





Urinary tract infection (lower): antimicrobial prescribing

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the <u>Yellow Card Scheme</u>.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

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This guideline is the basis of QS90.

This guideline should be read in conjunction with NG111 and NG112.

Overview

This guideline sets out an antimicrobial prescribing strategy for lower urinary tract infection (also called cystitis) in children, young people and adults who do not have a catheter. It aims to optimise antibiotic use and reduce antibiotic resistance.

See a <u>4-page visual summary of the recommendations</u>, including a table to support prescribing decisions.

There is also a <u>NICE guideline on antimicrobial stewardship</u>: systems and processes for <u>effective antimicrobial medicine use</u>.

Who is it for?

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

Recommendations

1.1 Managing lower urinary tract infection

- 1.1.1 Be aware that lower urinary tract infection (UTI) 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 <u>recommendations</u> on <u>self-care</u>) 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 (to use if symptoms do not start to improve within 48 hours or worsen at any time) or an immediate antibiotic prescription (see the <u>recommendations on choice of antibiotic</u>) 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 immunosuppression
 - the evidence for back-up antibiotic prescriptions, which was only in nonpregnant women with lower UTI where immediate antibiotic treatment was not considered necessary
 - 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 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

- 1.1.5 Offer an immediate antibiotic prescription (see the <u>recommendations on choice of antibiotic</u>) 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.
- 1.1.6 Obtain a midstream urine sample from pregnant women and men before antibiotics are taken, and send for culture and susceptibility testing.
- 1.1.7 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.
- 1.1.8 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

1.1.9 Obtain a urine sample from children and young people with lower UTI before

- antibiotics are taken, and dipstick test or send for culture and susceptibility testing in line with the NICE guideline on urinary tract infection in under 16s.
- 1.1.10 Assess and manage children under 5 with lower UTI who present with fever as outlined in the NICE guideline on fever in under 5s.
- Offer an immediate antibiotic prescription (see the <u>recommendations on choice of antibiotic</u>) 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.
- 1.1.12 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

- 1.1.13 When a back-up antibiotic prescription is given, as well as the <u>general advice on</u> <u>self-care</u>, 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 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 or

- symptoms do not start to improve within 48 hours of taking the antibiotic
 or
- the person becomes systemically very unwell.
- 1.1.14 When an immediate antibiotic prescription is given, as well as the <u>general advice</u> on <u>self-care</u>, 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.

Reassessment

- 1.1.15 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 1.1.4, 1.1.7, 1.1.8 and 1.1.12).

Referral

1.1.16 Refer people aged 16 years and over with lower UTI to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, sepsis).

1.1.17 Refer children or young people with lower UTI to hospital in line with the <u>NICE</u> guideline on urinary tract infection in under 16s.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on antibiotics.

Full details of the evidence and the committee's discussion are in the evidence review.

1.2 Managing asymptomatic bacteriuria

- 1.2.1 Be aware that asymptomatic bacteriuria:
 - is significant levels of bacteria (greater than 10⁵ 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 treated with antibiotics in pregnant women because it is a risk factor for pyelonephritis and premature delivery (see the <u>recommendations on choice</u> 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.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on antibiotics.

Full details of the evidence and the committee's discussion are in the evidence review.

1.3 Self-care

- 1.3.1 Advise people with lower UTI about using paracetamol for pain, or if preferred and suitable ibuprofen.
- 1.3.2 Advise people with lower UTI about drinking enough fluids to avoid dehydration.
- 1.3.3 Be aware that no evidence was found on cranberry products or urine alkalinising agents to treat lower UTI.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on self-care.

Full details of the evidence and the committee's discussion are in the evidence review.

1.4 Choice of antibiotic

- 1.4.1 When prescribing antibiotic treatment for lower UTI, take account of <u>local</u> antimicrobial resistance data and follow:
 - table 1 for non-pregnant women aged 16 years and over
 - table 2 for pregnant women aged 12 years and over
 - table 3 for men aged 16 years and over
 - table 4 for children and young people under 16 years.

