Urinary Tract Infections in Older Women:

A Clinical Review

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Abstract

IMPORTANCE—Asymptomatic bacteriuria and symptomatic urinary tract infections (UTIs) in older women are commonly encountered in outpatient practice.

OBJECTIVE—To review management of asymptomatic bacteriuria and symptomatic UTI and review prevention of recurrent UTIs in older community-dwelling women.

EVIDENCE REVIEW—A search of Ovid (Medline, PsycINFO, Embase) for English-language human studies conducted among adults aged 65 years and older and published in peer-reviewed journals from 1946 to November 20, 2013.

RESULTS—The clinical spectrum of UTIs ranges from asymptomatic bacteriuria, to symptomatic and recurrent UTIs, to sepsis associated with UTI requiring hospitalization. Recent evidence helps differentiate asymptomatic bacteriuria from symptomatic UTI. Asymptomatic bacteriuria is transient in older women, often resolves without any treatment, and is not associated with morbidity or mortality. The diagnosis of symptomatic UTI is made when a patient has both clinical features and laboratory evidence of a urinary infection. Absent other causes, patients presenting with any 2 of the following meet the clinical diagnostic criteria for symptomatic UTI: fever, worsened urinary urgency or frequency, acute dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness. A positive urine culture (10^5 CFU/mL) with no more

than 2 uropathogens and pyuria confirms the diagnosis of UTI. Risk factors for recurrent symptomatic UTI include diabetes, functional disability, recent sexual intercourse, prior history of urogynecologic surgery, urinary retention, and urinary incontinence. Testing for UTI is easily performed in the clinic using dipstick tests. When there is a low pretest probability of UTI, a negative dipstick result for leukocyte esterase and nitrites excludes infection. Antibiotics are selected by identifying the uropathogen, knowing local resistance rates, and considering adverse effect profiles. Chronic suppressive antibiotics for 6 to 12 months and vaginal estrogen therapy effectively reduce symptomatic UTI episodes and should be considered in patients with recurrent UTIs.

CONCLUSIONS AND RELEVANCE—Establishing a diagnosis of symptomatic UTI in older women requires careful clinical evaluation with possible laboratory assessment using urinalysis and urine culture. Asymptomatic bacteriuria should be differentiated from symptomatic UTI. Asymptomatic bacteriuria in older women should not be treated.

The Patient's Story

Mrs M is 91 years old and lives in a retirement community with her male partner. Her medical problems include coronary artery disease, hyperlipidemia, hypertension, diabetes mellitus, cerebrovascular disease, and hypothyroidism. She recently visited Dr N, her primary care physician for many years, for worsening chronic urinary frequency and incontinence. Mrs M began having urinary tract infections (UTIs) in her college years and for the past several years, urinary incontinence. Currently, she has urinary frequency (every 2–3 hours) and nocturia (awakening her as often as every 2 hours). In 2008, Mrs M was instructed by her primary care physician to limit fluid intake at dinner to 1 cup, and then drink only enough water to take her nighttime medications. During the past few months, Mrs M noted an increase in her urinary frequency and incontinence. Recently, she started wearing adult diapers every day. Mrs M is sexually active. Dysuria or hematuria are not present. She has felt more "spacey" and unsteady but does not have dizziness or lightheadedness. She does not have syncopal symptoms and has not fallen. Drug treatment of an overactive bladder with oxybutynin and tolterodine was not effective and she experienced only transient improvement with desipramine and solifenacin. All these agents were stopped. Six times in the past year, Mrs M's urine cultures were positive for more than 10^5 colony-forming units (CFU)/mL of *Escherichia coli* (*E coli*). Worsening incontinence resulted in Mrs M's treating physicians obtaining urine cultures. She has received multiple courses of antibiotics but states that the antibiotics don't make her incontinence or spaciness any better.

Overview of UTI

UTI is the most common bacterial infection, accounting for more than 8 million office visits and 1 million emergency department visits each year in the United States, eventually resulting in approximately 100 000 hospitalizations.[1,2] The overall number of office visits for UTIs are twice as common among women of all ages compared with men.[1]

UTI is broadly defined as an infection of the urinary system and may involve the lower urinary tract or the lower and upper urinary tracts combined.[3] The spectrum of urinary

conditions ranges from asymptomatic bacteriuria, to symptomatic UTI, to sepsis associated with UTI requiring hospitalization (Table 1).[8] Asymptomatic bacteriuria in women is defined as presence of at least 10^5 CFU/mL of the same uropathogen in 2 consecutive clean-catch midstream urine samples obtained from patients without any symptoms or signs attributable to urinary infection. Asymptomatic bacteriuria is a colonization state and does not indicate an infection that requires treatment.[4,5,9] Establishing a diagnosis of symptomatic UTI requires a patient to have symptoms and signs of a UTI and laboratory tests confirming the diagnosis (bacteriuria 10^5 CFU/mL and pyuria 10 white blood cells/high-powered field). Uncomplicated symptomatic UTI is present when there is a symptomatic bladder infection manifested by fever, worsened urinary urgency or frequency, dysuria, suprapubic tenderness, costovertebral angle pain or tenderness with no recognized cause, and laboratory tests revealing UTI. Fever is usually not present in symptomatic UTI localized to the bladder. Complicated UTI is defined as having a symptomatic UTI in patients caused by a functional or structural abnormality; having had urinary instrumentation; having systemic diseases such as renal insufficiency, diabetes, or immunodeficiency; or having undergone organ transplantation.[6,7,10,11] Pyuria is the presence of leukocytes in the urine. However, when superimposed with high prevalence of chronic genitourinary symptoms, increasing cognitive impairment, and a high comorbidity load with advancing age, diagnosis and management of a symptomatic UTI remains a challenge.

Mrs M has several risk factors for symptomatic UTI including being postmenopausal,[12–14] having urinary incontinence,[12,15,16] having prior history of symptomatic UTI,[12–14] and being sexually active.[17,18] Some evidence suggests that recurrent UTIs could have a genetic component[19–21] (Table 2).[12–23] Diabetes is also considered an important risk factor for recurrent UTIs in women.[22,23] Recurrent UTIs with the same or different uropathogens are common in outpatient settings, leading to repeated outpatient visits and increased therapeutic or prophylactic antibiotic use, anxiety, and low morale.[24,25] Mrs M does not meet the criteria for symptomatic UTI since her only symptom is worsening urinary frequency without other UTI-specific symptoms. She likely has worsening of chronic urinary incontinence because of continued diuretic use or as a natural progression of her incontinence. Antibiotics did not improve Mrs M's incontinence, also suggesting that her UTI should not be categorized as symptomatic.

