NICE National Institute for Health and Care Excellence

NICE Pathways

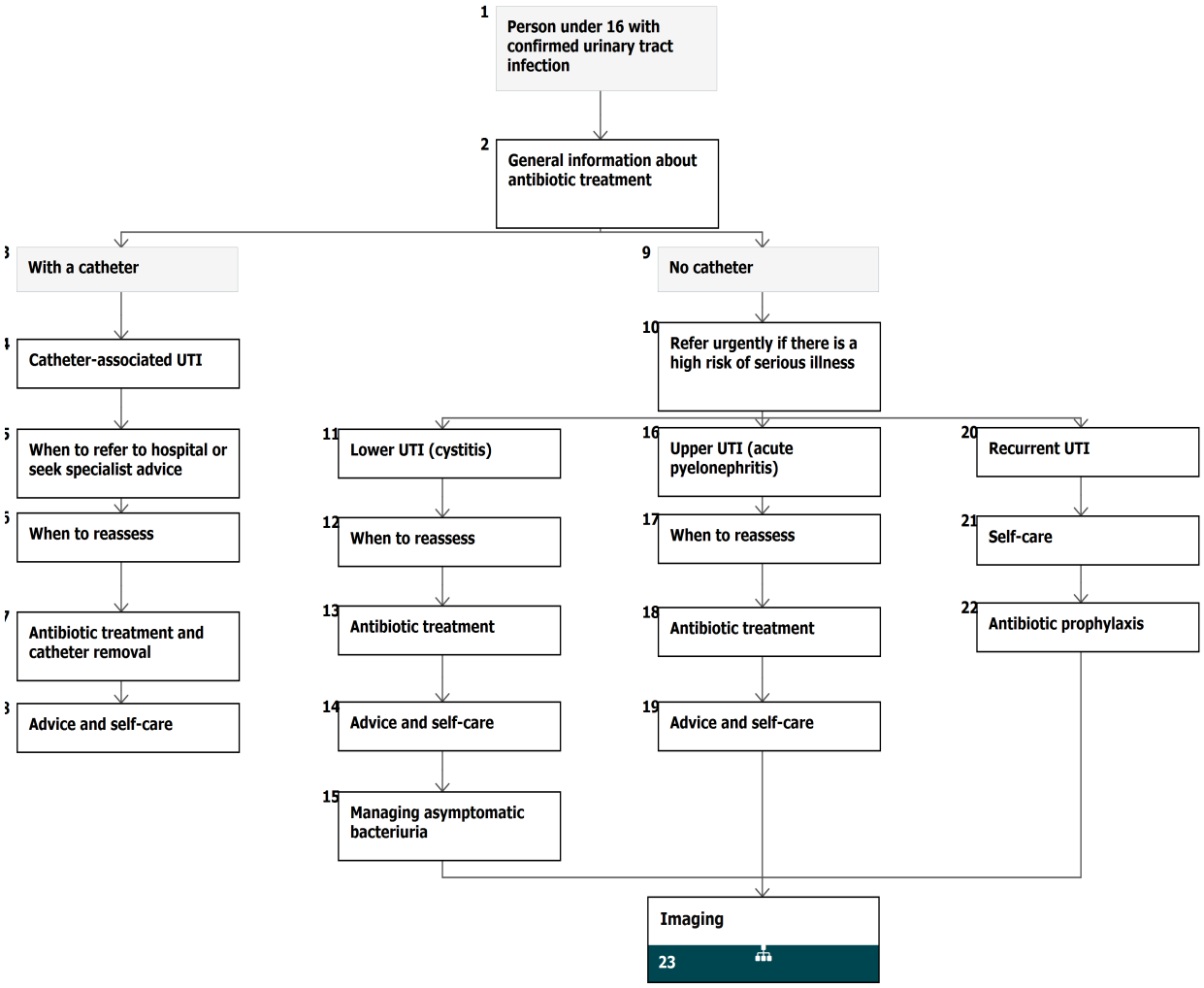
Management of urinary tract infection in under 16s

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/urinary-tract-infections
NICE Pathway last updated: 14 February 2019

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Person under 16 with confirmed urinary tract infection

No additional information

2 General information about antibiotic treatment

Note that the antibiotic requirements for infants and children with conditions that are outside the scope of this guidance (for example, infants and children already known to have significant pre-existing uropathies) have not been addressed and may be different from those given here.

Laboratories should monitor resistance patterns of urinary pathogens and make this information routinely available to prescribers.

See what NICE says on antimicrobial stewardship and medicines optimisation.

3 With a catheter

No additional information

4 Catheter-associated UTI

Be aware that:

- a catheter-associated UTI [See page 19] is a symptomatic infection of the bladder or kidneys in a person with a urinary catheter
- the longer a catheter is in place, the more likely bacteria will be found in the urine; after 1 month nearly all people have bacteriuria
- antibiotic treatment is not routinely needed for asymptomatic bacteriuria in people with a catheter (see recommendations on lower UTI for managing asymptomatic bacteriuria in pregnant women).

NICE has produced a visual summary on antimicrobial prescribing for catheter-associated urinary tract infections.

See why we made the recommendations on antibiotics for managing catheter-associated UTI [See page 35].

Preventing catheter-associated urinary tract infections

Do not routinely offer antibiotic prophylaxis to prevent catheter-associated UTI in people with a short-term or a long-term (indwelling or intermittent) catheter.

Give advice about seeking medical help if symptoms of an acute UTI develop.

See preventing infection related to long-term urinary catheters in NICE's recommendations on prevention and control of healthcare-associated infections.

See why we made the recommendations on antibiotic prophylaxis for catheter-associated UTI [See page 33].

5 When to refer to hospital or seek specialist advice

Refer people with catheter-associated UTI [See page 19] to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, sepsis).

Consider referring or seeking specialist advice for people with catheter-associated UTI if they:

- are significantly dehydrated or unable to take oral fluids and medicines **or**
- are pregnant **or**
- have a higher risk of developing complications (for example, people with known or suspected structural or functional abnormality of the genitourinary tract or underlying disease [such as diabetes or immunosuppression]) **or**
- have recurrent catheter-associated UTIs **or**
- have bacteria that are resistant to oral antibiotics.

NICE has produced a visual summary on antimicrobial prescribing for catheter-associated urinary tract infections.

See what NICE says on sepsis.

Rationale

See why we made the recommendations on antibiotics for managing catheter-associated UTI [See page 35].

6 When to reassess

Reassess people with catheter-associated UTI [See page 19] if symptoms worsen 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 sepsis
- previous antibiotic use, which may have led to resistant bacteria.

NICE has produced a visual summary on antimicrobial prescribing for catheter-associated urinary tract infections.

