Diagnosis of uncomplicated cystitis (UC)

Guido Schmiemann[1]
Klaus Gebhardt[2]
[1]Abteilung Versorgungsforschung, Institut für Public Health und Pflegeforschung, Universität Bremen, Bremen, Germany
[2]Gemeinschaftspraxis Gebhardt/Thielen, Bremen, Germany

Abstract

Urinary tract infections are among the most common bacterial infections and are responsible for 25% of antibiotic prescriptions in primary care. This chapter presents current evidence from a systematic literature search with a focus on systematic reviews and recent guidelines on diagnosing uncomplicated cystitis (UC). Starting with a general approach on the diagnostic process in suspected UC the pros and cons of different diagnostic strategies are discussed.

Due to the high prevalence of UC the value of typical risk factors (like sexual intercourse) in increasing the pre-test probability is limited. In contrast the clinical presentation and the presence of typical symptoms are a cornerstone in diagnosing UC and differentiating it from complicated infections needing another diagnostic approach. The impact of typical symptoms like dysuria, frequency and hematuria based on their ability to increase the post-test probability are presented. In recent years diagnostic algorithms have been developed to increase the diagnostic accuracy of patients' history alone or in combination with point of care tests. According to a diagnostic study the combination of three questions "Does the patient think she has a UTI?" "Is there at least considerable pain on micturition?" and "Is there vaginal irritation?" has the highest accuracy. When followed by dipstick testing (nitrite and blood) accuracy can be increased further. Other point of care tests including dipslide and microscopy are discussed as well. The ongoing debate about the most appropriate technique to obtain a urine sample is discussed based on a recent systematic review and a clinical trial. Management strategies using telephone-based algorithms or based on patients self-diagnosis have proven their clinical effectiveness. Nevertheless, their study design allows only limited conclusions regarding the diagnostic accuracy.

Summary of recommendations

Clinical diagnosis:

The diagnosis of acute uncomplicated cystitis can be made with a high probability based on a focused history of urinary irritative symptoms (dysuria, frequency and urgency) and the absence of new vaginal discharge, in those women who have no other risk factors for complicated urinary tract infections (LoE 2a, GoR B).

Explore alternative diagnoses and consider pelvic examination for women with symptoms of vaginal itch or discharge (LoE 2a GoR B).

Laboratory diagnosis:

1. In women with medium or high pretest probability urine dipstick testing can be used to increase probability of acute uncomplicated cystitis (LoE 1b, GoR A).
2. Urine cultures are recommended for women with: i) suspected pyelonephritis; ii) recurrent infections or infections that do not resolve after adequate treatment; iii) if the diagnosis remains unclear (LoE 4, GoR B).
3. Colony-forming units (CFU) $\geq 10^3$ of a typical uropathogen is suggestive of acute uncomplicated cystitis in women presenting with symptoms of dysuria (LoE 3, GoR B).

Additional diagnostic studies:

Women who present with atypical symptoms of either acute uncomplicated cystitis or acute uncomplicated pyelonephritis, as well as those who fail to respond to appropriate antimicrobial therapy should be considered for additional diagnostic studies (LoE 4, GoR B).

GMS
10.5680/lhuii000004

1 Introduction

This chapter will focus on uncomplicated cystitis (UC) in women. UC is among the most common bacterial infections. More than every third (37%) of all women >15years reported at least one infection in their lifetime. Recurrence is high with 29% of the women reporting more than one episode [1]. Despite the frequency and clinical relevance diagnosing UC still is a challenging task. After discussing some general aspects of diagnosing UC a current overview on the value of clinical symptoms, urine sampling techniques, diagnostic validity of dipstick test and diagnostic algorithms will be given.

2 Methods

The literature search was conducted using the search strategy applied during the update on the German guideline on urinary tract infection. Next to a general search strategy a search strategy specific for diagnostic studies was used.

