



THE IOU STUDY

IMPROVING OUTCOMES OF UTI

TOOL KIT



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INTRODUCTION

Implementing antibiotic stewardship programs in post-acute and long-term care (PALTC) settings is a major priority. This can be a daunting challenge, since many health care providers are uncertain where to start. This toolkit is designed to help PALTC facilities implement an antibiotic stewardship program centered on improving the management of urinary tract infections or UTI. In particular, the toolkit focuses on a specific type of UTI—uncomplicated bladder infections or cystitis.

Suspected UTI is the most common reason for antibiotic use in PALTC settings, making it a high priority condition. Uncomplicated cystitis is the most common presentation of UTI. Yet accurate diagnosis of uncomplicated cystitis can be difficult. Separating uncomplicated cystitis from asymptomatic bacteriuria—a condition in which there is bacteria in the urine, but no infection—poses a challenge for even the most seasoned clinician.

Making an accurate distinction between uncomplicated cystitis and asymptomatic bacteriuria is important. Not only is treatment for asymptomatic bacteriuria wasteful, but it may contribute to patient harm. Decades of studies confirm that treatment of asymptomatic bacteriuria in PALTC residents does not improve patient outcomes. Treatment of asymptomatic bacteriuria does not reduce falls, morbidity, or mortality. Treatment of asymptomatic bacteriuria does increase bacterial resistance, adverse drug events, and *Clostridioides* (formerly *Clostridium*) *difficile*. Treatment of asymptomatic bacteriuria appears to increase the risk of subsequent true symptomatic UTI. This may be in part due to disruption of the microbiome.

This toolkit provides practical materials developed and tested as part of the ARHQ-funded study, “Improving Outcomes of UTI Management in Long-Term Care,” or the IOU Study. The latter study was led by researchers and PALTC clinicians at the University of Pittsburgh, the University of Wisconsin, and AMDA – The Society for Post-Acute and Long-Term Care Medicine.

As part of the IOU Study, clinical recommendations for the diagnosis and management of uncomplicated cystitis were developed. The recommendations are based upon extensive literature review and expert consensus panels composed of clinicians with experience with frail older adults and/or the PALTC environment. These guidelines are unique in that they are focused on uncomplicated cystitis, thus avoiding some of the confusion created by lumping all UTI presentations together. They also are meant to guide decisions on empiric antibiotic use pending confirmation of infection and culture/sensitivity results. The tools included in this toolkit are designed to help facilities educate nursing home staff, prescribing clinicians and residents/families about the diagnosis and treatment of uncomplicated cystitis. The tools also are designed to effect systems change and promote quality assessment/performance improvement (QAPI) efforts. These tools have been piloted as part of the IOU Study. This toolkit makes them available for further dissemination.



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Clinical Recommendations for the Diagnosis of Uncomplicated Cystitis in Long-Term Care Residents

The Improving Outcomes of UTI Management in Long-Term Care Project (IOU) Consensus Guidelines for the Diagnosis of Uncomplicated Cystitis in Nursing Home Residents

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Original Study

The Improving Outcomes of UTI Management in Long-Term Care Project (IOU) Consensus Guidelines for the Diagnosis of Uncomplicated Cystitis in Nursing Home Residents



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A B S T R A C T

Keywords:

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cystitis
diagnostic guidelines
nursing facilities

Objectives: To identify a set of signs and symptoms most likely to indicate uncomplicated cystitis in noncatheterized nursing home residents ≥ 65 years of age using consensus-based methods informed by a literature review.

Design: Literature review and modified Delphi survey with strict inclusion criteria.

Setting and Participants: Expert panel of 20 physicians certified in geriatric medicine and/or medical direction, actively practicing in post-acute and long-term care settings.

Methods: The authors performed a literature review to produce a comprehensive list of potential signs and symptoms of presumptive uncomplicated cystitis, including nonspecific “quality control” items deemed unlikely to indicate uncomplicated cystitis. The expert panel rated their agreement for each sign/symptom using a 5-point Likert-type scale (1 = strongly disagree to 5 = strongly agree). Agreed upon signs and symptoms were summarized using a diagnostic algorithm for easy clinical use.

Results: The literature review identified 16 signs and symptoms that were evaluated in 3 Delphi survey rounds. The response rate was 100% for round 1 and 95% for the second 2 rounds. Consensus agreement for inclusion was achieved for dysuria on round 1 with exclusion of the 3 quality controls, and “offensive smelling urine.” Consensus in the second round was reached for including 4 additional items (gross hematuria, suprapubic pain, urinary frequency, and urinary urgency). Round 3 evaluated dysuria alone and combinations of symptoms. Consensus that dysuria alone is sufficient for diagnosis of cystitis was not reached.

Conclusions/Implications: The panel identified 5 signs and symptoms likely indicative of uncomplicated cystitis in nursing home residents and developed a diagnostic algorithm that can be used to promote antibiotic stewardship in nursing homes. Given similarities in populations, the algorithm may also be applicable to the older adult and the broader post-acute/long-term care populations.

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Suspected urinary tract infection (UTI) is the most commonly diagnosed infection, and the leading reason for antibiotic use, in nursing homes.^{1–3} Unfortunately, much of the treatment for suspected UTI is unnecessary, placing residents at risk of harm from adverse drug events; *Clostridium difficile* infections; and risk of development of, or exposure to, antibiotic-resistant organisms.^{3–8}

Clinical uncertainty surrounding asymptomatic bacteriuria (ASB) is the major driver for overtreatment of UTI.^{9–11} By definition, individuals with ASB do not have any specific urinary symptoms despite growth of bacteria on a urine culture. It is clear from numerous studies over the past 4 decades that ASB in older adults should not be treated.³ Several professional societies have issued statements discouraging urine testing and antibiotic treatment in the absence of urinary symptoms.^{12,13} However, many clinicians continue to treat ASB in older adults, citing uncertainty regarding the exact signs and symptoms of UTI in this population.^{14,15}

Several sets of diagnostic criteria for UTI in the long-term care setting have been developed to aid clinicians in decision making.^{16–19} These criteria serve various purposes such as promoting retrospective comparative benchmarking or establishing minimum criteria necessary to initiate antibiotic therapy. These criteria are frequently not followed because of lack of awareness, complexity, as well as concerns of low sensitivity and poor positive predictive value.^{3,20} Another drawback of these criteria is that they consider UTI as a broad clinical entity. In truth, UTI includes a spectrum of diseases that can range from uncomplicated cystitis to catheter-associated UTI, prostatitis, epididymitis, pyelonephritis, and urosepsis.^{21,22} The epidemiology and natural history of each of these subtypes will differ, and management should be ideally tailored to the presenting condition.²¹ It is widely accepted that uncomplicated cystitis is the most common type of suspected UTI and is generally less severe than pyelonephritis or urosepsis.^{22–25} Clinicians are frequently challenged when differentiating uncomplicated cystitis from ASB. Given this, identifying a set of diagnostic criteria for uncomplicated cystitis is an important need.

The objective of this study was to identify a set of signs and symptoms most likely to indicate uncomplicated cystitis in non-catheterized nursing home residents ≥ 65 years of age using consensus-based methods informed by a literature review. We used a modified Delphi approach involving an extensive background literature search and a series of structured surveys completed by a panel of practicing experts in geriatric, post-acute, and long-term care medicine.^{26–33} We then created an algorithm to aid nursing home clinicians in the diagnosis of uncomplicated cystitis.

Methods

Comprehensive Literature Review and Survey Development

The authors worked with 2 medical librarians at the University of Pittsburgh to conduct a literature review restricted to English-language articles in PubMed and Embase from 1980 to 2016 using a combination of terms including *urinary tract infections, urinary tract, infections, nursing homes, cognitively impaired, and aged*. The search strategy for the overarching question is in [Appendix 1](#). Article abstracts were reviewed and those evaluating the presence of signs and symptoms of cystitis were selected for full review. Moreover, existing guidelines for the diagnosis of UTI in nursing home residents were reviewed.^{16–19} A preliminary list of potential signs and symptoms to be assessed in the Delphi survey rounds was assembled. Three signs and symptoms *not* considered indicative of uncomplicated cystitis were also identified for use as quality controls. It was expected that these 3 quality control items would be rejected.

Expert Panel for Delphi

Accurate diagnosis of infections in post-acute and long-term care (PA/LTC) presents many challenges because of the unique characteristics of this population. As such, the expert panel members for the Delphi survey had to have both working knowledge of the PA/LTC environment as well as clinical expertise in the care of nursing home residents, including those unable to report symptoms due to advanced dementia, aphasia, or other conditions. A national panel of 20 physicians actively practicing in the PA/LTC setting was assembled. Participants had to be board certified in geriatric medicine, be board certified in medical direction, or have completed a fellowship in geriatric medicine. [Appendix 2](#) lists the experts and their current affiliations.

Data Collection and Analysis

The first round of the Delphi survey was conducted individually by e-mail, and participants were blind to the identity of other panel members. The expert panel was asked to rate their agreement for each sign/symptom given the following instructions: “This set of questions pertains to the diagnosis of uncomplicated cystitis (in non-catheterized residents), in the absence of warning signs that suggest complicated disease such as pyelonephritis or prostatitis. Regardless of general prevalence, please indicate your level of agreement that new onset or worsening of the following signs and symptoms indicate uncomplicated bladder infection in nursing home residents.” Agreement was measured using a 5-point Likert-type scale (1 = strongly disagree; 2 = disagree; 3 = equivocal; 4 = agree; 5 = strongly agree). In the first round, the goal was to conservatively determine signs/symptoms to include and exclude under strict criteria. Criteria reaching consensus for inclusion would be considered as potential “stand alone” criteria for evaluation in subsequent rounds. For this round, consensus agreement was defined as a 95% lower confidence interval limit of ≥ 4.0 for the item, whereas consensus disagreement was defined as an upper 95% confidence limit of ≤ 3.0 for the item. All items for which consensus could not be reached during the first round were returned to the panel in the second round, along with their initial rating and the mean rating for all panel members. Consensus agreement in the second round was defined as two-thirds of the panel giving a rating of ≥ 4.0 for the item. Finally, a third-round survey was conducted to solicit the two-thirds-majority expert panel opinion on single or combinations of individual signs/symptoms identified in the first 2 rounds of the modified Delphi. The results were summarized as a diagnostic flowchart to facilitate clinical use. The University of Pittsburgh Institutional Review Board reviewed and approved the Delphi survey as exempt.

Results

The literature search revealed 712 studies in PubMed and 1048 in Embase, yielding a total of 1219 articles after duplicates were removed. Following abstract review, 90 were deemed relevant for full review and 19 reported prevalence of 1 or more symptoms. Thirteen symptoms that might be and 3 unlikely to be (quality controls) related to a urinary tract infection were included in the first round of the Delphi survey ([Table 1](#)). Of the twenty panel members, 50% were female, 15 held board certifications in geriatric medicine, 15 in medical direction, and 17 had completed a geriatric medicine fellowship. Eighteen panel members met more than 1 inclusion criteria.

The first-round response rate was 100%. One symptom, “dysuria,” reached consensus criteria for inclusion. In addition, the panel agreed on excluding the 3 nonspecific quality control items (“insomnia,” “depression,” “radiating thigh pain”), and “offensive-smelling urine” as being indicative of uncomplicated cystitis. The remaining 11 items that did not reach consensus were included in the second round of the survey.