Rationale

See why we made the recommendations on antibiotics for managing catheter-associated UTI [See page 35].

7 Antibiotic treatment and catheter removal

Consider removing or, if this cannot be done, changing the catheter as soon as possible in people with a catheter-associated UTI [See page 19] if it has been in place for more than 7 days. Do not allow catheter removal or change to delay antibiotic treatment.

Obtain a urine sample before antibiotics are taken. Take the sample from the catheter, via a sampling port if provided, and use an aseptic technique (see catheter maintenance in NICE's recommendations on prevention and control of healthcare-associated infections).

- If the catheter has been changed, obtain the sample from the new catheter.
- If the catheter has been removed obtain a midstream specimen of urine.

Send the urine sample for culture and susceptibility testing, noting a suspected catheter-associated infection and any antibiotic prescribed.

Offer an antibiotic (see the recommendations on choice of antibiotic below) to people with catheter-associated UTI. 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

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

When urine culture and susceptibility results are available:

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

NICE has produced a visual summary on antimicrobial prescribing for catheter-associated urinary tract infections.

Choice of antibiotic

When prescribing an antibiotic for catheter-associated UTI, take account of local antimicrobial resistance data and:

- follow the table on antibiotics for children and young people under 16 years with catheter-associated UTI [See page 20]
- follow the table on antibiotics for pregnant women aged 12 years and over with catheter-associated UTI [See page 29].

Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Rationale

See why we made the recommendations on antibiotics for managing catheter-associated UTI [See page 35].

8 Advice and self-care

Give advice about managing symptoms with self-care to all people with catheter-associated UTI [See page 19].

NICE has produced a visual summary on antimicrobial prescribing for catheter-associated urinary tract infections.

Self-care

Advise people with catheter-associated UTI about using paracetamol for pain.

Advise people with catheter-associated UTI about drinking enough fluids to avoid dehydration.

See why we made the recommendations on self-care for catheter-associated UTI [See page 41].

Advice

When an antibiotic is given, as well as the general advice on self-care, give advice about:

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

See why we made the recommendations on antibiotics for managing catheter-associated UTI [See page 35].

9 No catheter

No additional information

10 Refer urgently if there is a high risk of serious illness

Infants and children with a high risk of serious illness should be referred urgently to the care of a paediatric specialist.

11 Lower UTI (cystitis)

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

NICE has produced a visual summary on antimicrobial prescribing for lower urinary tract infections.

Rationale

See why we made the recommendations on antibiotics for lower UTIs [See page 23].

12 When to reassess

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.

NICE has produced a visual summary on antimicrobial prescribing for lower urinary tract infections.

13 Antibiotic treatment

NICE has produced a visual summary on antimicrobial prescribing for lower urinary tract infections.

Infants under 3 months

Infants younger than 3 months with a possible UTI should be referred immediately to the care of a paediatric specialist. Treatment should be with parenteral antibiotics in line with NICE's recommendations on managing feverish illness in children with signs of immediately life-threatening illness.

Infants, children or young people aged 3 months – 15 years

For infants and children 3 months or older with cystitis/lower UTI:

- treat with antibiotics in line with the recommendations below.

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 urine testing.

Assess and manage children under 5 with lower UTI who present with fever as outlined in the NICE recommendations on fever in under 5s.

Offer an immediate antibiotic prescription (see the table on choice of antibiotic for children and young people under 16 years [See page 66]) 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.

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.

See what NICE says on preventing recurrence of UTIs.

Pregnant girls aged 12–15 years

Offer an immediate antibiotic prescription (see the table on choice of antibiotic for pregnant women aged 12 years and over [See page 40]) to pregnant women with lower UTI. Take account of:

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

Obtain a midstream urine sample from pregnant women before antibiotics are taken, and send for culture and susceptibility testing.

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.

Rationale

See why we made the recommendations on choice of antibiotic for lower UTIs [See page 50] and why we made the recommendations on antibiotic course length for lower UTIs [See page 56].

14 Advice and self-care

Give advice about managing symptoms with self-care to all people with lower UTI.

NICE has produced a visual summary on antimicrobial prescribing for lower urinary tract infections.

Self-care

Advise people with lower UTI about using paracetamol for pain, or if preferred and suitable ibuprofen.

Advise people with lower UTI about drinking enough fluids to avoid dehydration.

Be aware that no evidence was found on cranberry products or urine alkalinising agents to treat lower UTI.

See why we made the recommendations on self-care for lower UTIs [See page 19].

Advice when an antibiotic prescription is given

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 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.

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.

See why we made the recommendations on antibiotics for lower UTIs [See page 23].

15 Managing asymptomatic bacteriuria

Be aware that asymptomatic bacteriuria:

- is significant levels of bacteria (greater than 10^5 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 table on choice of antibiotic for pregnant women aged 12 years and over [See page 40]).

Asymptomatic bacteriuria in infants and children should not be treated with antibiotics.

NICE has produced a visual summary on antimicrobial prescribing for lower urinary tract infections.

Pregnant girls aged 12–15 years

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.

Rationale

See why we made the recommendations on managing asymptomatic bacteriuria [See page 49].

16 Upper UTI (acute pyelonephritis)

Be aware that acute pyelonephritis is an infection of one or both kidneys usually caused by bacteria travelling up from the bladder.

NICE has produced a visual summary on antimicrobial prescribing for upper urinary tract infections.

Rationale

See why we made the recommendations on choice of antibiotics for upper UTIs [See page 26].

17 When to reassess

Reassess if symptoms worsen 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 sepsis
- previous antibiotic use, which may have led to resistant bacteria.

NICE has produced a visual summary on antimicrobial prescribing for upper urinary tract infections.

18 Antibiotic treatment

NICE has produced a visual summary on antimicrobial prescribing for upper urinary tract infections.

Infants under 3 months

Infants younger than 3 months with a possible UTI should be referred immediately to the care of a paediatric specialist. Treatment should be with parenteral antibiotics in line with NICE's recommendations on managing feverish illness in children with signs of immediately life-threatening illness.

Infants, children or young people aged 3 months – 15 years

For infants and children 3 months or older with acute pyelonephritis/upper UTI:

- consider referral to a paediatric specialist
- treat with antibiotics in line with the recommendations below.

In children and young people under 16 years with acute pyelonephritis, obtain a urine sample before antibiotics are taken and send for culture and susceptibility testing in line with urine testing.

Assess and manage children under 5 with acute pyelonephritis who present with fever as outlined in the NICE recommendations on fever in under 5s.

Offer an antibiotic (see the table on choice of antibiotic for children and young people under 16 years with acute pyelonephritis [See page 60] and table on choice of antibiotic for pregnant women aged 12 years and over with acute pyelonephritis [See page 34]) to people with acute pyelonephritis. 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
- previous urine culture and susceptibility results
- previous antibiotic use, which may have led to resistant bacteria.

Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

When results of urine cultures are available:

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

See what NICE says on preventing recurrence of UTIs.

Rationale

See why we made the recommendations on choice of antibiotics for upper UTIs [See page 26], why we made the recommendations on antibiotic course length for upper UTIs [See page 53], and why we made the recommendations on antibiotic route of administration for upper UTIs [See page 55].

19 Advice and self-care

Self-care

Advise people with acute pyelonephritis about using paracetamol for pain, with the possible

addition of a low-dose weak opioid such as codeine for people over 12 years.

Advise people with acute pyelonephritis about drinking enough fluids to avoid dehydration.

NICE has produced a visual summary on antimicrobial prescribing for upper urinary tract infections.

See why we made the recommendations on self-care for upper UTIs [See page 19].

Advice when an antibiotic prescription is given

When an antibiotic is given, as well as the general advice on self-care, give advice about:

- possible adverse effects of the antibiotic, particularly diarrhoea and nausea
- nausea with vomiting also being a possible indication of worsening pyelonephritis
- seeking medical help if:
  - symptoms worsen at any time **or**
  - symptoms do not start to improve within 48 hours of taking the antibiotic **or**
  - the person becomes systemically very unwell.

See why we made the recommendations on choice of antibiotics for upper UTIs [See page 26].

20 Recurrent UTI

Be aware that recurrent UTI [See page 20]:

- includes lower UTI and upper UTI (acute pyelonephritis)
- may be due to relapse (with the same strain of organism) or reinfection (with a different strain or species of organism)
- is particularly common in women.

NICE has produced a visual summary on antimicrobial prescribing for recurrent urinary tract infections.

Rationale

See why we made the recommendations on antibiotic prophylaxis for recurrent UTIs [See page 57].

21 Self-care

Give advice to people with recurrent UTI [See page 20] about behavioural and personal hygiene measures and self-care treatments that may help to reduce the risk of UTI.

Be aware that:

- some women with recurrent UTI may wish to try D-mannose[1] if they are not pregnant
- some women with recurrent UTI may wish to try cranberry products if they are not pregnant (evidence of benefit is uncertain and there is no evidence of benefit for older women)
- some children and young people under 16 years with recurrent UTI may wish to try cranberry products with the advice of a paediatric specialist (evidence of benefit is uncertain).

Advise people taking cranberry products or D-mannose about the sugar content of these products, which should be considered as part of the person's daily sugar intake.

Be aware that evidence is inconclusive about whether probiotics (lactobacillus) reduce the risk of UTI in people with recurrent UTI.

NICE has produced a visual summary on antimicrobial prescribing for recurrent urinary tract infections.

Rationale

See why we made the recommendations on self-care for recurrent UTIs [See page 54].

22 Antibiotic prophylaxis

NICE has produced a visual summary on antimicrobial prescribing for recurrent urinary tract infections.

Infants under 3 months

Infants younger than 3 months with a possible UTI should be referred immediately to the care of a paediatric specialist. Treatment should be with parenteral antibiotics in line with NICE's recommendations on managing feverish illness in children with signs of immediately life-threatening illness.

[1] The evidence was based on a study where D-mannose was taken as 200 ml of 1% solution once daily in the

evening. D-mannose is a sugar that is available to buy as powder or tablets; it is not a medicine.

Infants, children or young people aged 3 months – 15 years

For children and young people under 16 years with recurrent UTI [See page 20], ensure that any current UTI has been adequately treated then consider a trial of daily antibiotic prophylaxis (see the table on choice of antibiotic for children and young people under 16 years with recurrent UTI [See page 42]) if behavioural and personal hygiene measures alone are not effective or not appropriate, with specialist advice. Take account of:

- underlying causes following specialist assessment and investigations
- the uncertain evidence of benefit of antibiotic prophylaxis for reducing the risk of recurrent UTI and the rate of deterioration of renal scars
- the severity and frequency of previous symptoms
- the risks of long-term antibiotic use
- the risk of developing complications
- previous urine culture and susceptibility results
- previous antibiotic use, which may have led to resistant bacteria
- preferences for antibiotic use.

When a trial of daily antibiotic prophylaxis is given, give advice about:

- the risk of resistance with long-term antibiotics, which means they may be less effective in the future
- possible adverse effects of long-term antibiotics
- returning for review within 6 months
- seeking medical help if there are symptoms of an acute UTI.

Review antibiotic prophylaxis for recurrent UTI at least every 6 months, with the review to include:

- assessing the success of prophylaxis
- discussion of continuing, stopping or changing prophylaxis (taking into account the person's preferences for antibiotic use and the risk of antimicrobial resistance)
- a reminder about behavioural and personal hygiene measures and self-care treatments.

If antibiotic prophylaxis is stopped, ensure that people have rapid access to treatment if they have an acute UTI.

See what NICE says on preventing recurrence of UTIs.

Rationale

See why we made the recommendations on antibiotic prophylaxis for recurrent UTIs [See page 57], why we made the recommendations on choice of antibiotic prophylaxis for recurrent UTIs [See page 63], and why we made the recommendations on antibiotic dosing and course length for recurrent UTIs [See page 65].

23 Imaging

See Urinary tract infections/Urinary tract infections in children and young people under 16 years /Imaging

Rationale: self-care for lower UTIs

- 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 self-management 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.

For more information see self-care in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Catheter-associated UTI

Catheter-associated UTI is defined as the presence of symptoms or signs compatible with a UTI in people with a catheter with no other identified source of infection plus significant levels of bacteria in a catheter or a midstream urine specimen when the catheter has been removed within the previous 48 hours (adapted from Infectious Diseases Society of America's guideline on catheter-associated UTI [2009]).

Rationale: self-care for upper UTIs

- There was no evidence for the use of oral analgesia in acute pyelonephritis. However, paracetamol has a well-established efficacy and safety profile for managing pain. The committee agreed that it was reasonable to advise people about paracetamol for self-management of pain. A low-dose weak opioid, such as codeine, could be taken with paracetamol by adults and young people over 12 years for more severe pain.
- Non-steroidal anti-inflammatory drugs, such as ibuprofen, are generally not recommended for people with acute pyelonephritis because of concerns about renal safety.
- The committee discussed the need for an adequate intake of fluids to ensure a high urine output, which is believed to help resolve acute pyelonephritis through a mechanical flushing of bacteria from the kidney. No evidence was found for this and there was no evidence of what constitutes adequate hydration. However, 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.

For more information see self-care in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing.