Search term: (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR diagnose[Title/Abstract] OR diagnosed[Title/Abstract] OR diagnoses[Title/Abstract] OR diagnosing[Title/Abstract] OR diagnosis[Title/Abstract] OR diagnostic[Title/Abstract] OR diagnosis[MeSH:noexp] OR diagnostic * [MeSH:noexp] OR diagnosis, differential [MeSH:noexp] OR diagnosis[Subheading:noexp]) and 1. exp urinary tract infections/ 2. urinary tract infection$.tw. 3. uti.tw. 4. cystitis/ or cystitis, interstitial/ 5. pyelonephritis/ 6. dysuria.tw. 7. perinephric abscess.tw. 8. bacteriuria/ 9. cystitis.tw. 10. pyelonephriti$.tw. 11. exp urinary tract/ 12. exp bacterial infections/ 13. 11 and 12 14. or/1-10,13 15. *Urethritis/ 16. 14 not 15

The search term was applied to PubMed. For searches in Embase and in the Cochrane Library adapted searches were used, the search included articles till 31.12.2015. An additional search for guidelines on urinary tract infections was conducted including the following websites: http://www.g-i-n.org; http://www.sign.ac.uk; http://www.nice.org.uk; Nederlands Huisartsen Genootschap. http://nhg.artsennet.nl; Dutch Institute for Healthcare Improvement. http://www.diliguide.nl; http://www.domusmedica.be; http://www.awmf.org; http://www.uroweb.org/guidelines/; http://www.ncbi.nlm.nih.gov/pubmed.

3 Results

The diagnostic process

When discussing the diagnostic workup of a disease, several aspects have to be taken into account:

- morbidity and mortality of the disease. How do physician and patient judge the disease? The more serious the disease the higher the intensity and diagnostic accuracy we should aim for. As UC is a potentially self-limiting disease costs and potential harms of a diagnostic work-up have to be considered carefully. This is in contrast to complicated infections like pyelonephritis, where a higher degree of diagnostic accuracy is warranted.
- applicability and usability of the diagnostic test.
- risks or harms associated with the tests
- patient preferences related to the diagnostic work-up

The aim of every diagnostic test is to increase the post-test probability. The extent to which a diagnostic test can increase the posttest probability depends on the quality of the test used. This quality is best described by the tests sensitivity, specificity and likelihood ratio (LR).

Posttest probability further depends on pre test probability (i.e prevalence of the disease within the specific setting – for example prevalence of UC in women with dysuria presenting in emergency departments).

Like in any other diagnostic process the clinician has to decide which diagnostic approach is warranted. The options are

- a high sensitivity (majority of patients with the diagnosis are detected including a high rate of false positive results – this approach may include a high number of unnecessary antibiotic prescriptions) or

- a high specificity with a lower number of false positive but a higher number of false negative.

Diagnostic accuracy although depends on some relevant pretest probabilities like the prevalence of asymptomatic bacteruria (ABU) and UC in the setting under examination. The prevalence of asymptomatic bacteriuria depends on the age and setting. While in premenopausal women the rate of ABU is around 5% [2] this rate increases with age up to 20% in non-institutionalized female octogenarians [3].

Prevalence of ABU is important, as this condition increases the rate of false positive dipstick results. The consequence is that in patients with urinary catheter (leading to a rate of nearly 100% ABU) dipstick results cannot be used to rule in the diagnosis of UC.

Prevalence of UC in clinical studies ranges from 27–79% when women with suspected UC were to be included [4].

Diagnosing UC

The diagnosis of UC can be established in a woman with typical symptoms and the confirmation of typical pathogens in the patients urine.

While sounding quite straightforward this diagnostic process can be challenging for several reasons.

1. typical symptoms
   Which symptoms are specific for UC?
2. patients' urine
   How to obtain a urine sample to prove a UC?
3. confirmation of pathogens
   Direct or indirect ways to confirm the presence of bacteria?

The gold standard for diagnosing UC is the presence of typical uropathogens in urine obtained by suprapubic aspiration and confirmed by urine culture. The presence of 10^5 cfu/ml of a single uropathogen, has been the reference standard in the past [5]. In recent years lower colony count up to 10^3 cfu/ml have been accepted. This change has to be taken into account, when comparing results of diagnostic studies.

Several barriers prevent this diagnostic gold standard to be applied in routine practice. Results of a urine culture need time and are therefore not available at the point of care. Nearly equivalent substitutes like gram stained microscopy requires the infrastructure and expertise often not available in the primary care setting.