Table 1
Modified Delphi Survey Rounds 1 and 2*

Sign or Symptom	Round 1			Round 2
	Consensus Reached to Exclude Sign/Symptom From Final Criteria	Consensus Reached to Include Sign/Symptom in Final Criteria	Consensus Not Reached to Include Signs/Symptom (Assessed Again in Round 2)	Consensus Reached to Include Sign/Symptom in Final Criteria
Literature-based signs/symptoms potentially related to UTI				
1. Chills or rigors			X	
2. Dysuria		X		
3. Fever ($\geq 100^\circ\text{F}$, or repeated temperatures $>99^\circ\text{F}$, and/or increase of $\geq 2^\circ\text{F}$ above baseline temperature)			X	
4. Urinary frequency			X	X
5. Hematuria (gross)			X	X
6. Incontinence			X	
7. Mental status change (delirium, altered level of consciousness, confusion)			X	
8. Malaise			X	
9. Nocturia			X	
10. Offensive-smelling urine	X			
11. Suprapubic pain			X	X
12. Turbid urine			X	
13. Urinary urgency			X	X
Signs/symptoms used as quality control variables [†]				
14. Depressive symptoms	X			
15. Insomnia	X			
16. Radiating thigh pain	X			

*Rounds 1 and 2 identified individual specific signs/symptoms to include or exclude from final criteria. A third round (not shown) was conducted to assess whether single or combinations of signs/symptoms were adequate criteria.

[†]Signs or symptoms not likely to be related to cystitis. These were included to assess result validity.

The second-round response rate was 95%. Consensus was reached on including 4 additional symptoms (urinary frequency, urinary urgency, suprapubic pain, and gross hematuria).

The third round addressed combinations of individual symptoms. The panel failed to reach a two-thirds majority on dysuria being a sufficient minimal criterion by itself; the combination of hematuria and frequency or urgency was deemed sufficient minimal criteria in absence of dysuria, as was the combination of suprapubic pain and

frequency or urgency being a sufficient minimal criterion in absence of dysuria. The results are qualitatively summarized in Figure 1 to enable easy clinical use.

Discussion

In this study, a panel of physicians with expertise in geriatrics and PA/LTC medicine was able to achieve consensus agreement on a set of

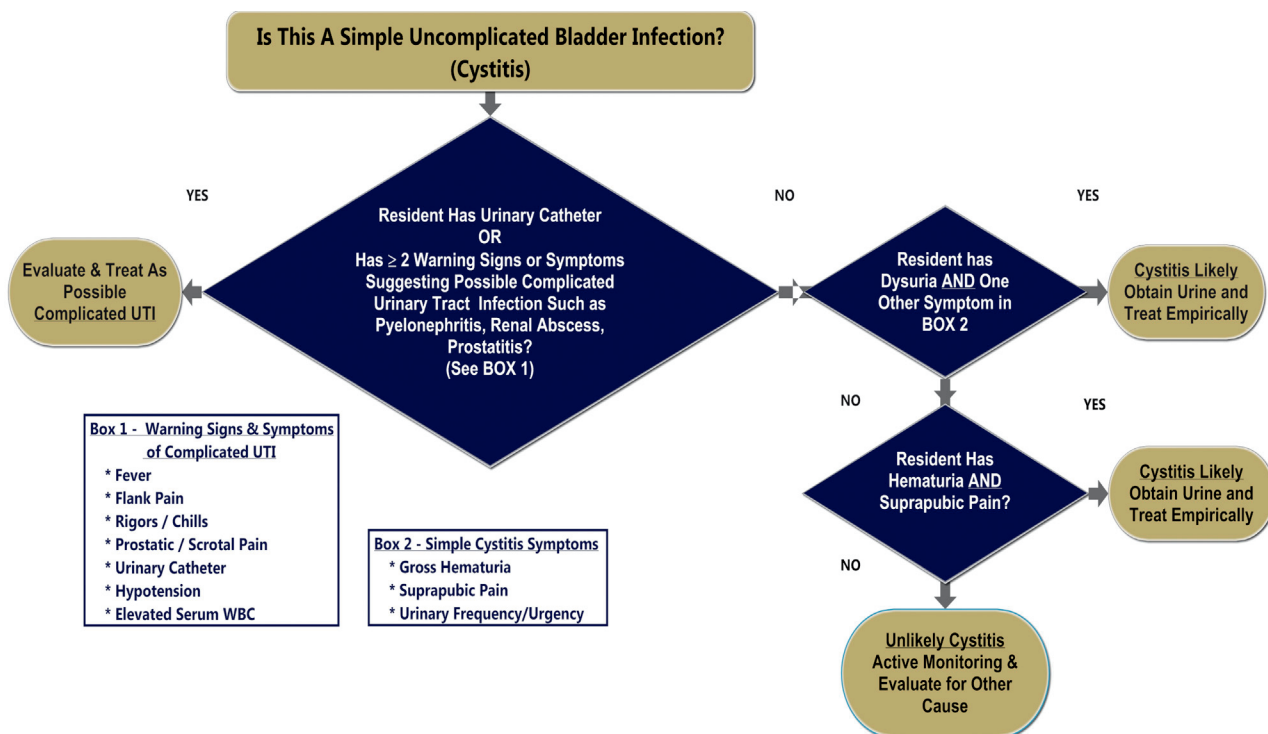


Fig. 1. Algorithm for the diagnostic approach to uncomplicated cystitis in noncatheterized nursing home residents.

signs and symptoms likely to be related to uncomplicated cystitis in noncatheterized older nursing home residents. The panel members' agreement on exclusion of the 3 quality control signs and symptoms unlikely to be UTI-related was reassuring. Using this information, we were able to create a streamlined algorithm to facilitate the diagnosis of uncomplicated cystitis in this population.

This diagnostic algorithm is unique in that it deconstructs the concept of suspected UTI into 3 potential domains: *complicated UTI* or *other non-UTI infection*, *likely cystitis*, and *unlikely cystitis* (eg, ASB). The advantage of this algorithm is that it provides the clinician with a guided framework for the diagnostic approach to UTI. Considering UTI as one large homogenous category clouds diagnosis given the multitude of possible symptoms. The main focus of this work was the differentiation of uncomplicated cystitis from ASB. The algorithm highlights signs and/or symptoms that would suggest the presence of complicated UTI or other non-UTI infection, but does not attempt to define criteria for each of these possibilities. Individuals meeting the criteria for complicated UTI or other non-UTI infection should be evaluated by a clinician, with decisions for additional diagnostic testing and/or treatment based on the results of the evaluation and the individual's clinical and hemodynamic status. Also, although this work addressed the nursing home population, we believe the algorithm is applicable to the older adult and PA/LTC populations given their similarities.

This study has several limitations. Given a limited evidence base, we had to rely on expert consensus methods to develop our diagnostic guideline. However, the modified Delphi process is a widely accepted research methodology to reach consensus, which employs several strategies to reduce biases.^{26–32,34} These include the use of a thorough baseline literature search as well as steps to ensure blinding of the panel members to each other's identity, thus promoting equal panel member input. Like all current diagnostic guidelines for suspected UTI, it is not possible to determine the exact sensitivity or specificity of this algorithm because no gold standard for the diagnosis of UTI exists.^{3,14,35} Our diagnostic guideline is being tested in a cluster randomized trial.

Individuals with dementia represent a significant proportion of the nursing home population. Obtaining a history from individuals with advanced stage dementia can prove challenging. However, we do not believe this decreases the applicability of the algorithm for several reasons. Although prevalence rates will vary from facility to facility, the vast majority of nursing home residents do not have advanced-stage dementia that would preclude their ability to communicate acute symptoms.^{36,37} Also, it is possible to determine the presence of physical signs (eg, suprapubic pain, hematuria, increased voiding frequency, or obvious discomfort during voiding) during clinical care and examination of such residents by the nursing staff or clinicians. Also, risk of nontreatment must be questioned. Prior studies of ASB included residents with dementia and showed no benefit in the absence of urinary symptoms; no survival benefit was found in a cohort study of residents with advanced dementia and suspected UTI, and many cases of uncomplicated cystitis resolve spontaneously and without progression to pyelonephritis.^{3,38–41} As always, clinicians should use clinical judgment when applying guidelines such as this algorithm.

There are a number of strengths of this study. The systematic literature search strategies ensured current foundational background knowledge. As noted, the Delphi process is widely accepted and is preferred over other consensus methods such as nominal group techniques.^{26,27} The Delphi panel was composed of a national group of skilled and practicing PA/LTC physicians. Panel members had practical knowledge of PA/LTC environment. Panel members also had direct knowledge of the challenge of diagnosing UTI in the nursing home population, including those with cognitive or communication impairment. As such, the work should be generalizable to the larger

nursing home population. Also, the response rate among panel members was very high, suggesting the issue at hand is “near and dear” to them.

Implementing clinical guidelines or algorithms in the PA/LTC setting is challenging. Although it may be possible to implement change on a single unit or facility, promoting practice change across many facilities is difficult. Identifying strategies to implement this algorithm in a group of PA/LTC homes is a priority and is the focus of an ongoing AHRQ-funded dissemination project by the authors and AMDA—The Society for Post-Acute and Long-Term Care Medicine (AHRQ - R18 HS023779).

Conclusions/Relevance

We used a modified Delphi process to identify 5 signs and symptoms likely indicative of uncomplicated cystitis, one of the most common problems encountered in PA/LTC residents. The diagnostic algorithm developed as part of this project should be of use to nursing home clinicians and can be used to promote antibiotic stewardship efforts as required under the revised Centers for Medicare and Medicaid Services (CMS) requirements of participation.⁴² We believe it is also applicable for use in the older adult and broader PA/LTC populations. Dissemination and implementation of this algorithm is currently being evaluated in an ongoing national project.

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Appendix 1. Literature Search Strategy for Diagnosis of UTI in Nursing Home Residents

PubMed

Part 1 UTIs

"Aging/urine"[Mesh]
 OR
 "Antigens, Bacterial/urine"[Mesh]
 OR
 "Bacterial Infections/urine"[Mesh]
 OR
 "Bacteriuria"[Mesh]
 OR
 "Cystitis"[Mesh]
 OR
 "Infection/urine"[Mesh:NoExp]
 OR
 "Pyuria"[Mesh]
 OR
 "Urinary Tract Infections"[Mesh:NoExp]
 OR
 "Urine/analysis"[Mesh]
 OR
 "Urine/chemistry"[Mesh]
 OR
 "Urine/cytology"[Mesh]
 OR
 "Urine/diagnosis"[Mesh]
 OR
 "Urine/microbiology"[Mesh]
 OR
 bacteriuri*[tiab]
 OR
 bladder infection*[All Fields]
 OR
 cystitis[tiab]
 OR
 mcgeer[tiab]
 OR
 pyelocystitis[tiab]
 OR
 pyuria[tiab]
 OR
 UTI[tiab]
 OR
 UTI s[tiab]
 OR
 UTIs[tiab]
 OR
 urinary infection[tiab]
 OR
 urinary infections[tiab]
 OR
 urinary tract infection[tiab]
 OR
 urinary tract infections[tiab]
 OR
 urological infection[tiab]
 OR
 urological infections[tiab]
 OR
 bacteriuri*[ot]
 OR

cystitis[ot]
 OR
 pyelocystitis[ot]
 OR
 pyuria[ot]
 OR
 urinary infection[ot]
 OR
 urinary tract infection[ot]
 OR
 urinary tract infections[ot]
 OR
 UTI[ot]
 OR
 UTIs[ot]
 OR
 ((urinary tract[tiab] OR urinary tract[ot]) AND (infection*
 [tiab] OR infection*[ot]))
 Part 2 Nursing Homes
 "Institutionalization"[Mesh]
 OR
 "Long-Term Care"[Mesh]
 OR
 "Residential Facilities"[Mesh]
 OR
 loeb M[au]
 OR
 loeb MB[au]
 OR
 aged care[tiab]
 OR
 assisted living[tiab]
 OR
 chronic care facilit*[tiab]
 OR
 community hous*[tiab]
 OR
 extended care[tiab]
 OR
 homes for the aged[tiab]
 OR
 institutional care[tiab]
 OR
 institutional living[tiab]
 OR
 institutionalis*[tiab]
 OR
 institutionalized elder*[tiab]
 OR
 intermediate care[tiab]
 OR
 geriatric facilit*[tiab]
 OR
 LTCF[tiab]
 OR
 loeb[tiab]
 OR
 long term care[tiab]
 OR
 longterm care[tiab]
 OR
 nursing home[tiab]
 OR
 nursing homes[tiab]
 OR