Recurrent UTI

Recurrent UTI in adults is defined as repeated UTI with a frequency of 2 or more UTIs in the last 6 months or 3 or more UTIs in the last 12 months (European Association of Urology (EAU) guidelines on urological infections [2017]).

Recurrent UTI is diagnosed in children and young people under 16 years if they have:

- 2 or more episodes of UTI with acute pyelonephritis/upper UTI **or**
- 1 episode of UTI with acute pyelonephritis plus 1 or more episode of UTI with cystitis/lower UTI **or**
- 3 or more episodes of UTI with cystitis/lower UTI.

Antibiotics for children and young people under 16 years with catheter-associated UTI

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 recommendations on fever in under 5s.	
Children aged 3 months and over	
First-choice oral antibiotics[3]	
Trimethoprim – if low risk of resistance[4]	3 to 5 months, 4 mg/kg (maximum 200 mg per dose) or 25 mg twice a day for 7 to 10 days

	6 months to 5 years, 4 mg/kg (maximum 200 mg per dose) or 50 mg twice a day for 7 to 10 days 6 to 11 years, 4 mg/kg (maximum 200 mg per dose) or 100 mg twice a day for 7 to 10 days 12 to 15 years, 200 mg twice a day for 7 to 10 days
Amoxicillin (only if culture results available and susceptible)	3 to 11 months, 125 mg three times a day for 7 to 10 days 1 to 4 years, 250 mg three times a day for 7 to 10 days 5 to 15 years, 500 mg three times a day for 7 to 10 days
Cefalexin	3 to 11 months, 12.5 mg/kg or 125 mg twice a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 1 to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 5 to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 12 to 15 years, 500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
Co-amoxiclav (only if culture results available and susceptible)	3 to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 1 to 5 years, 0.25 ml/kg of 125/31 suspension or 5 ml of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection)

	6 to 11 years, 0.15 ml/kg of 250/62 suspension or 5 ml of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 12 to 15 years, 250/125 mg or 500/125 mg three times a day for 7 to 10 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if susceptibility or sepsis a concern[3,5,6]	
Co-amoxiclav (only in combination unless culture results confirm susceptibility)	3 months to 15 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)
Cefuroxime	3 months to 15 years, 20 mg/kg three times a day (maximum 750 mg per dose); (50 to 60 mg/kg three or four times a day [maximum 1.5 g per dose] for severe infections)
Ceftriaxone	3 months to 11 years (up to 50 kg), 50 to 80 mg/kg once a day (maximum 4 g per day) 9 to 11 years (50 kg and above), 1 to 2 g once a day 12 to 15 years, 1 to 2 g once a day
Gentamicin	Initially 7mg /kg once a day, subsequent doses adjusted according to serum gentamicin concentration[7]
Amikacin	Initially 15 mg/kg once a day, subsequent doses adjusted according to serum amikacin concentration[7]
Second choice intravenous antibiotic	

Consult local microbiologist
[1] See BNF for children (BNFC) for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics. See the table on antibiotics for pregnant women aged 12 years and over with catheter-associated UTI [See page 29] if a young woman is pregnant. [2] The 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. [3] Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly. If a child or young person is receiving prophylactic antibiotics, treatment should be with a different antibiotic, not a higher dose of the same antibiotic. [4] A lower risk of resistance is likely if not 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 suggest resistance is low. A higher risk of resistance is likely with recent use. [5] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total antibiotic course of 10 days. [6] If intravenous treatment is not possible, consider intramuscular treatment if suitable. [7] Therapeutic drug monitoring and assessment of renal function is required (BNFC, August 2018).

Rationale: antibiotics for lower UTIs

- 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 NICE guideline on urinary tract infection in under 16s 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.

For more information see antibiotics in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Rationale: choice of antibiotics for upper UTIs

- Based on evidence and experience, the committee agreed that acute pyelonephritis is a bacterial infection needing treatment with antibiotics that reach therapeutic concentrations in the kidney. Antibiotics that don't achieve adequate levels in renal tissue, such as nitrofurantoin, fosfomycin and pivmecillinam, are to be avoided.
- A urine sample should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee reviewed the available evidence comparing different antibiotics in adults and children and agreed that it was limited by its setting (most studies in adults were undertaken in a hospital, and in children the setting of the studies was not reported). The studies included various different antibiotics, which may not reflect those chosen in UK practice. The committee discussed the evidence for a benefit of the intravenous third-generation cephalosporins, ceftolozane/tazobactam or ceftazidime, over an intravenous fluoroquinolone, but this was mainly limited to a benefit for composite cure (which included clinical cure, microbiological eradication and microbiological cure) and the absolute benefits were small.
- The committee agreed, based on experience, that several oral and intravenous antibiotics should be available for people with acute pyelonephritis. This enables antibiotics to be selected based on the severity of illness, antibiotic susceptibilities from culture results when available, local resistance patterns, risk of resistant bacteria, the setting, and known patient factors (such as whether the person has a higher risk of developing complications). In line with antimicrobial stewardship, narrower-spectrum antibiotics should be used wherever possible.
- Nationally for England, resistance of *E. coli* (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
    - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
    - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
    - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
    - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%)

(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.
- The committee agreed that any recent previous urine culture and susceptibility results, and antibiotic prescribing, should be reviewed before choosing an antibiotic.
- Based on experience, the committee agreed that if the results of urine culture suggest the bacteria are resistant to the antibiotic given, people with acute pyelonephritis should be contacted and the antibiotic changed regardless of whether symptoms are improving or not. The committee agreed that acute pyelonephritis is a serious infection and antibiotics should be changed to ensure cure.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed to recommend a choice of first-line **oral antibiotics**, at usual doses for acute pyelonephritis. These are:
    - **cefalexin** (a first-generation cephalosporin); based on its broad spectrum of activity and acceptable levels of resistance
    - **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor); which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
    - **trimethoprim**; which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
    - **ciprofloxacin** (a fluoroquinolone); based on its broad spectrum of activity and acceptable levels of resistance (particularly for people who have had previous treatment with penicillins, or cannot tolerate or are allergic to penicillins).
- The committee noted that use of broad-spectrum antibiotics, such as later-generation cephalosporins, fluoroquinolones or co-amoxiclav, can create a selective advantage for bacteria resistant to these second-line broad-spectrum agents, allowing such strains to proliferate and spread. And, by disrupting normal flora, broad-spectrum antibiotics can leave people susceptible to harmful bacteria such as *Clostridium difficile* in community settings. However, these antibiotics are appropriate for the empirical treatment of acute pyelonephritis, where coverage of more resistant strains of common bacterial pathogens is required.
- The committee was aware of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. However, they discussed that fluoroquinolone antibiotics are a valuable option for the treatment of acute pyelonephritis, which is a severe infection. Resistant gram-negative organisms are a particular concern in acute pyelonephritis. The committee agreed that ciprofloxacin should remain a first-choice option because gram-negative organisms are likely to be sensitive to it and acute pyelonephritis can be a complex infection. The committee was keen to point out, however, that cefalexin, co-amoxiclav and trimethoprim are also first-choice options, and antibiotics should be chosen on an individual patient basis, taking fluoroquinolone safety concerns, as well as susceptibility and resistance, into account.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for people with acute pyelonephritis who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:
    - **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible)
    - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-

