culture to guide change of antibiotic. **Referral** Recurrent UTI is a common reason for referral of women to urologists but no evidence was found describing criteria for referral or about which investigations to undertake. There is good evidence to support prevention of recurrent bacterial UTI in women with antibiotics and cranberry products. These strategies should be explored before referral for specialist investigation.

UMHS (2005)	**Follow-up**
	
	• **No tests if asymptomatic**. No laboratory follow-up is necessary if asymptomatic *[B]*.
	• **For recurrent UTIs**. In patients with recurrent UTIs (>3/year):
	  • Consider prophylaxis/self-initiated therapy *[A]*
	  • Urologic structural evaluation rarely indicated *[D]*
	
	Follow up urinalysis and urine culture and sensitivity (UAC & S) should be considered in women with recurrent UTIs or complicating factors.

EDUCATION	
ICSI (2006)	**Urinalysis (UA)/Hold for Urine Culture (UC)/Patient Education** Instructions on collecting a clean-catch, midstream urine specimen should be given to the patient. A dipstick and microscopic urinalysis is performed and the specimen is saved for possible culture. Education should also be given to the patient regarding urinary tract infection. (Refer to Support for Implementation section, "Other

	Resources Available" in the original guideline document.) **<u>Clinical Highlights</u>** All patients should be provided patient education about the prescribed therapy and the need to return to clinic if the symptoms do not subside. *(Annotation #9, 13)* **Patient/Provider Preference for Phone Treatment Without UA?** Treatment of uncomplicated UTI over the phone (using a well developed protocol) for women between the ages of 18 and 65 is a reasonable practice. Patient education should be provided over the phone, handed out at the pharmacy, or mailed to the patient, and should include the following information: • Prescribed therapy • Prevention techniques • **The need to return to the clinic if symptoms do not subside**
SIGN (2006)	**General Advice** Healthcare professionals should offer: • Information on cranberries. Patients should be advised that further research is required to determine the best way to take cranberries, for example, juice, tablets, or a combination; in what concentration; routinely or preventatively; and how often. • Advice on "complicated" versus "uncomplicated" infections. The distinction between a 3-day versus a 7-day course of pills and the reasons for using one or the other should also be explained to the patient. These issues could affect concordance. • Contraception advice. This and the role of sexual activity is a critical issue for women, and one which may affect concordance. This issue should be explicitly dealt with by healthcare professionals prescribing and dispensing treatment. • A reminder to patients and carers that the presence of bacteriuria does not always indicate disease. Especially in elderly patients, asymptomatic bacteriuria is a normal condition and should not be treated with antibiotics.
UMHS (2005)	**Information the Patient Needs to Know** • **Cause.** UTI are caused by bacteria and require antibiotic treatment. • **Complete treatment.** Antibiotic must be taken for the full

	prescribed duration, even if symptoms disappear. • **Fluids.** You should drink at least 8 glasses of fluids per day to help flush the urinary system. • **Possible side effects of treatment.** Side effects of antibiotics include rash, nausea, diarrhea, and vaginitis. If your doctor prescribes a urinary analgesic, phenazopyridine (Pyridium), to help with pain, it may turn your urine an orange color. • **Call for early follow-up.** Symptoms that require early follow-up included: persistent fever or discomfort persisting greater than 72 hours after starting therapy, inability to take antibiotic due to nausea or vomiting, development of any new symptoms. • **Call if symptoms return.** If your symptoms of urinary tract infection return after completing your antibiotic, you should contact your physician.