residential care[tiab]
 OR
 residential home[tiab]
 OR
 residential homes[tiab]
 OR
 residential facilit*[tiab]
 OR
 retirement hom*[tiab]
 OR
 skilled nursing facilit*[tiab]
 OR
 aged care[ot]
 OR
 assisted living[ot]
 OR
 homes for the aged[ot]
 OR
 institutional care[ot]
 OR
 intermediate care[ot]
 OR
 geriatric facilit*[ot]
 OR
 long term care[ot]
 OR
 longterm care[ot]
 OR
 nursing home[ot]
 OR
 nursing homes[ot]
 OR
 residential care[ot]
 OR
 residential home[ot]
 OR
 residential homes[ot]
 OR
 residential facilit*[ot]
 OR
 retirement hom*[ot]
 OR
 skilled nursing facilit*[ot]
 OR
 "The annals of long-term care: the official journal of the
 American Medical Directors Association"[Journal]
 OR
 "Director"[Journal]
 OR
 "J Long Term Care Adm"[Journal]
 OR
 "Journal of the American Medical Directors
 Association"[Jour]
 OR
 "Mod Nurs Home"[Journal]
 OR
 "Nurs Homes"[Journal]
 OR
 "Nurs Homes Sr Citiz Care"[Journal]
 OR
 "Prof Nurs Home"[Journal]
 OR
 "Todays Nurs Home"[Journal]
 OR
 ((Institutionalized[tiab] OR Institutionalized[ot]) AND (aged[tiab]
 OR elderly[tiab] OR older[tiab] OR setting[tiab] OR settings[tiab] OR
 aged[ot] OR elderly[ot] OR older[ot] OR setting[ot] OR settings[ot]))
 Part 3
 Part 1 AND Part 2
 Part 4
 "English"[Language]
 Part 5
 "1980/01/01"[PDAT]: "2016/12/31"[PDAT]
 EMBASE.com
 Part 1 UTIs
 'cystitis'/exp
 OR
 bacteriuri*
 OR
 bladder NEXT/1 infect*
 OR
 'cystitis'
 OR
 mcgeer*:ab,ti
 OR
 'pyuria'
 OR
 'uti'
 OR
 'utis'
 OR
 urinary NEXT/1 infect*
 OR
 urinary NEXT/1 tract NEXT/1 infect*
 OR
 urine NEXT/1 infect*
 OR
 urine NEXT/1 tract NEXT/1 infect*
 OR
 urolog* NEXT/1 infect*
 OR
 ('aging'/exp OR 'bacterial infection'/exp AND 'urine'/exp)
 OR
 ('urinary tract':ab,ti AND infect*:ab,ti)
 Part 2 Nursing Homes
 'aged care'
 OR
 assisted NEXT/1 liv*
 OR
 chronic NEXT/1 care NEXT/1 facilit*
 OR
 community NEXT/1 hous*
 OR
 convalescence NEXT/1 home*
 OR
 convalescence NEXT/1 hospital*
 OR
 elderly NEXT/1 care NEXT/1 facilit*
 OR

extended NEXT/1 care NEXT/1 facilit*
 OR
 geriat* NEXT/3 facilit*
 OR
 'home for the aged'
 OR
 institution* NEXT/1 liv*
 OR
 'institutional care'
 OR
 institutionalis*
 OR
 'institutionalization'
 OR
 institutionalized NEXT/1 elder*
 OR
 'intermediate care'
 OR
 Ltcf
 OR
 loeb:ab,ti
 OR
 'loeb m':au
 OR
 'long term care'
 OR
 'longterm care'
 OR
 'nursing home'
 OR
 'nursing homes'

OR
 old NEXT/1 age NEXT/1 home*
 OR
 old NEXT/1 people NEXT/1 home*
 OR
 resident* NEXT/1 hom*
 OR
 residential NEXT/3 care
 OR
 residential NEXT/3 facilit*
 OR
 retire* NEXT/1 hom*
 OR
 skilled NEXT/1 nursing NEXT/1 facilit*
 OR
 (institutionaliz* AND (aged OR elderly OR older OR setting OR settings))

Part 3
 Part 1 AND Part 2
 Part 4
 [english]/lim
 Part 5
 [1980-2016]/py
 Part 6
 Part 3 AND Part 4 AND Part 5
 Part 7
 'conference abstract'/it
 Part 8
 Part 6 NOT Part 7

Appendix 2

Delphi Panel Members for Diagnostic Guideline

Physician Name	Affiliation	City	State
Namita Ahuja, MD	University of Pittsburgh Medical Center (UPMC)	Pittsburgh	PA
Laurie Archbald-Pannone, MD	University of Virginia	Charlottesville	VA
Seki Balogun, MD	University of Virginia	Charlottesville	VA
Kenneth Brubaker, MD	Division of Geriatric Medicine, Lancaster General Hospital	Elizabethtown	PA
Chuck Crecelius, MD	Washington University School of Medicine	St Louis	MO
Swati Gaur, MD	Community Health Services of Georgia	Gainesville	GA
Catherine Glew, MD	Center for Healthy Aging, Lehigh Valley Health Network	Allentown	PA
Daniel Haimowitz, MD	Genesis PACE Program	Levittown	PA
Steven Handler, MD	University of Pittsburgh	Pittsburgh	PA
Leon Kraybill, MD	Division of Geriatric Medicine, Lancaster General Hospital	Lancaster	PA
Susan Levy, MD	SML Geriatric Medicine Consulting	Bethany Beach	DE
Dheeraj Mahajan, MD	Chicago Internal Medicine Practise and Research (CIMPAR)	Melrose Park	IL
David Mehr, MD	University of Missouri	Columbia	MO
Naushira Pandya, MD	NOVA Southeastern College of Osteopathic Medicine	Ft Lauderdale	FL
Neelofer Sohail, MD	Division of Geriatric Medicine, Lancaster General Hospital	Lancaster	PA
Karl Steinberg, MD	Mariner Health Center	Oceanside	CA
Matt Wayne, MD	Summa Health System	Akron	OH
Heidi White, MD	Duke University	Durham	NC
Brian Wilson, MD	University of Pittsburgh Medical Center	Pittsburgh	PA
Rollin Wright, MD	University of Pittsburgh	Pittsburgh	PA



Clinical Recommendations for the Empiric Treatment of Uncomplicated Cystitis in Long-Term Care Residents Pending Culture & Sensitivity Results

The IOU Consensus Recommendations for Empirical Therapy of Cystitis in Nursing Home Residents and Reference

Hanlon JT, Perera S, Drinka PJ, et al. The IOU consensus recommendations for empirical therapy of cystitis in nursing home residents. *J Am Geriatr Soc.* 2018 Dec 24. doi: 10.1111/jgs.15726 [Epub ahead of print]



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The IOU Consensus Recommendations for Empirical Therapy of Cystitis in Nursing Home Residents

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OBJECTIVE: To establish consensus recommendations for empirical treatment of uncomplicated cystitis with anti-infectives in noncatheterized older nursing home residents to be implemented in the Improving Outcomes of UTI Management in Long-Term Care Project (IOU) funded by the Agency for Healthcare Research and Quality.

DESIGN: Two-round modified Delphi survey.

PARTICIPANTS: Expert panel of 19 clinical pharmacists.

MEASUREMENTS: Comprehensive literature search and development/review/edit of draft survey by the investigative group (one geriatric clinical pharmacist, two geriatric medicine physicians, and one infectious disease physician). The expert panel members rated their agreement with each of 31 recommendations for drugs of choice, dosing medications at various levels of renal function, drug-drug interactions to avoid, and duration of therapy by sex on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Consensus agreement was defined as a lower 95%

confidence limit of 4.0 or higher for the recommendation-specific mean score.

RESULTS: The response rate was 95% for the first round, and three recommendations achieved consensus (dosing for nitrofurantoin and trimethoprim/sulfamethoxazole in those without chronic kidney disease, and drug-drug interaction between trimethoprim/sulfamethoxazole and warfarin). In the second round, 90% responded and reached consensus on an additional eight recommendations (two for nitrofurantoin or trimethoprim/sulfamethoxazole as initial drugs of choice, three for dosing ciprofloxacin, nitrofurantoin, and trimethoprim/sulfamethoxazole at various levels of chronic kidney disease, and three drug-drug interactions to avoid: trimethoprim/sulfamethoxazole with phenytoin and ciprofloxacin with theophylline or with tizanidine).

CONCLUSION: An expert panel of clinical pharmacists was able to reach consensus on a set of recommendations for the empirical treatment of cystitis with oral anti-infective medications in older nursing home residents. The recommendations were incorporated into a treatment algorithm for uncomplicated cystitis in noncatheterized nursing home residents and used in educational materials for health professionals in an ongoing controlled intervention study. *J Am Geriatr Soc* 00:1–7, 2018.

Key words: aged; nursing homes; cystitis; urinary tract infection; antibacterial agents

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Suspected uncomplicated urinary tract infection (UTI) is the most common reason that antibiotics are prescribed to older nursing home residents.^{1–3} Most cases of suspected uncomplicated UTIs are in fact asymptomatic bacteriuria for which antibiotics are unnecessary.^{1,4} Some cases of suspected uncomplicated UTIs are due to cystitis in which

residents are typically not severely ill and present with lower urinary symptoms such as dysuria, urinary urgency/frequency, or suprapubic pain.^{4–8} Warning signs or symptoms such as rigors, flank pain, hypotension, or prostatic pain, particularly when associated with significant fever, suggest more complicated upper tract disease or prostatitis⁸ (Supplementary Appendix S1).

The appropriateness of antibiotics is important because they can have considerable unintended consequences such as adverse drug events and promoting the development of antibiotic-resistant organisms.^{1,9} Antibiotic resistance may directly harm an individual through treatment failures, increased need for postacute and long-term care services, prolonged stays, and increased mortality.¹⁰ Moreover, antibiotic-resistant urinary tract organisms are associated with increased transfers to acute care facilities and with mortality.^{1,10} In addition, suboptimal antibiotic use is the leading cause of *Clostridium difficile* infections that can result in serious and life-threatening complications.^{1,11}

Much of the antibiotic use for cystitis among nursing home residents is potentially suboptimal. For example, Rotjanapan and colleagues conducted a 6-month study in two Rhode Island nursing homes (total of 270 beds) and found that 72% of residents, all aged 65 and older, with cystitis received unnecessarily broad-spectrum antibiotic therapy.¹² In addition, 46% of antibiotics given had a suboptimal dosage, and nearly 70% of residents were given an antibiotic for an excessive duration. Another study by Miller and colleagues reported on the appropriateness of antibiotic prescribing for 282 residents aged 65 and older who received an antibiotic for cystitis in 18 US nursing homes over a 12-month period.¹³ Overall, 40% of antibiotics were deemed to be potentially suboptimal. The most common problem was excessive doses of primarily renally cleared antibiotics in 19% of residents. Other problems seen included the use of higher cost antibiotics, therapeutic duplication, impractical directions, prolonged duration, and drug interactions.¹³

Although there are consensus recommendations for defining, evaluating, and monitoring infections in nursing home residents, they are not specific to the optimal use of antibiotics in treating uncomplicated cystitis.^{14–18} Given this background, the study objective was to establish consensus recommendations for the optimal prescribing of empirical anti-infectives for uncomplicated cystitis in noncatheterized older nursing home residents via a modified Delphi survey of an expert panel of clinical pharmacists.^{19,20} The expert recommendations were developed as part of the Improving Outcomes of UTI Management in Long-Term Care Project (IOU), an implementation and dissemination project funded by the Agency for Healthcare Research and Quality aimed at improving antimicrobial stewardship for nursing home acquired cystitis. It should be noted that these expert recommendations provide *initial* empirical treatment suggestions pending the results of urine culture and sensitivities. The recommendations would not account for any history of prior resistance or recent antimicrobial exposure that a clinician should always consider.

