

Urinary tract infection (lower): antimicrobial prescribing

NICE guideline

Draft for consultation, May 2018

This guideline sets out an antimicrobial prescribing strategy for lower urinary tract infection (cystitis), which is an infection of the bladder. It aims to optimise antibiotic use and reduce antibiotic resistance.

See a 3-page visual summary of the recommendations, including tables to support prescribing decisions.

Who is it for?

- Health professionals
- People with lower urinary tract infection (cystitis), their families and carers

The guideline contains:

- the draft recommendations
- summary of the evidence.

Information about how the guideline was developed is on the [guideline's page](#) on the NICE website. This includes the full evidence review, details of the committee and any declarations of interest.

Recommendations

The recommendations in this guideline are for managing lower urinary tract infection (UTI, also called cystitis) in adults, young people and children who do not have a catheter.

1.1 *Managing lower urinary tract infection (cystitis)*

1.1.1 Be aware that lower UTI (cystitis) is an infection of the bladder usually caused by bacteria from the gastrointestinal tract entering the urethra and travelling up to the bladder.

1.1.2 Give advice about managing symptoms with self-care (see the recommendations on [self-care](#)) to all people with lower UTI.

Treatment for women with lower UTI who are not pregnant

1.1.3 Consider a back-up antibiotic prescription or an immediate antibiotic prescription (see the recommendations on [choice of antibiotic](#)) for women with lower UTI who are not pregnant. Take account of:

- the severity of symptoms
- the risk of developing complications, which is higher in people with known or suspected structural or functional abnormality of the genitourinary tract or underlying disease (such as diabetes or immunosuppression)
- previous urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria
- preferences of the woman for antibiotic use.

1.1.4 Taking account of the severity of symptoms, consider waiting until any microbiological results are available before prescribing an antibiotic for a woman with lower UTI who is not pregnant.

1.1.5 If a urine sample has been sent for culture and susceptibility testing and an antibiotic prescription has been given:

- review the choice of antibiotic when microbiological results are available, **and**
- change the antibiotic according to susceptibility results if bacteria are resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible.

Treatment for pregnant women and men with lower UTI

1.1.6 Obtain a midstream urine sample before prescribing antibiotics for pregnant women and men with lower UTI and send for culture and susceptibility testing.

1.1.7 Offer an immediate antibiotic prescription (see the recommendations on [choice of antibiotic](#)) to pregnant women and men with lower UTI. Take account of:

- previous urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria.

1.1.8 For pregnant women with lower UTI:

- review the choice of antibiotic when microbiological results are available, **and**
- change the antibiotic according to susceptibility results if the bacteria are resistant, using a narrow spectrum antibiotic wherever possible.

1.1.9 For men with lower UTI:

- review the choice of antibiotic when microbiological results are available, **and**
- change the antibiotic according to susceptibility results if the bacteria are resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible.

Treatment for children and young people under 16 years with lower UTI

1.1.10 Obtain a midstream urine sample from children and young people with lower UTI and dipstick test or send for culture and

susceptibility testing in line with the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#).

1.1.11 Assess and manage children under 5 with lower UTI who present with fever as outlined in the NICE guideline on [fever in under 5s](#).

1.1.12 Offer an immediate antibiotic prescription (see the recommendations on [choice of antibiotic](#)) for children and young people under 16 years with lower UTI. Take account of:

- previous urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria.

1.1.13 If a urine sample has been sent for culture and sensitivity testing when an antibiotic prescription has been given:

- review the choice of antibiotic when microbiological results are available, **and**
- change the antibiotic according to susceptibility results if the bacteria are resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible.

Advice for all people with lower UTI when an antibiotic prescription is given

1.1.14 When a back-up antibiotic prescription is given, as well as the general advice on [self-care](#), give advice about:

- an antibiotic not being needed immediately
- using the back-up prescription if symptoms do not start to improve within 48 hours or if they worsen rapidly or significantly at any time
- possible adverse effects of antibiotics, particularly diarrhoea and nausea
- seeking medical help if antibiotics are taken and symptoms worsen rapidly or significantly at any time, do not start to

improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell.

1.1.15 When an immediate antibiotic prescription is given, as well as the general advice on [self-care](#), give advice about:

- possible adverse effects of the antibiotic, particularly diarrhoea and nausea
- seeking medical help if symptoms worsen rapidly or significantly at any time, do not start to improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell.

Reassessing symptoms

1.1.16 Reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of:

- other possible diagnoses
- any symptoms or signs suggesting a more serious illness or condition, such as pyelonephritis
- previous antibiotic use, which may have led to resistant bacteria.

Send a urine sample for culture and susceptibility testing if this has not already been done and review treatment when results are available (see recommendations 1.1.5, 1.1.8, 1.1.9 and 1.1.13).

Referring to hospital

1.1.17 Refer adults and young people aged 16 years and over with lower UTI to hospital if they have a severe systemic infection (any of the high risk criteria from the NICE guideline on [sepsis](#)).

1.1.18 Refer children or young people with lower UTI to hospital in line with the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#).

See the evidence and committee discussion on [antibiotics](#).

1.2 *Managing asymptomatic bacteriuria*

1.2.1 Be aware that asymptomatic bacteriuria:

- is clinically significant levels of bacteria (greater than 10,000 colony forming units/ml) in the urine with no symptoms of UTI
- is not routinely screened for, or treated, in women who are not pregnant, men, young people and children
- is routinely screened for, and treated with antibiotics, in pregnant women because it is a risk factor for pyelonephritis and premature delivery (see the recommendations on [choice of antibiotic](#)).

