

Possible urinary signs & symptoms	The outcome	Recommended care	When should I get help? Contact your GP practice or contact NHS 111
<p>Key signs/symptoms:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Dysuria: Burning pain when passing urine (wee) ^{1,2} <input type="checkbox"/> New nocturia: Needing to pass urine in the night³ <input type="checkbox"/> Cloudy urine: Visible cloudy colour when passing urine⁴ <p>Other signs/symptoms to consider:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Frequency: Passing urine more often than usual¹ <input type="checkbox"/> Urgency: Feeling the need to pass urine immediately¹ <input type="checkbox"/> Haematuria: Blood in your urine¹ <input type="checkbox"/> Suprapubic pain: Pain in your lower tummy¹ <p>Other things to consider: ¹</p> <p>Recent sexual history ^{2,5}</p> <ul style="list-style-type: none"> <input type="checkbox"/> Inflammation due to sexual activity can feel similar to the symptoms of a UTI. ⁶ <input type="checkbox"/> Some sexually transmitted infections (STIs) can have symptoms similar to those of a UTI. ⁶ <p>Changes during menopause ^{7,8,9}</p> <ul style="list-style-type: none"> • Some changes during the menopause can have symptoms similar to those of a UTI 	<p>Non-pregnant women:</p> <p><input type="checkbox"/> If none or only one of: dysuria, new nocturia, cloudy urine; AND/OR vaginal discharge ^{4,10} →</p> <ul style="list-style-type: none"> • UTI much less likely^{4,10} • You may need a urine test to check for a UTI^{4,10} • Antibiotics less likely to help¹⁰ • Usually lasts 5 to 7 days^{11,12} <p><input type="checkbox"/> If 2 or more of: dysuria, new nocturia, cloudy urine; AND NO vaginal discharge →</p> <ul style="list-style-type: none"> • UTI more likely¹³ • You should start to improve within 48 hours¹³ • Symptoms usually last 3 days¹³ <p>Pregnant women:</p> <p><input type="checkbox"/> If suspected UTI →</p>	<p><input type="checkbox"/> Self-care and pain relief. ¹¹</p> <ul style="list-style-type: none"> • Symptoms may get better on their own.^{10,12} <p><input type="checkbox"/> Recommend GP visit if symptoms:</p> <ul style="list-style-type: none"> • Get worse¹³ • Do not get a little better with self-care within 48 hours¹³ • Are persistent and ongoing <p><input type="checkbox"/> If mild symptoms, recommend self-care AND GP visit if symptoms:</p> <ul style="list-style-type: none"> • Get worse¹³ • Do not get a little better with self-care within 48 hours <p><input type="checkbox"/> Recommend immediate GP visit/ NHS111 and self-care</p> <p><input type="checkbox"/> Immediate GP referral</p>	<p>The following symptoms are possible signs of serious infection and should be assessed urgently. ^{1,17,27}</p> <p>Phone for advice if you are not sure how urgent the symptoms are.</p> <ol style="list-style-type: none"> 1. You have shivering, chills and muscle pain¹ 2. You feel confused, or are very drowsy²⁸ 3. You have not passed urine all day^{28,29} 4. You are vomiting² 5. You see blood in your urine¹ 6. Your temperature is above 38°C or less than 36°C.²⁷ 7. You have kidney pain in your back just under the ribs^{1,2} 8. Your symptoms get worse¹³ 9. Your symptoms are not starting to improve within 48 hours of taking antibiotics
<p>Self-care to help yourself get better more quickly</p>	<p>Options to help prevent a UTI</p>	<p>Antibiotic Resistance</p>	<p>Community Pharmacy notes</p>
<ul style="list-style-type: none"> • Drink enough fluids to stop you feeling thirsty. Aim to drink 6 to 8 glasses^{14,15} • Avoid too much alcohol, fizzy drinks or caffeine that can irritate your bladder^{14,15} • Take paracetamol or ibuprofen at regular intervals for pain relief, if you can and have had no previous side effects^{11,16} • There is currently no evidence to support taking cranberry products or cystitis sachets to improve your symptoms^{16,17} • Consider the risk factors in the 'Options to help prevent UTI' column to reduce future UTIs¹⁴ 	<p>It may help you to consider these risk factors: ¹⁴</p> <ul style="list-style-type: none"> • Stop bacteria spreading from your bowel into your bladder. ¹⁸ Wipe from front (vagina) to back (bottom) after using the toilet. ¹⁸ • Avoid waiting to pass urine. ¹⁴ Pass urine as soon as you need. ¹⁴ • Go for a wee after having sex to flush out any bacteria that may be near the opening to the urethra. ^{14,18} • Wash the external vagina area with water before and after sex to wash away any bacteria that may be near the opening to the urethra. ^{5,18} • Drink enough fluids to make sure you wee regularly throughout the day, especially during hot weather. ^{14,15,16} <p>If you have a recurrent UTI, the following may help ¹⁹</p> <ul style="list-style-type: none"> • Cranberry products and D-mannose: There is some evidence to say that these work to help prevent recurrent UTI. ^{19,20,21,22} • After the menopause: Topical hormonal treatment may help^{19,23} for example, vaginal pessaries. • Antibiotics at night or after sex may be considered. ¹⁹ 	<p>Antibiotics can be lifesaving. But antibiotics are not always needed for urinary symptoms. ^{16,24}</p> <p style="text-align: center;">↓</p> <p>Antibiotics taken by mouth, for any reason, affect our gut bacteria making some resistant. ²⁵</p> <p style="text-align: center;">↓</p> <p>This may make future UTI more difficult to treat. ^{24,25}</p> <p style="text-align: center;">↓</p> <p>Common side effects to taking antibiotics include thrush, rashes, vomiting and diarrhoea. ²⁶ Seek medical advice if you are worried.</p> <p style="text-align: center;">↓</p> <p>Keep antibiotics working; only take them when advised by a health professional. ²⁴ This way they are more likely to work for a future UTI. ²⁵</p>	