METHODS

To develop the modified Delphi survey, the investigative team worked with two medical librarians at the University of Pittsburgh to conduct a comprehensive literature review

restricted to English-language articles in PubMed and Embase using a combination of terms including *urinary tract infections, cystitis, antibacterial agents, nursing homes, and aged* (ie, persons 65 y and older). Inclusion criteria included those using randomized controlled trial, cohort or case-control, or experimental pharmacokinetic designs. Abstracts of the articles were reviewed. Studies deemed relevant underwent a full article review. In addition, reference lists from review and retrieved articles were scanned for any additional relevant studies.

Using the identified literature and considering four important aspects of medication appropriateness (ie, drugs of choice, dosing medications at various levels of renal function, drug-drug interactions to avoid, and duration of therapy by sex), a clinical pharmacist researcher developed the initial draft of the Delphi survey.^{19,20} This draft survey was further refined by three internal medicine physician investigators (two from geriatric medicine and one from infectious disease).

The final survey included 31 recommendations and supporting references to be considered by an expert panel (Supplementary Appendix S2). The expert panel consisted of 19 clinical pharmacists (Acknowledgment section lists the details), and they were sent the modified Delphi survey via e-mail and were blinded to the identity of other panel members. They were asked to rate their agreement with each of 31 recommendations on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). After receipt of the completed surveys, means and 95% confidence intervals were estimated for each recommendation. Consensus on agreeing to a recommendation was achieved when the lower 95% confidence limit calculated from participant responses was greater than or equal to 4.0. Consensus on disagreeing to a recommendation was achieved when the upper 95% confidence limit calculated from participant responses was less than or equal to 3.0, and the remainder was treated as failure to reach consensus.

Recommendations that did not achieve consensus in the first round were included in a second round. The same expert panel was asked to further consider the recommendation after providing the group rating mean for each item from the first round and additional targeted or suggested items from the expert panel to better glean consensus. This approach is consistent with previous published work.^{21,22} For all statistical analyses, SAS v.9.3 (SAS Institute, Cary, NC) was used. The University of Pittsburgh institutional review board approved the study as exempt. The results were summarized into simple treatment recommendations to facilitate clinical use.

RESULTS

The literature search yielded 253 treatment studies in PubMed and 332 in Embase for a total of 462 unique articles, of which 53 were deemed relevant after abstract review. No additional studies were identified from reference lists. There were a few articles from randomized controlled trials. Three-quarters (75%) of the expert panel members were female. Additionally, 68% were board-certified geriatric pharmacists, and an additional 26% were board certified in another specialty. A total of 68% had long-term care experience, and 95% worked with frail older adults.

The first-round response rate was 95%. After the first round of the survey, consensus was reached for three

Table 1. Clinical pharmacist expert panel round 1 survey responses for antibiotic treatment of cystitis in older nursing home residents

Appropriateness domain	Recommendations	Mean (95% CI)
Drugs of choice for empirical treatment	With adequate renal function or sulfonamide allergy, nitrofurantoin	4.22 (3.86-4.59)
	With adequate renal function but without sulfonamide allergy, TMP/SMZ	4.28 (3.90-4.65)
Renal dosing	Fosfomycin is always the first choice ^a	1.61 (1.26-1.96)
	When CrCl <60, avoid nitrofurantoin ^a	1.89 (1.65-2.12)
	When CrCl <40, avoid nitrofurantoin	3.17 (2.50-3.83)
	When CrCl <30, avoid nitrofurantoin	4.44 (3.96-4.83)
	When CrCl <30, avoid TMP/SMZ ^a	2.22 (1.75-2.69)
	When CrCl <15, avoid TMP/SMZ	4.33 (3.91-4.75)
	With adequate renal function, nitrofurantoin 100 mg twice a day ^b	4.56 (4.30-4.81)
	With adequate renal function, trimethoprim-sulfamethoxazole 160/800 mg twice a day ^b	4.61 (4.36-4.86)
	With reduced renal function but not to the level it should be avoided, TMP/SMZ 160/800 mg per day	4.00 (3.58-4.42)
Clinically significant drug-drug interactions	When CrCl <30, ciprofloxacin 250 mg/d	3.56 (3.04-4.07)
	With adequate renal function, ciprofloxacin 250 mg twice a day	4.17 (3.68-4.66)
	Regardless of renal function, fosfomycin 3 g single dose	4.17 (3.71-4.63)
	Ciprofloxacin and theophylline	4.28 (3.90-4.65)
	Ciprofloxacin and corticosteroids	3.22 (2.79-3.66)
	Ciprofloxacin and warfarin	4.06 (3.69-4.42)
	Ciprofloxacin and glipizide/glyburide ^a	2.33 (1.77-2.90)
	TMP/SMZ and procainamide	3.83 (3.31-4.35)
	TMP/SMZ and phenytoin	4.33 (3.95-4.71)
Minimum duration of anti-infective treatment	TMP/SMZ and warfarin ^b	4.89 (4.73-5.05)
	TMP/SMZ and methotrexate	3.94 (3.45-4.44)
	TMP/SMZ and angiotensin-converting enzyme inhibitors	3.72 (3.35-4.10)
	TMP/SMZ and angiotensin receptor blockers	3.72 (3.35-4.10)
	TMP/SMZ and sulfonylureas	3.50 (3.11-3.89)
	In women, 3 d	3.83 (3.34-4.32)
	In women, 5 d	2.89 (2.35-3.43)
	In men, 5 d ^a	2.06 (1.69-2.42)
	In men, 7 d	4.11 (3.73-4.49)
Cost of treatment	In men, 10 d	2.67 (2.15-3.18)
	Fosfomycin is the least expensive choice ^a	1.50 (1.15-1.85)

Abbreviations: CI, confidence interval; CrCl, creatinine clearance in milliliters per minute; TMP/SMZ, trimethoprim/sulfamethoxazole.

^aConsensus disagreement.

^bConsensus agreement.

recommendations (using nitrofurantoin 100 mg twice a day and trimethoprim/sulfamethoxazole 160/800 mg twice a day in those without chronic kidney disease, and avoiding a drug-drug interaction between trimethoprim/sulfamethoxazole and warfarin) (Table 1). The panel also reached consensus against considering fosfomycin as a drug of choice, avoiding nitrofurantoin in those with a creatinine clearance (CrCl) lower than 60 mL/min, avoiding trimethoprim/sulfamethoxazole in those with a CrCl lower than 30 mL/min, avoiding ciprofloxacin in patients concurrently receiving glipizide/glyburide, 5 days as the minimum treatment duration for men, and fosfomycin as the cheapest alternative (Table 1).

The second-round response rate was 90%. Four new recommendations were added. The panel reached consensus agreement on nitrofurantoin as the drug of choice for empirical treatment of cystitis for individuals with adequate renal function and a sulfonamide allergy; trimethoprim/sulfamethoxazole as the drug of choice in those with adequate renal function and without a sulfonamide allergy; avoiding

nitrofurantoin in those with a CrCl lower than 30 mL/min; avoiding trimethoprim/sulfamethoxazole in those with a CrCl lower than 15 mL/min; for those with adequate renal function, 250 mg twice a day as the appropriate dose of ciprofloxacin; significance of the drug-drug interaction between ciprofloxacin and theophylline, between ciprofloxacin and tizanidine, and that between trimethoprim/sulfamethoxazole and phenytoin (Table 2). The panel disagreed that ciprofloxacin and sulfonylureas constitute a significant drug-drug interaction and that men should be treated for a minimum of 10 days (Table 2). Consensus was not reached for the remaining items (Table 2). Figure 1 operationally summarizes the survey results as treatment recommendations.

DISCUSSION

We found that an expert panel of clinical pharmacists could achieve consensus agreement on the optimal prescribing of empirical oral anti-infectives in uncomplicated cystitis in older nursing home residents. Regarding drugs of choice,

Table 2. Clinical pharmacist expert panel round 2 survey responses for antibiotic treatment of cystitis in older nursing home residents

Appropriateness domain	Recommendations	Mean (95% CI)
Drugs of choice for empirical treatment	With adequate renal function or sulfonamide allergy, nitrofurantoin ^a	4.41 (4.15-4.67)
Renal dosing	With adequate renal function but without sulfonamide allergy, TMP/SMZ ^a	4.35 (4.04-4.66)
	When CrCl <60, avoid nitrofurantoin	3.35 (2.72-3.98)
	When CrCl <30, avoid nitrofurantoin ^a	4.82 (4.62-5.03)
	When CrCl <15, avoid TMP/SMZ ^a	4.41 (4.00-4.82)
	With reduced renal function but not to the level it should be avoided, TMP/SMZ 160/800 mg per day	4.12 (3.72-4.52)
	When CrCl <30, ciprofloxacin 250 mg/d	3.76 (3.34-4.19)
	When CrCl <30, ciprofloxacin 500 mg/d ^b	3.06 (2.44-3.67)
	With adequate renal function, ciprofloxacin 250 mg twice a day ^a	4.47 (4.21-4.74)
Clinically significant drug-drug interactions	With adequate renal function, ciprofloxacin 500 mg twice a day ^b	2.53 (1.90-3.16)
	Regardless of renal function, fosfomycin 3 g single dose	4.24 (3.74-4.73)
	Ciprofloxacin and theophylline ^a	4.41 (4.09-4.73)
	Ciprofloxacin and corticosteroids	3.06 (2.72-3.40)
	Ciprofloxacin and warfarin	4.06 (3.72-4.40)
	Ciprofloxacin and glipizide/glyburide ^c	2.35 (1.91-2.80)
	Ciprofloxacin and tizanidine ^{a,b}	4.41 (4.05-4.78)
	TMP/SMZ and procainamide	4.06 (3.72-4.40)
	TMP/SMZ and phenytoin ^a	4.41 (4.15-4.67)
	TMP/SMZ and methotrexate	4.06 (3.67-4.44)
	TMP/SMZ and angiotensin-converting enzyme inhibitors	3.71 (3.31-4.10)
	TMP/SMZ and angiotensin receptor blockers (or potassium supplements) ^b	3.71 (3.31-4.10)
Minimum duration of anti-infective treatment	TMP/SMZ and sulfonyleureas	3.59 (3.22-3.95)
	In women, 3 d	4.00 (3.69-4.31)
	In women, 5 d	2.71 (2.27-3.14)
	In men, 7 d	4.00 (3.64-4.36)
	In men, 10 d ^c	2.47 (2.06-2.88)

Abbreviations: CI, confidence interval; CrCl, estimated creatinine clearance in milliliters per minute; TMP/SMZ, trimethoprim/sulfamethoxazole.

^aConsensus agreement.

^bNew recommendation added in round 2.