The Evidence: Diagnosis, Management, and Prevention

We searched Ovid (MEDLINE, PsycINFO, EMBASE) for English-language human studies conducted among adults aged 65 years and older and published in peer-reviewed journals from 1946 to November 20, 2013. We focused on community-dwelling older adults. Search terms included *UTI*, *asymptomatic bacteriuria*, *risk factors and UTI*, *community-onset UTI*, *functional decline and UTI*, *delirium and UTI*, *dehydration and UTI*, *diagnosis and UTI, diet and drug therapy and UTI, prevention and UTI*, and *urine tests and UTI.* We also searched for recently published Cochrane reviews regarding treatment and prevention of UTI in community-dwelling older adults. The recommendations that follow are based on evaluation of the existing evidence.

Presentation and Diagnosis of Asymptomatic Bacteriuria and Symptomatic UTI in Older Adults

> Dr N: *Do you feel ill from the bladder infection that you can tell?*
>
> Mrs M: *Just in my head. … I don't have any of the accompanying symptoms. There's no odor, there's no burning or anything like that. But for the past at least half-dozen years, it just has been there, that's all. Every time they took a test, there was a very small amount of E coli. Whatever that means.*
>
> Dr N: *For me, it's just so challenging. We're taught in medical school that you don't treat asymptomatic bacteriuria in people. It doesn't help them. The problem when people have chronic urinary symptoms is that we are trying to determine if this is now a symptomatic bacterial infection and how do I figure out what is a UTI sign or symptom in somebody who has these chronic voiding problems to begin with. So, that's always been the tricky part. She has been hospitalized a couple of times for UTIs. She basically presented with dizziness, had trouble walking, confusion, and low blood pressure. She was admitted and found to have a UTI based on urine cultures. She was treated with antibiotics [and] intravenous fluids and got better.*

Asymptomatic bacteriuria is common and its incidence increases with age. The incidence of asymptomatic bacteriuria increases from 3.5% in the general population to 16% to 18% in women older than aged 70 years and some longitudinal studies report that it affects 50% of older women.[4,5] Asymptomatic bacteriuria is generally benign in this population. Older adults with or without bacteriuria will often have specific genitourinary symptoms including worsening urgency, incontinence, and dysuria, and nonspecific symptoms such as anorexia, fatigue, malaise, and weakness—as reported with Mrs M's experience. In one longitudinal prospective series of ambulatory older adults, patterns of bacteriuria observed in urine samples obtained at 6-month intervals[5] revealed more than 30% of patients had spontaneously resolving bacteriuria and another 30% who initially did not have bacteriuria subsequently developed it (Table 3). Chronically incontinent and disabled older adults may have a prevalence of pyuria (10 white blood cells) of 45% and bacteriuria (10^5 CFU/mL) of 43%.[26] Women with asymptomatic bacteriuria with pyuria fulfill the laboratory criterion for symptomatic UTI but do not have symptomatic UTI because they lack the signs and symptoms for UTI. As with Mrs M's experience, chronic urinary incontinence can make it difficult to differentiate asymptomatic bacteriuria (which is benign) from symptomatic UTI (which has the potential to evoke urosepsis or pyelonephritis). Hematuria without bacteriuria and pyuria may be unrelated to infection. In recognizing the greater prevalence of genitourinary symptoms in older adults, most studies evaluating symptomatic UTI in older women require both signs and symptoms of UTI (2 genitourinary signs and symptoms) and laboratory confirmation of UTI (bacteriuria and pyuria) to establish a diagnosis of UTI in the elderly patient (Table 2).

Fluctuations in urinary urgency and incontinence occur in older women such as Mrs M even without a urinary infection. Chronic dysuria is also prevalent and can get worse with age (Table 4). Several recent studies provide guidance for differentiating asymptomatic bacteriuria from symptomatic UTI by defining the effectiveness of clinical features of UTI

with subsequent laboratory evidence of UTI. In frail older adults who are institutionalized, there was significant association between laboratory-confirmed UTI and acute dysuria (relative risk [RR], 1.58; 95% CI, 1.10–2.03), change in character of urine (RR, 1.42; 95% CI, 1.07–1.79), and change in mental status (RR, 1.38; 95% CI, 1.03–1.74).[34] Of these clinical features, acute dysuria (<1 week in duration) most effectively predicted laboratory confirmation of UTI. An epidemiologic study from Spain involving 343 women aged 14 to 90 years showed that pretest probability of having a UTI among patients with new urinary symptoms was 0.48; positive likelihood ratio (LR) for new dysuria was 1.31 (95% CI, 1.12–1.54), new urgency 1.29 (95% CI, 1.12–1.50), and new urinary frequency 1.16 (95% CI, 1.06–1.28).[35] This study reinforces the notion that new dysuria is the most discriminating clinical finding for symptomatic UTI. When evaluating new dysuria, timing, severity, and location are important. Worsening urinary frequency or urgency occurs both in UTI and urinary incontinence. Consequently, these symptoms are not reliable indictors for UTI. In contrast, new dysuria is specific for symptomatic UTI and, if present, indicates a need for further diagnostic evaluation.