1.2.2 Offer an immediate antibiotic prescription to pregnant women with asymptomatic bacteriuria, taking account of:

- recent urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria.

See the evidence and committee discussion on [antibiotics](#).

1.3 *Self-care*

1.3.1 Consider paracetamol for pain, or if preferred and suitable ibuprofen, in people with lower UTI.

1.3.2 Advise people with lower UTI about the adequate intake of fluids.

1.3.3 Explain that no evidence was found on cranberry products to treat a lower UTI.

See the evidence and committee discussion on [self-care](#).

1.4 *Choice of antibiotic*

1.4.1 When prescribing antibiotic treatment for lower UTI:

- follow table 1 for non-pregnant women aged 16 years and over
- follow table 2 for pregnant women aged 12 years and over

- follow table 3 for men aged 16 years and over
- follow table 4 for children and young people under 16 years.

Table 1. Antibiotics for non-pregnant women aged 16 years and over

Antibiotic ¹	Dosage and course length ²
First choice³	
Nitrofurantoin – if eGFR ≥45 ml/minute	50 mg four times a day or 100 mg modified-release twice a day for 3 days
Trimethoprim – if low risk of resistance and not used in the past 3 months	200 mg twice a day for 3 days
Second choice (no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice not suitable)^{3,4}	
Nitrofurantoin – if eGFR ≥45 ml/minute and not used as first choice	50 mg four times as day or 100 mg modified-release twice a day for 3 days
Pivmecillinam	400 mg initial dose, then 200 mg three times a day for a total of 3 days
Fosfomycin	3 g single dose sachet
¹ See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment and breastfeeding. ² Doses given are by mouth using immediate-release medicines, unless otherwise stated. ³ Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly. ⁴ If there are symptoms of pyelonephritis or sepsis, see the recommendations on choice of antibiotic in the NICE guideline on acute pyelonephritis.	
Abbreviations: eGFR, estimated glomerular filtration rate.	

Table 2. Antibiotics for pregnant women aged 12 years and over

Antibiotic ¹	Dosage and course length ²
Treatment of lower UTI	
First choice³	
Nitrofurantoin – if eGFR ≥45 ml/minute ⁴	50 mg four times as day or 100 mg modified-release twice a day for 7 days
Second choice (no improvement in lower UTI symptoms on first choice taken for at least 48 hours or when first choice not suitable)^{3,5}	
Cefalexin	500 mg twice a day for 7 days
Amoxicillin (only if culture results available and susceptible)	500 mg three times a day for 7 days

Alternative second choices	Consult local microbiologist, choose antibiotics based on culture and susceptibility results
Treatment of asymptomatic bacteriuria	
Choose from cefalexin, amoxicillin or nitrofurantoin based on recent culture and susceptibility results	
<p>¹See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment.</p> <p>²Doses given are by mouth using immediate-release medicines, unless otherwise stated.</p> <p>³Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.</p> <p>⁴Avoid at term in pregnancy; may produce neonatal haemolysis (BNF, April 2018).</p> <p>⁵If there are symptoms of pyelonephritis or sepsis, see the recommendations on choice of antibiotic in the NICE guideline on acute pyelonephritis.</p>	
Abbreviations: eGFR, estimated glomerular filtration rate.	

Table 3. Antibiotics for men aged 16 years and over

Antibiotic ¹	Dosage and course length ²
First choice³	
Trimethoprim	200 mg twice a day for 7 days
Nitrofurantoin – if eGFR ≥45 ml/minute ⁴	50 mg four times as day or 100 mg modified-release twice a day for 7 days
Second choice (no improvement in UTI symptoms on first choice taken for at least 48 hours or when first choice not suitable)³	
Consider alternative diagnoses and follow recommendations in the NICE guideline on acute pyelonephritis or acute prostatitis, basing antibiotic choice on recent culture and susceptibility results.	
<p>¹See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment.</p> <p>²Doses given are by mouth using immediate-release medicines, unless otherwise stated.</p> <p>³Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.</p> <p>⁴Nitrofurantoin is not recommended for men with suspected prostate involvement because it is unlikely to reach therapeutic levels in the prostate.</p>	
Abbreviations: eGFR, estimated glomerular filtration rate.	

Table 4. Antibiotics for children and young people under 16 years

Antibiotic ¹	Dosage and course length ²
Children under 3 months	
Refer to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s .	
Children aged 3 months and over	