- – generation cephalosporin)
  - **ciprofloxacin** (taking safety concerns into account)
  - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours. Gentamicin is the preferred aminoglycoside in the UK, but shortages of certain antibiotics may result in the use of alternatives; for example amikacin in place of gentamicin.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

Pregnant women with acute pyelonephritis

- Based on experience and resistance data, the committee agreed to recommend **cefalexin** (a first-generation cephalosporin) as the first-choice oral antibiotic for pregnant women who don't require intravenous antibiotics, and **cefuroxime** (a second-generation cephalosporin) as the first-choice intravenous antibiotic.
- Ciprofloxacin and trimethoprim are not recommended because they should be avoided in pregnancy. Co-amoxiclav was not recommended because of high resistance levels nationally and the risks of treatment failure in pregnancy.
- The committee agreed, based on experience, that local microbiologists should be consulted for advice on second-choice antibiotics, or combining antibiotics if susceptibility or sepsis is a concern.

Children and young people with acute pyelonephritis

- The committee was aware that the NICE guideline on urinary tract infection in under 16s makes recommendations on diagnosing acute pyelonephritis and considering referral to a paediatric specialist.
- Based on evidence, their experience and resistance data, the committee agreed to recommend **cefalexin** or **co-amoxiclav** (only if culture results are available and bacteria are susceptible) at usual doses for acute pyelonephritis, as first-choice **oral antibiotics**.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for children and young people who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:

  – **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible); which can be given intravenously

  – **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation

- cephalosporin); which would be suitable alternatives to co-amoxiclav

  – **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some children and young people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours.

- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of children and young people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

For more information see choice of antibiotic in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing.

Antibiotics for pregnant women aged 12 years and over with catheter-associated UTI

Antibiotic[1]	Dosage and course length
First-choice oral antibiotic[2]	
Cefalexin	500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell)[2,3]	
Cefuroxime	750 mg to 1.5 g three or four times a day
Second-choice antibiotics or combining antibiotics if susceptibility or sepsis a concern	
Consult local microbiologist	

[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics.

[2] Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

[3] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Antibiotics for non-pregnant women and men aged 16 years and over with catheter-associated UTI

Antibiotic[1]	Dosage and course length
First-choice oral antibiotic if no upper UTI symptoms[2]	
Nitrofurantoin – if eGFR ≥45 ml/minute[3,4]	100 mg modified-release twice a day for 7 days
Trimethoprim – if low risk of resistance[5]	200 mg twice a day for 7 days
Amoxicillin (only if culture results available and susceptible)	500 mg three times a day for 7 days
Second-choice oral antibiotic if no upper UTI symptoms (when first-choice not suitable)[2]	
Pivmecillinam (a penicillin)[4]	400 mg initial dose, then 200 mg three times a day for a total of

	7 days
First-choice oral antibiotic if upper UTI symptoms[2]	
Cefalexin	500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
Co-amoxiclav (only if culture results available and susceptible)	500/125 mg three times a day for 7 to 10 days
Trimethoprim (only if culture results available and susceptible)	200 mg twice a day for 14 days
Ciprofloxacin (consider safety issues[6])	500 mg twice a day for 7 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if susceptibility or sepsis a concern[2,7]	
Co-amoxiclav (only in combination, unless culture results confirm susceptibility)	1.2 g three times a day
Cefuroxime	750 mg to 1.5 g three or four times a day
Ceftriaxone	1 to 2 g once a day
Ciprofloxacin (consider safety issues[6])	400 mg twice or three times a day

Gentamicin	Initially 5 to 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration[8]
Amikacin	Initially 15 mg/kg once a day (maximum per dose 1.5 g once a day), subsequent doses adjusted according to serum amikacin concentration (maximum 15 g per course)[8]
Second-choice intravenous antibiotic	
Consult local microbiologist	

[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment and breastfeeding, and administering intravenous antibiotics.

[2] Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

[3] May be used with caution if eGFR 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).

[4] Nitrofurantoin and pivmecillinam are only licensed for uncomplicated lower UTIs, and are not suitable for people with upper UTI symptoms or a blocked catheter.

[5] A lower risk of resistance is likely if not 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 suggest resistance is low. A higher risk of resistance is likely with recent use and in older people in care homes.

[6] The European Medicines Agency's Pharmacovigilance Risk Assessment Committee has recommended restricting the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons, bones and the nervous system (press release October 2018), but they are an option in catheter-associated

UTI with upper UTI symptoms, which is a severe infection.

[7] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

[8] Therapeutic drug monitoring and assessment of renal function is required (BNF, August 2018).

Rationale: antibiotic prophylaxis for preventing catheter-associated UTI

- The committee discussed the evidence on antibiotic prophylaxis for catheter-associated UTI in various populations.
- Based on evidence, their experience and resistance data, the committee agreed that antibiotic prophylaxis should not be routinely offered to people with a **long-term (indwelling or intermittent) catheter**.
    - The benefit of antibiotic prophylaxis for symptomatic bacteriuria was mixed.
    - The committee noted that although there was evidence of benefit (reduced rate of UTIs per year) from 1 RCT in adults who used intermittent self-catheterisation and had recurrent UTI, there was also evidence of increasing antibiotic resistance in the microorganisms found in the group taking antibiotics for prophylaxis. The committee discussed that routine antibiotic prophylaxis would be a change in practice, which is not warranted because of increasing resistance. Decisions around prophylaxis for people who self-catheterise and have recurrent UTIs may, however, be made on an individual basis, with shared decision-making and a discussion of the risks and benefits.
    - The committee discussed that people should be advised to seek medical help if symptoms of a UTI develop, which would be managed as an acute UTI, rather than people receiving long-term antibiotic prophylaxis.
    - The committee was aware of recommendations in the NICE guideline on healthcare-associated infections that antibiotic prophylaxis should not be offered routinely when changing long-term indwelling catheters, but should be considered for people with a history of symptomatic UTI after catheter change or an experience of trauma (frank haematuria after catheterisation or 2 or more attempts of catheterisation). The committee for the healthcare-associated infections guideline agreed that for these groups, the benefits of antibiotic prophylaxis outweigh the risks of antimicrobial resistance. These groups are likely to be at high risk of a UTI and at risk of complications if a UTI develops.
- Based on evidence, the committee agreed not to recommend routine antibiotic prophylaxis to prevent catheter-associated UTI in people with a short-term catheter in hospital.