Suprapubic aspiration is considered as too invasive by most general practitioners.

Therefore diagnosing of UC during the encounter has to rely on adequate history taking, clinical examination and results of available point of care testing like urinary dipstick.

Risk factors for UC

Risk factors are important in diagnosing UTI as their presence increases the pretest probability. However many of the risk factors known have a high prevalence themselves and their relevance in clinical practice remains doubtful. Some risk factors are more relevant, when discussing individual strategies in recurrent UTI.

In younger women sexual intercourse and the use of diaphragm with spermicide have been described as a major risk factor [6].

Regarding postmenopausal women prospective cohort studies confirmed sexual intercourse as a risk factor [7]. In Table 1 common established risk factors are presented.

Table 1: HR=Hazard ratio OR=Odds ratio RR=Relative risk, HMO=Health maintenance organization, CI=Confidence interval

Risk factor	Findings
Antecedent antibiotic use	RR 2.57 (1.24–5.32; 95% CI) when AB used 15–28d before [5]
Sexual intercourse	dose–response relation (RR for 1,3,5 days with intercourse in the last 7d 1.37 (2.56–4.81 95% CI) (University cohort), 1.24 (1.91–2.96 95% CI) (HMO cohort) [6]
Sexually active (postmenopausal)	OR, 1.42 (1.1–1.9 95% CI) [8] HR, 3.42; 1.49–7.8 95% CI) [7]
History of recurrent infection	RR 2.10 (1.23–3.57 95% CI) (HMO cohort) RR 5.58 (3.24–9.63 95% CI) (university cohort) [6]
Incontinence (postmenopausal women)	OR, 1.36 (1.03–1.8 95% CI) [7], [8] HR 2.0 (1.4–2.9 95% CI) [9]
History of UTI before menopause	OR, 4.9 (1.7–13.8 95% CI) [10] OR, 4.2 (3.3–5.4 95% CI) [8]
Diabetes mellitus	HR 1.0 (0.6, 1.6 95% CI) [9] RR 1.8, (1.2–2.7 95% CI) [11]
Severe cognitive impairment (MMSE <19)	HR 2.7 (1.9, 3.9 95% CI) 85y and older; [9]
Stool incontinence	HR 3.2 (2.2, 4.8 95% CI) [9]

Clinical symptoms in UC

Typical symptoms in patients with UC include dysuria (painful voiding), frequency (frequent voiding of urine), urgency (the urge to void immediately), and hematuria (presence of blood in urine), nocturia (awakening from sleep). Especially in elderly patients new episodes of urine incontinence or changes in the mental status can be found.

Giessen et al. [4] evaluated the diagnostic accuracy in UTI when using different reference standards (10^2, 10^3 and 10^5 cfu/ml), they found six symptoms with diagnostic value (see table 2).

Irrespective of the threshold used dysuria and frequency had the highest sensitivity – that means they increase the probability that an UC is present. Hematuria has the highest specificity, if positive the presence of hematuria helps to rule in the diagnosis.

With a threshold of 10^3 cfu the following symptoms increase the probability of a UC (see Table 2).

Table 2: Symptoms and their predictive value in diagnosing UC
(Results for vaginal discharge refer on a level of 10^2 cfu/ml all other symptoms refer to a threshold of 10^3 cfu/ml [4].

Symptom	Sensitivity	Specificity	Likelihood ratio
Dysuria	0.79 (0.72–0.85)	0.39 (0.31–0.49)	1.31 (1.18–1.45)
Frequency	0.88 (0.83–0.92)	0.21 (0.14–0.31)	1.12 (1.03–1.19)
Hematuria	0.22 (0.18–0.27)	0.87 (0.81–0.91)	1.68 (1.06–2.66)
Nocturia	0.59 (0.48–0.70)	0.57 (0.51–0.62)	1.37 (1.13–1.65)
Urgency	0.62 (0.46–0.76)	0.51 (0.35–0.68)	1.28 (1.11–1.47)

Vaginal discharge	0.15 (0.08–0.26)	0.77 (0.62–0.88)	0.65 (0.51–0.83)

The results are partly supported by another systematic review [12].