References:

Note

The information contained in this leaflet resource relates to the following NICE guidelines

- **NG15 Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use:** 1.1.11, 1.1.31, 1.1.33, 1.1.34
- **NG63 Antimicrobial stewardship: changing risk-related behaviours in the general population:** 1.3.2, 1.5.5, 1.5.6
- **NG109 Urinary tract infection (lower): antimicrobial prescribing:** 1.1.1, 1.1.2, 1.1.3, 1.1.5, 1.3
- **NG 112 Urinary tract infection (recurrent): antimicrobial prescribing:** 1.1.3, 1.1.5, 1.2, 1.2.1

1. Scottish Intercollegiate Guidelines Network (SIGN). Management of bacterial urinary tract infection in adults. 2012 Jul. Available from:
<http://www.sign.ac.uk/pdf/sign88.pdf>.

RATIONALE: A SIGN guideline, outlining symptoms of bacterial urinary tract infections as: dysuria; frequency of urination; suprapubic tenderness; urgency; polyuria; haematuria. Expert consensus is that, in women with symptoms of vaginal itch or discharge, alternative diagnoses to UTI should be explored. This guideline also provides details of UTI symptoms suggestive of pyelonephritis, including: loin pain; flank tenderness; fever; rigors; other manifestations of systemic inflammatory response, and suggests admission to hospital if there is no response to antibiotic treatment within 24 hours.

2. Bent S, Nallamotheu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002 May; 287(20):2701- 2710. Available from:
<https://www.ncbi.nlm.nih.gov/pubmed/12020306>.

RATIONALE: A systematic review of diagnostic studies, aiming to review the accuracy and precision of history taking and physical examination for the diagnosis of UTI in women. Results indicated that the presence of vaginal discharge or vaginal irritation substantially reduced the probability of UTI to around 20%. Additionally, this review states that dysuria with frequency together increase the chances of UTI to 90%. This review also identifies symptoms of pyelonephritis as: fever; back pain; nausea; vomiting.

3. Jackson S. Lower urinary tract symptoms and nocturia in men and women: prevalence, aetiology and diagnosis. *BJUJ*. 1999 Dec; 84(1):5-8. Available from:
<http://onlinelibrary.wiley.com/doi/10.1046/j.1464-410X.84.s1.6.x/epdf>.

RATIONALE: An editorial, exploring the prevalence of nocturia in different age groups of both men and women with lower urinary tract infections. Results indicate that whilst nocturia is more prevalent in adults over the age of 75, it does occur in all ages with bacterial urinary tract infections. As there is no universally accepted definition of nocturia, there is a wide variation in the reported prevalence of nocturia. Nevertheless, nocturia is a common symptom, with similar prevalence in both men and women across all ages, with proven UTI (men 16% to 55%; women 9% to 51%).

4. Little, P., et al. 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; 60(576): 495-500. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894378/>

RATIONALE: A validation study to determine the value of using urinary symptoms and signs and urine dipsticks for diagnosis of confirmed UTI. The study individuals included 434 women with at least 2 urinary symptoms of UTI and no vaginal discharge from across 62 different practices in England. Clinical symptoms and dipstick results were assessed against laboratory cultures. 66% of women had a confirmed UTI. No symptoms or signs or combination was able to confirm UTI with absolute certainty. The negative predictive value when nitrite, leukocytes, and blood are all negative was 76%. The positive predictive value for having nitrite and either blood or leukocytes was 92%. When clinical variables were examined, the positive predictive value was 82% for women with all three of cloudy urine, dysuria of any degree, and new nocturia to any degree; 74% for two, 68% for one. The negative predictive value was 67% for none of these three features. The authors conclude that though dipsticks can moderately improve diagnostic precision, they are poor at ruling out infection. Clinical strategies need to take into account poor negative predictive values. *Therefore the steering group in discussion agreed that a strategy of using a combination of clinical score and urine dipstick will optimise correct use of antibiotics. As at least 74% with two of dysuria, cloudy urine or nocturia will have a proven UTI it is reasonable to prescribe empirically in these patients. In patients with only one of dysuria, cloudy urine or nocturia, or none of these symptoms but they have other severe urinary symptoms a urine dipstick will help determine who should be given empirical antibiotics: if nitrite is*

positive or Both WBC and RBC are positive UTI is likely, if Nitrite is negative and WBC positive only half will have UTI, if all dipstick results are negative UTI is much less likely. Depending on the likelihood of UTI and severity of symptoms, then an immediate or back-up or no antibiotic strategy can be discussed with the patient.