- Prophylaxis is not recommended routinely before insertion of a short-term catheter for surgical, non-surgical or urodynamic procedures, while the catheter is in place, or at the time of removal.
    - Before or during short-term catheterisation, there is only limited evidence of benefit with antibiotic prophylaxis for symptomatic bacteriuria in surgical patients.
    - During short-term catheterisation for urodynamic studies, antibiotic prophylaxis did not reduce episodes of symptomatic UTI.
    - At the time of catheter removal, there is evidence of benefit for antibiotic prophylaxis for symptomatic UTI, but in subgroup analysis this was limited to surgical patients, and predominantly those who had either prostate surgery or had a catheter in place for longer than 5 days. The committee discussed that antibiotic prophylaxis for all short-term catheter removal in hospital would be a change in practice, and widespread prophylaxis is not warranted taking into account the principles of antimicrobial stewardship.

For more information see antibiotic prophylaxis for preventing catheter-associated UTI in the NICE guideline on urinary tract infection (catheter-associated): antimicrobial prescribing.

Antibiotics for pregnant women aged 12 years and over

When prescribing an antibiotic for acute pyelonephritis, take account of local antimicrobial resistance data and follow the table below for pregnant women aged 12 years and over.

Antibiotic[1]	**Dosage and course length**
First-choice oral antibiotic[2]	
Cefalexin	500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell)[2,3]	
Cefuroxime	750 mg to 1.5 g three or four times a day
Second-choice antibiotics or combining antibiotics if susceptibility or sepsis a concern	

Consult local microbiologist
[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics. [2] Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly. [3] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Rationale: antibiotics for managing catheter-associated UTI

- Based on evidence and experience, the committee agreed that people with a symptomatic catheter-associated UTI should be offered an antibiotic.
- Urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment decisions. The committee discussed and agreed that a comment should be added to the microbiology request form to alert the laboratory to a suspected catheter-associated infection and the name of any antibiotic prescribed.
- The committee agreed that the evidence for antibiotic treatment for catheter-associated UTI specifically was limited, but that evidence for antibiotic treatment for acute pyelonephritis could be extrapolated. The evidence for acute pyelonephritis included some people with complicated UTI, some of whom had a catheter (see the NICE guideline on acute pyelonephritis: antimicrobial prescribing).
- Limited evidence suggested that catheters should be removed or changed before antibiotics are given, but the committee discussed safety concerns with this approach and practical considerations about possible delays in primary care settings. They agreed that catheter removal or change should not delay treatment with antibiotics. The longer a catheter is in place, the more likely bacteria will be found in the urine, and the committee agreed that catheters should be removed rather than changed, where possible. Changing the catheter is based on evidence from 1 small RCT, which found higher cure or improvement rates and reduced mortality (from urosepsis) when the catheter was changed before starting antibiotics. The committee based when to remove or change the catheter (after 7 days) on their experience.
- Based on evidence and experience, the committee agreed that screening and antibiotic treatment for asymptomatic bacteriuria is not routine in people with a catheter because it is not generally a risk factor for harm. Pregnant women (including those with a catheter) have routine screening and antibiotic treatment for asymptomatic bacteriuria because it is a risk factor for pyelonephritis and preterm labour.

Committee discussion on choice of antibiotic

- The committee agreed, based on evidence, experience and resistance data, that several oral and intravenous antibiotics should be available for people with a catheter-associated UTI. Having a choice enables antibiotics to be selected based on the severity of illness, presence or absence of upper UTI symptoms, antibiotic susceptibilities from culture results when available, local resistance patterns, risk of resistant bacteria, setting and known patient factors. In line with antimicrobial stewardship, narrower-spectrum antibiotics should be used wherever possible.
- Nationally for England, resistance of *E. coli* (the main causative organism of 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%)
    - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
    - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)

(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.
- The committee agreed that any recent previous urine culture and susceptibility results, and antibiotic prescribing, should be reviewed before choosing an antibiotic.
- 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, the antibiotic should be changed, using a narrow-spectrum antibiotic where possible.

Non-pregnant women and men with catheter-associated UTI

- Based on evidence, their experience and resistance data, the committee agreed to recommend **nitrofurantoin**, **trimethoprim** or **amoxicillin** at usual doses as first-choice **oral antibiotics** for adults with a catheter-associated UTI but no upper UTI symptoms.
    - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute. It may be used with caution if eGFR is 30 to 44 ml/minute to treat uncomplicated lower UTI caused by suspected or proven multidrug-resistant bacteria, and only if the potential benefit outweighs risk (BNF, August 2018). The committee noted that nitrofurantoin is only licensed for uncomplicated lower UTI. However, they agreed that for adults with a catheter-associated UTI without upper UTI symptoms, nitrofurantoin is an option (unless they have a blocked catheter, where *Proteus mirabilis* could be the causative organism). Based on experience, the committee felt it was important to offer 'lower UTI' antibiotics as an option for adults with

- – catheter-associated UTI without upper UTI symptoms, otherwise all adults with a catheter-associated UTI would need to be offered a broader-spectrum 'upper UTI' antibiotic, where their symptoms may not warrant this.
  - The committee agreed to recommend the modified-release preparation of nitrofurantoin over the immediate-release preparation because of the twice-daily dosing of the modified-release preparation and, in their experience, better tolerability with this preparation.
  - Trimethoprim has high resistance levels nationally and should only be prescribed if a lower risk of resistance is thought to be likely. A lower risk of resistance is 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 suggest resistance is lower. There is a higher risk of trimethoprim resistance with recent use and in older people in care homes.
  - Amoxicillin is recommended only if culture results are available and bacteria are susceptible because resistance rates are high.
- If nitrofurantoin, trimethoprim or amoxicillin are not suitable, the second-choice oral antibiotic for adults with a catheter-associated UTI but no upper UTI symptoms is **pivmecillinam** (a penicillin) at its usual dose. The committee acknowledged that prescribers may be less familiar with this antibiotic, but it is often used in other European countries. The committee noted that pivmecillinam is only licensed for uncomplicated lower UTI. However, as with nitrofurantoin, they agreed that for adults with a catheter-associated UTI without upper UTI symptoms, 'lower UTI' antibiotics are an option.
- For adults with upper UTI symptoms, nitrofurantoin, amoxicillin and pivmecillinam are not appropriate, and **cefalexin** (a first generation cephalosporin), **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor), **trimethoprim** or **ciprofloxacin** (a fluoroquinolone), at usual doses, are recommended to cover a broader range of bacterial pathogens. Co-amoxiclav and trimethoprim are only suitable if culture results are available and bacteria are susceptible, because resistance rates are high.
- The committee noted that use of broad-spectrum antibiotics, such as later-generation cephalosporins, fluoroquinolones or co-amoxiclav, can create a selective advantage for bacteria resistant to these second-line broad-spectrum agents, allowing such strains to proliferate and spread. By disrupting normal flora, broad-spectrum antibiotics can leave people susceptible to harmful bacteria such as *Clostridium difficile* in community settings. However, these antibiotics are appropriate for the empirical treatment of catheter-associated UTI with upper UTI symptoms, where coverage of more resistant strains of common bacterial pathogens is required.
- The committee was aware of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects, mainly involving muscles, tendons and bones, and the nervous system. However, they discussed that fluoroquinolone antibiotics are a valuable option for the treatment of catheter-associated UTI with upper UTI symptoms, which is a severe infection, and it is appropriate to reserve