First choice^{3,4}	
Trimethoprim – if low risk of resistance and not used in the past 3 months	3 to 5 months, 4 mg/kg or 25 mg twice a day for 3 days 6 months to 5 years, 4 mg/kg or 50 mg twice a day for 3 days 6 to 11 years, 4 mg/kg or 100 mg twice a day for 3 days 12 to 17 years, 200 mg twice a day for 3 days
Nitrofurantoin – if eGFR ≥45 ml/minute	3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 to 17 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days
Second choice (no improvement in lower UTI symptoms on first choice taken for at least 48 hours or when first choice not suitable)^{3,4,5}	
Nitrofurantoin – if eGFR ≥45 ml/minute and not used as first choice	3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 to 17 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days
Cefalexin	3 to 11 months, 12.5 mg/kg or 125 mg twice a day for 3 days 1 to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 3 days 5 to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 3 days 12 to 17 years, 500 mg two or three times a day for 3 days
Amoxicillin (only if culture results available and susceptible)	1 to 11 months, 125 mg three times a day for 3 days 1 to 4 years, 250 mg three times a day for 3 days 5 to 11 years, 500 mg three times a day for 3 days 12 to 17 years, 500 mg three times a day for 3 days
<p>¹See BNF for children for appropriate use and dosing in specific populations, for example hepatic and renal impairment. See table 2 if the young woman is pregnant.</p> <p>²The age bands apply to children of average size and, in practice, the prescriber will use the age bands in conjunction with other factors such as the severity of the condition being treated and the child's size in relation to the average size of children of the same age. Doses given are by mouth using immediate-release medicines, unless otherwise stated.</p> <p>³Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly. Where a child or young person is receiving prophylactic antibiotics, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.</p> <p>⁴If 2 or more antibiotics are appropriate, choose the antibiotic with the lowest acquisition cost.</p> <p>⁵If there are symptoms of pyelonephritis or sepsis, see the recommendations on choice of antibiotic in the NICE guideline on acute pyelonephritis.</p>	

Abbreviations: eGFR, estimated glomerular filtration rate.
--

See the evidence and committee discussion on [choice of antibiotic](#) and [antibiotic course length](#).

Summary of the evidence

Self-care

Oral analgesia (ibuprofen)

- Two RCTs ([Bleidorn et al. 2010](#) and [Gagyor et al. 2015](#)) in non-pregnant women found conflicting evidence regarding the effectiveness of ibuprofen compared with antibiotics. One small RCT, Bleidorn et al. 2010, found no significant differences between ibuprofen and ciprofloxacin in reducing symptoms and symptom duration (very low to low quality evidence). However, a more recent larger RCT, Gagyor et al. 2015, found that women using ibuprofen were more likely to report a higher burden of symptoms over the first 7 days after the start of their treatment, compared with women using fosfomycin (moderate quality evidence).
- Subgroup analyses, based on the results of urine culture prior to treatment, showed that women who received ibuprofen had significantly fewer antibiotic courses per patient compared with women who received fosfomycin (Gagyor et al. 2015; moderate quality evidence). However, this effect was driven mostly by the randomisation process, rather than the effect of the treatment itself.
- Women who received ibuprofen (irrespective of urine culture) were significantly more likely to receive an additional antibiotic prescription to treat a UTI during 12 months of follow-up (31.1% versus 12.3%; high quality evidence), but were less likely to experience a recurrent UTI between days 15 to 28 of follow up (5.8% versus 11.1%; moderate quality evidence). The authors noted that this result could be because the baseline risk of having recurrent UTI was greater in the fosfomycin group, as more women had experienced a UTI in the past year.

- Bleidorn et al. (2010) did not report any safety or tolerability outcomes. However, Gagyor et al. (2015) found no significant difference between ibuprofen and fosfomycin in the incidence of pyelonephritis, febrile UTIs, patient-reported adverse events, or serious drug-related adverse effects (low to moderate quality evidence).

Cranberry products

- Two RCTs ([Wing et al. 2008](#) and [Wing et al. 2015](#)) assessed the clinical effectiveness and safety of cranberry products for the prevention of asymptomatic bacteriuria in healthy pregnant women.
- Wing et al. (2008) found that cranberry juice was not effective in preventing episodes of asymptomatic bacteriuria or UTI. However, a significant reduction in compliance was seen in women receiving cranberry juice compared with placebo (very low quality evidence).
- Wing et al. (2015) assessed the safety and tolerability of cranberry capsules and found no significant difference in the number of babies born with a 1 minute Apgar score <7 in women who received cranberry capsules compared with placebo (21.4% versus 0%; very low quality evidence).

Other non-pharmacological or non-antimicrobial interventions

- No systematic reviews or RCTs of any non-pharmacological or non-antimicrobial interventions were identified in men, older people or children.
- No systematic reviews or RCTs of paracetamol were identified.
- No systematic reviews or RCTs of hydration were identified.

Committee discussion on self-care

- Based on experience, the committee agreed that it was reasonable to consider paracetamol for managing pain in adults, young people and children with lower UTI as this medicine has a well-established efficacy and safety profile for managing pain and fever.
- The committee agreed, based on the evidence and their experience, that it was also reasonable to consider ibuprofen for managing pain in adults, young people and children with lower UTI if this was preferred and suitable, taking account of safety concerns with NSAIDs, for example renal impairment.
- The committee agreed that people should be told that no evidence was found for using cranberry products to treat lower UTI or asymptomatic bacteriuria. The only evidence found assessed the efficacy and safety of cranberry products for the prevention of asymptomatic bacteriuria in healthy pregnant women.
- Based on experience, the committee agreed that people should be advised about the adequate intake of fluids because maintaining full hydration is important in people with a UTI.

Antibiotics

- In most cases, managing lower UTI (cystitis) will require antibiotic treatment. However, acute, uncomplicated cystitis in non-pregnant women can be self-limiting and for some women delaying antibiotic treatment with a back-up prescription to see if symptoms will resolve without antibiotic treatment, or delaying the antibiotic until microbiological results are available, may be an option.
- The most common causative pathogen in uncomplicated UTIs is *Escherichia coli* (in 70-95% of cases). *Staphylococcus saprophyticus* accounts for 5-10% of cases and occasionally other Enterobacteriaceae, such as *Proteus mirabilis* and Klebsiella species are isolated ([European Association of Urology guidelines on urological infections 2017](#)).