- Scholes D, Hooton TM, Roberts PL, Stapleton AE, Gupta K, Stamm WE. Risk factors for recurrent urinary tract infections in young women. *J Infect Dis.* 2000 Oct; 182(4):1177-1182. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/10979915>.

RATIONALE: A case-control study of two populations in Seattle (USA), in which 229 university women and female health maintenance organisation enrollees with recurrent urinary tract infections were recruited. Independent risk factors for recurrent UTIs included: intercourse frequency within the previous month without washing (OR 5.8; 95% CI 3.1 to 10.6); spermicide use in the last 12 months (OR 1.8; 95% CI 1.1 to 2.9); new sexual partner during the past year (OR 1.9; 95% CI 1.2 to 3.2). Advice is given on how to prevent recurrent UTIs, including: voiding after intercourse; increased fluid intake; avoiding use of condoms with spermicide-coated lubricants.

- Huppert JS, Biro F, Lan D, Mortensen JE, Reed J, Slap GB. Urinary symptoms in adolescent females: STI or UTI? *J Adolesc Health.* 2007 May; 40(5):418-424. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1976261/pdf/nihms22080.pdf>.

RATIONALE: A cross-sectional sample study, aiming to determine if urinary symptoms or urinary tract infections were associated with sexually transmitted infections, and which history, clinical, and laboratory findings could distinguish these infections in symptomatic women. 296 sexually active females between the ages of 14 and 22 attending a hospital-based teen health centre or emergency department were recruited. Genitourinary symptoms, medical and sexual history, and urinalysis results were recorded. An STI was defined as a vaginal swab positive for *Trichomonas vaginalis*, or a urine nucleic acid amplification test positive for *Neisseria gonorrhoeae*, or *Chlamydia trachomatis*. A urine culture with >10,000 colonies of a single pathogen was considered to be a positive UTI. In the full sample, prevalence of UTI and STI were 17% and 33%, respectively, and neither urinary symptoms or confirmed UTI were significantly associated with STI. Further analyses of the 51% with urinary symptoms indicated that positive urine leukocytes, more than one partner in the last three months, and a history of STI predicted STI. Urinalysis results identified four groups: normal urinalysis (67% had no infection); positive nitrites or protein (55% had UTI); positive leukocytes or blood (62% had STI); both nitrites/protein and leukocytes/blood positive (28% had STI and 65% had UTI). The authors conclude that, since there is a similarity in symptoms, adolescent females with urinary symptoms should be tested for both UTI and STIs. Urinalysis results may also be helpful to direct initial therapy.

- Michaels T, Sands J. Dysuria: Evaluation and Differential Diagnosis in Adults. *American Family Physician.* 2015;92(9). Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26554471>

RATIONALE: A review of evidence based approaches for the evaluation of adult patients with dysuria. The authors state that the most common cause of acute dysuria is infection, especially cystitis. Other infectious causes include urethritis, sexually transmitted infections, and vaginitis. Non-infectious inflammatory causes include a foreign body in the urinary tract and dermatologic conditions. Non-inflammatory causes of dysuria include medication use, urethral anatomic abnormalities, local trauma, and interstitial cystitis/bladder pain syndrome. An initial targeted history includes features of a local cause (e.g., vaginal or urethral irritation), risk factors for a complicated urinary tract infection (e.g., male sex, pregnancy, presence of urologic obstruction, recent procedure), and symptoms of pyelonephritis. Women with vulvovaginal symptoms should be evaluated for vaginitis. Any complicating features or recurrent symptoms warrant a history, physical examination, urinalysis, and urine culture. Findings from the secondary evaluation, selected laboratory tests, and directed imaging studies enable physicians to progress through a logical evaluation and determine the cause of dysuria or make an appropriate referral.

- Portman DJ, Gass ML. Vulvovaginal Atrophy Terminology Consensus Conference P. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas.* 2014;79(3):349-54. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/25179577>
RATIONALE: Consensus report from 2012. The Board of Directors of the International Society for the Study of Women's Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) acknowledged the need to review current terminology associated with genitourinary tract symptoms related to menopause. To do this they cosponsored a terminology consensus conference, which was held in May 2013 and agreed that the term genitourinary syndrome of menopause (GSM) is a medically more accurate, all-encompassing, and more publicly acceptable term than vulvovaginal atrophy. Symptoms of GSM are associated with a decrease in oestrogen and other sex steroids involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra and bladder. The syndrome may include but is not limited to genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, discomfort or pain, and impaired function; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all of the signs and symptoms. The term was presented and discussed at the annual meeting of each society. GSM is currently used as the as a term to cover both atrophic vaginitis and vaginal atrophy in more recent references found during the review for the diagnostic guidance.