^cConsensus disagreement.

the panel reached agreement that the preferred drugs were nitrofurantoin and trimethoprim/sulfamethoxazole. This is consistent with recent guidelines and reviews and also is clinically sensible because both drugs are capable of successfully treating *Escherichia coli* (*E. coli*) and *Klebsiella* spp that together account for up to 83% of cases of UTI in nursing home populations.^{17,23–30} Trimethoprim/sulfamethoxazole is more active against *Proteus* spp, although nitrofurantoin would be preferred when treating *Enterococcus*. It should also be noted that overall resistance to nitrofurantoin is minimal, and it is a good choice in those with a sulfa allergy.²³ Where resistance to *E. coli* is less than 20%, trimethoprim/sulfamethoxazole may be a reasonable alternative because its average wholesale price is less than nitrofurantoin and avoids the small risk of pulmonary reactions that can be seen with nitrofurantoin.^{23,24,29,31,32}

The expert panel agreement also provides guidance regarding the renal dosing recommendations for several anti-infectives consistent with a previous Delphi survey.²² Although controversial, nitrofurantoin should not be used in residents with an estimated CrCl lower than 30 mL/min because urinary concentrations may be insufficient for it to be effective.³³ In those whose CrCl is higher than 15 mL/min, trimethoprim/

sulfamethoxazole is an acceptable alternative. Below this level of renal function, the risk of hyperkalemia with trimethoprim/sulfamethoxazole is greater, and alternatives such as ciprofloxacin or fosfomycin should be considered.^{24,31,34}

The panel also identified four clinically important drug-drug interactions, three of which involved narrow therapeutic range drugs (warfarin, phenytoin, and theophylline). A case-control study from Canada found that trimethoprim/sulfamethoxazole in combination with warfarin increased the risk of upper gastrointestinal hemorrhage by nearly 4-fold (adjusted odds ratio [aOR] = 3.84).³⁵ A nearly 2-fold increased risk was also found with ciprofloxacin (aOR = 1.94).³⁵ The finding with trimethoprim/sulfamethoxazole was confirmed by another case-control study from the United States where the risk of bleeding with warfarin was increased by nearly 3-fold (aOR = 2.70).³⁶ This same anti-infective was found in another case-control study to be the culprit interacting with phenytoin in which the risk of toxicity requiring hospitalization was increased more than 2-fold (aOR = 2.11).³⁷ Ciprofloxacin increases the risk of theophylline toxicity by nearly 2-fold (aOR = 1.86).³⁸ Finally, when possible the use of tizanidine should be avoided in those taking ciprofloxacin to avoid toxicity. (Anon. Approved product labeling for ZANAFLEX

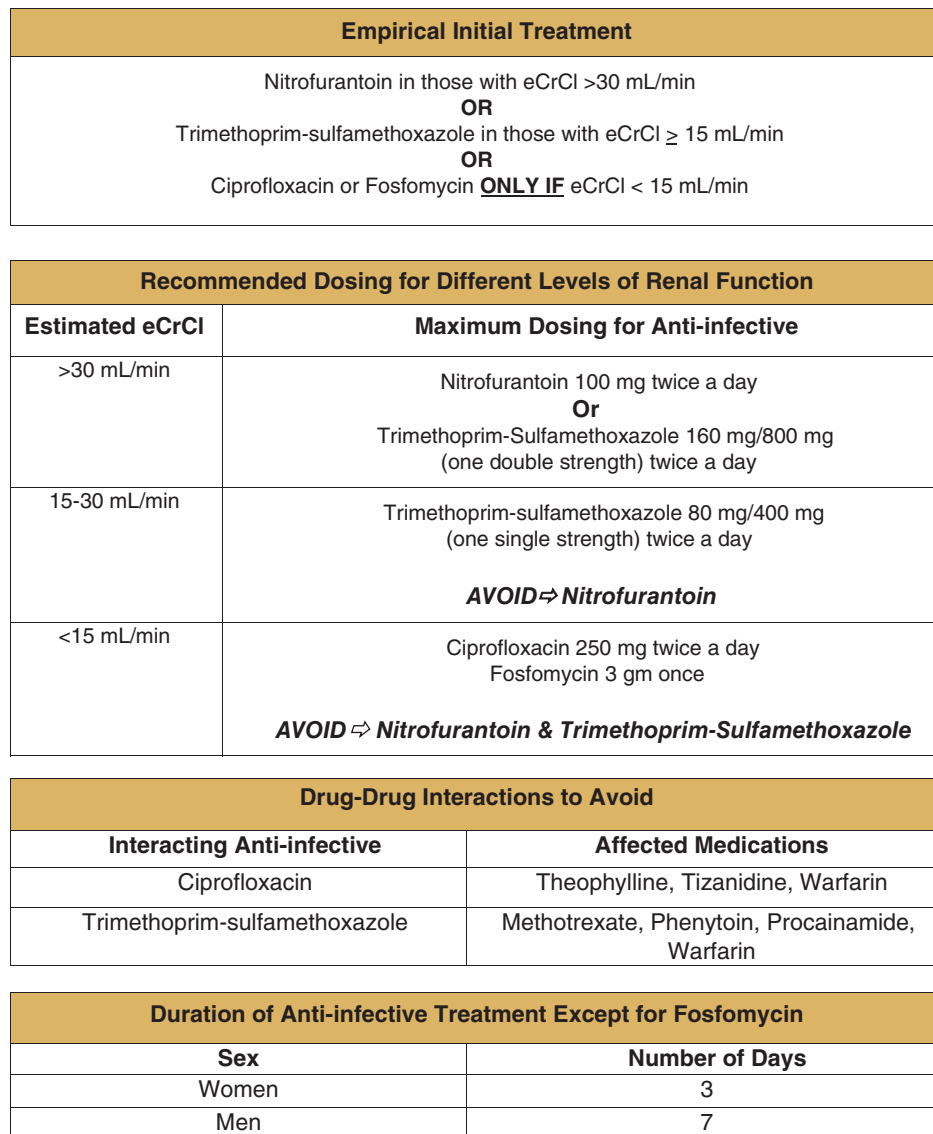


Figure 1. Empirical treatment of uncomplicated bladder infection (cystitis) in nursing home residents 65 years of age and older without a urinary catheter. eCrCl = estimated creatinine clearance.

(Tizanidine), https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021447s011_020397s026lbl.pdf. Accessed September 5, 2018).

Our study had several potential limitations. First, although the panel agreed that anti-infective treatment in men more than 5 days but less than 10 days in duration was acceptable for uncomplicated cystitis, we were unable to reach consensus regarding the optimal duration of treatment. For women, most sources are clear that the duration of use for anti-infectives for cystitis should range between 3 and 7 days.^{23,24,28,29} Therefore, we operationalized the duration of use as 7 days for men and 3 days for women in the final recommendations (Figure 1). We included nitrofurantoin in these duration recommendations based on the expert opinion of the Delphi panel. Although not routinely recommended in men because of the concern for prostatitis, our recommendations specifically focus on cystitis for which nitrofurantoin is indicated. We do not suggest use of nitrofurantoin for complicated UTI. Although a 5-day course of nitrofurantoin is often recommended in women, this is due to a dearth of

studies looking at 3-day courses. Only a few studies using a 3-day course have been conducted, and these involved younger women. Treatment success was observed in these studies.^{40,41} Pharmacodynamic effects of nitrofurantoin include a short static kill time for *E. coli* (complete eradication in 8 hours), although a dynamic kill time appears to be influenced more by dosing rather than duration of treatment.⁴² Given that clinical trials have not established an optimal duration of therapy for nitrofurantoin, and that our work here is based on expert opinion, it is reasonable that clinicians might consider using a 5-day course of nitrofurantoin. Future studies are clearly needed to define the optimal dose and duration of therapy for nitrofurantoin in cystitis.

Second, we used a convenience sample of clinical pharmacists for this modified Delphi survey. However, they came from 10 states and included clinical pharmacists from academia, community-based care, and managed care. Third, face-to-face meetings of the panelists were not held due to the prohibitive cost and other practical considerations. However, remote participation was believed to be advantageous in maintaining

blinding and limits confounding arising from dominant personalities.³⁹ Finally, as new research contributes additional information about emerging resistance patterns, optimal durations of therapy, and safe and effective medication use in older adults, the list of anti-infective drugs and associated prescribing information will likely need to be updated.

As with all treatment recommendations, clinical judgment is paramount. It is important to note that active patient monitoring without empirical antibiotic use may also be acceptable while awaiting culture results. These guidelines are meant for empirical treatment pending culture results. Clinicians should reassess a patient's clinical progress along with antibiotic appropriateness once culture results and sensitivities return. Referred to as an antibiotic time-out, this reassessment offers the clinician an opportunity to refine antibiotic prescribing by narrowing the antimicrobial spectrum, reducing treatment duration, and potentially discontinuing unnecessary additional treatment. When using this treatment recommendation, clinicians should also be mindful of local resistance patterns in their facility as well as disease severity, recent antibiotic use, and/or prior history of antimicrobial resistance in an individual patient because these factors may influence the choice of the empirical antimicrobial selected.

In conclusion, an expert panel of clinical pharmacists was largely able to reach consensus agreement on a set of recommendations for the empirical treatment of uncomplicated cystitis with oral anti-infective medications in older nursing home residents. These recommendations were incorporated into a consensus-based treatment algorithm for uncomplicated cystitis in noncatheterized older nursing home residents and used in educational materials for health professionals in an ongoing controlled intervention study (AHRQ R18 HS023779). Although these recommendations are a starting point to assist in current clinical care, future research is needed to better inform decisions regarding antibiotic selection and optimal durations of therapy, particularly with nitrofurantoin, for nursing home residents with uncomplicated cystitis.

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Author Contributions: *Study concept and design:* All authors. *Acquisition of subjects and/or data:* Hanlon and Saracco. *Data analysis:* Hanlon, Nace, and Perera. *Interpretation of data:* Hanlon, Perera, Drinka, Crinch, Nace, and Schweon. *Preparation of manuscript:* All authors.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Appendix S1. The IOU Consensus Recommendations for the diagnosis of uncomplicated cystitis in nursing home residents

Appendix S2. Delphi Treatment Survey.



Physician Order Set for Suspected UTI

Resident Name _____

Date _____

Facility _____ DOB _____

Room Number _____

A Active Monitoring Orders

- Encourage _____ ounces of liquid intake _____ times daily
- Record fluid intake
- Vital signs, including temp, every shift for _____ days
- Vital signs, including temp, every _____ hours for _____ days
- Notify physician / NP / PA if symptoms worsen or are unresolved in _____ hours
- Other _____

B Laboratory Testing

- CBC Electrolytes, BUN, Cr Comprehensive Metabolic Panel
- Blood Cultures Urine Culture Urine analysis _____
(Other)

_____ Medications - Complete only if starting empiric antibiotics at this time _____

C Residents with Symptoms of Uncomplicated Bladder Infection (Non-Catheterized)

<input type="checkbox"/> Start the following antibiotics (mark the selected antibiotic in the ✓ column)						
✓	Renal Function	Antibiotic	Dose	Route	Freq	Duration
	>30 ml/min	Trimethoprim-Sulfamethoxazole	160mg/800mg (One Double Strength)		BID	days
	>30 ml/min	Nitrofurantoin	100mg		BID	days
	15-30 ml/min	Trimethoprim-Sulfamethoxazole	80mg/400mg (One Single Strength)		BID	days
	<15 ml/min	Ciprofloxacin	250mg		BID	days
	<15 ml/min	Fosfomycin	3gm		Daily	days

D Residents with Symptoms of Complicated UTI (e.g. Pyelonephritis, Prostatitis, Catheterized)