SELECTED SUPPORTING REFERENCES **Note from NGC: Bolded references are cited in more than one guideline. Refer to the original guideline documents for a complete listing of supporting references.**	
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TABLE 5: BENEFITS AND HARMS	
Benefits	
ICSI (2006)	• Symptom relief • Accurate diagnosis of UTI • Appropriate antibiotic use • Decreased use of urine culture as a guide in therapy of uncomplicated UTI
SIGN (2006)	• Relief of symptoms from UTI • Prevention of adverse treatments effects • Prevention of UTI recurrence • Prevention of symptom development in asymptomatic UTI patients

UMHS (2005)	• Clinical care resources are utilized appropriately and good clinical outcomes are obtained when a cost-effective strategy is used for the diagnosis and treatment of uncomplicated urinary tract infection.
	• A review of 28 treatment trials of adult women with uncomplicated cystitis concluded that no benefit was achieved by increasing the length of therapy beyond 5 days. Specific benefits of shorter course (<5 days) antibiotic therapy include:
	  • Decreased costs of antibiotics
	  • Improved patient compliance
	  • Decreased adverse effects of antibiotic treatments (e.g., amoxicillin-associated vaginitis)
	• A recent study in Seattle examined a phone triage guideline. Use of the guideline decreased cost and increased appropriate antibiotic use without any increase in adverse outcomes.

HARMS	
ICSI (2006)	• Sulfa and ciprofloxacin may cause an increase in international normalized ratio (INR) values for patients taking warfarin. • Increasing resistance to trimethoprim-sulfa is a growing concern and is being monitored closely. • Alarming increases in quinolone resistance are emerging internationally, which underscores the need to reserve ciprofloxacin

	for serious infection.
SIGN (2006)	Adverse effects of antibiotic treatment
UMHS (2005)	• Side effects of antibiotic treatment include rash, nausea, diarrhea, and vaginitis. Adverse effects associated with the use of trimethoprim/sulfamethoxazole (TMP/SMX) increase markedly if treatment is continued past 3 days. • Flouoroquinolones increase the risk of tendon rupture in those over age 60, in kidney, heart, and lung transplant recipients, and with concomitant steroid therapy.

TABLE 6: EVIDENCE RATING SCHEMES AND REFERENCES	
ICSI (2006)	**Classes of Research Reports:** A. Primary Reports of New Data Collection: Class A: • Randomized, controlled trial Class B: • Cohort study Class C: • Nonrandomized trial with concurrent or historical controls • Case-control study • Study of sensitivity and specificity of a diagnostic test • Population-based descriptive study Class D: • Cross-sectional study • Case series • Case reports B. Reports that Synthesize or Reflect upon Collections of Primary

	Reports Class M: • Meta-analysis • Systematic review • Decision analysis • Cost-effectiveness analysis Class R: • Consensus statement • Consensus report • Narrative review Class X: • Medical opinion
SIGN (2006)	**Description of Levels of Evidence** **Levels of Evidence** **1++**: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias **1+**: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias **1-**: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias **2++**: High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal **2+**: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal **2-**: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal **3**: Non-analytic studies (e.g. case reports, case series)

	4: Expert opinion **Grades of Recommendation** Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation. **A**: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; *or* A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results **B**: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1++ or 1+ **C**: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2++ **D**: Evidence level 3 or 4; *or* Extrapolated evidence from studies rated as 2+ **Good Practice Points**: Recommended best practice based on the clinical experience of the guideline development group
UMHS (2005)	**Rating Scheme for the Strength of the Evidence** Levels of evidence for the most significant recommendations: A. Randomized controlled trials B. Controlled trials, no randomization C. Observational trials D. Opinion of expert panel

GUIDELINE CONTENT COMPARISON

The Institute for Clinical Systems Improvement (ICSI), Scottish Intercollegiate Guidelines Network (SIGN), and University of Michigan Health System (UMHS) present recommendations for the diagnosis and treatment of uncomplicated lower UTIs and provide explicit reasoning behind their judgments.