In summary the absence of symptoms like dysuria and frequency helps to rule out the diagnosis of UC while the presence of hematuria helps to rule in the diagnosis. The presence of vaginal discharge reduces the probability of UC. One has to remind that the likelihood ratios of the different symptoms are quite small, meaning that the gain in diagnostic accuracy when applying the results is still small. For example: Assuming a pretest probability (prevalence) of 50% the presence of dysuria (LR 1.31) alone would increase the posttest probability to 56.7%.

Presenting pattern

Not all women suffering from UC are seeking medical help [1]. Those presenting to primary care have symptoms for a median of 3 days with urgency and dysuria being the dominating symptoms [13], [14]. Regarding severity daytime frequency was the most common symptom rated as moderately severe (78%) [13].

The role of lower abdominal pain remains unclear as two systematic reviews show different results. While Medina et al. [12] found, that suprapubic pain was a weak predictor (LR 0.81 (0.73–0.89)) for the absence of an uUTI, Giessen [4] found lower abdominal pain/suprapubic pain as a weak positive predictor (LR 1.06 (0.88–1.29)) – both using different effect models.

Clinical scores can result in high positive predictive value. Little et al. [15] found a PPV of 82% for patients with the combination of urine cloudiness, burning dysuria of any degree and nocturia of any degree. However the NPV were still quite low (40%).

History taking in UTI

Variables from patients history that increase the likelihood of an UTI were assessed in a prospective trial. Knottnerus et al. [16] found that having at least considerable pain during micturition, having any vaginal irritation, patients suspecting a UC can further help to assess the probability of a UC. The likelihood of women who think they have a UC does not depend on their previous experience [16].

A questionnaire to be filled out by the patient (acute cystitis symptom score) was developed by Alidjanov et al. [17]. The questionnaire inquires after typical symptoms (frequency, urgency, dysuria, suprapubic pain, hematuria) rated on a 4 point Likert scale. The authors report a 94% sensitivity and 90% specificity to predict UC when using a threshold of 6 points [17].

Algorithm and self-diagnosis in UTI

Different algorithms have tried to increase the diagnostic accuracy. A swedish RCT in an out-of-hour service could demonstrate no significant differences in terms of diagnostic accuracy (44 vs. 31% positive cultures) or time to symptom resolution (79% vs 72% at day four) between standard and algorithm based care. The algorithm only included typical symptoms and their severity (mild, moderate, strong), dipstick results were not considered in the algorithm [18].

Knottnerus et al. [16] tried to take into account the interdependency of different signs and symptoms. They found that three questions regarding the history

1. Does the patient think she has a UTI?
2. Is there at least considerable pain on micturition?
3. Is there vaginal irritation?

followed by a dipstick test on nitrite and blood can help to correctly classify 73% of all patients for having a high risk (>70% probability of UC) or low risk (<30%).

A diagnosis without direct patient contact is possible and has been successfully evaluated in some studies on telephone management [19], [20], [21], [22] or using an interactive computer kiosk [23]. While

this approach proved to be feasible in terms of patient satisfaction and cure rates most of the studies used a retrospective design and did not assess diagnostic accuracy.

Smell and visual aspect of urine

An offensive smell is a weak predictor for UTI (2.02 (1.05–3.90) [24]. Urine cloudiness is a weak predicto 2.32 (1.40–3.85) [24]. When including both symptoms in a prediction model, only urine cloudiness remained significant [24].

Urine sample technique

There is an ongoing debate about the ideal sample techniques. For doctor and patients alike the sampling technique should be easy to apply, convenient, reliable and with a low level of risks associated.

One can assume that contamination rates increases in the following order

a. suprapubic puncture,
b. urethral catheterization
c. midstream clean catch (after cleaning the labia before voiding using tap water, soap or disinfectants),
d. midstream urine (without cleaning before voiding)
e. random samples (without further instructions)
f. home-voided urine.