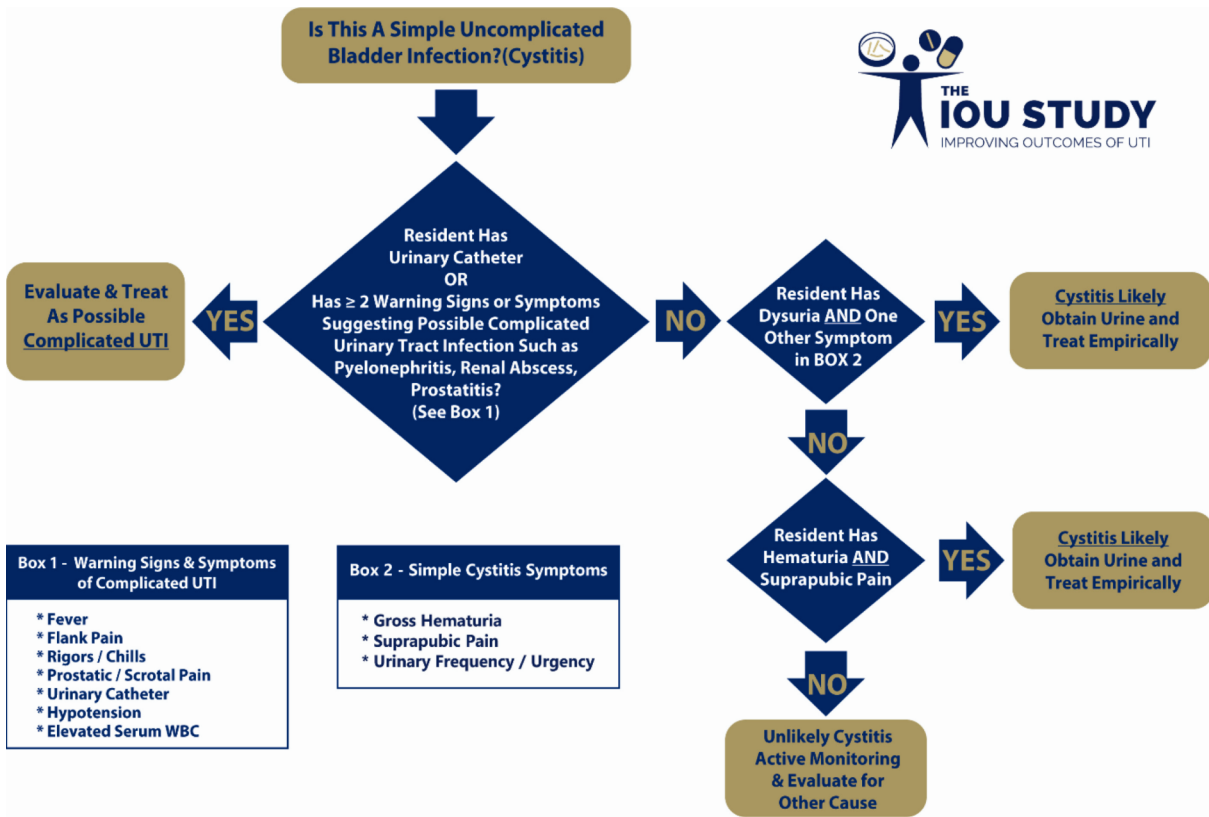
<input type="checkbox"/> Start the following antibiotics	Dose	Route	Duration
			days
			days
			days

E Additional Orders OR Orders for Residents with Complicated UTI

- _____
- _____

Physician Signature / Date

Nurse Signature / Date



Treatment of Uncomplicated Bladder Infection (Cystitis) In Nursing Home Residents ≥ 65 Years Without a Urinary Catheter

Empiric Initial Treatment	
Nitrofurantoin in those with eCrClr >30 ml/min OR Trimethoprim-sulfamethoxazole in those with eCrClr > 15 ml/min OR Ciprofloxacin or Fosfomycin <u>only if</u> eCrClr < 15 ml/min	
Recommended Dosing for Different Levels of Renal Function	
Estimated CrClr	Maximum Dosing for Anti-infective
>30 ml/min	Nitrofurantoin 100mg twice daily Or Trimethoprim-Sulfamethoxazole 160mg/800mg (one double strength) twice daily
15-30ml/min	Trimethoprim-sulfamethoxazole 80mg/400mg (one single strength) twice daily
<15 ml/min	AVOID \Rightarrow Nitrofurantoin Ciprofloxacin 250mg twice daily Fosfomycin 3gm daily AVOID \Rightarrow Nitrofurantoin & Trimethoprim-Sulfamethoxazole
Drug-Drug Interactions to Avoid	
Interacting Anti-infective	Affected Medications
Ciprofloxacin	Theophylline, Tizanidine, Warfarin
Trimethoprim-sulfamethoxazole	Methotrexate, Phenytoin, Procainamide, Warfarin
Maximum Duration of Anti-infective Treatment Except for Fosfomycin	
Gender	Number of Days
Women	3
Men	7



Active Monitoring for Urinary Symptoms

Resident Name _____ MRN _____
 Facility _____ DOB _____ Room Number _____

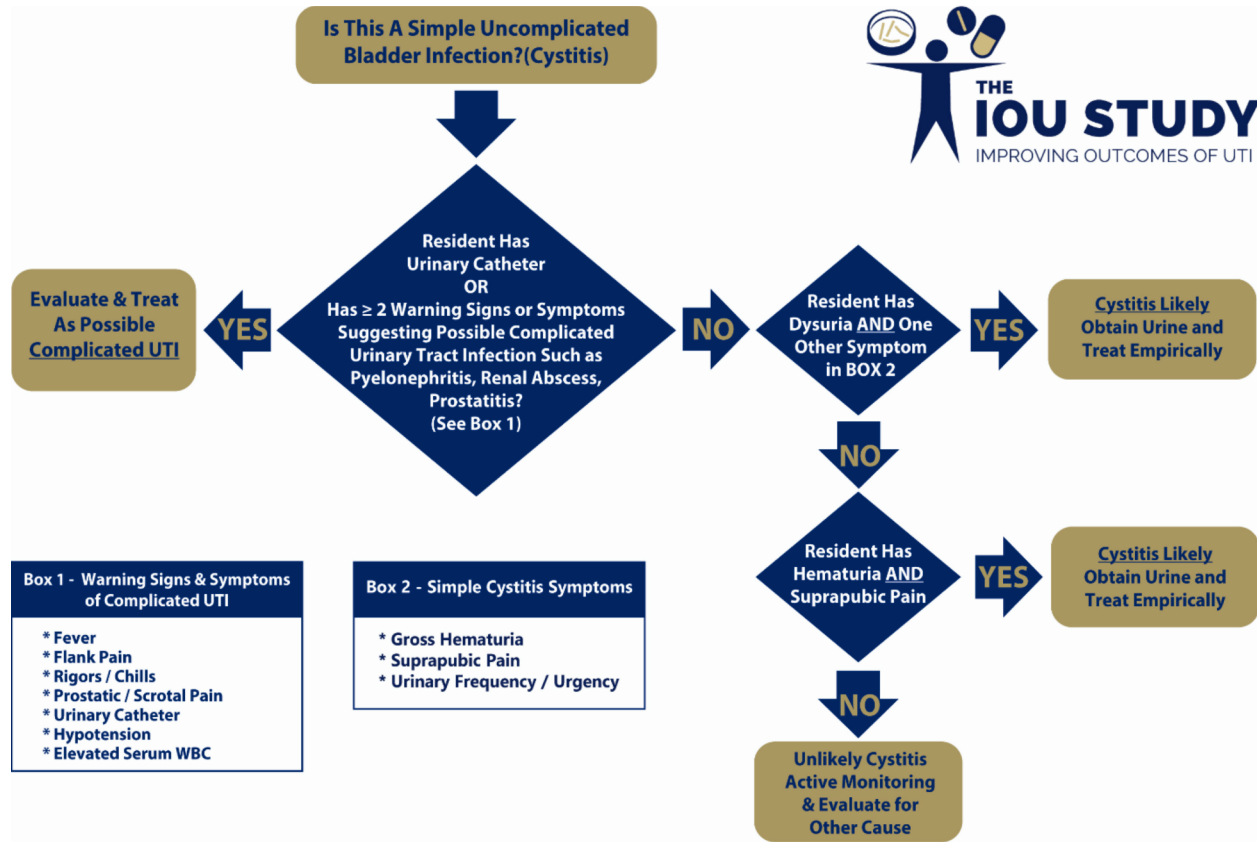
A. Systemic Symptoms & Signs – 2 or More Suggest COMPLICATED UTI or Other Infection												
Symptoms or Signs	Date				Date				Date			
	D	E	N		D	E	N		D	E	N	
Single fever 100 F or greater or multiple recurrent temperatures of 99 or greater												
Flank pain or costovertebral angle tenderness												
Rigors (shaking chills)												
Pain or swelling of the testes, epididymis or prostate												
Urinary Catheter Present												
Hypotension												
Elevated WBC on CBC												

B. Urinary Specific Symptoms & Signs - 2 or More Suggest UNCOMPLICATED CYSTITIS												
Symptoms or Signs	Date				Date				Date			
	D	E	N		D	E	N		D	E	N	
Acute dysuria – burning / pain on urination												
Gross hematuria												
Suprapubic pain – either reported or noted when pressing on abdomen												
New urinary frequency or urgency												

C. Non-Specific Signs and Symptoms												
These DO NOT SUPPORT the Diagnosis of UTI IN ABSENCE of Symptoms & Signs Above												
Symptoms or Signs	Date				Date				Date			In absence of symptoms or signs in the tables above, these findings do not support work-up or treatment for UTI.
	D	E	N		D	E	N		D	E	N	
Urinary incontinence												
Foul smelling or dark urine												
New fatigue												
New confusion or delirium												
Change in behavior												
Less interactive												
Other												

Evaluate resident for symptoms/signs above each shift. Check appropriate box if present.

D = Day Shift; E = Evening Shift, N = Night Shift



Treatment of Uncomplicated Bladder Infection (Cystitis) In Nursing Home Residents ≥ 65 Years Without a Urinary Catheter

Empiric Initial Treatment	
Nitrofurantoin in those with eCrCl >30ml/min OR Trimethoprim-sulfamethoxazole in those with eCrCl > 15ml/min OR Ciprofloxacin or Fosfomycin <u>only if</u> eCrCl < 15ml/min	
Recommended Dosing for Different Levels of Renal Function	
Estimated CrCl	Maximum Dosing for Anti-infective
>30ml/min	Nitrofurantoin 100mg twice daily Or Trimethoprim-Sulfamethoxazole 160mg/800mg (one double strength) twice daily
15-30ml/min	Trimethoprim-sulfamethoxazole 80mg/400mg (one single strength) twice daily
<15ml/min	AVOID ⇒ Nitrofurantoin Ciprofloxacin 250mg twice daily Fosfomycin 3gm daily AVOID ⇒ Nitrofurantoin & Trimethoprim-Sulfamethoxazole
Drug-Drug Interactions to Avoid	
Interacting Anti-infective	Affected Medications
Ciprofloxacin	Theophylline, Tizanidine, Warfarin
Trimethoprim-sulfamethoxazole	Methotrexate, Phenytoin, Procainamide, Warfarin
Maximum Duration of Anti-infective Treatment Except for Fosfomycin	
Gender	Number of Days
Women	3
Men	7



Bladder Infection or Missing Something Else?

All cases used in this series are real cases. Any individual names have been changed.

Case 1

Harriet is a 90 year old female nursing home resident with a history of late stage Alzheimer's disease and breast cancer. She had an episode of urosepsis with fever, dysuria, urgency, and hypotension 4 years previously. While she can engage in casual conversation, she is unable to recall most recent events. The hospice nurse requests a urine culture because she believes Harriet has a bladder infection. Her primary nurse reports no fever, flank pain, or complaints of dysuria, hematuria, suprapubic pain, urgency or frequency. Harriet vitals are normal, but she is noted to be less interactive over the past day and is not eating as well.