- Palma F, Volpe A, Villa P, Cagnacci A, Writing group of As. Vaginal atrophy of women in post-menopause. Results from a multicentric observational study: The AGATA study. *Maturitas.* 2016;83:40-4. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26421474>
RATIONALE: This multi-centric study was performed in order to provide nation-wide data on the prevalence and management of genitourinary signs of menopause (GSM) conducted by the Atrophy of the vagina in women in post-menopause in Italy (AGATA) group. Nine hundred thirteen females, 59.3 ± 7.4 years old asking for a routine gynaecological examination were recruited. Diagnosis of GSM was based on patient sensation of vaginal dryness, any objective sign of vulvar vaginal atrophy and a pH > 5. 722/913 (79.1%) women were diagnosed with GSM with a prevalence ranging from 64.7% to 84.2%, starting from 1 to 6 years after menopause. Recent vaginal infection was more likely in women with GSM (OR 2.48, 95% CI: 1.33-4.62; p = 0.0041). Symptoms reported by women with GSM were vaginal dryness (100%), dyspareunia (77.6%), burning (56.9%), itching (56.6%) and dysuria (36.1%). Signs detected by gynaecologists were mucosal dryness (99%), thinning of vaginal rugae (92.1%), pallor of the mucosa (90.7%), mucosal fragility (71.9%) and petechiae (46.7%). Only 274 (30%) of women had had a previous diagnosis of VVA/GSM. These were treated either with no therapy (9.8%), systemic hormone (9.2%), local hormone (44.5%) or local non-hormonal (36.5%) therapy, and at the time of investigation 266 of them (97.1%) still had the disorder. GSM is a common, under-diagnosed and under-treated disorder. Measures to improve its early detection and its appropriate management are needed.

10. Public Health England (PHE). Diagnosis of UTI: Quick reference guide for primary care. 2018 October. Available from: <https://www.gov.uk/government/publications/urinary-tract-infection-diagnosis> in October

RATIONALE: A PHE reference guide, suggesting that, PHE UTI diagnostic flowchart for women (under 65 years) with suspected UTI suggests that 2 or 3 of the key diagnostic symptoms/signs indicate that a UTI is likely. The symptoms/signs to look out for are: dysuria (burning pain when passing urine), new nocturia (passing urine more often at night), urine cloudy to the naked eye.

11. Gagyor 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; 23(351):1-11. Available from: <http://www.bmj.com/content/bmj/351/bmj.h6544.full.pdf>.

RATIONALE: A randomised controlled trial across 42 German general practices, aiming to determine if treatment of symptoms of uncomplicated UTI with ibuprofen can reduce the rate of antibiotic prescriptions without a significant increase in symptoms, recurrences, or complications. 494 women aged between 18 and 65 with typical symptoms of uncomplicated UTI were included and randomly assigned to one of two treatment arms: a single dose of fosfomycin 3g for three days (n=246), or ibuprofen 3 x 400mg for three days (n=248). In both groups, additional antibiotic treatment was subsequently prescribed as necessary for persistent, worsening, or recurrent symptoms. Results indicated that, out of the 248 women in the ibuprofen group, two thirds treated symptomatically recovered without any antibiotics. Recurrent urinary tract infections were more common in the fosfomycin group. This trial also indicated that mild to moderate urinary symptoms given an anti-inflammatory agent and not treated with empirical therapy can last for a mean average of 5.6 days. The authors conclude that, although they cannot generally recommend ibuprofen as first-line treatment for uncomplicated UTI in women, the treatment option can be discussed with women with mild to moderate symptoms in a shared decision making approach, or within a strategy of delayed prescribing.

12. Ferry SA, Holm SE, Stenlund H, Lundholm R, Monsen TJ. The natural course of uncomplicated lower urinary tract infection in women illustrated by a randomized placebo controlled study. *Scand J Infect Dis*. 2004 Apr; 36(4):296-301. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/15198188>.

RATIONALE: A prospective, multicentre, randomised double-blind and placebo controlled trial, including 1,143 women over 18 consulting for symptoms suggestive of uncomplicated lower UTI. This trial described natural course as the spontaneous eradication of both symptoms and bacteriuria. Spontaneous cure rate of symptoms was recorded at 28% after seven days, and 37% had neither symptoms nor bacteriuria by five to seven weeks. At seven days, however, the majority of uropathogens responsible for uncomplicated UTIs were starting to be eradicated, including *E. coli* (170 isolates).

