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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Abstract

Objectives: 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.

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 non-specific “quality control” items deemed unlikely to indicate uncomplicated cystitis. The expert panel rated their agreement for each sign/symptom using a 5-point Likert 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 three Delphi survey rounds. The response rate was 100% for round one and 95% for the second two rounds. Consensus agreement for inclusion was achieved for dysuria on round one with exclusion of the three 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 three 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.

Keywords
Urinary Tract Infection; UTI; Cystitis; Diagnostic Guidelines; Nursing Facilities

INTRODUCTION

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 four 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 due to lack of awareness, complexity, as well as concerns of low sensitivity and poor positive predictive

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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 two 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 three 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 owing to 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 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 2/3 of the panel giving a rating of ≥4.0 for the item. Finally, a third round survey was conducted to solicit the 2/3 majority expert panel opinion on single or combinations of individual signs/symptoms identified in the first two 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 one or more symptoms. Thirteen symptoms that might be and three 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 one 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 three nonspecific quality control items (“insomnia”, “depression”, “radiating thigh pain”), and “offensive smelling urine” as being indicative of uncomplicated cystitis. The remaining 11 items which did not reach consensus were included in the second round of the survey.

The second round response rate was 95%. Consensus was reached on including four 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 2/3 majority on dysuria being a sufficient minimal criterion by itself; the combination of hematuria and frequency or urgency being a sufficient minimal criteria in absence of dysuria; and 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 signs and symptoms likely to be related to uncomplicated cystitis in non-catheterized older nursing home residents. The panel member’s agreement on exclusion of the three 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 three potential domains: complicated UTI or other non-UTI infection, likely cystitis, and unlikely cystitis (e.g., 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 upon the results of the evaluation and the individual’s clinical and hemodynamic status. Also, while this work addressed the nursing home population, we believe the algorithm is applicable to the older adult and post-acute / long-term care 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 since 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. While 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 (e.g. 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 non-treatment 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 be 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 comprised 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. While 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 five 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 post-acute / long-term care populations. Dissemination and implementation of this algorithm is currently being evaluated in an ongoing national project.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Benoit SR, et al., Factors associated with antimicrobial use in nursing homes: a multilevel model. J Am Geriatr Soc, 2008. 56(11): p. 2039–44. [PubMed: 19016937]
2. Dwyer LL, et al., Infections in long-term care populations in the United States. J Am Geriatr Soc, 2013. 61(3): p. 342–9. [PubMed: 23496650]
3. Nace DA, Drinka PJ, and Crnich CJ, Clinical uncertainties in the approach to long term care residents with possible urinary tract infection. Journal of the American Medical Directors Association, 2014. 15(2): p. 133–9. [PubMed: 24461240]
4. Crnich CJ, et al., Antibiotic resistance in non-major metropolitan skilled nursing facilities: prevalence and interfacility variation. Infection Control & Hospital Epidemiology, 2012. 33(11): p. 1172–4. [PubMed: 23041821]
5. Daneman N, et al., Variability in Antibiotic Use Across Nursing Homes and the Risk of Antibiotic-Related Adverse Outcomes for Individual Residents. JAMA Internal Medicine, 2015. 175(8): p. 1331–9. [PubMed: 26121537]
6. Drinka PJ, Crnich CJ, and Nace DA, An antibiotic prescription induces resistance at the individual level more than the group level. Journal of the American Medical Directors Association, 2013. 14(9): p. 707–8. [PubMed: 23773302]
7. Fisch J, et al., New acquisition of antibiotic-resistant organisms in skilled nursing facilities. Journal of Clinical Microbiology, 2012. 50(5): p. 1698–703. [PubMed: 22378900]
8. Rotjanapan P, Dosa D, and Thomas KS, Potentially inappropriate treatment of urinary tract infections in two Rhode Island nursing homes. Archives of Internal Medicine, 2011. 171(5): p. 438–43. [PubMed: 21403040]
9. Crnich CJ and Drinka P, Improving the management of urinary tract infections in nursing homes: It’s time to stop the tail rom wagging the dog. Annals of Long-Term Care: Clinical Care and Aging, 2014. 22(9): p. 32–36.
10. Nace DA and Drinka PJ, Cranberry capsules reducing the incidence of what? Journal of the American Geriatrics Society, 2014. 62(8): p. 1616–7. [PubMed: 25116998]
11. Nicolle LE, Symptomatic urinary tract infection in nursing home residents. Journal of the American Geriatrics Society, 2009. 57(6): p. 1113–4. [PubMed: 19490245]
12. Vance J, AMDA-choosing wisely. Journal of the American Medical Directors Association, 2013. 14(9): p. 639–41. [PubMed: 24011659]
13. Workgroup AGSCW, American Geriatrics Society identifies another five things that healthcare providers and patients should question. Journal of the American Geriatrics Society, 2014. 62(5): p. 950–60. [PubMed: 24575770]
14. Juthani-Mehta M, et al., Clinical features to identify urinary tract infection in nursing home residents: a cohort study. Journal of the American Geriatrics Society, 2009. 57(6): p. 963–70. [PubMed: 19490243]
15. Nicolle LE, Asymptomatic bacteriuria. Current Opinion in Infectious Diseases, 2014. 27(1): p. 90–6. [PubMed: 24275697]
16. Loeb M, et al., Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. Infection Control & Hospital Epidemiology, 2001. 22(2): p. 120–4. [PubMed: 11232875]
17. Loeb M, et al., Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial. BMJ, 2005. 331(7518): p. 669. [PubMed: 16150741]
18. McGeer A, et al., Definitions of infection for surveillance in long-term care facilities. American Journal of Infection Control, 1991. 19(1): p. 1–7. [PubMed: 1902352]
19. Stone ND, et al., Surveillance definitions of infections in long-term care facilities: revisiting the McGeer criteria. Infection Control & Hospital Epidemiology, 2012. 33(10): p. 965–77. [PubMed: 22961014]