What Really Is a Bladder Infection?

The term "UTI", or urinary tract infection, has been applied to a wide range of conditions – from simple bladder infections or cystitis; to prostatitis and epididymitis in men; to upper pole disease such as pyelonephritis. Most clinicians have no trouble recognizing pyelonephritis with its classic symptoms of fever, flank pain, and hypotension occurring in the presence of more common lower tract symptoms (dysuria, urgency, frequency, suprapubic pain). However, determining if cystitis is present may prove challenging due to the common finding of asymptomatic bacteriuria (ASB) in the nursing home setting.

ASB is found in 50% or more of clinically nursing home residents. Numerous studies have consistently shown no benefits to treatment – no reductions in falls, hospitalizations, or mortality. **Treatment of ASB does not prevent symptomatic bladder infections, and in fact antibiotic treatment appears to increase the risk of future bladder infections.** ASB appears to be protective against recurrent bladder infections. This has led some successful trials of actually establishing ASB in patients with a history of symptomatic bladder infections.

Nursing home residents presenting without urinary symptoms are no more likely to have bladder infections than any other acute change in condition. Taking a shotgun approach may harm the resident by ignoring the true cause for a change in condition and greatly increasing the risk of adverse events such as adverse drug events, drug interactions, Clostridium difficile infections, and resistant bacteria. Unnecessary treatment increases costs to the patient and may contribute to avoidable hospitalizations.

Diagnosis of cystitis is based on clinical signs and symptoms not culture results

Alternatives to the Knee Jerk Urine Culture Order

All residents with a change in condition should be thoughtfully evaluated. Consideration of alternative diagnoses is important. Practitioners should always ask about recent medication changes or new conditions.

If the resident is stable (no urinary symptoms and no systemic signs of infection such as fever or hypotension are present), close monitoring of vital signs, intake and behavior is appropriate. Blood work may be helpful as well. Box 1 is an example of a standardized active monitoring order set for use by practitioners and facilities.

If the resident doesn't improve and there are no urinary or infectious symptoms, the resident should be evaluated by a practitioner.

Box 1 - Example of an Active Monitoring Order Set

- Obtain vital signs (BP, Pulse, Resp Rate, Temp, Pulse Ox) every ____ hours for ____ days.
- Record fluid intake each shift for ____ days.
- Notify physician if fluid intake is less than _____ cc daily.
- Offer resident ____ ounces of water / juice every ____ hours.
- Notify physician, NP, or PA if condition worsens, or if no improvement in ____ hours.
- Obtain the following blood work _____ .
- Consult pharmacist to review medication regimen.
- Contact the physician, NP, PA with an update on the resident's condition on _____.

Case 1 Follow-Up

Because Harriet did not have urinary signs or symptoms, she was evaluated by her primary care physician who noted that she had a new left facial droop and was slurring her words. The primary nurse reported she had been having trouble understanding Harriet's speech, but hadn't recognized the facial droop. **If the physician had ordered the urine culture and risked treating ASB, he would have missed the fact she had a stroke.** Harriet was treated conservatively. No urine culture was ordered. Her speech deficit improved and she remains alive, happy and symptom free three years later.

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Doesn't Dementia Change Things?

All cases used in this series are real cases. Any individual names have been changed.

Case 2

Mildred is a 94 year old nursing home resident with a history of late stage Alzheimer's disease, depression, and severe knee arthritis. She was admitted to the nursing home because of her dementia, arthritis and inability to ambulate. The family reports a history of recurrent "urinary tract infections". She has no prior hospitalizations. One month after admission, the nurses report Mildred has had a change in condition. She has become irritable and quite nasty towards the staff. She insults the nurses and physically pushes the aides away when they attempt to provide care. She has no fever, no urinary symptoms and her vitals are stable. The daughter requests a urine test because this is "how her mother presents when she has a UTI".

Still Take a History in Residents with Dementia

Nursing home residents, **including those with significant dementia**, who present without urinary symptoms are no more likely to have UTI than any other acute change in condition.

Dementia can certainly interfere with the ability to report symptoms. However, residents with dementia who have even limited verbal skills can often still report acute bothersome symptoms. The diagnosis of dementia should not stop one from asking about symptoms simply because of the belief that responses won't be accurate. Take time to obtain a slow, but thoughtful history. Staff and practitioners should specifically ask about urinary symptoms and determine the existence of tenderness of flank, suprapubic, or scrotal areas. Repeating questions during the interview helps establish response consistency.

ASB is found in 50% or more of clinically stable nursing home residents. Numerous studies have consistently shown no benefits to treatment – no reductions in falls, hospitalizations, or mortality. **Treatment of ASB does not prevent symptomatic bladder infections, and in fact increases the risk of future bladder infections.** ASB appears to be protective against recurrent bladder infections.

Shotgun approaches to diagnostic testing may harm the resident by ignoring the true cause for a change in condition and greatly increasing the risk of adverse events such as adverse drug events, drug interactions, Clostridium difficile infections, and resistant bacteria. Unnecessary treatment increases costs to the patient and may contribute to avoidable hospitalizations.

Diagnosis of cystitis is based on clinical signs and symptoms not culture results

Approach to the Patient with Dementia

Residents with dementia and who have a change in condition should be thoughtfully evaluated. Never make the assumption a person cannot communicate based on their diagnosis. Box 1 provides suggestions to improve the practitioner's evaluation of such residents. Consideration of alternative diagnoses is very important in this population. Practitioners should always ask about recent medication changes or new conditions, particularly any new psychotropic medications.

If the resident is stable (no urinary symptoms and no systemic signs of infection such as fever or hypotension are present), close monitoring of vital signs, intake and behavior is appropriate. If the resident doesn't improve and there are no urinary or infectious symptoms, the resident should be evaluated by a practitioner.

Box 1 – Evaluating the Resident with Dementia for Possible Bladder Infection

- Speak to the resident directly and in a quiet setting.
- Minimize distractions by turning off the TV, loud music, and closing the door.
- Establish a calm, relaxed rapport with the resident.
- Use yes / no type questions and use visual clues.
- Give the resident time to respond to questions.
- When asking specific questions about urinary symptom, rephrase the questions using a variety of alternative descriptors. For example, when investigating whether a resident has dysuria, ask not just about burning on urination, but also ask about discomfort, pain, “hurting when you pee”.
- Weave repeated questions into your conversation.
- Suprapubic, flank, and scrotal pain are both symptoms and an exam findings. Always perform an abdominal exam when assessing for suprapubic pain.

Case 2 Follow-Up

Mildred had no urinary symptoms. Because she presented with aggressive behaviors, had significant knee arthritis, and declined to get out of bed, her physician considered pain as a cause following examination. Pain commonly presents as irritability or physical aggression in residents with dementia. Scheduled acetaminophen was begun and by the next day, she had improved without antibiotics. This scenario repeated itself over the next year, but the physician was finally able to convince the daughter that her behavioral changes were not related to UTI.

References:

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- 2) Cai T, Mazzoli S, Mondaini N, et al. The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: To treat or not to treat? *Clin Infect Dis* 2012;55(6):771-7.
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There Are No Tests of Cure!

All cases used in this series are real cases. Any individual names have been changed.

Case 3

Louis is a 78 year old male who has a history of mild Alzheimer's disease, rheumatoid arthritis, gait impairment, and BPH. He is frustrated because he is not able to drive or live independently. He is seen by his urologist in follow up of a bladder infection two months ago. Louis currently has no fever or urinary symptoms. His urologist obtains a urine culture to verify eradication of the infection.

Determining Success of Treatment

Treatment of bladder infections with appropriately selected (according to sensitivities) and dosed antibiotics will lead to clinical cure of the infection as evidenced by improvement in symptoms over the course of treatment.

Persistence of urinary symptoms should prompt reassessment of the diagnosis. For example persistent, or even worsening, dysuria in a female patient may not be due to a bladder infection. Atrophic vaginitis and yeast infections are very common in this population and frequently manifest as dysuria.

Once a treatment course has been completed and there is resolution of symptoms, no repeat testing should be done. **There is no role for so-called tests of cure in UTI. Testing in the absence of symptoms places the resident at great risk of treatment for asymptomatic bacteriuria (ASB) and is a costly and wasteful action.**

ASB is found in 50% or more of clinically nursing home residents. It is defined as the presence of bacteria in a urine culture without the presence of any urinary symptoms. Numerous studies have consistently shown no benefits to treatment of ASB – no reductions in falls, hospitalizations, or mortality. **Treatment of ASB does not prevent bladder infections, and in fact appears to increase the risk of future bladder infections.** ASB appears to be protective against bladder infections. This has led to some successful trials of actually establishing ASB in patients with a history of symptomatic bladder infections.

Numerous studies confirm that the simple act of ordering a urine culture drives antibiotic use, most of which is inappropriate.

Diagnosis of cystitis is based on clinical signs and symptoms not culture results

Steps to Reduce Inappropriate Urine Culture Orders

AMDA – The Society for Post-Acute and Long-Term Care Medicine has released a Choosing Wisely statement recommending against the ordering of urine cultures in the absence of urinary symptoms.

There are many situations in which urine cultures are not helpful and actually present significant risks of harm. These are outlined in Box 1.

Box 1 – Don't Order A Urine Culture:

- In residents without urinary symptoms or signs of systemic infection (fever, rigor, leukocytosis)
- In residents with functional decline or non-specific symptoms alone in the absence of urinary or other systemic infectious signs
- As part of a routine yearly physical
- Based on standing orders in residents without symptoms
- To verify eradication after antibiotic treatment
- To evaluate foul smelling urine in the absence of urinary symptoms
- To evaluate urine characteristics such as cloudiness, turbidity, or color

Facilities should establish policies which:

- Outline when urine cultures are inappropriate
- How urine culture reports are communicated and addressed by covering physicians
- How urine culture orders given by consultants are reviewed and approved

Case 3 Follow-Up

Louis's urine culture returned with 10 X 6 colonies of *Escherichia coli*. The nursing staff contacted a covering physician who, based upon sensitivities, ordered amoxicillin for 7 days. Five days into this course, the patient developed profuse watery diarrhea. He was diagnosed with *Clostridium difficile*. His amoxicillin was discontinued and metronidazole was started. Following the course of metronidazole, he had a relapse and received a second course of metronidazole. Louis experienced anorexia and weight loss, becoming debilitated. He required physical therapy and multiple physician visits. Since this event, he has avoided all antibiotics. His bowel pattern finally returned to normal one year later.

References:

- 1) Nace DA, Drinka PJ, Crnich CJ. Clinical uncertainties in the approach to LTC residents with possible UTI. *J Am Med Dir Assoc*. 2014 Feb;15(2):133-9. PMID: 24461240.
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Start Simple, Limit Collateral Damage

All cases used in this series are real cases. Any individual names have been changed.

Case 4

Hazel is a 90 year old female who has a history of moderately severe Alzheimer's disease, major depression, osteoporosis and DJD who developed new onset dysuria and urinary frequency. Staff report that she often moans when urinating. A urine culture is ordered. Because of the severity of her symptoms, she is treated empirically with ciprofloxacin 500 mg by mouth BID.

She has no allergies. Her only medications include sertraline, oxycodone, and a combination calcium-vitamin D supplement. She is not on warfarin. Her last Cr was 0.5 with an estimated creatinine clearance using the Cockcroft-Gault equation (<https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation>) of 42 ml/min.

Picking the Right Empiric Antibiotic

Treatment of bladder infections with appropriately selected (according to sensitivities) and renally dosed antibiotics will lead to clinical cure of the infection as evidenced by improvement in symptoms over the course of treatment.