A recent systematic review [25] compared these techniques in non-pregnant women with symptoms suggesting an UTI in primary care. The authors concluded that there is no evidence to suggest that sampling technique affects the accuracy of the microbiological diagnosis. However, the evidence is indirect and a study by Hooton et al. [26] comparing midstream collection with urethral catheterization found high correlations regarding the causative agent in UTI caused by *Escherichia coli* but very low correlations when *Enterococci* and *group B streptococci* were found.

As a consequence the lower specificity for causative agents in voided urine samples compared to invasive techniques will result in overdiagnosing of 5–10% healthy patients [25] but reducing the possible complications and risks of infection accompanied by invasive techniques.

Dipstick results

Dipsticks are among the most frequently used point of care tests in primary care. Reasons for false positive/false negative results have to be taken into account. The most useful tests included in the dipstick are test for blood, leucocytes and nitrite.

Leucocytes: Positive if leukocyteesterase is present – an indirect evidence for the presence of leukocytes.

Nitrite: Some bacteria reduce nitrate to nitrite by the help of the enzyme nitrate reductase. A positive result is dependent of a certain concentration of bacteria. False positive results for leucocytes (nitrite) occur through:

a. contamination with vaginal secretion
b. long waiting time before processing
c. colouring agents like beetroots.

False negative results for leukocytes (nitrite) occur through vitamin C, high concentration of bilirubin, glucosuria >20 g/l, proteinuria >5 g/l, boric acid, very acidic urine, infection by pathogen without the ability to produce nitratreductase i.e enterococci, staphylococci.

Bladder incubation time of more than 4 hours did not increase the UTI probability in the model developed by Knottnerus et al. [16].

Dipslide

A dipslide coated on each side with a different culture medium is recommended in some guidelines (NHG) and used in screening for asymptomatic bacteriuria in pregnancy [27], [28]. The dipslide has 98.0% sensitivity and 99.6% specificity for detecting ASB in pregnancy [27], when used to diagnose UC in daily practice sensitivity was 73% (CI 66–80%), specificity 94% (CI 88–98%) resulting in a positive (negative) predictive value of 95% [11] (CI 90–98%) and 68% (CI 60–76%) [29]. In a more recent study the added value of a dipslide was rated. The authors concluded that “dipslide appear to add little information to what is already known from history and dipstick results, implying that performance of these expensive, time-consuming tests might be abandoned” [16].

Microscopy

The result of microscopy is dependent on the skill of the microscoper. A positive test for pyuria and bacteriuria rules in UTI with a high probability (pooled LR for pyuria and bacteriuria positive: LR+ 37.0, LR– 0.21), in contrast a negative result for both bacteriuria and pyuria generally rules out a UTI (pooled LR for pyuria or bacteriuria positive: LR+ 4.2, LR– 0.11) [30]. Gram-staining and using phase-contrast microscopy improve the diagnostic accuracy [31], [32]. The benefit of microscopy is the rapidity and the higher diagnostic accuracy compared with dipsticks. If available microscopy should be used to clarify the diagnosis in suspected urinary tract infections.

Urine flow cytometry is a laboratory based method to standardize urine sediment analysis. The automated analyzers are capable to quantify for examples white blood counts (WBC) or bacteria. While clinical performance with sensitivities (specifities) of 0.87 (0.67) for WBCs and 0.92 (0.60) for bacteria seems promising a systematic review and metaanalysis [33] concluded that due to methodological shortcomings further studies are needed.

Further examination

Physical examination is not necessary in UC and does not help to increase the diagnosis. However, when a complicated infection is suspected signs and symptoms as costovertebral angle tenderness and fever should be looked for.

Further diagnostic studies like radiological imaging or ultrasound scan are usually not indicated in UC and should be reserved for complicated infections.

Differential diagnosis

Sexually transmitted infections are the most important differential diagnosis in women presenting with symptoms suggestive of a UC. Especially in infections with *Chlamydia trachomatis* the clinical presentation often is indistinguishable and the diagnostic workup incomplete [34]. Presence of vaginal discharge and sexual history can be used to stratify the risk.