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

Treatment	Antibiotic, dosage and course length
	Nitrofurantoin (if estimated glomerular filtration rate [eGFR] is 45 ml/minute or more):
First choices If there are symptoms of pyelonephritis (such as fever) or a complicated urinary tract infection (UTI), see the NICE guideline on acute pyelonephritis for antibiotic choices.	100 mg modified-release twice a day (or, if unavailable, 50 mg four times a day) for 3 days
	Trimethoprim (if there is a low risk of resistance):
	200 mg twice a day for 3 days
	Nitrofurantoin (if eGFR is 45 ml/minute or more, and it was not used as first-choice):
Second choices (if no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice is not suitable)	45 ml/minute or more, and it
symptoms on first choice taken for at least 48 hours, or when first choice is not suitable) If there are symptoms of pyelonephritis (such as fever)	45 ml/minute or more, and it was not used as first-choice): 100 mg modified-release twice a day (or, if unavailable, 50 mg four times a day) for
symptoms on first choice taken for at least 48 hours, or when first choice is not suitable)	45 ml/minute or more, and it was not used as first-choice): 100 mg modified-release twice a day (or, if unavailable, 50 mg four times a day) for 3 days
symptoms on first choice taken for at least 48 hours, or when first choice is not suitable) If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the NICE guideline on acute	45 ml/minute or more, and it was not used as first-choice): 100 mg modified-release twice a day (or, if unavailable, 50 mg four times a day) for 3 days Pivmecillinam (a penicillin): 400 mg initial dose, then 200 mg three times a day for

See the <u>BNF</u> for appropriate use and dosing in specific populations, for example, in hepatic or renal impairment, and breastfeeding.

Check any previous urine culture and susceptibility results, and antibiotic prescribing, and choose antibiotics accordingly.

See the MHRA advice on monitoring for pulmonary and hepatic adverse reactions to nitrofurantoin. Nitrofurantoin may be used with caution if eGFR is 30 ml/minute to 44 ml/

minute to treat uncomplicated lower UTIs caused by suspected or proven multidrugresistant bacteria and only if potential benefit outweighs risk (BNF, August 2018).

A lower risk of resistance may be more likely if trimethoprim has not been used in the past 3 months, previous urine culture suggests susceptibility (but this was not used), and in younger people in areas where local epidemiology data suggests resistance is low. A higher risk of resistance may be more likely with recent use and in older people in residential facilities.

Table 2 Antibiotics for pregnant women aged 12 years and over

Treatment	Antibiotic, dosage and course length
First choice If there are symptoms of pyelonephritis (such as fever) or a complicated urinary tract infection (UTI), see the NICE guideline on acute pyelonephritis for antibiotic choices.	Nitrofurantoin (if estimated glomerular filtration rate [eGFR] is 45 ml/minute or more): 100 mg modified-release twice a day (or, if unavailable, 50 mg
	four times a day) for 7 days Avoid at term because it may produce neonatal haemolysis (BNF, August 2018)
Second choices (if no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice is not suitable) If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the NICE guideline on acute pyelonephritis for antibiotic choices.	Amoxicillin (only if culture results are available and susceptible): 500 mg three times a day for 7 days Cefalexin: 500 mg twice a day for 7 days
Alternative second choices	Consult local microbiologist, and choose antibiotics based on culture and susceptibility results
Treatment of asymptomatic bacteriuria	Choose from nitrofurantoin, amoxicillin or cefalexin based on recent culture and susceptibility results

See the <u>BNF</u> for appropriate use and dosing in specific populations, for example, in hepatic or renal impairment.

Check any previous urine culture and susceptibility results, and antibiotic prescribing, and choose antibiotics accordingly.

See the MHRA advice on monitoring for pulmonary and hepatic adverse reactions to nitrofurantoin. Nitrofurantoin may be used with caution if eGFR is 30 ml/minute to 44 ml/minute to treat uncomplicated lower UTIs caused by suspected or proven multidrugresistant bacteria and only if potential benefit outweighs risk (BNF, August 2018).