Diagnosis and Treatment of Uncomplicated Lower Urinary Tract Infection: Comparison of ICSI, SIGN and UMHS Recommendations	
ICSI (2006)	*Diagnosis*: Based on history. If laboratory testing performed, dipstick analysis is preferred to urine microscopy or culture. *First-line Treatment*: Trimethoprim/sulfamethoxazole double-strength BID x 3 days or trimethoprim 100 mg BID x 3 days. *Second-line Treatment*: Nitrofurantoin 100 mg BID x 7 days or ciprofloxacin 250 mg BID x 3 days.
SIGN (2006)	*Diagnosis*: Based on history. If laboratory testing performed, dipstick analysis is preferred, but perform only for women with limited signs and symptoms. *First-line Treatment*: Trimethoprim or nitrofurantoin x 3 days. *Second-line Treatment*: There is no clear first-choice alternative to trimethoprim or nitrofurantoin. For patients who don't respond to these, a change in antibiotic should be based on urine culture for sensitivities.
UMHS (2005)	*Diagnosis*: Based on history. If laboratory testing performed, dipstick analysis is preferred to urine microscopy or culture. *First-line Treatment*: Trimethoprim/sulfamethoxazole double-strength BID x 3 days. *Second-line Treatment*: Quinolone x 3 days or nitrofurantoin, amoxicillin or cephalosporin x 7 days.

Guideline Methodology

All three organizations performed a systematic review of the literature which included applying quality criteria to published studies to select those suitable for evidence review and guideline formulation. All three organizations also graded or classified the included studies as a means of assessing the strength of the

evidence. The guidelines all relied on expert consensus to formulate recommendations based on the literature review and the assigned evidence grades. In its guideline, ICSI provides the classes of research reports that support each recommendation, along with reference citations. This guideline also provides a table summarizing findings of studies of the effectiveness of antibiotic treatment durations. SIGN provides an evidence grade for each recommendation based on a ranking of the type and quality of evidence. SIGN also reviews the evidence in narrative form and provides specific citations. A SIGN companion document discusses number needed to treat and number needed to screen for UTI. The UMHS guideline provides the classes of research reports that support each recommendation and discusses the evidence in narrative form, but does not cite references. However, an annotated reference list is provided at the end of the document. All three guidelines include one or more flow-chart algorithms to guide diagnosis and treatment of lower urinary tract infections.

Areas of Agreement

Diagnosis

The three guidelines are in general agreement concerning the diagnosis of UTI, with minor differences. SIGN states that although the clinical encounter typically involves taking a history and performing a physical examination, the diagnostic accuracy of the clinical assessment for UTI remains uncertain; UMHS states that no formal physical exam is needed unless a pelvic exam is indicated or the patient has signs and symptoms suggestive of pyelonephritis. All the guidelines indicate the need to assess for complicating factors, such as back pain or fever indicative of pyelonephritis, and signs of sexually transmitted disease (STD), such as vaginal itch or discharge. ICSI and UMHS list complicating factors and medical conditions that increase the risk for pyelonephritis or infection with resistant organisms, including diabetes, immunosuppression, and recent hospitalization or catheterization. The guidelines agree it may be appropriate to treat uncomplicated UTI empirically on the basis of symptoms alone, but all three groups also provide diagnostic testing recommendations for cases when laboratory evaluation is preferred by the provider. SIGN states that although tests that suggest or prove the presence of bacteria or white cells in the urine may contribute additional information to inform management, they rarely have important implications for diagnosis.

Laboratory Tests

When testing is undertaken, urinalysis by dipstick or microscopy is preferred over urine culture by all three guidelines, and dipstick urinalysis is preferred to microscopy. According to ICSI, urinary dipstick testing has largely supplanted microscopy and urine-culture analysis, because the dipstick method is cheaper, faster, and more convenient. UMHS concludes that if diagnostic testing is desired, dipstick UA (the cheapest and quickest test) should be performed first. If this confirms a high likelihood of UTI, no further testing need be done, and treatment can be initiated. If dipstick UA is equivocal, possible next steps would be to perform a pelvic exam, perform urine microscopy, and/or defer treatment and send urine for culture. SIGN provides recommendations similar to ICSI and UMHS, stating that urine microscopy note be undertaken in clinical settings in primary or secondary care. They provide recommendations for dipstick testing, noting that it

should be used as a diagnostic test in women with only limited signs and symptoms. According to UMHS, none of the available tests are ideal screening tools.