20. Phillips CD, et al., Asymptomatic bacteriuria, antibiotic use, and suspected urinary tract infections in four nursing homes. BMC Geriatrics, 2012. 12: p. 73. [PubMed: 23176555]

21. Gupta K, Grigoryan L, and Trautner B, Urinary Tract Infection. Annals of Internal Medicine, 2017. 167(7): p. ITC49–ITC64. [PubMed: 28973215]

22. Johansen TE, et al., Critical review of current definitions of urinary tract infections and proposal of an EAU/ESIU classification system. International Journal of Antimicrobial Agents, 2011. 38 Suppl: p. 64–70. [PubMed: 22018988]

23. Anger JT, et al., Urologic disease burden in the United States: veteran users of Department of Veterans Affairs healthcare. Urology, 2008. 72(1): p. 37–41; discussion 41. [PubMed: 18342928]

24. Foxman B, Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infectious Disease Clinics of North America, 2014. 28(1): p. 1–13. [PubMed: 24484571]

25. Willems CS, et al., Cystitis: antibiotic prescribing, consultation, attitudes and opinions. Family Practice, 2014. 31(2): p. 149–55. [PubMed: 24317602]

26. Campbell SM and Cantrill JA, Consensus methods in prescribing research. J Clin Pharm Ther, 2001. 26(1): p. 5–14. [PubMed: 11286603]

27. Hsu CC and Sandfor BA, The Delphi technique: Making sense of consensus. Practical Assessment, Research & Evaluation, 2007. 12(10): p. 1–8.

28. Jones J and Hunter D, Consensus methods for medical and health services research. BMJ, 1995. 311(7001): p. 376–80. [PubMed: 7640549]

29. Okoli C and Pawlowski SD, The Delphi method as a research tool: An example, design considerations and applications. Information & Management, 2004. 42: p. 15–29.

30. Verhagen AP, et al., The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 1998. 51(12): p. 1235–41. [PubMed: 10086815]

31. Jurgens T, et al., Development and evaluation of an instrument for the critical appraisal of randomized controlled trials of natural products. BMC Complementary & Alternative Medicine, 2009. 9: p. 11. [PubMed: 19389240]

32. Annear MJ, et al., What should we know about dementia in the 21st century? A Delphi consensus study. BMC Geriatrics, 2015. 15: p. 5. [PubMed: 25656075]

33. Lewthwaite H, et al., Improving physical activity, sedentary behavior and sleep in COPD: perspectives of people with COPD and experts via a Delphi approach. PeerJ, 2018. 6: p. e4604. [PubMed: 29719731]

34. Hanlon JT, et al., Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. J Am Geriatr Soc, 2009. 57(2): p. 335–40. [PubMed: 19170784]

35. D’Agata E, Loeb MB, and Mitchell SL, Challenges in assessing nursing home residents with advanced dementia for suspected urinary tract infections. Journal of the American Geriatrics Society, 2013. 61(1): p. 62–6. [PubMed: 23311553]

36. Services, C.f.M.a.M., Nursing Home Data Compendium 2015 Edition. 2015.

37. Mitchell SL, Kiely DK, and Hamel MB, Dying with advanced dementia in the nursing home. Archives of Internal Medicine, 2004. 164(3): p. 321–6. [PubMed: 14769629]

38. Bleidorn J, et al., Symptomatic treatment (ibuprofen) or antibiotics (ciprofloxacin) for uncomplicated urinary tract infection?--results of a randomized controlled pilot trial. BMC Medicine, 2010. 8: p. 30. [PubMed: 20504298]

39. Dufour AB, et al., Survival After Suspected Urinary Tract Infection in Individuals with Advanced Dementia. J Am Geriatr Soc, 2015. 63(12): p. 2472–2477. [PubMed: 26613981]

40. Finucane TE, “Urinary Tract Infection”–Requiem for a Heavyweight. Journal of the American Geriatrics Society, 2017. 65(8): p. 1650–1655. [PubMed: 28542707]

41. Hooton TM, Clinical practice. Uncomplicated urinary tract infection. New England Journal of Medicine, 2012. 366(11): p. 1028–37.
42. Centers for Medicare & Medicaid Services (CMS), H., Medicare and Medicaid Programs; Reform of Requirements for Long-Term Care Facilities. Federal Register, 2016. 81(192): p. 68688–68872. [PubMed: 27731960]
Figure 1.
Algorithm for the Diagnostic Approach to Uncomplicated Cystitis in Non-Catheterized Nursing Home Residents
| Sign or Symptom                                                                 | Round 1 | Round 2 | Round 1 | Round 2 |
|--------------------------------------------------------------------------------|---------|---------|---------|---------|
| **Literature Based Signs/Symptoms Potentially Related to UTI**                  |         |         |         |         |
| 1. Chills or Rigors                                                            |         |         | X       |         |
| 2. Dysuria                                                                     |         |         |         | X       |
| 3. Fever (≥100 F or repeated temperatures > 99 F, and/or increase of ≥2 degrees 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 & 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.*

*S Signs or symptoms not likely to be related to cystitis. These were included to assess result validity.*