Table 3 Antibiotics for men aged 16 years and over

Treatment Antibiotic, dosage and course length		
	Trimethoprim:	
First choices	200 mg twice a day for 7 days	
If there are symptoms of pyelonephritis (such as fever) or	Nitrofurantoin (if estimated glomerular filtration rate [eGFR] is 45 ml/minute or more):	
a complicated urinary tract infection (UTI), see the NICE	100 mg modified-release twice a day (or, if unavailable, 50 mg four times a day) for 7 days	
guideline on acute pyelonephritis for antibiotic choices.	Nitrofurantoin is not recommended for men with suspected prostate involvement because it is unlikely to reach therapeutic levels in the prostate.	
Second choices (if no improvement in lower UTI		
symptoms on first choice taken for at least 48 hours, or when first choice is not suitable)	Consider alternative diagnoses and follow recommendations in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing or	
If there are symptoms of pyelonephritis (such as fever) or a complicated UTI, see the NICE guideline on acute pyelonephritis	the NICE guideline on prostatitis (acute): antimicrobial prescribing, basing antibiotic choice on recent culture and susceptibility results.	
for antibiotic choices.		

See the <u>BNF</u> for appropriate use and dosing in specific populations, for example, in hepatic or renal impairment.

Check any previous urine culture and susceptibility results, and antibiotic prescribing, and choose antibiotics accordingly.

See the MHRA advice on monitoring for pulmonary and hepatic adverse reactions to <u>nitrofurantoin</u>. Nitrofurantoin may be used with caution if eGFR is 30 ml/minute to 44 ml/minute to treat uncomplicated lower UTIs caused by suspected or proven multidrugresistant bacteria and only if potential benefit outweighs risk (BNF, August 2018).

Table 4 Antibiotics for children and young people under 16 years

Treatment	Antibiotic, dosage and course length
	Refer to a paediatric specialist
	and treat with intravenous
Children under 3 months	antibiotics in line with the
	NICE guideline on fever in
	<u>under 5s</u>

Treatment Antibiotic, dosage and course length **Trimethoprim** (if there is a low risk of resistance): 3 months to 5 months, 4 mg/ kg (maximum 200 mg per dose) or 25 mg twice a day for 3 days 6 months to 5 years, 4 mg/kg (maximum 200 mg per dose) or 50 mg twice a day for 3 days First choices for children aged 3 months and over If there are symptoms of pyelonephritis (such as fever) 6 years to 11 years, 4 mg/kg (maximum 200 mg per dose) or a complicated UTI, see the NICE guideline on acute or 100 mg twice a day for pyelonephritis for antibiotic choices. 3 days If 2 or more antibiotics are appropriate, choose the 12 years to 15 years, 200 mg antibiotic with the lowest acquisition cost. Some twice a day for 3 days children may also be able to take a tablet or part-tablet, rather than a liquid formulation, if the dose is Nitrofurantoin (if estimated appropriate. glomerular filtration rate (eGFR) is 45 ml/minute or more): 3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 years to 15 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days

Treatment Antibiotic, dosage and course length Nitrofurantoin (if eGFR is 45 ml/minute or more and it was not used as first-choice): 3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 years to 15 years, 50 mg four times a day or 100 mg modified-release twice a day for 3 days Amoxicillin (only if culture Second choices for children aged 3 months and over results available and (if no improvement in lower UTI symptoms on first susceptible): choice taken for at least 48 hours, or when first choice 3 months to 11 months, is not suitable) 125 mg three times a day for If there are symptoms of pyelonephritis (such as fever) 3 days or a complicated UTI, see the NICE guideline on acute 1 year to 4 years, 250 mg pyelonephritis for antibiotic choices. three times a day for 3 days If 2 or more antibiotics are appropriate, choose the 5 years to 15 years, 500 mg antibiotic with the lowest acquisition cost. Some three times a day for 3 days children may also be able to take a tablet or part-tablet, rather than a liquid formulation, if the dose is Cefalexin: appropriate. 3 months to 11 months, 12.5 mg/kg or 125 mg twice a day for 3 days 1 year to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 3 days 5 years to 11 years, 12.5 mg/ kg twice a day or 250 mg three times a day for 3 days 12 years to 15 years, 500 mg twice a day for 3 days

See the <u>BNF for children</u> (BNFC) for appropriate use and dosing in specific populations, for example, in hepatic or renal impairment. See <u>table 2</u> if a young woman is pregnant.