Antibiotic Treatment

Concerning first-line therapy, the guidelines agree that short course therapy (3-6 days) with antibiotics is as effective as longer therapy and has fewer side effects. ICSI and UMHS recommend trimethoprim/sulfamethoxazole twice daily for 3 days. ICSI also recommends trimethoprim alone twice daily for 3 days. SIGN recommends either trimethoprim or nitrofurantoin for 3 days. In contrast to SIGN, both ICSI and UMHS recommend a longer course of 7 days when nitrofurantoin is used. Although SIGN notes that the Infectious Diseases Society of America (IDSA) recommends 7 days of treatment with nitrofurantoin, it states there is no direct evidence comparing 3-day therapy with 7-day therapy. In support of its recommendation for 3-day nitrofurantoin therapy, SIGN cites a study by Christiaens et al (2002) that showed 3-day nitrofurantoin therapy was effective in non-pregnant women with uncomplicated UTI. ICSI points out that two studies have demonstrated high effectiveness with 7 days of nitrofurantoin, but that 3-day treatment appears to be less effective than trimethoprim-sulfamethoxazole.

According to UMHS, single-dose regimens are less efficient at eradicating bacteriuria than are 3 to 5 day regimens, but there is no benefit to increasing therapy duration beyond 3 days with either trimethoprim/sulfamethoxazole or trimethoprim. The increasing bacterial resistance to trimethoprim-sulfa and other antibiotics is discussed by all three guidelines.

Other Treatment

SIGN and UMHS recommend cranberry products for prophylaxis of recurrent UTI; SIGN also recommends methenamine hippurate. ICSI does not address non-antibiotic therapies.

UTI in Pregnancy

SIGN and UMHS agree that pregnant women should be screened with urine culture at the first prenatal visit. SIGN further specifies that a positive culture should be confirmed with a second culture. Both guidelines agree that asymptomatic bacteriuria should be treated with an antibiotic. SIGN does not specify the antibiotic to use; UMHS recommends a variety of FDA category B drugs. SIGN also recommends treatment of symptomatic bacteriuria in pregnant women with antibiotics (unspecified), whereas UMHS does not address this topic. However, for symptomatic cystitis in pregnancy, UMHS recommends follow-up similar to that for asymptomatic bacteriuria.

Areas of Disagreement

Antibiotics

As mentioned above, SIGN recommends 3 days of nitrofurantoin therapy, whereas UMHS and ICSI both recommend 7 days.

Treatment via Telephone

According to ICSI, treatment of uncomplicated UTI over the phone is a reasonable approach for women age 18 to 65, as long as a well-developed protocol is used. UMHS agrees, stating that most UTIs in women are uncomplicated and will resolve with a short course of antibiotics. According to this guideline, many women can be assessed and safely managed without the need for an office visit or laboratory test. UMHS also points out that one study found telephone triage and management lowered costs, increased the appropriate use of antibiotics, and did not lead to an increase in adverse outcomes (Saint et al., Am J Med 1999;106:636-641). SIGN, on the other hand, explicitly recommends against telephone management, stating that it cannot be recommended as an alternative to standard consultation. SIGN's conclusion is based in part on the same study by Saint et al cited by UMHS, which showed an increase in return visits for STDs after nurse telephone consultation. SIGN's other reason for recommending against telephone consultation is that a Department of Health advisory recommends limiting antibiotic prescribing over the telephone.

Conclusion

There is general agreement between the guidelines that available laboratory tests for UTI are of uncertain validity, but that when laboratory evaluation is preferred by the physician, that dipstick urinalysis is the cheapest and fastest method. There is also agreement that uncomplicated UTI can be treated empirically. First-line therapeutic options include trimethoprim, either alone or in combination with sulfamethoxazole, and nitrofurantoin. The SIGN guideline differs from ICSI and UMHS in recommending 3 days of treatment when nitrofurantoin is used; ICSI and UMHS recommend 7 days. SIGN also differs from both ICSI and UMHS regarding the appropriateness of telephone triage/treatment. While ICSI and UMHS find this approach to be effective and safe, SIGN recommends against it.

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