- fluoroquinolone use for such conditions. Resistant gram-negative organisms are a particular concern in catheter-associated UTI with upper UTI symptoms, and the committee agreed that ciprofloxacin should remain a first-choice option to cover what can be a complex infection. The committee was keen to point out, however, that cefalexin, co amoxiclav and trimethoprim are also first-choice options, and antibiotics should be chosen on an individual patient basis, taking fluoroquinolone safety concerns, as well as susceptibility and resistance, into account.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for adults who are unable to take oral antibiotics because of nausea and vomiting, or are more severely unwell. These are:
    - **co-amoxiclav** (only in combination unless culture results confirm bacteria are susceptible)
    - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin)
    - **ciprofloxacin** (taking safety concerns into account)
    - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some people with catheter-associated UTI, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed by 48 hours. Gentamicin is the preferred aminoglycoside in the UK, but shortages of certain antibiotics may result in the use of alternatives; for example amikacin in place of gentamicin.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

Pregnant women with catheter-associated UTI

- Based on evidence, experience and resistance data, the committee agreed to recommend **cefalexin** (a first-generation cephalosporin) as the first-choice oral antibiotic for pregnant women who don't need intravenous antibiotics, and **cefuroxime** (a second-generation cephalosporin) as the first-choice intravenous antibiotic.
- Ciprofloxacin and trimethoprim are not recommended because they should be avoided in pregnancy. Co-amoxiclav was not recommended because of high resistance levels nationally and the risks of treatment failure in pregnancy.
- The committee agreed, based on experience, that local microbiologists should be consulted for advice on second-choice antibiotics, or combining antibiotics if susceptibility or sepsis is a concern.

Children and young people with catheter-associated UTI

- Based on evidence, experience and resistance data, the committee agreed to recommend

- **trimethoprim** (if low risk of resistance), **amoxicillin** (only if culture results are available and bacteria are susceptible), **cefalexin** or **co-amoxiclav** (only if culture results are available and bacteria are susceptible) at usual doses as first-choice **oral antibiotics** for children and young people with catheter-associated UTI.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics** at usual doses for children and young people who are unable to take oral antibiotics because of nausea and vomiting, or are more severely unwell. These are:
    - **co-amoxiclav** (only in combination unless culture results confirm bacteria are susceptible); which can be given intravenously
    - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin)
    - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some children and young people with upper UTI symptoms, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of children and young people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

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.
- In line with the NICE guideline on antimicrobial stewardship and Public Health England's Start smart – then focus, the committee agreed that the use of intravenous antibiotics should be reviewed by 48 hours (taking into account the response to treatment and susceptibility results from urine culture) and switched to oral treatment where possible.

Course length for non-pregnant women, pregnant women, men, children and young people with catheter-associated UTI

- Based on evidence, experience and resistance data, the committee agreed that, for oral treatment, at least a 7-day course of all the recommended antibiotics was needed to treat catheter-associated UTI to ensure complete cure. This is because people with a catheter are more at risk of complications from a UTI. For adults with a catheter-associated UTI and upper UTI symptoms, pregnant women, and children and young people, course lengths are the same as those for acute pyelonephritis (see the NICE guideline on acute pyelonephritis).
- For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible.

For more information see antibiotics for managing catheter-associated UTI in the NICE guideline on urinary tract infection (catheter-associated): antimicrobial prescribing.

Antibiotics for pregnant women aged 12 years and over

When prescribing antibiotic treatment for lower UTI, take account of local antimicrobial resistance data and follow the table below for pregnant women aged 12 years and over.

Antibiotic[1]	Dosage and course length[2]
Treatment of lower UTI	
First-choice[3]	
Nitrofurantoin (avoid at term) – if eGFR ≥45 ml/minute[4,5]	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)[3,6]	
Amoxicillin (only if culture results 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, choose antibiotics based on culture and susceptibility results
Treatment of asymptomatic bacteriuria	
Choose from nitrofurantoin[4,5], amoxicillin or cefalexin based on recent culture and	

susceptibility results
[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment. [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] Avoid at term in pregnancy; may produce neonatal haemolysis (BNF, August 2018). [5] May be used with caution if eGFR 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). [6] If there are symptoms of 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), see antibiotic treatment in the NICE recommendations on acute pyelonephritis.

Rationale: self-care for catheter-associated UTI

- There was no evidence for the use of oral analgesia in catheter-associated-UTI. However, paracetamol has a well-established efficacy and safety profile for managing pain. The committee agreed that it was reasonable to consider paracetamol for managing pain in people with a catheter-associated UTI.
- 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.
- The committee agreed that the evidence for use of cranberry in preventing catheter-associated UTI (which showed no effect) was limited to a specific population in the immediate postoperative period, and could not be extrapolated to other populations or settings. The committee was, therefore, unable to make a recommendation on its use.

For more information see self-care in the NICE guideline on urinary tract infection (catheter-associated): antimicrobial prescribing.

Recurrent UTI

Recurrent UTI in adults is defined as repeated UTI with a frequency of 2 or more UTIs in the last 6 months or 3 or more UTIs in the last 12 months (European Association of Urology (EAU) guidelines on urological infections [2017]).

Recurrent UTI is diagnosed in children and young people under 16 years if they have:

- 2 or more episodes of UTI with acute pyelonephritis/upper UTI **or**
- 1 episode of UTI with acute pyelonephritis plus 1 or more episode of UTI with cystitis/lower UTI **or**
- 3 or more episodes of UTI with cystitis/lower UTI.

Antibiotics for children and young people under 16 years with recurrent UTI

When prescribing antibiotic prophylaxis for recurrent UTI [See page 20], take account of local antimicrobial resistance data and follow the recommendations in the table below for children and young people under 16 years.