The age bands apply to children of average size and, in practice, the prescriber will use the age bands 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.

Check any previous urine culture and susceptibility results, and antibiotic prescribing. and choose antibiotics accordingly. When a child or young person is having prophylactic antibiotics, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.

See the MHRA advice on monitoring for pulmonary and hepatic adverse reactions to nitrofurantoin. Nitrofurantoin may be used with caution if eGFR is 30 ml/minute to 44 ml/minute to treat uncomplicated lower UTIs caused by suspected or proven multidrugresistant bacteria and only if potential benefit outweighs risk (BNFC, August 2018).

A lower risk of resistance may be more likely if trimethoprim has not been used in the past 3 months, previous urine culture suggests susceptibility (but this was not used), and in younger people in areas where local epidemiology data suggests resistance is low. A higher risk of resistance may be more likely with recent use and in older people in residential facilities.

For a short explanation of why the committee made these recommendations, see the <u>evidence and committee discussion on choice of antibiotic</u> and <u>antibiotic course</u> length.

Full details of the evidence and the committee's discussion are in the evidence review.

Summary of the evidence

Self-care

Recommendations 1.3.1 to 1.3.3

Oral analgesia (ibuprofen)

- Two randomised controlled trials (RCTs) (<u>Bleidorn et al. 2010</u> and <u>Gagyor et al. 2015</u>) 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 urinary tract infection (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 (<u>Wing et al. 2008</u> and <u>Wing et al. 2015</u>) assessed the clinical effectiveness and safety of cranberry products for preventing 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 adherence 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 advise
 people with lower UTI about using paracetamol for self-management of pain as
 this medicine has a well-established efficacy and safety profile.
- The committee agreed, based on evidence and experience, that it was also reasonable to advise people with lower UTI about using ibuprofen for selfmanagement of pain if this was preferred and suitable, taking account of safety concerns with NSAIDs, for example, renal impairment.
- Based on committee experience that dehydration is often cited as a cause of UTIs, the committee agreed that people should be advised about drinking enough fluids to avoid dehydration.
- No evidence was found for using cranberry products or alkalinising agents to treat lower UTI or asymptomatic bacteriuria. There was only evidence assessing the efficacy and safety of cranberry products for preventing asymptomatic bacteriuria in healthy pregnant women.

Return to recommendations

Antibiotics

Recommendations 1.1.1 to 1.1.17

Recommendations 1.2.1 to 1.2.2

- In most cases, managing lower UTI will require antibiotic treatment. However, acute, uncomplicated lower UTI 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 may be an option.
- The most common causative pathogen in uncomplicated UTIs is Escherichia coli (in 70 to 95% of cases). Staphylococcus saprophyticus accounts for 5 to 10% of cases and occasionally other Enterobacteriaceae, such as Proteus mirabilis and Klebsiella species are isolated (<u>European Association of Urology guidelines on urological infections 2017</u>).

- The main complication of lower UTI 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 preterm 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 lower UTI, 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, such as in pregnant women (<u>European Association of Urology guidelines on</u> urological infections 2017).
 - In pregnancy, asymptomatic bacteriuria can lead to pyelonephritis and preterm labour (<u>NICE clinical knowledge summary on UTI (lower) - women</u> and pyelonephritis).

Efficacy of antibiotics

- One systematic review of RCTs (<u>Falagas et al. 2009</u>) 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 (0.14% 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 (<u>Smaill et al. 2015</u>) and 1 RCT (<u>Kazemier et al. 2015</u>) 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 nonspontaneous 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 (<u>NICE clinical knowledge summary on diarrhoea –</u> antibiotic associated).
- About 10% of the general population claim to have a penicillin allergy; this is often
 because of a skin rash that occurred while taking a course of penicillin as a child.
 Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See
 the NICE guideline on drug allergy for more information.
- People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (BNF, August 2018).
- Nitrofurantoin should be used with caution in those with renal impairment (MHRA Drug Safety Update, September 2014). It should be avoided at term in pregnancy because it may produce neonatal haemolysis. Adults (especially older adults) and children on long-term therapy should have monitoring for liver function and pulmonary symptoms

(BNF, August 2018).