Establishing a diagnosis of symptomatic UTI in an older women like Mrs M who have a high prevalence of asymptomatic bacteriuria and progressively worsening urinary incontinence requires assessment for new presenting signs and symptoms of genitourinary tract disease and consideration of other diagnoses. There is no clear answer how urgent this evaluation is. Although UTI can be a serious problem, several randomized controlled trials found that 25% to 50% of women presenting with UTI symptoms will have recovered in 1 week without using antibiotics.[36,37] Spontaneous symptom improvement occurs in 50% of community-dwelling noncatheterized women who delay antibiotic treatment (Table 3).[29] Thus, delaying antibiotic treatment while evaluating a symptomatic UTI generally does not lead to adverse outcomes. Symptoms such as dizziness and confusion alone should not be attributed to UTI. In clinical scenarios similar to Mrs M's, it is likely that hydration was received during hospitalization, in addition to antibiotic therapy, and it is equally likely that restoration of hydration status resulted in clinical improvement. Women with urinary urgency are often told to restrict fluid intake, leading to dehydration.[30] Hence when the diagnosis of symptomatic UTI is in doubt, delaying antibiotic treatment while conducting further evaluation, but offering supportive treatment such as increased fluid intake, should be considered (Table 3).[29]

Role of Urinary Testing in Diagnosing Symptomatic UTIs in Older Adults

The utility of urinary dipstick testing, urinalysis, and urine culture is challenging in the older adult because of the high prevalence of bacteriuria and pyuria that may not be clinically important. As in the case of Mrs M, all urinary studies to evaluate for leukocyte esterase, nitrites, pyuria, and bacteriuria over a 2-year period were positive.

The urinary dipstick, although easy and convenient, has variable test characteristics.[38] Sensitivity and specificity for urinary dipstick testing to evaluate for leukocyte esterase, nitrites, or both vary in older adults by the age of study participants, clinical suspicion of UTI, and laboratory definition for UTI used (ie, bacteriuria alone, level of bacteriuria [>10^2–10^5 CFU/mL], or bacteriuria plus pyuria). The sensitivity and specificity for a positive

dipstick test in older patients with was 82% (95% CI, 74%–92%) and 71% (95% CI, 55%–71%), respectively.[27] Other studies of elderly patients showed the negative predictive value for dipstick testing ranges from 92% to 100%.[4,28] Urinary dipstick analysis should be performed in the out-patient setting primarily to rule out and not to establish a diagnosis of UTI. In a patient with a low pretest probability of UTI, if the dipstick is negative for leukocyte esterase and nitrites, it excludes the presence of infection and mitigates the need to obtain urinalysis and urine culture (Table 3). High false-positive rates limit dipstick testing effectiveness.[27] Further urinary studies are warranted for patients with a high pretest probability of UTI.

Laboratory-based clean-catch urinalysis confirms the presence of pyuria if there at least 10 white blood cells per high-powered field and urine culture is positive if there are at least 10^5 CFU/mL of an organism and if the culture identifies the uropathogen.

In the outpatient setting, a clean-catch urine specimen should be collected by the patient. For female patients, the labia should be separated and the urethral area cleansed with an antiseptic soap solution wiping front to back before voiding. The initial urinary flow should be allowed to drain into the toilet or bedpan, catching the midstream urine into a sterile container. If a clean-catch urine specimen is challenging for a patient to obtain (eg, obesity, arthritis), a simple voided specimen, although less ideal, can be used.[39]

When to Send Urine Tests

It is challenging for clinicians caring for older patients with chronic nonspecific symptoms to know when to send urine laboratory studies. Because of the high prevalence of asymptomatic bacteriuria among elderly women, the pretest probability for positive urinalysis or urine culture tests is high. An exacerbation of multiple comorbidities can lead to urinary symptoms (eg, urgency, frequency, and dysuria). A study of elderly patients complaining of poor well-being (anorexia, difficulty in falling asleep, difficulty in staying asleep, fatigue, malaise, weakness) found they were frequently incontinent of urine irrespective of the presence of bacteriuria.[40] Therefore, when chronic urinary nocturia, incontinence, or a general sense of lack of well-being is present, urine studies should not be routinely sent. When there is fever, acute dysuria (<1 week in duration), new or worsening urinary urgency, frequency, new urinary incontinence, gross hematuria, suprapubic or costovertebral angle pain or tenderness, urine studies should be obtained. Acute dysuria is more discriminating for UTI than other genitourinary symptoms (Figure). In a cognitively impaired patient, persistent change in mental status and change in character of the urine not responsive to other interventions (ie, hydration) suggests the need for urine studies. Given the known transient and recurring nature of bacteriuria in older patients,[4,5] a test of cure should not be performed after treatment of UTI. Evaluation of clinical response should be based on symptom improvement without a need to repeat urinary studies. The Figure depicts a pragmatic clinical algorithm, though not clinically validated, that can be applied to the care of the older patient.

Treatment Considerations in Older Adults

> Dr N: *She told me that her incontinence had definitely gotten worse in the last couple of weeks. I had noticed that another physician had sent a urine culture that had grown more than 10^5 CFU/mL of E coli that was sensitive to all antibiotics. Assuming that this was asymptomatic bacteriuria, it was not treated with antibiotics. A repeat urine culture again showed more than 10^5 CFU/mL of E coli, again it was pan sensitive. Given her symptoms, I treated her with a 7-day course of an antibiotic. However the antibiotics didn't really make a difference.*

Studies have shown that treatment of asymptomatic bacteriuria does eradicate bacteriuria.[41] However, reinfection rates (1.67 vs 0.87 per patient-year of follow-up), adverse antimicrobial drug effects, and isolation of increasingly resistant organisms occur more commonly in the therapy vs nontherapy groups. No differences in genitourinary morbidity or mortality were observed between the 2 groups.[42]

For the past 3 decades, infectious disease physicians have recommended against screening or treating asymptomatic bacteriuria in community-dwelling or institutionalized older adults.[10] Nevertheless, geriatricians and primary caregivers of older adults have continued to struggle with determining if nonspecific changes could be related to UTI. In patients with dementia, 75% of patients not meeting accepted minimum criteria for antibiotic initiation for UTI still received antibiotic therapy.[43] The Figure demonstrates common clinical features clinicians should include when evaluating UTI in older adults. Two important issues require consideration when treating older patients for UTI: choice of antibiotic and duration of therapy. Choice of antibiotic should be guided by bacterial pathogens if known, local resistance rates, adverse effect profile, and co-morbidities of the patient. Among community-dwelling older women, the predominant pathogens are *E coli* (51.4%), *Klebsiella pneumoniae* (4.1%), *Proteus mirabilis* (3.3%), and *Enterococcus faecalis* (2.5%).[44] Resistance rates are variable, but outpatient urinary isolate resistance rates are higher in the United States compared with Canada.[45] Fluoroquinolone resistance is highest for patients aged 65 years and older.[45] Fluoroquinolones are now the most commonly prescribed antibiotics in ambulatory care.[46] Between 2005 and 2009 among outpatients older than aged 80 years, the incidence of fluoroquinolone resistant *E coli* isolates increased from 464 to 1116 per 100 000 person-years ($P < .001$). The incidence of *E coli* isolates resistant to fluoroquinolones plus trimethoprim-sulfamethoxazole increased from 274 to 512 per 100 000 person-years ($P < .05$).[47] Extended-spectrum β-lactamase-producing gram-negative pathogens are implicated in community-acquired acute uncomplicated UTI. These bacteria have high resistance rates to oral antimicrobial agents, including amoxicillin-clavulanic acid (69.6% resistant), ciprofloxacin (84.8% resistant), and trimethoprim-sulfamethoxazole (75.9% resistant). Nitrofurantoin (15% resistant) and fosfomycin (0% resistance) remain effective against these bacteria.[48]