4 Future perspectives

Technological solutions like portable systems using chromatic techniques [35], “isothermal microcalorimetry“ [36], “CultureStat Rapid UTI Detection System” [37] or the Flexicult [38] have been described. The impact of these technical solutions for a faster detection of bacteria and antimicrobial susceptibility or as a point of care test remains to be seen.

5 Conclusion

Despite technical advances in recent years the accurate patient history remains the cornerstone in assessing patients with symptoms suggestive of cystitis. Patients history is not only necessary to clarify if there is any risk for a complicated infection. Accurate history is although the most accurate predictor for diagnosing UC.

References

1. Butler CC, Hawking MK, Quigley A, McNulty CA. Incidence, severity, help seeking, and management of uncomplicated urinary tract infection: a population-based survey. Br J Gen Pract.

2015 Oct;65(639):e702-7. DOI: 10.3399/bjgp15X686965

2. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, Saint S, Schaeffer AJ, Tambayh PA, Tenke P, Nicolle LE; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010 Mar 1;50(5):625-63.
3. Rodhe N, Löfgren S, Matussek A, André M, Englund L, Kühn I, Mölstad S. Asymptomatic bacteriuria in the elderly: high prevalence and high turnover of strains. Scand J Infect Dis. 2008;40(10):804-10. DOI: 10.1080/00365540802195242
4. Giesen LG, Cousins G, Dimitrov BD, van de Laar FA, Fahey T. Predicting acute uncomplicated urinary tract infection in women: a systematic review of the diagnostic accuracy of symptoms and signs. BMC Fam Pract. 2010 Oct;11:78. DOI: 10.1186/1471-2296-11-78
5. KASS EH. Asymptomatic infections of the urinary tract. Trans Assoc Am Physicians. 1956;69:56-64.
6. Hooton TM, Scholes D, Hughes JP, Winter C, Roberts PL, Stapleton AE, Stergachis A, Stamm WE. A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med. 1996 Aug 15;335(7):468-74. DOI: 10.1056/NEJM199608153350703
7. Moore EE, Jackson SL, Boyko EJ, Scholes D, Fihn SD. Urinary incontinence and urinary tract infection: temporal relationships in postmenopausal women. Obstet Gynecol. 2008 Feb;111(2 Pt 1):317-23. DOI: 10.1097/AOG.0b013e318160d64a
8. Hu KK, Boyko EJ, Scholes D, Normand E, Chen CL, Grafton J, Fihn SD. Risk factors for urinary tract infections in postmenopausal women. Arch Intern Med. 2004 May 10;164(9):989-93. DOI: 10.1001/archinte.164.9.989
9. Caljouw MA, den Elzen WP, Cools HJ, Gussekloo J. Predictive factors of urinary tract infections among the oldest old in the general population. A population-based prospective follow-up study. BMC Med. 2011 May;9:57. DOI: 10.1186/1741-7015-9-57
10. Raz R, Gennesin Y, Wasser J, Stoler Z, Rosenfeld S, Rottensterich E, Stamm WE. Recurrent urinary tract infections in postmenopausal women. Clin Infect Dis. 2000 Jan;30(1):152-6. DOI: 10.1086/313596
11. Boyko EJ, Fihn SD, Scholes D, Abraham L, Monsey B. Risk of urinary tract infection and asymptomatic bacteriuria among diabetic and nondiabetic postmenopausal women. Am J Epidemiol. 2005 Mar 15;161(6):557-64. DOI: 10.1093/aje/kwi078
12. Medina-Bombardó D, Jover-Palmer A. Does clinical examination aid in the diagnosis of urinary tract infections in women? A systematic review and meta-analysis. BMC Fam Pract. 2011 Oct;12:111. DOI: 10.1186/1471-2296-12-111
13. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, Smith H, Hawke C, Leydon G, Arscott A, Turner D, Mullee M. Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial. BMJ. 2010 Feb 5;340:c199. DOI: 10.1136/bmj.c199
14. Gágyor I, Bleidorn J, Kochen MM, Schmiemann G, Wegscheider K, Hummers-Pradier E. Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ. 2015 Dec;351:h6544. DOI: 10.1136/bmj.h6544
15. Little P, Turner S, Rumsby K, Jones R, Warner G, Moore M, Lowes JA, Smith H, Hawke C, Leydon G, Mullee M. Validating the prediction of lower urinary tract infection in primary care: sensitivity and specificity of urinary dipsticks and clinical scores in women. Br J Gen Pract. 2010 Jul;60(576):495-500. DOI: 10.3399/bjgp10X514747
16. Knottnerus BJ, Geerlings SE, Moll van Charante EP, Ter Riet G. Toward a simple diagnostic index for acute uncomplicated urinary tract infections. Ann Fam Med. 2013 Sep-Oct;11(5):442-51. DOI: 10.1370/afm.1513.
17. Alidjanov JF, Abdufattaev UA, Makhsudov SA, Pilatz A, Akilov FA, Naber KG, Wagenlehner FM. New self-reporting questionnaire to assess urinary tract infections and differential diagnosis: acute cystitis symptom score. Urol Int. 2014;92(2):230-6. DOI: 10.1159/000356177
18. Bollestad M, Grude N, Lindbaek M. A randomized controlled trial of a diagnostic algorithm for symptoms of uncomplicated cystitis at an out-of-hours service. Scand J Prim Health Care. 2015 Jun;33(2):57-64. DOI: 10.3109/02813432.2015.1041827
19. Saint S, Scholes D, Fihn SD, Farrell RG, Stamm WE. The effectiveness of a clinical practice guideline for the management of presumed uncomplicated urinary tract infection in women. Am J