- The main complication of lower UTI (cystitis) is ascending infection leading to upper UTI (acute pyelonephritis). Most episodes of acute pyelonephritis are uncomplicated and result in no residual kidney damage. However, complications can include impaired renal function or renal failure, septicaemia and pre-term labour in pregnancy (NICE clinical knowledge summary on [pyelonephritis](#)).
 - In men, prostate involvement is common, which may lead to acute prostatitis, chronic bacterial prostatitis or a prostatic abscess; urinary stones are also a possibility (NICE clinical knowledge summary on [UTI \(lower\) - men](#)).
 - In children, UTIs can lead to renal scarring, but more often this is preceded by acute pyelonephritis rather than cystitis, and it is more common in children with vesicoureteral reflux (NICE clinical knowledge summary on [UTI - children](#)).
- Asymptomatic bacteriuria, where there is significant bacteriuria but no symptoms or signs of infection, is not routinely screened for or treated, except if it is considered a risk factor in clearly defined situations, such as in pregnant women ([European Association of Urology guidelines on urological infections 2017](#)).
 - In pregnancy, asymptomatic bacteriuria can lead to pyelonephritis and pre-term labour (NICE clinical knowledge summary on [UTI \(lower\) - women](#) and [pyelonephritis](#)).

Efficacy of antibiotics

- One systematic review of RCTs ([Falagas et al. 2009](#)) in non-pregnant women found that women who were treated with antibiotics were more likely to have complete symptom resolution (61.8% versus 25.7%; NNT 3 [range 3 to 4]; high quality evidence) and microbiological success (defined as negative urine culture) (90% versus 33.3%; NNT 2 [range 2 to 2]; moderate quality evidence), and less likely to experience relapse after the end of treatment (15.8% versus 41.6%; NNT 3 [range 3 to 5]; moderate quality evidence), compared with placebo. There was no significant difference between groups in the incidence of pyelonephritis (0.21% versus 0.75%; low quality evidence), although due to the very low incidence of

pyelonephritis, it is likely the studies lacked statistical power to detect a clinically important difference.

- One systematic review ([Smaill et al. 2015](#)) and 1 RCT ([Kazemier et al. 2015](#)) assessed antibiotics compared with placebo or no treatment for managing asymptomatic bacteriuria in pregnant women. Smaill et al. (2015) found that pregnant women who received antibiotics for asymptomatic bacteriuria had a reduced incidence of persistent bacteriuria (20.3% versus 66.3%; NNT 2 [range 2 to 3]; low quality evidence); were less likely to develop pyelonephritis (5.6% versus 20.8%; NNT 7 [range 6 to 9]; moderate quality evidence) or deliver a preterm baby (<37 weeks) (5.8% versus 22.1%; NNT 7 [range 4 to 13]; moderate quality evidence), compared with those who received no treatment.
- Smaill et al. (2015) found no significant difference between antibiotics and placebo in serious adverse neonatal outcomes (very low quality evidence).
- Kazemier et al. (2015) found no significant difference between nitrofurantoin and placebo in reducing the incidence of symptomatic UTI, pyelonephritis or preterm birth (<34 weeks; very low quality evidence). Significantly more women had non-spontaneous onset of labour with nitrofurantoin compared with placebo, but there is considerable uncertainty with these results (very low quality evidence).
- [Zalmanovici-Trestioreanu et al. \(2015\)](#) found that there was a greater incidence of bacteriological cure in older people who received antibiotics for treating asymptomatic bacteriuria compared with those who received placebo or no treatment (61% versus 17%; NNT 3 [range 2 to 3]; high quality evidence). However, there was no significant benefit in reducing symptomatic UTI (very low quality evidence) and people who received antibiotics were more likely to report adverse events (high quality evidence).

Safety of antibiotics

- Antibiotic-associated diarrhoea occurs in 2 to 25% of people taking antibiotics, depending on the antibiotic used ([NICE Clinical Knowledge Summary \[CKS\]: diarrhoea – antibiotic associated](#)).

- Allergic reactions to penicillins occur in 1 to 10% of people and anaphylactic reactions occur in less than 0.05%. People with a history of atopic allergy (for example, asthma, eczema and hay fever) are at a higher risk of anaphylactic reactions to penicillins. People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics ([BNF, April 2018](#)). See the NICE guideline on [drug allergy: diagnosis and management](#) for more information.
- Nitrofurantoin should be used with caution in those with renal impairment. It should be avoided at term in pregnancy because it may produce neonatal haemolysis. Adults (especially the elderly) and children on long-term therapy should be monitored for liver function and pulmonary symptoms ([BNF, April 2018](#)).
- Trimethoprim has a teratogenic risk in the first trimester of pregnancy (folate antagonist; [BNF, April 2018](#)). The manufacturers advise that it is contraindicated in pregnancy ([trimethoprim summary of product characteristics](#)).
- One RCT ([Falagas et al. 2009](#)) in non-pregnant women found a significant increase in the total number of adverse events with antibiotics compared with placebo (19.2% versus 12.9%; NNH 15 [range 9 to 16]; moderate quality evidence). However there was no significant difference between antibiotics and placebo in the number of withdrawals due to adverse events with antibiotics compared with placebo.
- [Zalmanovici-Trestioreanu et al. \(2015\)](#) assessed the safety of antibiotics in the management of asymptomatic bacteriuria in older people. There was a significant increase in the incidence of adverse events in those treated with antibiotics compared with placebo or no treatment (4.2% versus 1.0%; NNH 31 [range 19 to 82]; high quality evidence).
- See the [summaries of product characteristics](#) for information on contraindications, cautions and adverse effects of individual medicines.