- Trimethoprim has a teratogenic risk in the first trimester of pregnancy (folate antagonist; <u>BNF</u>, <u>August 2018</u>). The manufacturers advise that it is contraindicated in pregnancy (<u>trimethoprim summary of product characteristics</u>).
- A systematic review (<u>Falagas et al. 2009</u>) 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.
- 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 <u>summaries of product characteristics</u> for information on contraindications, cautions and adverse effects of individual medicines.

Back-up antibiotics

- One RCT (<u>Little et al. 2010</u>) assessed various antibiotic prescribing strategies in non-pregnant women with acute uncomplicated lower UTI, where immediate antibiotic treatment was not necessary. The women included in the study had a mean age of 39 to 45 years and had moderate symptoms (mean score of 1.7 to 1.8, on a scale of 0=no problem, 1=mild problem, 2=moderately bad problem, 3=severe problem) at baseline. 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. Lower UTI is generally confirmed by symptoms and signs of infection together with dipstick testing of urine for some people. 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.
- The committee discussed that the evidence for back-up prescribing was only in non-pregnant women aged 18 to 70 years (mean age of 39 to 45 years) with, on average, moderate symptoms of an acute uncomplicated lower UTI, where immediate antibiotic treatment was not necessary. In this population, 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.
- The committee agreed that 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 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, but increased adverse events. There was no significant difference between antibiotics and placebo for the development of pyelonephritis (a complication of lower UTI). However, due to the very low incidence of pyelonephritis, it is likely the studies

lacked statistical power to detect a clinically important difference.

• Based on experience, the committee agreed that if a urine culture has been taken, and results suggest the bacteria are resistant to the antibiotic given, the woman should be contacted and the antibiotic changed if symptoms are not already improving. The committee agreed that for non-pregnant women where 3-day courses of antibiotics are given, only changing antibiotics according to susceptibility results if symptoms are not already improving is appropriate. Often, susceptibility results may not be back before short courses are nearly completed, and because of differences between the in vitro and in vivo effectiveness of antibiotics, susceptibility results may not always be accurate. For some populations, where symptoms of the UTI are already improving, an additional course of antibiotics may be unnecessary treatment.

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.
- Based on experience, the committee agreed that when results of urine cultures are available, if the results suggest the bacteria are resistant to the antibiotic given, pregnant woman should be contacted and the antibiotic changed regardless of whether symptoms are improving or not. The committee agreed there was a greater risk from UTIs in pregnant women and antibiotics should be changed to ensure cure.
- The committee discussed that no evidence was identified on antibiotic treatment for men with a lower UTI, apart from 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 resistant to the antibiotic given, men should be contacted and, if symptoms are not already improving, the antibiotic should be changed. The committee agreed that for men, only changing antibiotics according to susceptibility results if symptoms are not already improving is appropriate. Often, susceptibility results may not be back for some days, and because of differences between the in vitro and in vivo effectiveness of antibiotics, susceptibility results may not always be accurate. For some populations, where symptoms of the UTI are already improving, an additional course of antibiotics may be unnecessary treatment.

Children and young people with a lower UTI

- The committee was aware that the <u>NICE guideline on urinary tract infection in under 16s</u> makes recommendations on diagnosing lower UTIs (including the use of dipsticks and urine culture).
- Based on experience, the committee agreed that if a urine culture has been taken, and results suggest the bacteria are resistant to the antibiotic given, the child or young person should be contacted and, if symptoms are not already improving, the antibiotic changed. The committee agreed that for children and young people where 3-day courses of antibiotics are given, only changing antibiotics according to susceptibility results if symptoms are not already improving is appropriate. Often, susceptibility results may not be back before short courses are nearly completed, and because of differences between the in vitro and in vivo effectiveness of antibiotics, susceptibility results may not always be accurate. For some populations, where symptoms of the UTI are already improving, an additional course of antibiotics may be unnecessary treatment.