Med. 1999 Jun;106(6):636-41. DOI: 10.1016/S0002-9343(99)00122-9
20. Vinson DR, Quesenberry CP Jr. The safety of telephone management of presumed cystitis in women. Arch Intern Med. 2004 May 10;164(9):1026-9. DOI: 10.1001/archinte.164.9.1026
21. Schauberger CW, Merkitch KW, Prell AM. Acute cystitis in women: experience with a telephone-based algorithm. WMJ. 2007 Sep;106(6):326-9.
22. Barry HC, Hickner J, Ebell MH, Ettenhofer T. A randomized controlled trial of telephone management of suspected urinary tract infections in women. J Fam Pract. 2001 Jul;50(7):589-94.
23. Aagaard EM, Nadler P, Adler J, Maselli J, Gonzales R. An interactive computer kiosk module for the treatment of recurrent uncomplicated cystitis in women. J Gen Intern Med. 2006 Nov;21(11):1156-9. DOI: 10.1111/j.1525-1497.2006.00575.x
24. Little P, Turner S, Rumsby K, Warner G, Moore M, Lowes JA, Smith H, Hawke C, Turner D, Leydon GM, Arscott A, Mullee M. Dipsticks and diagnostic algorithms in urinary tract infection: development and validation, randomised trial, economic analysis, observational cohort and qualitative study. Health Technol Assess. 2009 Mar;13(19):iii-iv, ix-xi, 1-73. DOI: 10.3310/hta13190
25. Holm A, Aabenhus R. Urine sampling techniques in symptomatic primary-care patients: a diagnostic accuracy review. BMC Fam Pract. 2016 Jun 8;17:72. DOI: 10.1186/s12875-016-0465-4
26. Hooton TM, Roberts PL, Cox ME, Stapleton AE. Voided midstream urine culture and acute cystitis in premenopausal women. N Engl J Med. 2013 Nov 14;369(20):1883-91. DOI: 10.1056/NEJMoa1302186
27. Mignini L, Carroli G, Abalos E, Widmer M, Amigot S, Nardin JM, Giordano D, Merialdi M, Arciero G, Del Carmen Hourquescos M; World Health Organization Asymptomatic Bacteriuria Trial Group. Accuracy of diagnostic tests to detect asymptomatic bacteriuria during pregnancy. Obstet Gynecol. 2009 Feb;113(2 Pt 1):346-52. DOI: 10.1097/AOG.0b013e318194f109
28. Kazemier BM, Schneeberger C, De Miranda E, Van Wassenaer A, Bossuyt PM, Vogelvang TE, Reijnders FJ, Delemarre FM, Verhoeven CJ, Oudijk MA, Van Der Ven JA, Kuiper PN, Feiertag N, Ott A, De Groot CJ, Mol BW, Geerlings SE. Costs and effects of screening and treating low risk women with a singleton pregnancy for asymptomatic bacteriuria, the ASB study. BMC Pregnancy Childbirth. 2012 Jun;12:52. DOI: 10.1186/1471-2393-12-52
29. Winkens R, Nelissen-Arets H, Stobberingh E. Validity of the urine dipslide under daily practice conditions. Fam Pract. 2003 Aug;20(4):410-2.
30. Whiting P, Westwood M, Watt I, Cooper J, Kleijnen J. Rapid tests and urine sampling techniques for the diagnosis of urinary tract infection (UTI) in children under five years: a systematic review. BMC Pediatr. 2005 Apr;5(1):4. DOI: 10.1186/1471-2431-5-4