Back-up antibiotics

- One RCT ([Little et al. 2010](#)) assessed various antibiotic prescribing strategies in non-pregnant women with acute uncomplicated lower UTI, where immediate antibiotic treatment was not necessary. Although

bacterial confirmation was not essential for inclusion into the study, the proportion of women who had urine culture ranged from 23% to 89% ($p < 0.001$), across 5 treatment groups. Immediate empirical antibiotics were compared with back-up (delayed by 48 hours) empirical antibiotics, and immediate antibiotics based on either a symptom severity score >2 , a positive dipstick test, or a midstream urine culture result. Only two thirds of women randomised to receive antibiotics based on a midstream urine result had a positive urine culture.

- There was no difference between the different prescribing strategies (immediate empirical antibiotics; back-up empirical antibiotics; immediate antibiotics based on symptom severity score >2 , positive dipstick test or midstream urine culture result) in the severity or duration of symptoms during follow-up, or in the time to reconsultation (low to very low quality evidence). However, significantly more women who were prescribed immediate antibiotics used them, compared with all other prescribing strategy groups, except immediate antibiotics based on symptom severity scoring (very low quality evidence). There were also significantly fewer women waiting 48 hours before taking their antibiotics in the immediate antibiotics group, compared with all other prescribing strategy groups, except immediate antibiotics based on symptom severity score (low to very low quality evidence).
- Little et al. (2010) found that despite randomisation, all groups delayed starting their antibiotic course by at least 24 hours (very low quality evidence). However, a delay of more than 48 hours was associated with a longer duration of moderately bad symptoms (very low quality evidence).
- No systematic reviews or RCTs of back-up antibiotic prescribing strategies were identified in men, pregnant women, older people or children.

Committee discussion on antibiotics

- The committee recognised the equality considerations for managing a lower UTI in transgender people, due to anatomical differences between women and men.

Non-pregnant women with lower UTI

- Based on evidence and experience, the committee agreed that either a back-up antibiotic prescription or an immediate antibiotic prescription could be prescribed for non-pregnant women with a lower UTI. The committee discussed that sending a urine sample for culture and susceptibility testing is not usual practice in most young, non-pregnant women with a first lower UTI, and lower UTI is generally confirmed by symptoms and signs of infection together with dipstick testing of urine. If urine culture has been taken, delaying the antibiotic until microbiological results are available could also be considered, depending on the severity of symptoms. Decisions around prescribing strategies should be individualised, taking account of the severity of symptoms, the risk of developing complications or having treatment failure, and preference for back-up or immediate antibiotics, or awaiting the results of urine culture. A back-up antibiotic prescription could be used if symptoms do not start to improve within 48 hours (by which point most UTIs should be starting to improve) or if they worsen rapidly or significantly at any time.
- Based on evidence, the committee agreed that antibiotics were effective in curing lower UTI symptoms and reducing relapse in non-pregnant women. There was no significant difference between antibiotics and placebo for pyelonephritis (although due to the very low incidence of pyelonephritis, it is likely the studies lacked statistical power to detect a clinically important difference), and antibiotics increased adverse events.
- Based on evidence in a population of women under 75 years, without dementia, the committee agreed that back-up empirical antibiotics were as effective as immediate empirical antibiotics for the severity or duration of UTI symptoms and the time to reconsultation. Back-up antibiotics (particularly a forward dated prescription) also reduced antibiotic use.

- Based on experience, the committee agreed that if a urine culture has been taken, and results suggest the bacteria are not susceptible to the antibiotic given, the woman should be contacted and the antibiotic changed if symptoms are not already improving.

Pregnant women and men with a lower UTI

- The committee discussed that no evidence was identified on antibiotic treatment for pregnant women with a symptomatic lower UTI. However, evidence in pregnant women with asymptomatic bacteriuria showed that antibiotics were effective in reducing persistent bacteriuria, pyelonephritis and the delivery of a preterm baby.
- Based on limited evidence and experience, the committee agreed that pregnant women with a lower UTI should be offered an immediate antibiotic, and urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee discussed that no evidence was identified on antibiotic treatment for men with a lower UTI, apart from in 1 systematic review where about 10% of the study population were men.
- Based on experience, the committee agreed that men with a lower UTI should be offered an immediate antibiotic, and urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- Based on experience, the committee agreed that when results of urine cultures are available, if the results suggest the bacteria are not susceptible to the antibiotic given, pregnant woman should be contacted and the antibiotic changed regardless of whether symptoms are improving or not. Men should be contacted if the bacteria are not susceptible to the antibiotic given and, if symptoms are not already improving, the antibiotic should be changed.

Children and young people with a lower UTI

- The committee was aware that the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#) makes

recommendations on diagnosing lower UTIs (including the use of dipsticks and urine culture) and offering immediate antibiotic treatment where appropriate.