While a number of antibiotics may be used to empirically treat UTI, prescribers should preferentially use antibiotics that are unlikely to have high rates of resistance, have reasonably narrow spectrums, be cost effective, and which are dosed appropriately for the patient's renal function.

Fluoroquinolones, which include ciprofloxacin, are the class of antibiotics most commonly used to treat UTI in the nursing home setting. This is despite fluorquinolone resistance rates up to 50% for common gram negative urinary bacteria. Fluoroquinolones carry a proportionally higher risk of *Clostridium difficile* infection compared to several other antibiotics, interact with other common medications such as warfarin, and pose increased risk for specific adverse drug events.

A number of clinical guidelines recommend either nitrofurantoin or trimethoprim-sulfamethoxazole as first line treatment for uncomplicated UTI. Recent evidence now supports use of nitrofurantoin in older adults with estimate creatinine clearance levels as low as 30ml/min. Both are less expensive and pose lower risk of *Clostridium difficile* infection.

Nitrofurantoin or trimethoprim-sulfamethoxazole are first line treatments for uncomplicated UTI in older adults.

The IOU Guideline for Treatment of Uncomplicated Cystitis

The attached guideline was created following an extensive literature search of UTI treatment trials in older adults and with the input of a panel of experts with expertise in post-acute and long-term care prescribing.

Case 3 Follow-Up

Hazel did not improve with the ciprofloxacin. Her urine culture returned with 10 X 6 colonies of *Escherichia coli*. Sensitivities showed it was resistance to ciprofloxacin and levofloxacin, but was sensitive to nitrofurantoin and trimethoprim-sulfamethoxazole. The ciprofloxacin was stopped and nitrofurantoin prescribed. Her symptoms resolved fully over the next several days.

References:

- 1) Beveridge LA, Davey PG, Phillips G. Optimal management of urinary tract infections in older people. *Clin Interv Aging* 2011;6:173-180.
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FREQUENTLY ASKED QUESTIONS ABOUT ANTIBIOTIC TREATMENT OF UNCOMPLICATED CYSTITIS

1. **Is It Okay To Use Nitrofurantoin In Older Adults?** – **YES**. In the past, nitrofurantoin use in older adults was discouraged. Prior to 2015, the American Geriatric Society's *Beer's List for Potentially Inappropriate Medication Use in Older Adults* included nitrofurantoin due to concerns around possible side effects and lack of efficacy in those with a creatinine clearance below 60 mL/min. In 2015, the Beer's Criteria Update Panel changed this recommendation based on a more thorough look at the literature. **The panel concluded nitrofurantoin can be used safely and effectively in older adults having a creatinine clearance of 30 or better.**
2. **Can Nitrofurantoin Be Used In Men With Uncomplicated Cystitis?** – **YES**. Nitrofurantoin is indicated for the treatment of acute uncomplicated cystitis in men or women. It is not indicated for the treatment of complicated infections such as pyelonephritis or prostatitis. Symptoms of uncomplicated cystitis may include dysuria, urinary urgency/frequency, suprapubic pain and/or hematuria. Men who have prostatic, epididymal, and/or flank pain are not likely to have uncomplicated cystitis. The presence of such symptoms would suggest complicated UTI for which nitrofurantoin is not indicated.
3. **Do Nitrofurantoin And Trimethoprim/Sulfamethoxazole Cover Bacteria Which Commonly Cause Cystitis?** – **YES**. *Escherichia coli* and *Klebsiella species* together account for up to 83% of urinary tract infections. Both nitrofurantoin and trimethoprim/sulfamethoxazole are effective against these agents. Clinicians should always be aware of their facility's local resistance pattern which may be significant. Local resistance can be identified by construction and review of the facility urinary antibiogram. Nitrofurantoin may have an advantage in areas where resistance to trimethoprim/sulfamethoxazole is 20% or higher. *Proteus species* and *Enterococcus species* may also cause urinary tract infections, though in a minority of cases. Trimethoprim/sulfamethoxazole is active against susceptible strains of *Proteus*, while nitrofurantoin is effective against *Enterococcus*. Clinicians should also consider past culture data for those individuals with frequently diagnosed UTI. A urine culture should be obtained prior to initiating empiric therapy. Once culture and sensitivity data becomes available, antibiotic prescribing should be reviewed with an eye to narrowing, stopping or shortening the course as indicated.

4. **Is Ciprofloxacin A First Line Antibiotic For Uncomplicated Cystitis? – NO.** Ciprofloxacin is not recommended as a first line antibiotic for uncomplicated cystitis. Ciprofloxacin is linked to a number of serious adverse events including tendinitis, tendon rupture, peripheral neuropathy, central nervous system effects including psychosis, and exacerbations of myasthenia gravis. In addition, bacterial resistance to ciprofloxacin has increased. Several long-term care studies have found a rate of antibiotic resistance of roughly 50%. Fluoroquinolones are also associated with *Clostridium difficile* infection. The package insert now includes a black box warning which states ***ciprofloxacin should be reserved for those who have no alternative treatment options for uncomplicated cystitis.***

5. **Is Ciprofloxacin Safer Than Other Antibiotics? – NO.** Ciprofloxacin can cause a number of adverse effects, including serious ones. Serious adverse events related to ciprofloxacin include tendonitis, tendon rupture, central nervous system effects, and exacerbations of myasthenia gravis. Aortic rupture is also associated with use of fluoroquinolones though causation is not firmly established.

6. **Isn't It Better To Use Broad Spectrum Antibiotics When Treating Uncomplicated Cystitis Empirically – NO.** Empiric antibiotic therapy should be targeted to the organisms that most commonly cause the infection being treated. When treating uncomplicated cystitis, this includes *Escherichia coli* and *Klebsiella species*. The routine use of overly broad antibiotics such as third or fourth generation cephalosporin antibiotics will unnecessarily increase the risk of antibiotic resistance. In addition, when antibiotics are prescribed in long-term care facilities for cystitis, narrowing of therapy based on culture and sensitivity reports – though recommended – is rarely performed.

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**Treatment of
Uncomplicated Bladder Infection (Cystitis)
In Nursing Home Residents
≥ 65 Years Without a Urinary Catheter**

Empiric Initial Treatment

Nitrofurantoin in those with eCrClr >30ml/min
OR Trimethoprim-sulfamethoxazole in those with eCrClr > 15ml/min
OR Ciprofloxacin or Fosfomycin **only if** eCrClr < 15ml/min

**Recommended Dosing for Different
Levels of Renal Function**

Estimated CrClr	Maximum Dosing for Anti-infective
>30ml/min	Nitrofurantoin 100mg twice daily Or Trimethoprim-Sulfamethoxazole 160mg/800mg (one double strength) twice daily
15-30ml/min	Trimethoprim-sulfamethoxazole 80mg/400mg (one single strength) twice daily AVOID → Nitrofurantoin
<15ml/min	Ciprofloxacin 250mg twice daily Fosfomycin 3gm daily AVOID → Nitrofurantoin & Trimethoprim-Sulfamethoxazole

Drug-Drug Interactions to Avoid

Interacting Anti-infective	Affected Medications
Ciprofloxacin	Theophylline, Tizanidine, Warfarin
Trimethoprim- sulfamethoxazole	Methotrexate, Phenytoin, Procainamide, Warfarin

**Maximum Duration of Anti-infective
Treatment Except for Fosfomycin**

Gender	Number of Days
Women	3
Men	7



THE IOU STUDY
 IMPROVING OUTCOMES OF UTI
TOOL KIT

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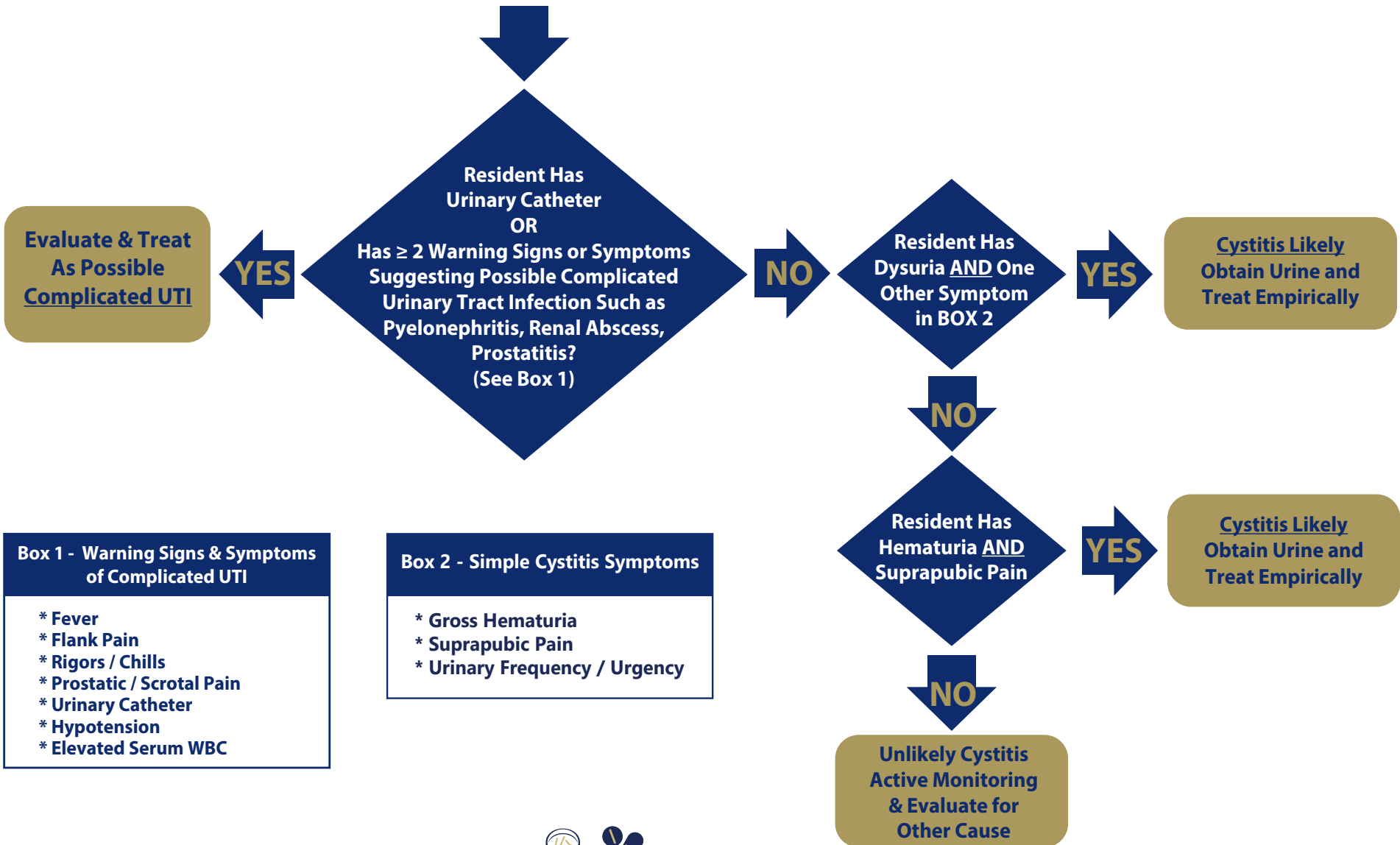


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Is This A Simple Uncomplicated Bladder Infection?(Cystitis)



- Box 1 - Warning Signs & Symptoms of Complicated UTI**
- * Fever
 - * Flank Pain
 - * Rigors / Chills
 - * Prostatic / Scrotal Pain
 - * Urinary Catheter
 - * Hypotension
 - * Elevated Serum WBC

- Box 2 - Simple Cystitis Symptoms**
- * Gross Hematuria
 - * Suprapubic Pain
 - * Urinary Frequency / Urgency

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