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. [In May 2022, we removed the reference to routine screening in pregnancy from recommendation 1.2.1, in line with amended recommendations from the UK National Screening Committee.]

 Based on evidence, the committee agreed that antibiotics reduce persistent bacteriuria, pyelonephritis and the delivery of a preterm baby in pregnant women with asymptomatic bacteriuria.

Return to recommendations

Choice of antibiotic

Recommendation 1.4.1

- Three systematic reviews (<u>Falagas et al. 2010</u>, <u>Rafalsky et al. 2006</u> and <u>Zalmanovici-Trestioreanu et al. 2010</u>) 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 among 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 lower UTI. No quinolone showed additional benefit over another (very low to high quality evidence).
- One systematic review (<u>Guinto et al. 2010</u>) 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 (<u>Fitzgerald et al. 2012</u>) 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 nonpregnant 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 <u>summaries of product characteristics</u> 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.
- Nationally for England, resistance of E. coli (the main causative organism of lower UTIs) in laboratory-processed urine specimens to the following antibiotics is:
 - nitrofurantoin: 2.5% (varies by area from 2.0 to 3.6%)
 - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%)
 - pivmecillinam: 7.5% (varies by area from 4.1 to 15.7%)
 - cefalexin: 9.9% (varies by area from 8.1 to 11.4%).
 (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)
- The committee also discussed that prescribers should be aware of their local antimicrobial prescribing data, because resistance rates do vary by area.

Non-pregnant women with a lower UTI

 Based on evidence, experience and resistance data, the committee agreed to recommend nitrofurantoin or trimethoprim at usual doses as first-choice

antibiotics.

- Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute. It may be used with caution if eGFR is 30–44 ml/minute to treat uncomplicated lower UTI caused by suspected or proven multidrug resistant bacteria and only if potential benefit outweighs risk (BNF, August 2018).
- The committee agreed to recommend either the modified-release preparation of nitrofurantoin or the immediate-release preparation. However, because of its twice daily dosing and, in their experience, better tolerability, the committee was keen to point out that the modified-release preparation was preferred unless it was unavailable. The committee also discussed that, in their experience, immediate-release preparations containing nitrofurantoin in a macrocrystalline form may be better tolerated than those containing nitrofurantoin in a microcrystalline form.
- Trimethoprim should only be prescribed if a lower risk of resistance is likely because of high resistance levels nationally. Based on experience, the committee agreed that a lower risk of resistance may be more likely 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 people in areas where local epidemiology data suggests resistance is low. A higher risk of trimethoprim resistance may be more likely with recent use (the committee was aware of evidence that trimethoprim is significantly associated with resistant E. coli infections treated in the previous 2 to 3 months), and in older people in residential facilities.
- Based on evidence, their experience and resistance data, the committee agreed
 to recommend nitrofurantoin (if not used as first-choice), pivmecillinam (a
 penicillin) 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 or first-choice antibiotics are not suitable. The committee acknowledged
 that prescribers may be less familiar with pivmecillinam or fosfomycin, but these
 antibiotics are often used in other European countries.
- If there are symptoms of upper UTI (acute pyelonephritis) or the person has a complicated UTI (associated with a structural or functional abnormality, or

underlying disease, which increases the risk of a more serious outcome or treatment failure), antibiotics recommended in the <u>NICE guideline on pyelonephritis (acute): antimicrobial prescribing</u> should be prescribed.