- Based on experience, the committee agreed that if a urine culture has been taken, and results suggest the bacteria are not susceptible to the antibiotic given, the child or young person should be contacted and, if symptoms are not already improving, the antibiotic changed.

Managing asymptomatic bacteriuria

- Based on evidence and experience, the committee agreed that asymptomatic bacteriuria is not routinely screened for, or treated with antibiotics, in non-pregnant women, men, young people or children because it is not a risk factor for harm in these groups. It is routinely screened for, and treated with antibiotics, in pregnant women because it is a risk factor for harm.
- Based on evidence, the committee agreed that antibiotics reduce persistent bacteriuria, pyelonephritis and the delivery of a pre-term baby in pregnant women with asymptomatic bacteriuria.

Choice of antibiotic

- Three systematic reviews ([Falagas et al. 2010](#), [Rafalsky et al. 2006](#) and [Zalmanovici-Trestioreanu et al. 2010](#)) assessed the appropriate choice of antibiotics when treating UTIs in non-pregnant women.
- In Zalmanovici-Trestioreanu et al. (2010) there were no major differences in treatment outcomes amongst various antibiotics and antibiotic classes: nitrofurantoin, trimethoprim, co-trimoxazole, beta-lactams, and quinolones (very low to high quality evidence).
- Falagas et al. (2010) showed that fosfomycin did not offer any additional benefit over other antibiotics, despite it having a single-dose regimen (very low to moderate quality evidence). Fosfomycin did not reduce the rate of adverse events or withdrawal from treatment compared with other antibiotics (very low to low quality evidence).

- Rafalsky et al. (2006) reviewed the efficacy and safety of quinolones for the treatment of acute uncomplicated cystitis. No quinolone showed additional benefit over another (very low to high quality evidence).
- One systematic review ([Guinto et al. 2010](#)) assessed the effectiveness of different antibiotics for the treatment of asymptomatic bacteriuria in pregnant women. There was no significant difference between fosfomycin and cefuroxime in reducing the incidence of persistent infection, or in the number of women who required a change of antibiotic (very low quality evidence). Similarly, there was no significant difference between pivmecillinam and ampicillin in the number of women with persistent infection after treatment or in the incidence of recurrent infection (very low quality evidence).
- One systematic review ([Fitzgerald et al. 2012](#)) assessed choice of antibiotic in children with uncomplicated lower UTI. Overall, there were no significant differences between antibiotics of any class or course length (very low quality evidence).
- Zalmonovici-Trestioreanu et al. (2010) compared the safety of different antibiotic classes in non-pregnant women with uncomplicated lower UTI. There was no significant difference in the number of adverse events reported, or in the number of women who discontinued treatment due to an adverse event, for quinolones compared with co-trimoxazole; beta-lactams compared with co-trimoxazole; nitrofurantoin compared with beta-lactams; quinolones compared with beta-lactams; or nitrofurantoin compared with co-trimoxazole (very low to high quality evidence).
- Rafalsky et al. (2006) compared the safety of different quinolone antibiotics in non-pregnant women with uncomplicated lower UTI and found no significant difference in the number of adverse events reported, or withdrawals from treatment due to adverse events, for ciprofloxacin compared with ofloxacin; levofloxacin compared with ofloxacin; or standard-release ciprofloxacin compared with extended-release ciprofloxacin (very low to moderate quality evidence).
- Falagas et al. (2010) compared the safety of fosfomycin to other antibiotics in the treatment of UTI in non-pregnant women. There was no significant

difference in the number of adverse events reported or in the number of women withdrawing from treatment due to an adverse event in the fosfomycin group compared with those who received other antibiotics (very low to low quality evidence).

- See the [summaries of product characteristics](#) for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on choice of antibiotic

- Based on evidence of no major differences in clinical effectiveness between classes of antibiotics, the committee agreed that the choice of antibiotic should largely be driven by minimising the risk of resistance. Resistant bacteria are a particular concern in UTIs and, where possible, any previous urine culture and susceptibility results, and antibiotic prescribing, should be checked and antibiotics chosen accordingly.
- The committee discussed that, if an antibiotic is needed to treat an infection that is not life threatening, a narrow-spectrum antibiotic should generally be first choice. Indiscriminate use of broad-spectrum antibiotics creates a selective advantage for bacteria resistant even to these 'last-line' broad-spectrum agents, and also kills normal commensal flora leaving people susceptible to antibiotic-resistant harmful bacteria such as *Clostridium difficile*. For infections that are not life threatening, broad-spectrum antibiotics need to be reserved for second-choice treatment when narrow-spectrum antibiotics are ineffective.

Non-pregnant women with a lower UTI

- Based on evidence, their experience and resistance data, the committee agreed to recommend **nitrofurantoin** or **trimethoprim** at usual doses as first-choice antibiotics.
 - Trimethoprim should only be prescribed if a lower risk of resistance is likely, for example if trimethoprim has not been used in the past 3 months, if previous urine culture results suggest trimethoprim susceptibility (but this was not used as treatment) and in younger women in areas where local epidemiology data suggest resistance is low. There is a higher risk of trimethoprim resistance with recent use (the committee was aware of evidence that trimethoprim is significantly associated with resistant *Escherichia coli* infections treated in the previous 2-3 months), and in older people in residential facilities.
 - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute.