Three days of trimethoprim-sulfamethoxazole is recommended as standard UTI therapy for otherwise healthy women. Fluoroquinolones are only recommended as first-line empirical therapy in communities with trimethoprim-sulfamethoxazole resistance rates greater than 10% to 20%.[49] Despite these recommendations, the use of trimethoprim-sulfamethoxazole has not significantly changed (odds ratio [OR], 0.89; 95% CI, 0.60–1.30), while use of

ciprofloxacin increased (OR, 1.75; 95% CI, 1.11–2.75).[50] Current guidelines still recommend trimethoprim-sulfamethoxazole as a first-line empirical therapy in patients living in communities having resistance rates of less than 20%.[51]

Recent, revised guidelines place nitrofurantoin as one of the first-line agents for UTI. However, the US Food and Drug Administration states that this drug is contraindicated for use among patients with a creatinine clearance of less than 60 mL/min/1.73 m^2. Evidence supporting this contraindication is limited and is based on inadequate nitrofurantoin concentration in the urine of patients with creatinine clearance of less than 60 mL/min/1.73 m^2. Recent data suggests that nitrofurantoin can be safely administered to patients with creatinine clearance of at least 40 mL/min/1.73 m^2.[52,53] Nitrofurantoin achieves very low plasma concentrations, 40% of it is excreted in the urine, it maintains very low rates of resistance after 60 years of use,[53] and it is cost effective.[54] Nitrofurantoin should be considered for treatment of cystitis only in older adults. Nitrofurantoin can have pulmonary toxicity. Patients receiving this drug having new pulmonary symptoms should be promptly evaluated.

For more highly resistant bacterial isolates, fosfomycin may be effective for older adults. It is more expensive than other oral agents.[55] Vancomycin-resistant enterococci (VRE), methicillin-resistant *S aureus* (MRSA), and extended-spectrum β-lactamase (ESBL)–producing gram-negative rods are usually susceptible to fosfomycin, and although the bacterial efficacy is lower than other first-line agents, it is an appealing oral outpatient alternative for resistant isolates.[51] Alternatively, when all oral agents have been exhausted, referral to an infectious disease physician for possible short-course outpatient parenteral antibiotic therapy is another viable alternative to prevent hospitalization.[56] Table 5 represents additional suggested antibiotic regimens that are based on published literature in older adults. Antibiotic therapy for UTI was recently reviewed in The Medical Letter and is reprinted in this issue of *JAMA*.[66]

Among older adults, the optimal duration of therapy is unknown. A recent review of 15 studies (1644 older women) showed no difference (RR, 0.98; 95% CI, 0.62–1.54) in short-term clinical failure between short-course (3–6 days) and long-course (7–14 days) oral antibiotic therapy.[67] Although single-dose therapy was preferred by most patients, the rate of persistent UTI was higher with single-dose therapy compared with short-course treatment (RR, 2.01; 95% CI, 1.05–3.84).[67]

Ongoing Management of UTI

> Dr N: *So, she's going to come in next week and give a urine sample. We'll see if the E coli has been cleared and then try to figure out what the next step will be.*

Urine testing should be in response to symptoms as outlined in the Figure. Repeated urine testing as a test of cure is not warranted among older patients. Among patients with recurrent symptomatic UTI (Table 1), use of chronic suppressive antibiotics for 6 to 12 months are effective at reducing UTI episodes and should be considered.[68] Nitrofurantoin given at 50 mg daily is used in older patients with minimal adverse effects and no growth of nitrofurantoin-resistant fecal flora after 1 year of treatment.[69] Six months of trimethoprim-

sulfamethoxazole (40 mg/200 mg daily), trimethoprim (100 mg daily), and nitrofurantoin (100 mg daily) are also effective,[70] but trimethoprim-sulfamethoxazole resistant *E coli* fecal isolates were more common in patients treated with trimethoprim-based regimens.[71]

Prevention

> Mrs M: *My companion of 5 years and I practice a kind of senior teenage sex, I guess you'd call it. We enjoy each other very much.*

Recent studies on postmenopausal women show that sexual intercourse results in a higher incidence of symptomatic UTIs, suggesting that postcoital symptomatic UTIs can occur in older women.[18] It is important to ask older women about recent sexual intercourse, especially with new partners. Sexually transmitted infections (STIs) can cause urinary symptoms and if vaginal discharge is present, an evaluation of STI should be performed. As with younger women, it is appropriate to advise early postcoital voiding as well as liberalizing fluid intake during the daytime hours. Additionally, a trial of postcoital antibiotic prophylaxis may be considered since it has been shown to prevent UTI in younger women.[68]

In older women, a study showed that 300 mL of cranberry juice cocktail could reduce the laboratory evidence of UTI at 6 months.[72] Subsequent studies yielded conflicting results, in part because of inadequate standardization of the cranberry active ingredient.[73] Current evidence suggests that in older women with a history of recurrent UTI, cranberry products may be effective at reducing the risk of UTI (Table 6).[74] Oral estrogen therapy has not been found to be effective at reducing UTI risk compared with placebo (4 studies, 2798 women: RR, 1.08; 95% CI, 0.88–1.33); however, vaginal estrogen cream reduced UTI in 2 studies (RR, 0.25; 95% CI, 0.13–0.50 in one study and RR, 0.64;, 95% CI, 0.47–0.86 in the second study).[75] Prior to initiating one of these prevention strategies, an evaluation of medications contributing to urinary retention and a urologic evaluation for predisposing conditions to UTI, such as pelvic organ prolapse, bladder lesions, or kidney stones, should be performed.