Pregnant women with a lower UTI

- Based on evidence, experience and resistance data, the committee agreed to recommend usual dose **nitrofurantoin** as the first-choice antibiotic (with the cautions outlined above):
 - Nitrofurantoin is not recommended at term in pregnancy because it may produce neonatal haemolysis (<u>BNF</u>, <u>August 2018</u>).
 - 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 (<u>BNF</u>, <u>August 2018</u>). However, the committee acknowledged that trimethoprim is sometimes used in pregnancy when given with folic acid 5 mg daily in the first trimester (<u>NICE clinical knowledge</u> summary on UTI (lower) – women).
- Based on evidence, experience and resistance data, the committee agreed to recommend amoxicillin, cefalexin 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 or first-choice antibiotics are not suitable.
 - 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 the person has a complicated UTI (associated with a structural or functional abnormality, or underlying disease, which increases the risk of a more serious outcome or treatment failure), antibiotics recommended in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing should be prescribed.
- Based on evidence, experience and resistance data, the committee agreed to

recommend a course of nitrofurantoin, amoxicillin or cefalexin, (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 experience and resistance data, the committee agreed to recommend trimethoprim or nitrofurantoin at usual doses as first-choice antibiotics (with the cautions outlined above).
 - 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 <u>NICE guideline on prostatitis</u> (acute): antimicrobial prescribing).
 - Nitrofurantoin is not recommended for men with suspected prostate involvement because it is unlikely to reach therapeutic levels in the prostate.
- Based on 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

- Based on evidence, experience and resistance data, the committee agreed to recommend trimethoprim or nitrofurantoin at usual doses as first-choice antibiotics (with the cautions outlined above).
 - 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 evidence, experience and resistance data, the committee agreed to recommend nitrofurantoin (if not used as first-choice), amoxicillin or cefalexin 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 or first-choice antibiotics are not suitable.

- 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 the person has a complicated UTI (associated with a structural or functional abnormality, or underlying disease, which increases the risk of a more serious outcome or treatment failure), antibiotics recommended in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing should be prescribed.

Return to recommendation

Antibiotic course length

Recommendation 1.4.1

- 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). However, long-term bacteriological failure (at 4 to 10 weeks) was significantly higher with 3-day courses of any antibiotic compared with longer courses of any antibiotic (low 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 2,500 g compared with no treatment (low quality evidence). Singledose, 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 (<u>Lutters et al. 2008</u>) 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 significantly fewer adverse events. The committee
 agreed that a longer course may increase the likelihood of complete
 bacteriological eradication, which may be important for some women (for
 example, women who experience repeated lower UTIs). However, it was not
 possible to analyse data separately for people with repeated lower UTIs.
- 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, 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. If women
 have a complicated UTI (associated with a structural or functional abnormality, or
 underlying disease, which increases the risk of a more serious outcome or
 treatment failure), antibiotics recommended in the NICE guideline on
 pyelonephritis (acute): antimicrobial prescribing should be prescribed.

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

- 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 evidence, 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. If children and young people have a complicated
 UTI (associated with a structural or functional abnormality, or underlying disease,
 which increases the risk of a more serious outcome or treatment failure),
 antibiotics recommended in the NICE guideline on pyelonephritis (acute):
 antimicrobial prescribing should be prescribed.

Return to recommendation

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 urinary tract infection (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 <u>Drug Tariff</u> for costs.
- Nitrofurantoin 25 mg/5 ml oral suspension is more expensive than other oral suspensions, such as trimethoprim 50 mg/5 ml. The cost of a 300-ml bottle of nitrofurantoin is £446.95 compared with £4.87 for a 100-ml bottle of trimethoprim (<u>Drug Tariff</u>, September 2018).

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the <u>NICE</u> topic page on antimicrobial stewardship.

For full details of the evidence and the guideline committee's discussion, see the <u>evidence</u> <u>review</u>. You can also find information about <u>how the guideline was developed</u>, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put this guidance into practice.

Update information

Minor updates since publication

May 2025: We added links to the MHRA advice on monitoring for pulmonary and hepatic adverse reactions to nitrofurantoin.

May 2022: We removed the reference to routine screening in pregnancy from recommendation 1.2.1, in line with amended UK National Screening Committee recommendations.

July 2019: The antibiotic prescribing tables have been amended to recommend either the modified-release, or if unavailable the immediate-release, formulations of nitrofurantoin.

February 2019: Minor corrections to one of the evidence summaries.

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