- Based on evidence, their experience and resistance data, the committee agreed to recommend **nitrofurantoin** (if not used as first-choice), **pivmecillinam** or **fosfomycin** at usual doses as second-choice antibiotics for use if lower UTI symptoms do not improve on a first-choice antibiotic taken for at least 48 hours.
- If there are symptoms of upper UTI (acute pyelonephritis) or sepsis, these antibiotic choices are not appropriate and antibiotics recommended in the NICE antimicrobial prescribing guideline on acute pyelonephritis should be prescribed.

Pregnant women with a lower UTI

- Based on evidence, their experience and resistance data, the committee agreed to recommend usual dose **nitrofurantoin** as the first-choice antibiotic:
 - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute.
 - Nitrofurantoin is not recommended at term in pregnancy because it may produce neonatal haemolysis.
 - Trimethoprim was not recommended because it is contraindicated in pregnancy. Trimethoprim is a folate antagonist and there is a teratogenic risk in the first trimester.
- Based on evidence, their experience and resistance data, the committee agreed to recommend **cefalexin**, **amoxicillin** or other antibiotics recommended by local microbiologists (based on culture and susceptibility results) at usual doses as second-choice antibiotics for use if lower UTI symptoms do not improve on a first-choice antibiotic taken for at least 48 hours.
 - Amoxicillin is recommended only if culture results are available and bacteria are susceptible because resistance rates are high.
 - If there are symptoms of upper UTI (acute pyelonephritis) or sepsis, these antibiotic choices are not appropriate and antibiotics recommended in the NICE antimicrobial prescribing guideline on acute pyelonephritis should be prescribed.

- Based on evidence, their experience and resistance data, the committee agreed to recommend a course of cefalexin, amoxicillin or nitrofurantoin (with the cautions outlined above) for the treatment of asymptomatic bacteriuria in pregnant women. Choice should be based on recent culture and susceptibility results.

Men with a lower UTI

- Based on their experience and resistance data, the committee agreed to recommend **trimethoprim** or **nitrofurantoin** at usual doses as first-choice antibiotics.
 - Trimethoprim generally has a lower risk of resistance in men, and can reach therapeutic prostate levels. However, if acute prostatitis is suspected, quinolones are the first-choice antibiotic (see the NICE antimicrobial prescribing guideline on acute prostatitis).
 - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute.
 - Nitrofurantoin is not recommended for men with suspected prostate involvement because it is unlikely to reach therapeutic levels in the prostate.
- Based on their experience, the committee agreed that alternative diagnoses (such as acute pyelonephritis or acute prostatitis) should be considered in men whose symptoms have not responded to a first-choice antibiotic, and second-choice antibiotics should be based on recent culture and susceptibility results.

Children and young people with a lower UTI

- The committee was aware that the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#) makes recommendations on antibiotic treatment for children and young people under 16 with a lower UTI, which it supported and provided more detail on.

- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed to recommend **trimethoprim** or **nitrofurantoin** at usual doses as first-choice antibiotics.
 - Trimethoprim should only be prescribed if a lower risk of resistance is likely, for example if trimethoprim has not been used in the past 3 months, if previous urine culture results suggest trimethoprim susceptibility (but this was not used as treatment) and in areas where local epidemiology data suggest resistance is low.
 - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute.
 - The committee was aware that nitrofurantoin suspension is currently substantially more expensive than trimethoprim suspension and, if both antibiotics are appropriate, the one with the lowest acquisition cost should be chosen.
- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed to recommend **nitrofurantoin** (if not used as first-choice), **cefalexin** or **amoxicillin** at usual doses as second-choice antibiotics for use if lower UTI symptoms get worse on a first-choice antibiotic taken for at least 48 hours.
 - Amoxicillin is recommended only if culture results are available and bacteria are susceptible, because resistance rates are high.
 - If there are symptoms of upper UTI (acute pyelonephritis) or sepsis, these antibiotic choices are not appropriate and antibiotics recommended in the NICE antimicrobial prescribing guideline on acute pyelonephritis should be prescribed.

Antibiotic course length

- One systematic review ([Milo et al. 2005](#)) assessed the effectiveness of 3-day courses compared with 5 to 10-day courses of antibiotics in the treatment of lower UTI in mainly non-pregnant women (some data [less than 10%] from men were included). Three-day courses of any antibiotic were not significantly different to longer courses (5 to 10 days) of any

antibiotic in preventing short-term or long-term symptomatic failure, short-term bacteriological failure, or the development of pyelonephritis (very low to high quality evidence). Subgroup analysis showed a significant increase in the number of women reporting short-term bacteriological failure with a 3-day course of a quinolone compared with a 5 to 10-day course of a quinolone (7.6% versus 5.1%; low quality evidence). However, there was no significant difference in long-term bacteriological failure (moderate quality evidence).