13. Little P, Turner S, Rumsby K, Warner G, Moore M, Lowes JA et al. 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):1-73. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/19364448>.

RATIONALE: A collation of six studies, aiming to estimate clinical and dipstick predictors of infection and develop and test clinical scores, and to compare management using clinical and dipstick scores with commonly used alternative strategies. The results showed that, in women with uncomplicated UTI, the negative predictive value when nitrite, leukocytes, and blood are all negative was 76%. The positive predictive value for having nitrite and either blood or leukocytes was 92%. Moderate to severe UTI is defined as having a higher symptom score of two or more of: urine cloudiness; smell; nocturia; dysuria.

Results also suggested that women suffer 3.5 days of moderately bad symptoms with immediate antibiotics, and 4.8 days if taking antibiotics is delayed for 48 hours. The authors conclude that, to achieve good symptom control and reduce antibiotic use, clinicians should either offer a 48-hour delayed antibiotic prescription to be used at the patient's discretion, or target antibiotic treatment by dipsticks (positive nitrite or positive leukocytes and blood) with the offer of a delayed prescription if dipstick results are negative. Those treated with empirical therapy should, however, seek further advice if their symptoms do not start to improve within 48 hours.

14. Scottish Antimicrobial Prescribing Group (SAPG). Guidance on management of recurrent urinary tract infection in non-pregnant women. 2016 Jun. Available from: https://www.scottishmedicines.org.uk/files/sapg1/Management_of_recurrent_lower_UTI_in_non-pregnant_women.pdf.

RATIONALE: An SAPG guideline, providing a thorough overview of the management of recurrent urinary tract infections. This guideline provides advice about simple measures to limit recurrent UTI, including: better hydration; urge initiated voiding and postcoital voiding; cranberry products; stand-by antibiotics; intra-vaginal or oral oestrogens for post-menopausal women. This guideline also stresses the importance of confirming UTI diagnoses, and investigating underlying causes if simple measures are not effective.

15. Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI). 5th Annual Report, April 2013 – March 2014. 2015 Feb. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/405295/ARHAI_annual_report.pdf.

RATIONALE: An ARHAI report, noting that mandatory surveillance over the past ten years has demonstrated a sustained increase in *E. coli* bacteraemia, that is unexplained by improved diagnosis. The analysis demonstrates that only a small proportion of infections are related to urinary catheterisation. Other risk factors, such as repeated urinary tract infections treated by sub-optimal antibiotic prescribing, and inadequate hydration, have a significant impact. The surveillance report shows that *E. coli* bacteraemia peaks in the summer months, which may also be due to poor urine output associated with dehydration. The report recommends that: all organisations providing care to patients with indwelling urinary catheters should ensure that the recommendations of EPIC 3 (short-term catheters) and NICE (long-term catheters) are being implemented, and provide evidence of compliance; hydration status must be a priority for those at risk of dehydration, particularly those in hospitals and long-term care facilities; treatment of UTI should be based on local antibiotic resistance patterns, and patients diagnosed with a UTI (especially those with a history of repeated infections) should be subject to a safety-netting procedure to ensure that treatment has been effective.

16. National Institute of Health and Care Excellence (NICE). Urinary tract infection (lower): antimicrobial prescribing. October 2018. Available from: <https://www.nice.org.uk/guidance/ng109>

RATIONALE: This NICE guideline sets out an antimicrobial prescribing strategy for lower urinary tract infection. This guideline aims to optimise antibiotic use and reduce antibiotic resistance. The recommendations state that advice should be given on self-care to all those with an expected lower UTI. This includes paracetamol for pain and adequate intake of fluids. Consider a back-up antibiotic prescription or an immediate antibiotic prescription for women with lower UTI who are not pregnant. If pregnant an immediate antibiotic should be given. Obtain a mid-stream urine sample

before prescribing antibiotics for pregnant women and send for culture and susceptibility testing. This guideline clearly states which antibiotics should be used for infections in tables in the text and also in visual summaries that accompany the guideline.

The evidence review for this guideline summarised non-pharmacological interventions in healthy pregnant women that could prevent future episodes of asymptomatic bacteriuria or uncomplicated urinary tract infection (UTI). No systematic reviews or randomised controlled trials (RCTs) were identified in non-pregnant women, men, older people and children. Two RCTs were found (Wing et al. 2008 and Wing et al. 2015) for pregnant women. Both studies assessed asymptomatic bacteriuria or UTI prevention in healthy pregnant women, who otherwise had no indication or risk of asymptomatic bacteriuria or UTI. They looked at cranberry capsules or cranberry juice drinks in pregnant women of less than 16 weeks gestation. The dose of proanthocyanidin (the active ingredient) was reported as equivalent as the same researchers conducted both studies (approximately 32-34 mg of proanthocyanidin). Overall, there were no significant differences in maternal or neonatal outcomes in either study.