Conclusions

Asymptomatic bacteriuria, urinary incontinence, and symptomatic UTI are prevalent in older women and identifying which patients warrant antibiotic therapy is difficult. Establishing a diagnosis of symptomatic UTI requires careful clinical assessment with possible laboratory assessment using urinalysis and urine culture. New-onset dysuria is one of the best indicators of a potential symptomatic UTI. In older patients who have a high prevalence of genitourinary symptoms, urinary studies should only be performed if a patient's symptoms worsen acutely and there is no other identifiable cause. Non-specific symptoms such as a general lack of well-being should not be the only reason for obtaining urinary studies. Once a diagnosis of symptomatic UTI is established, antibiotic selection should be made by knowing prior uropathogen susceptibility profiles, considering possible antibiotic adverse effects, potential interactions with other medications, and patient comorbidity.

Acknowledgments

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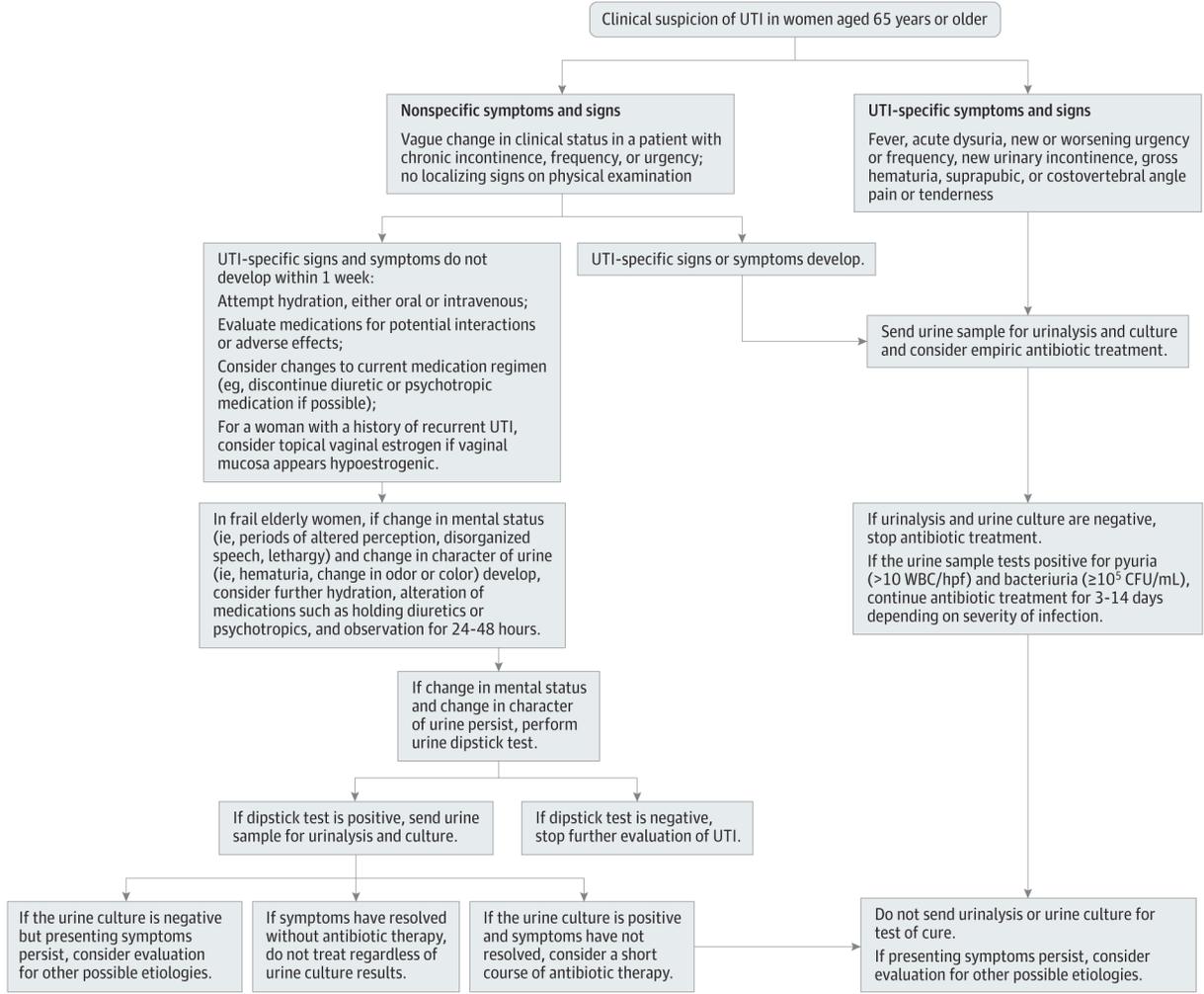
Figure.
Suggested Approach to the Evaluation and Treatment of Older Women With a Suspected UTI

CFU indicates colony-forming units; hpf, high-powered field; UTI, urinary tract infection; WBC, white blood cells.

Table 1

Suggested Approach to the Evaluation and Treatment of Older Women With a Suspected UTI

Condition	Definition
UTI	Presence of microbial pathogens within the urinary tract[4]
Asymptomatic bacteriuria	Bacteria or yeast isolated in appropriate quantitative counts from a urine culture without accompanying signs or symptoms attributable to the genitourinary tract[5] In women patients: 2 consecutive clean-catch midstream urine samples growing at least 10^5 colony-forming units/mL with no more than 2 species of microorganisms and no indwelling urinary catheter within 7 days of first urine culture
Symptomatic UTI (without indwelling urinary catheter)	Can include cystitis, pyelonephritis, urosepsis, septic shock, or all combined[5] Defined by at least 2 of following criteria: fever (>38°C) in a patient who is aged 65 years or older; frequency or urgency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness (not explained by other diagnoses); positive urine culture of at least 10^5 colony-forming units/mL with no more than 2 species of microorganisms; and pyuria (10 white blood cells/mm^3 of unspun urine)[6]
Uncomplicated UTI	Symptomatic UTI in a normal genitourinary tract with no prior instrumentation
Complicated UTI	Symptomatic UTI in patients with either functional or structural abnormality, a history of urinary instrumentation or systemic diseases such as renal insufficiency, transplantation, diabetes, or immunodeficiency
Recurrent UTI	Two or more symptomatic UTIs within 6 months or 3 or more infections within 1 year[7]
Urosepsis	Sepsis caused by UTI

Abbreviation: UTI, urinary tract infection.