31. Williams GJ, Macaskill P, Chan SF, Turner RM, Hodson E, Craig JC. Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: a meta-analysis. Lancet Infect Dis. 2010 Apr;10(4):240-50. DOI: 10.1016/S1473-3099(10)70031-1
32. Coulthard MG, Nelson A, Smith T, Perry JD. Point-of-care diagnostic tests for childhood urinary-tract infection: phase-contrast microscopy for bacteria, stick testing, and counting white blood cells. J Clin Pathol. 2010 Sep;63(9):823-9. DOI: 10.1136/jcp.2010.077990
33. Shang YJ, Wang QQ, Zhang JR, Xu YL, Zhang WW, Chen Y, Gu ML, Hu ZD, Deng AM. Systematic review and meta-analysis of flow cytometry in urinary tract infection screening. Clin Chim Acta. 2013 Sep;424:90-5. DOI: 10.1016/j.cca.2013.05.014
34. Wilbanks MD, Galbraith JW, Geisler WM. Dysuria in the emergency department: missed diagnosis of Chlamydia trachomatis. West J Emerg Med. 2014 Mar;15(2):227-30. DOI: 10.5811/westjem.2013.12.18989
35. Deakin AG, Jones GR, Spencer JW, Bongard EJ, Gal M, Sufian AT, Butler CC. A portable system for identifying urinary tract infection in primary care using a PC-based chromatic technique. Physiol Meas. 2014 May;35(5):793-805. DOI: 10.1088/0967-3334/35/5/793
36. Braissant O, Müller G, Egli A, Widmer A, Frei R, Halla A, Wirz D, Gasser TC, Bachmann A, Wagenlehner F, Bonkat G. Seven hours to adequate antimicrobial therapy in urosepsis using isothermal microcalorimetry. J Clin Microbiol. 2014 Feb;52(2):624-6. DOI: 10.1128/JCM.02374-13
37. Olsson C, Kapoor D, Howard G. A method for the rapid detection of urinary tract infections. Urology. 2012 Apr;79(4):761-5. DOI: 10.1016/j.urology.2011.12.040
38. Bates J, Thomas-Jones E, Pickles T, Kirby N, Gal M, Bongard E, Hood K, Francis N, Little P, Moore M, Rumsby K, Llor C, Burgman C, Verheij T, Cohen D, Wootton M, Howe R, Butler CC. Point of care testing for urinary tract infection in primary care (POETIC): protocol for a randomised controlled trial of the clinical and cost effectiveness of FLEXICULT™ informed management of

uncomplicated UTI in primary care. BMC Fam Pract. 2014 Nov;15:187. DOI: 10.1186/s12875-014-0187-4

Corresponding authors: PD Dr. med Guido Schmiemann MPH, Institut für Public Health und Pflegeforschung, Universität Bremen, Abteilung Versorgungsforschung Bremen, Germany, E-mail: schmiema@uni-bremen.de

Citation note: Schmiemann G, Gebhardt K. Diagnosis of uncomplicated cystitis (UC) . Version: 2017-11-22. In: Bjerklund Johansen TE, Wagenlehner FME, Matsumoto T, Cho YH, Krieger JN, Shoskes D, Naber KG, editors. Urogenital Infections and Inflammations. Duesseldorf: German Medical Science GMS Publishing House; 2017-. DOI: 10.5680/lhuii000004