17. Clinical Knowledge Summaries (CKS). Urinary tract infection (lower) – women. 2015 Jul. Available from: <https://cks.nice.org.uk/urinary-tract-infection-lower-women#!topicsummary>.
RATIONALE: A CKS guideline, providing advice for six different scenarios of uncomplicated urinary tract infections in women. For recurrent UTI, this guideline states that cranberry products and urine alkalinising agents should not be recommended, as there is currently no good evidence to support their use. This guideline also states that women should seek medical attention if they develop fever, loin pain, or do not respond to treatment.

18. Badran YA, El-Kashef TA, Abdelaziz AS, Ali MM. Impact of genital hygiene and sexual activity on urinary tract infection during pregnancy. *Urol Ann.* 2015 Oct; 7(4):478-481. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4660700/>.
RATIONALE: A retrospective study, aiming to determine the association of UTI with genital hygiene practices and sexual activity in pregnant women. 200 pregnant women attending prenatal clinics in Saudi Arabia between January 2011 and June 2014 were included. 80 women who had positive urine cultures were compared with the remaining 120 healthy women. Results indicated that *E. coli* was the infecting organism in 83% of cases. Factors associated with UTI included sexual intercourse more than three times a week (OR=5.62); recent UTI (OR=3.27); not washing genitals pre-coitus (OR=2.16); not washing genitals post-coitus (OR=8.62); wiping genitals from back to front (OR=2.96). The authors state that genital hygiene practices such as frequency of coitus, urinating after coitus, washing genitals pre- and post-coitus, taking baths, frequent replacing of underwear, and wiping genitals from front to back were associated with a reduced frequency of UTIs. Women who usually urinated within 15 minutes of intercourse also had a lower likelihood of developing a UTI than women who did not urinate after intercourse. The authors conclude that urinary tract infection in these women were primarily caused by bacteria from the stool (*E. coli*), and that hygiene habits and sexual behaviour may play a role in the occurrence of UTIs.

19. National Institute of Health and Care Excellence (NICE). Urinary tract infection (recurrent): antimicrobial prescribing. October 2018. Available from: <https://www.nice.org.uk/guidance/ng112>.
RATIONALE: This NICE guideline sets out an antimicrobial prescribing strategy for recurrent urinary tract infection (UTI). Recurrent UTI in adults is defined as repeated UTI with a frequency of 2 or more UTIs in the last 6 months or 3 or more UTIs in the last 12 months. The guideline states that recurrent UTI includes lower UTI and upper UTI (acute pyelonephritis), may be due to relapse or reinfection, and is particularly common in women. It outlines criteria that explain when you should refer someone with recurrent UTI and provides recommendations for groups including women who are and aren't pregnant, men, and children. For women with recurrent UTI who are not pregnant it suggests options for management. These include vaginal oestrogen (off-label use) for post-menopausal women and antibiotic prophylaxis (single dose to be given if trigger identifiable, daily dose if no trigger identifiable or if single dose ineffective). The review also recommends self-care measures for non-pregnant women including the use of D-mannose or cranberry products for which there is very weak evidence of a preventative effect in non-pregnant women with recurrent UTIs.

To support the recommendations around cranberry products and D-mannose, the evidence review highlights an RCT from Kranjcec et al. (2014) comparing D-mannose (200 ml of 1% solution once daily in the evening) with no treatment. All women in the study took antibiotics for their current UTI. Effectiveness was determined by the number of participants presenting with 1 recurrent UTI during the study period of 6 months. D-mannose was significantly more effective in preventing recurrent UTI in non-pregnant women compared with no treatment (Kranjcec et al. 2014, n=205: 14.6% versus 60.8%; RR 0.24, 95% CI 0.15 to 0.39; NNT 3 [95% CI 2 to 3]; high quality evidence). Two systematic reviews (Jepson et al. 2012 and Fu et al. 2017) assessed the efficacy of cranberry products for preventing recurrent UTIs in women. When comparing cranberry products to placebo or no treatment Jepson et al. 2012 found that prophylactic cranberry products for 3, 6 or 12 months did not show a significant benefit in the number of women who had one or more UTI during follow up (4 RCTs, n=594: 19.9% versus 22.8%; RR 0.74, 95% CI 0.42 to 1.31; very low quality evidence). Fu et al. (2017) compared cranberry in either juice or capsule form, for preventing UTIs in non-pregnant women, with a follow up of 6 to 12 months. Cranberry juice or capsules significantly reduced the incidence of UTI in non-pregnant women compared with placebo or no treatment (7 RCTs, n=1498: 20.7% versus 26.5%; RR 0.74, 95% CI 0.55 to 0.98; very low quality evidence). Cranberry juice did not significantly reduce the incidence of UTI, diagnosed either by symptom presence or culture confirmation, compared with placebo or no treatment (6 RCTs, n= 1272: 22.0% versus 26.6%; RR 0.79, 95% CI 0.59 to 1.06, very low quality evidence). However, cranberry tablets did significantly reduce incidence of UTI compared with placebo (2 RCTs, n= 276: 13.5% versus 28.0%; RR 0.48, 95% CI 0.29 to 0.79; low quality evidence).

20. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections (Review). *Cochrane Database Syst Rev.* 2012 Oct; 17(10):1-82. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/23076891>.
RATIONALE: A systematic review of 24 studies and 4,473 participants, comparing cranberry products with control or alternative treatments. There was a small trend towards fewer UTIs in people taking cranberry products, compared to placebo or no treatment, but this was not a significant finding. Many participants stopped drinking the juice, suggesting it may not be an acceptable intervention. In the long-term, cranberry products were ineffective, possibly due to the lack of potency of the active ingredient. Four of the five studies in women with recurrent UTI (n=594), which included a placebo group, provided data that could be combined in a meta-analysis. Results demonstrated a small, non-significant reduction in the risk of repeat symptomatic UTI with cranberry treatment, compared to placebo or no treatment (RR 0.74; 95% CI 0.42 to 1.31). Two studies in women with recurrent UTI, and one study in children, compared cranberry capsules or syrup with antibiotic prophylaxis. Meta-analysis of the two studies in women showed that cranberry products, compared to antibiotics, were equally as effective in reducing the risk of repeat UTI (RR 1.31; 95% CI 0.85 to 2.02). The study in children also showed that the cranberry products, compared to antibiotics, were equally as effective in reducing the risk of repeat symptomatic UTI (RR 0.69; 95% CI 0.32 to 1.51). The authors

conclude that given the large number of dropouts/withdrawals from studies (mainly attributed to the acceptability of consuming cranberry products particularly juice, over long periods), and the evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs. Other preparations (such as powders) need to be quantified using standardised methods to ensure the potency, and contain enough of the 'active' ingredient, before being evaluated in clinical studies or recommended for use.

21. Kranjčec B, Papeš D, Altarac S. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. *World J Urol*.

2014 Feb; 32(1):79-84. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/23633128>

RATIONALE: In 1 RCT Kranjčec et al 2014 (N=308) compared D-mannose (2gms in 200mls per day) with antibiotic prophylaxis (nitrofurantoin 50mg a day) and with no treatment. Patients in the D-mannose group and the antibiotic prophylaxis group had a significantly lower risk of recurrent UTI episodes during therapy compared to patients in the no treatment group (RR 0.239 and 0.335, P<0.0001). Patients in the D-mannose group had a significantly lower risk of side effects compared to patients in Nitrofurantoin group (RR 0.276, P<0.0001), but the clinical importance of this finding is low because Nitrofurantoin was well tolerated. D-mannose works by sticking to E.coli lectin on their fimbria preventing adhesion to the bladder, so promoting an immune response. This is high quality evidence and there is no reason why this should not give similar results in older women although further studies will be needed in both age groups to confirm these excellent results. Health professionals may want to consider recommending D-mannose as an alternative preventative treatment.

22. Fu Z, Liska D, Talan D, Chung M. Cranberry reduces the risk of urinary tract infection recurrence in otherwise healthy women: a systematic review and meta- analysis. *J Nutr*.

2017;147(12):2282-2288. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29046404>

RATIONALE: This meta-analysis assessed the effect of cranberry on the risk of UTI recurrence in otherwise healthy women. Literature published before January 2011 was obtained from 2 published systematic reviews. An updated search (through July 2017) identified 7 randomised controlled trials conducted in healthy women at risk of UTI (n = 1498 participants). Results of the meta-analysis showed that cranberry reduced the risk of UTI by 26% (pooled risk ratio: 0.74; 95% CI: 0.55, 0.98; I² = 54%). Risk of bias indicated that 2 studies had high loss to follow-up or selective outcome reporting.

Overall, the studies were relatively small, with only 2 having >300 participants. These results suggest that cranberry may be effective in preventing UTI recurrence in generally healthy women; however, larger high-quality studies are needed to confirm these findings.

23. Eriksen BC. A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. *Am J Obstet Gynecol*. 1999 May; 180(5):1072-1079. Available from: <http://www.sciencedirect.com/science/article/pii/S0002937899705971>.

RATIONALE: A randomised controlled trial, including 108 postmenopausal women, aiming to detect a difference in time until the first recurrence of a urinary tract infection during treatment with an estradiol-releasing silicone vaginal ring, versus no oestrogen treatment. 53 women were randomly assigned to the Estring group, and 55 were assigned to the control group. Results indicated that approximately 45% of the women with the vaginal ring remained free of disease, in comparison to approximately 20% in the control group (p=.008). Estring lowered vaginal pH, and the time to first recurrence was effectively prolonged by Estring treatment. The authors conclude that the use of vaginal oestrogen can be considered for the prevention of recurrent UTI in postmenopausal women.

24. Alanis AJ. Resistance to antibiotics: are we in the post-antibiotic era? *Arch Med Res*. 2005 Dec; 36(6):697-705. Available from:

<http://www.sciencedirect.com/science/article/pii/S0188440905002730>.