Table 2

Risk Factors for UTIs in Postmenopausal Women

Source	Study Characteristics	Participants		UTI Definition	Risk Factors			Findings
		No.	Age, y		Evaluated	Ascertainment		
Raz et al,[12] 2000	Design: case-control Setting: outpatient clinic, Israel Duration: not reported	149 Cases 53 controls	Mean (SD), 65.6 (7.2)	Recurrent symptomatic UTI: >3 culture-documented episodes of symptomatic UTI during the last year or 2 episodes during the last 6 months with dysuria, urgency and frequency (cystitis); and fever, chills, and/or loin pain (check study for clarifications)	General medical history, marital status, No. of pregnancies and deliveries, comorbidities, and previous surgical procedures, history of UTIs including age at first UTI, ABO blood group, secretor status, urinary incontinence, postvoid urine residual, and uterine, bladder, or rectal prolapse	Questionnaire, renal ultrasonography, gynecological examination, blood and saliva analysis		Incontinence (OR, 5.8; 95% CI, 2.1–16.2) History of UTI before menopause (OR, 4.9; 95% CI, 1.7–13.8) Nonsecretor status (OR, 2.9; 95% CI, 1.3–6.3)
Hu et al,[13] 2004	Design: population-based case-control Setting: HMO group, state of Washington Duration: 1994–1996	899 Cases 911 controls	Range, 55–75	Symptomatic UTI: presence of dysuria (increased frequency or urgency of urination for 2 weeks) and urine culture during the preceding month that grew 10^5 CFU/mL of a uropathogenic organism	Demographics; comorbidities including DM, obstetric, and gynecologic history; sexual activity and contraceptive practices	Interview, clinic visit for urine collection		Sexually active (OR, 1.42; 95% CI, 1.1–1.9) History of UTI (OR, 4.2; 95% CI, 3.3–5.4) DM (OR, 2.8; 95% CI, 1.8–4.4) Incontinence (OR, 1.36; 95% CI, 1.03–1.8) Oral estrogen replacement did not reduce UTI risk
Sheinfeld et al,[22] 1989	Design: prospective case-control Setting: Urology clinic, Northwestern University Medical School, Chicago, Illinois Duration: January–September 1984	98	Case group, range, 23–72; mean, 35 control group, range, 23–78; mean, 38	Symptomatic UTI: urinary frequency, dyuria, urgency, fever, chills, or flank pain with 10^5 CFU/mL bacteria in urine sample	ABO, P and Lewis blood groups	Blood sample phenotyping, clinic visit		ABO blood group (χ^2 = 2.02; UTI vs no UTI P = .60) P blood group (χ^2 = 0.23; UTI vs no UTI P = .63) Lewis blood group (χ^2 = 8.28; secretor phenotype (Le[a – b +])=74%; nonsecretor phenotype (Le[a+b –])=18%; recessive phenotype (Le[a-b –])=8% Le(a + b–) UTI vs no UTI (OR, 3.4; 95% CI, 1.5–7.9)

| Source | Study Characteristics | Participants | | Risk Factors | | | | Findings |
| | | No. | Age, y | UTI Definition | Evaluated | Ascertainment | | |

Source	Study Characteristics	No.	Age, y	UTI Definition	Evaluated	Ascertainment	Findings
Jackson et al,[14] 2004	Design: population-based, prospective cohort Setting: HMO group, state of Washington Duration: 1998–2002 plus 2-year follow-up	1017	Range, 55–75	Symptomatic UTI: midstream urine specimen with 10^5 CFU/mL of a uropathogenic organism in the presence of dysuria, urgency, or frequency 2 weeks	Demographic characteristics, comorbidities, urinary incontinence, sexual activity, personal and family history of UTI, postmenopausal hormone use	Interview, medical record review, urine and vaginal swab culture, blood glucose, bladder scan for postvoid residual volume	Insulin-dependent DM (HR, 3.4; 95% CI, 1.7–7.0) At least 6 lifetime UTIs (HR, 6.9; 95% CI, 3.5–13.6)
Moore et al,[15] 2008	Design: population-based, prospective cohort Setting: HMO group, state of Washington Duration: 1998–2002 plus 2-year follow-up	913	Range, 55–75	Symptomatic UTI: midstream, clean-catch, urine culture with 10^5 CFU/mL of uropathogens plus 2 acute urinary symptoms: dysuria, urgency, or frequency	Urinary incontinence, rate of urine loss	Daily diaries, questionnaires	Mean monthly rate of urine loss (No. of losses/mo): No UTI, 2.64/mo UTI, 4.60/mo ($P = .04$)
Czaja et al,[17] 2009	Design: prospective cohort Setting: student health center, University of Washington Duration: January 2003–December 2006	104	Range, 18–49	*E coli*–recurrent symptomatic UTI: presentation for medical evaluation of symptoms of acute cystitis (dysuria, frequency, or urgency) with a concentration of *E coli* in urine of $>10^2$ CFUs/mL	Demographics, sexual activity	Self-report	Prevalence of concurrent sex and periurethral carriage of rUTI strain: 14 days before rUTI = 7% 3 days before rUTI = 41%; ($P = .008$ for day 14 vs day 1)
Moore et al,[18] 2008	Design: prospective cohort Setting: HMO group, state of Washington Duration: 1998–2002 plus 2-year follow-up	913	Range, 55–75	Symptomatic UTI: midstream, clean-catch, urine specimen with 10^5 CFU/mL of a uropathogen confirmed by culture, plus 2 acute urinary symptoms: dysuria, urgency, or frequency	Demographics, physical function, DM, douching, smoking, vaginal dryness, hormone use, hysterectomy, incontinence, and UTI history	Subject diaries, interview, medical record review,	Risk of UTI 2 days after intercourse (HR, 3.42; 95% CI, 1.49–7.8) Risk in DM vs non-DM patients (HR, 1.97; 95% CI, 1.11–3.5)
Stapleton et al,[23] 1995	Design: prospective cohort Setting: student health clinic, University of Washington Duration: 6-month follow-up	40	With recurrent UTI, median, 22 without recurrent UTI, median, 26	Symptomatic *E coli* UTI: presence of typical lower urinary tract symptoms, pyuria (8 leukocytes/mm³), and *E coli* 10^2 CFU/mL in voided midstream urine; recurrent symptomatic	ABO blood group secretor status, UTI history	Daily diaries, clinic visits; saliva, blood and urine samples	Rectal F-fimbriated: nonsecretors with UTIs vs secretors with UTI (56% vs 27%; $P = .04$)