- Milo et al. (2005) found a significant reduction in the number of women reporting adverse events (16.3% versus 20.6%; NNH 23 [range 16 to 39]; very low quality evidence), withdrawing due to adverse events (1.5% versus 3.2%; very low quality evidence), or reporting gastrointestinal adverse effects (6.7% versus 8.5%; very low quality evidence) with a 3-day course compared with a 5- to 10-day course of antibiotics.
- Three systematic reviews ([Guinto et al. 2010](#), [Smaill et al. 2015](#) and [Widmer et al. 2015](#)) assessed the effectiveness of different antibiotic course lengths for treating asymptomatic bacteriuria in pregnant women. Smaill et al. (2015) conducted a subgroup analysis which found that women who received a short course of antibiotics (3 to 7 days) or continuous treatment were less likely to deliver preterm babies (before 37 weeks) compared with no treatment (low to moderate quality evidence). Continuous courses of antibiotics reduced the number of babies born with a birthweight below 2500 g compared with no treatment (low quality evidence). Single-dose, an intermediate course of 3 to 6 weeks and continuous antibiotics also significantly reduced the incidence of pyelonephritis compared with no treatment (low to moderate quality data). There was no significant difference between a short course of antibiotics and no treatment in the incidence of pyelonephritis (low quality evidence).
- Guinto et al. (2010) assessed the effectiveness of single-dose antibiotics compared with short courses of 7 days. Women who received a 1-day course of nitrofurantoin were more likely to have a persistent infection compared with women who received a 7-day course of nitrofurantoin (high

quality evidence). There was no significant difference in nausea or preterm delivery between treatment groups (moderate quality evidence).

- Widmer et al. (2015) found that women who received a single dose of antibiotics were more likely to deliver a baby with a low birthweight compared with those who received a short course (4 to 7 days) of antibiotics (moderate quality evidence). However, they found no significant difference between a single dose and a short course (4 to 7 days) for the number of women who reported no cure at the end of follow-up, experienced recurrent asymptomatic bacteriuria, developed pyelonephritis, or had a preterm delivery (very low to moderate quality evidence).
- One systematic review in older women with lower UTI ([Lutters et al. 2008](#)) found that single-dose antibiotics were associated with higher rates of persistent UTI compared with short courses (3 to 6 days) or long courses (7 to 14 days) of antibiotics in the short-term, but this was no longer significant in the long-term (very low to low quality evidence). Long courses did not offer any clinical benefit over short courses, and there was no significant difference between 3- or 5-day courses in reducing the incidence of persistent UTIs or clinical failure (very low to low quality evidence). Antibiotic course length, such as single-dose, short-course, or long-course, had no effect on adverse events, or on the number of withdrawals due to adverse events (very low to moderate quality evidence).
- Two systematic reviews ([Michael et al. 2003](#) and [Fitzgerald et al. 2012](#)) assessed the clinical effectiveness of varying antibiotic course lengths in children with uncomplicated lower UTI. Fitzgerald et al. (2012) found no significant difference between short-course (3 to 7 days) and long-course (10 to 14 days) antibiotics in the number of children with persistent bacteriuria; and course length did not affect the rate of reinfection or recurrence (very low quality evidence). Michael et al. (2003) found no significant difference between antibiotics given as either a short course (2 to 4 days) or a longer course (7 to 14 days) on the number of children with UTIs at the end of treatment, or the rate of recurrence of UTI (very low quality evidence).

Committee discussions on antibiotic course length

- The committee agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects.

Non-pregnant women with lower UTI

- Based on evidence, the committee agreed that a 3-day course of antibiotics was as effective as a 5- to 10-day course of antibiotics in non-pregnant women with lower UTI, and resulted in fewer adverse events.
- Based on evidence, the committee agreed that a 7- to 10-day course of antibiotics did not offer any clinical advantage over a 3- to 6-day course in older women with lower UTI.
- Based on evidence, their experience and resistance data, the committee agreed that a 3-day course of all the recommended antibiotics (apart from fosfomycin where a single dose is given) was sufficient to treat lower UTI in non-pregnant women of any age, with no longer duration of treatment required for older women.

Pregnant women with lower UTI

- Based on evidence and their experience, the committee agreed that a 7-day course of all the recommended antibiotics was required to treat bacteriuria in pregnant women with either symptomatic lower UTI or asymptomatic bacteriuria.
- A 7-day course is required to ensure complete cure because the risk of harm from a UTI is higher in pregnant women than in non-pregnant women.

Men with lower UTI

- Based on their experience, the committee agreed that a 7-day course of all the recommended antibiotics was required to treat lower UTI in men.
- A 7-day course is required to ensure complete cure because men are more at risk of complications from UTIs than women due to anatomical differences and possible outflow obstruction.

Children and young people with UTI

- The committee was aware that the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#) makes recommendations on antibiotic treatment for children and young people under 16 with a lower UTI, which it supported and provided more detail on.
- Based on evidence, the committee agreed that a 3- to 7-day course of antibiotics was as effective as a 7- to 14-day course of antibiotics in children and young people with lower UTI.
- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed that a 3-day course of all the recommended antibiotics was sufficient to treat lower UTI in children and young people.

See the full evidence review for more information.

Other considerations

Medicines adherence

- Medicines adherence may be a problem for some people with medicines that require frequent dosing or longer treatment duration (for example, some antibiotics). See the NICE guideline on [medicines adherence](#).

Resource implications

- There is a potential resource saving if a back-up antibiotic prescription strategy is used in non-pregnant women with lower UTI.
- Recommended antibiotics (nitrofurantoin, trimethoprim, amoxicillin, cefalexin and fosfomycin) are available as generic formulations, but there is currently no generic formulation of pivmecillinam, although the cost is comparable to other generic antibiotics, see [Drug Tariff](#) for costs.
- Nitrofurantoin 25mg/5ml oral suspension is more expensive than other oral suspensions, such as trimethoprim 50mg/5ml. The cost of a 300 ml bottle of nitrofurantoin is £446.95 compared with £2.30 for a 100 ml bottle of trimethoprim ([Drug Tariff](#), April 2018).