RATIONALE: A review article, stating that serious infections caused by bacteria that have become resistant to commonly used antibiotics have become a major global healthcare problem in the 21st century. This review states that the single largest cause of antibiotic resistance is the indiscriminate and inappropriate use of antibiotics in outpatient clinics, hospitalised patients, and in the food industry. The authors state that antibiotics should only be taken on advice from a healthcare professional for a bacterial infection that shows susceptibility to that particular antibiotic. This review also states that new mechanisms of resistance have resulted in the simultaneous development of resistance to several antibiotic classes, creating very dangerous multidrug- resistant bacterial strains, also known as 'super-bugs'. The potential negative consequences of this are that they put society at risk for the spread of potentially serious multi-drug resistant bacterial infections.

25. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients – systematic review and meta-analysis. *BMJ*. 2010 May; 18(340):1-11. Available from: <http://www.bmj.com/content/bmj/340/bmj.c2096.full.pdf>.

RATIONALE: A systematic review and meta-analysis, aiming to investigate subsequent antibiotic resistance in individuals prescribed antibiotics in primary care. 24 studies were included, 22 of which involved patients with symptomatic infection, and two of which involved healthy volunteers. In five studies of urinary tract bacteria (14,348 participants), the pooled odds ratio for resistance was 2.5 (95% CI 2.1 to 2.9) within two months of antibiotic treatment, and 1.33 (95% CI 1.2 to 1.5) within 12 months. Studies reporting the quantity of antibiotic prescribed found that longer duration and multiple courses were associated with higher rates of resistance. The authors conclude that individuals prescribed an antibiotic in primary care for a urinary infection develop bacterial resistance to that antibiotic. The effect is greatest in the month immediately following treatment, but may persist for up to 12 months. This effect not only increases the population carriage of organisms resistant to first line antibiotics, but also creates the conditions for increased use of second-line antibiotics in the community.

26. Leydon GM, Turner S, Smith H, Little P, UTIS Team. Women's views about management and cause of urinary tract infection: qualitative interview study. *BMJ*. 2010 Feb; 5(340):1-7. Available from: <http://www.bmj.com/content/bmj/340/bmj.c279.full.pdf>.

RATIONALE: A retrospective study, aiming to explore the views of women with urinary tract infections on the acceptability of different strategies for managing the infection, including delayed use of antibiotics, and the cause of infection. 21 women presenting to general practices across Southern England were included. Results indicated that women preferred not to take antibiotics, and were open to alternative management approaches, due to wanting to avoid the side-effects of antibiotic therapy. Most of the participants with experience of antibiotic use had developed thrush, skin rash, and gastrointestinal side-effects as a consequence, and this mediated their desire for antibiotic medication. The authors conclude that if women are asked to delay taking antibiotics, the clinician must

address the particular worries that women might have, and explain the rationale for not using antibiotics immediately.

27. National Institute of Health and Care Excellence (NICE). Sepsis: Recognition, diagnosis and early management. 2016 Jul. Available from:

<https://www.nice.org.uk/guidance/ng51/resources/sepsis-recognition-diagnosis-and-early-management-1837508256709>.

RATIONALE: A NICE guideline, stating that people with sepsis may have non-specific, non-localised presentations, such as feeling generally unwell without a high temperature of over 38°C. This guideline presents a risk stratification tool for adults, children and young people aged 12 years and over with suspected sepsis. Where high temperature is recognised as a cause for concern, this guideline also lists a tympanic temperature of less than 36°C as a moderate to high risk criteria for sepsis.

28. The UK Sepsis Trust. Do I have sepsis? 2016 Mar. Available from: <http://sepsistrust.org/public/do-i-have-sepsis/>.

RATIONALE: A UK Sepsis Trust website, stating that if someone has early signs of a flu-like illness, chest infection, diarrhoea and vomiting, or an inability to eat and drink, together with one of the symptoms of sepsis, immediate medical advice should be sought. This website defines the symptoms of sepsis as: slurred speech; extreme shivering or muscle pain; passing no urine (in a day); severe breathlessness; skin mottled or discoloured.

29. The UK Sepsis Trust. Sepsis: a guide for patients and relatives. 2013 Oct. Available from: [http://sepsistrust.org/wp-](http://sepsistrust.org/wp-content/uploads/2013/10/Sepsis_A5_final1.pdf)

[content/uploads/2013/10/Sepsis_A5_final1.pdf](http://sepsistrust.org/wp-content/uploads/2013/10/Sepsis_A5_final1.pdf).

RATIONALE: A UK Sepsis Trust guideline, stating that sepsis is caused by the way the body responds to an infection, which may have started anywhere in the body. This guideline also outlines the symptoms of sepsis as: a drop in blood pressure; fast heart beat; breathlessness; mottled skin; lack of urination; difficulty breathing; confusion and disorientation.