Source	Study Characteristics	Participants		Risk Factors			Findings
		No.	Age, y	UTI Definition	Evaluated	Ascertainment	
				UTI: 2 episodes within 12 months 2 episodes within 12 months			
Gorter et al,[19] 2010	Design: retrospective cohort Setting: the Netherlands Duration: 2000–2004	6958	30	Recurrent symptomatic UTI: new episode defined as UTI occurring after 6-week symptom-free period Relapse: the need to repeat prescribing antibiotics between 4 days and 6 weeks after first prescription Reinfection: need for a New prescription after 6 weeks Symptomatic UTI: defined as either: (1) *International Classification of Primary Care* code for cystitis (U71) or nonspecific urethritis (U72) when antibiotic was prescribed within 3 days of the patient's visit; or (2) stranguria, dysuria, frequency or urgency and/or culture, dip slide, leukocyte esterase or nitrite tests with positive findings if the patient's record indicated antibiotics had been prescribed	Age, socioeconomic status, urinary tract stones and atrophic or candida vaginitis, DM, DM medications, DM complications, antibiotics prescribed	Medical record review, coded diagnosis	Recurrent UTI: DM (OR, 2.0; 95% CI, 1.4–2.9) Oral blood glucose medications (OR, 2.1; 95% CI, 1.2–3.5) Taking insulin (OR, 3.0; 95% CI, 1.7–5.1) DM diagnosis 5y (OR, 2.9; 95% CI, 1.9–4.4) Retinopathy (OR, 4.1; 95% CI, 1.9–9.1)
Zafanello et al,[20] 2010	Design: review Setting: 9 studies included Duration: NA	NA	Children and adults	Recurrent UTI: definition not standardized	Genetic susceptibility markers for recurrent UTI		*HSPA1B, CXCR1 and CXCR2, TLR2, TLR4, TGF-β1* genes may be associated with susceptibility to recurrent UTI

Table 3

Testing and Treatment Considerations for UTIs

Issue	Consideration
Urinary dipstick testing	Should be used primarily to rule out a UTI, not to establish a diagnosis of UTI In a patient with a low pretest probability of UTI, if the dipstick is negative for leukocyte esterase and nitrites, it excludes the presence of infection and eliminates the need to obtain a laboratory-based urinalysis and urine culture[26–28]
Antibiotic treatment	In 25%–50% of women presenting with UTI, symptoms will have recovered or will show spontaneous improvement in 1 week without using antibiotics[29]
Supportive treatments	Diuretics should be avoided in older women with urinary incontinence Women with urinary urgency are often told to restrict fluid intake, leading to dehydration[30] When the diagnosis of symptomatic UTI is in doubt, delaying antibiotic treatment for 1 week but offering supportive treatment such as increased fluid intake is an acceptable therapeutic option[29]

Abbreviation: UTI, urinary tract infection.

Table 4

From *The Rational Clinical Examination:* Univariate Findings and Multivariate Approach for Diagnosing UTI in Adult Women[a,b]

Univariate Findings[c]	LR (95% CI)[d]	
	Present	**Absent**
Dysuria	1.5 (1.2–2.0)	0.5 (0.3–0.7)
Frequency	1.8 (1.1–3.0)	0.5 (0.4–1.0)
Vaginal discharge	0.3 (0.1–0.9)	3.1 (1.0–9.3)
Vaginal irritation	0.2 (0.1–0.9)	2.7 (0.9–8.5)
	Abnormal	**Normal**
Dipstick result[e]	4.2	0.3

Abbreviations: LR, likelihood ratio; UTI, urinary tract infection.

[a]A *Rational Clinical Examination* article evaluated the efficacy of various clinical features and urine dipstick testing for younger patients. The approach for older patients is different. Although the prevalence of asymptomatic bacteriuria in the general population is approximately 5%, it ranges from 15% to 17% in women older than 70 years and can be as high as 30%–50%. Chronic genitourinary symptoms, such as urinary frequency and urgency, are also very common in older women. It is important to distinguish between chronic symptoms and new or worsening urinary symptoms. In general, vaginal discharge is not a common presenting complaint among older women with or without a UTI. Considering these challenges, establishing a diagnosis in older women requires the presence of 2 clinical features such as fever, worsened urinary urgency or frequency, acute dysuria, suprapubic tenderness, costovertebral angle pain or tenderness, and the presence of bacteriuria or pyuria on urinalysis. Although not a common complaint, new dysuria is a very sensitive indicator of symptomatic UTI in older women.

[b]Adapted from *The Rational Clinical Examination: Evidence-Based Clinical Diagnosis*.[31] Data were derived from Bent et al.[32]

[c]For a multivariable approach, multiply the above individual LRs for combinations of findings (eg, dysuria present and vaginal discharge absent yields a combined LR = 4.7; dysuria absent and vaginal discharge present yields a combined LR = 0.15).

[d]LRs that are less than 1 are rounded off to make computation easier when combining findings.

[e]The dipstick values were selected from visual inspection of a summary receiver-operating characteristic curve to maximize the accuracy so CIs could not be determined.[33]

Table 5

Treatment Options in the United States for Uncomplicated UTI in the Outpatient Setting

Antibiotic	Dosage for Normal Renal Function[a]	Precautions	Study Type	Participant Characteristics	
				Mean Age, (Range) y	Sex
Nitrofurantoin	100 mg twice daily for 3–5 days	Avoid if pyelonephritis is suspected[51]	Prospective, randomized, double-blind, 3-group comparative[57]	34 (18–85)	Women only
			Prospective, randomized, double-masked comparative[58]	Nitrofurantoin: 33 (15–92) fosfomycin: 33 (16–80)	Women only
Trimethoprim-sulfamethoxazole	One 160 mg-800 mg tablet twice daily for 3 days	Hemorrhage while undergoing warfarin therapy[59], hyperkalemia while taking angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or spirinolactone[60,61]	Population-based, nested case-control[59]	80 (74–85)	Men 53%, women 47%
			Population-based, nested case-control study[60]	Case group 82 control group 81 (75–87)	Men 39%, women 61%
			Population-based, nested case-control[61]	Case group 82 control group 81 (75–87)	Men 31%, women 69%
			Prospective, randomized, comparative[62]	Cefpodoxime: 44 (29–59), trimethoprim-sulfamethoxazole: median 42 (26–58)	Women only
Ciprofloxacin	250 mg twice daily for 3 days	High rates of community-acquired isolates with resistance	Prospective, randomized, double-blind[63]	3-day group: 78.8 (SD 7.6) 7-day group: 78.6 (SD 7.3)	Women only
			Prospective, randomized, double-blind, 3-group comparative[57]	34 (18–85)	Women only
Fosfomycin trometamol	3 gm daily for 1 day	Avoid if pyelonephritis is suspected[51]	Prospective, randomized, double-masked comparative[58]	Fosfomycin: 33 (16–80) nitrofurantoin: 33 (15–92)	Women only
Cefpodoxime	100 mg twice daily for 3 days	Higher failure rates for UTI with β-lactam antibiotics[64]	Prospective, randomized, comparative[62]	Cefpodoxime: 44 (29–59) trimethoprim-sulfamethoxazole: median 42 (26–58)	Women only
Amoxicillin-clavulanate	875 mg twice daily for 3 days	Higher failure rates for UTI with β-lactam antibiotics[64]	Case-control[64]	Age >60: case group 63% control group 35%	Case group: women 77%, men 23%; control group: women 61%, men 39%
Gentamicin	5 mg/kg once daily for 3 days	Need outpatient parenteral antibiotic therapy; reserve for isolates with no oral alternative	Prospective, randomized, comparative trial[65]	Once daily: 53 (22–80) 3 × daily: 40 (20–74)	Women 86%, men 14%

Antibiotic	Dosage for Normal Renal Function[a]	Precautions	Study Type	Participant Characteristics	
				Mean Age, (Range) y	Sex
Ertapenem	1 gm daily intravenously for 3 days	Need outpatient parenteral antibiotic therapy; reserve for extended spectrum β-lactamases isolates[56]	Retrospective, descriptive[56]	58 (32–71)	Men 55%, women 45%

[a]Dosage for normal renal function indicates a creatinine clearance of more than 60 mL/min/1.73 m^2.

Table 6

Prevention of UTIs

Source	Study Design	No. of Participants	Outcome Definition	Dose and Concentration of Cranberry Product	Findings, Effect Size
Avorn et al,[72] 1994[a]	RCT	153	Asymptomatic bacteriuria: organisms numbering >10⁵ CFU/mL regardless of organism and pyuria in a clean-catch urine specimen	300 mL Cranberry juice cocktail daily	Bacteriuria with pyuria (OR, 0.42; 95% CI, 0.23–0.76; P =.004) Transition from bacteriuric-pyuria to nonbacteriuric-pyuria (OR, 0.27; P = .006)
Jepson and Craig,[73] 2008[b]	Review of 10 studies, meta-analysis of 4 RCTs	359 Cranberry group 306 placebo group	Symptomatic UTI: >10⁵ CFU/mL with pyuria in catheter collected midstream or clean catch-urine specimen with 1 spmptom: dysuria, frequency, or urgency Asymptomatic bacteriuria: >10⁵ CFU/mL bacteria Primary outcome: No. of UTIs in each group. Recurrent UTIs: 4 UTIs during the past year or 1 during the previous 3 months or 2 symptomatic, single-organism, culture-positive UTIs in the previous calendar year	Juice/cocktail: adults 30–300 mL/d children 15–300 mL/d Capsules: 400 mg–2 g Tablets: 1:30 concentrate twice daily	Incidence of UTI at 12 mo (RR, 0.66; 95% CI, 0.47–0.92) Subgroup RRs: women with recurrent UTI (RR, 0.61; 95% CI, 0.40–0.91) elderly men and women (RR, 0.51; 95% CI, 0.21–1.22) neuropathic bladder (RR, 1.06; 95% CI, 0.51–2.21)
Wang et al,[74] 2012[b]	Review of 13 studies, meta-analysis of 10 RCTs	Review: 1616, meta-analysis: 1494 (794 cranberry group, 700 control group)	Symptomatic UTI: >10⁴ or 10⁵ CFU/mL bacteria with or without pyuria, with symptoms	0.4–194.4 g cranberry	Incidence of all UTIs (RR, 0.62; 95% CI, 0.49–0.80) Subgroup RRs: women with recurrent UTIs (RR, 0.53; 95% CI, 0.33–0.83) elderly patients (RR, 0.51; 95% CI, 0.21–1.22) females (RR, 0.49; 95% CI, 0.34–0.73) children (RR, 0.33; 95% CI, 0.16–0.69) cranberry juice (RR, 0.47; 95% CI, 0.30–0.72) cranberry juice twice/d (RR, 0.58; 95% CI, 0.40–0.84)
Perrotta et al,[75] 2008[c]	Review of 9 studies; meta-analysis of 4 RCTs	Review: 3345, meta-analysis: 2798	Recurrent UTI: 3 UTI episodes in the last 12 mo or 2 episodes in the last 6 mo		Oral estrogens (RR, 1.08; 95% CI, 0.88–1.33) Nonpooled results of vaginal estrogens: intravaginal oestriol cream (RR, 0.25; 95% CI, 0.13–0.50) releasing silicone vaginal ring (RR, 0.64; 95% CI, 0.47–0.86) Estrogens vs antibiotics: study 1 at end of treatment (RR, 1.08; 95% CI, 1.01–1.68) study 2 at end of treatment (RR, 0.09; 95% CI, 0.02–0.36) 2 mo after end of treatment (RR, 0.56; 95% CI, 0.09–3.55)

Abbreviations: CFU, colony-forming units; OR, odds risk; RCT, randomized controlled trial; RR, relative risk; UTI, urinary tract infection.

[a] Study duration was 6 months. All participants were women and mean age was 78.5 years.

[b] Participants were men and women.

[c] All participants were postmenopausal women.