Antibiotic prophylaxis[1,2]	Dosage[3]
Children under 3 months	
Refer to paediatric specialist	
Children aged 3 months and over (specialist advice only)	
First-choice	
Trimethoprim[4]	3 to 5 months, 2 mg/kg at night (maximum 100 mg per dose) or 12.5 mg at night 6 months to 5 years, 2 mg/kg at night (maximum 100 mg per dose) or 25 mg at night

	6 to 11 years, 2 mg/kg at night (maximum 100 mg per dose) or 50 mg at night 12 to 15 years, 100 mg at night
Nitrofurantoin – if eGFR ≥45 ml/minute[5]	3 months to 11 years, 1 mg/kg at night 12 to 15 years, 50 to 100 mg at night
Second-choice	
Cefalexin	3 months to 15 years, 12.5 mg/kg at night (maximum 125 mg per dose)
Amoxicillin[6]	3 to 11 months, 62.5 mg at night 1 to 4 years, 125 mg at night 5 to 15 years, 250 mg at night

[1] See BNF for children (BNFC) for appropriate use and dosing in specific populations, for example hepatic and renal impairment.

[2] Choose antibiotics according to recent culture and susceptibility results where possible, with rotational use based on local policies. Select a different antibiotic for prophylaxis if treating an acute UTI. If 2 or more antibiotics are appropriate, choose the antibiotic with the lowest acquisition cost.

[3] The 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 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.

[4] Teratogenic risk in first trimester of pregnancy (folate antagonist; BNFC, August 2018).

Manufacturers advise contraindicated in pregnancy (trimethoprim summary of product characteristics).

[5] Avoid at term in pregnancy; may produce neonatal haemolysis (BNFC, August 2018).

[6] Amoxicillin is not licensed for preventing UTIs, so use for this indication would be off-label. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Rationale: antibiotics for lower UTIs

- 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 NICE guideline on urinary tract infection in under 16s 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.

For more information see antibiotics in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Rationale: choice of antibiotics for upper UTIs

- Based on evidence and experience, the committee agreed that acute pyelonephritis is a bacterial infection needing treatment with antibiotics that reach therapeutic concentrations in the kidney. Antibiotics that don't achieve adequate levels in renal tissue, such as nitrofurantoin, fosfomycin and pivmecillinam, are to be avoided.
- A urine sample should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee reviewed the available evidence comparing different antibiotics in adults and children and agreed that it was limited by its setting (most studies in adults were undertaken in a hospital, and in children the setting of the studies was not reported). The studies included various different antibiotics, which may not reflect those chosen in UK practice. The committee discussed the evidence for a benefit of the intravenous third-generation cephalosporins, ceftolozane/tazobactam or ceftazidime, over an intravenous fluoroquinolone, but this was mainly limited to a benefit for composite cure (which included clinical cure, microbiological eradication and microbiological cure) and the absolute benefits were small.
- The committee agreed, based on experience, that several oral and intravenous antibiotics should be available for people with acute pyelonephritis. This enables antibiotics to be selected based on the severity of illness, antibiotic susceptibilities from culture results when available, local resistance patterns, risk of resistant bacteria, the setting, and known patient factors (such as whether the person has a higher risk of developing complications). In line with antimicrobial stewardship, narrower-spectrum antibiotics should be used wherever

- possible.
- Nationally for England, resistance of *E. coli* (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
    - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
    - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
    - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)
    - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%)

(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.
- The committee agreed that any recent previous urine culture and susceptibility results, and antibiotic prescribing, should be reviewed before choosing an antibiotic.
- Based on experience, the committee agreed that if the results of urine culture suggest the bacteria are resistant to the antibiotic given, people with acute pyelonephritis should be contacted and the antibiotic changed regardless of whether symptoms are improving or not. The committee agreed that acute pyelonephritis is a serious infection and antibiotics should be changed to ensure cure.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed to recommend a choice of first-line **oral antibiotics**, at usual doses for acute pyelonephritis. These are:
    - **cefalexin** (a first-generation cephalosporin); based on its broad spectrum of activity and acceptable levels of resistance
    - **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor); which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
    - **trimethoprim**; which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
    - **ciprofloxacin** (a fluoroquinolone); based on its broad spectrum of activity and acceptable levels of resistance (particularly for people who have had previous treatment with penicillins, or cannot tolerate or are allergic to penicillins).
- The committee noted that use of broad-spectrum antibiotics, such as later-generation cephalosporins, fluoroquinolones or co-amoxiclav, can create a selective advantage for bacteria resistant to these second-line broad-spectrum agents, allowing such strains to proliferate and spread. And, by disrupting normal flora, broad-spectrum antibiotics can leave people susceptible to harmful bacteria such as *Clostridium difficile* in community settings. However, these antibiotics are appropriate for the empirical treatment of acute

- pyelonephritis, where coverage of more resistant strains of common bacterial pathogens is required.
- The committee was aware of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. However, they discussed that fluoroquinolone antibiotics are a valuable option for the treatment of acute pyelonephritis, which is a severe infection. Resistant gram-negative organisms are a particular concern in acute pyelonephritis. The committee agreed that ciprofloxacin should remain a first-choice option because gram-negative organisms are likely to be sensitive to it and acute pyelonephritis can be a complex infection. The committee was keen to point out, however, that cefalexin, co-amoxiclav and trimethoprim are also first-choice options, and antibiotics should be chosen on an individual patient basis, taking fluoroquinolone safety concerns, as well as susceptibility and resistance, into account.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for people with acute pyelonephritis who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:
    - **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible)
    - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin)
    - **ciprofloxacin** (taking safety concerns into account)
    - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours. Gentamicin is the preferred aminoglycoside in the UK, but shortages of certain antibiotics may result in the use of alternatives; for example amikacin in place of gentamicin.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

Pregnant women with acute pyelonephritis

- Based on experience and resistance data, the committee agreed to recommend **cefalexin** (a first-generation cephalosporin) as the first-choice oral antibiotic for pregnant women who don't require intravenous antibiotics, and **cefuroxime** (a second-generation cephalosporin) as the first-choice intravenous antibiotic.
- Ciprofloxacin and trimethoprim are not recommended because they should be avoided in pregnancy. Co-amoxiclav was not recommended because of high resistance levels nationally and the risks of treatment failure in pregnancy.

- The committee agreed, based on experience, that local microbiologists should be consulted for advice on second-choice antibiotics, or combining antibiotics if susceptibility or sepsis is a concern.

Children and young people with acute pyelonephritis

- The committee was aware that the NICE guideline on urinary tract infection in under 16s makes recommendations on diagnosing acute pyelonephritis and considering referral to a paediatric specialist.
- Based on evidence, their experience and resistance data, the committee agreed to recommend **cefalexin** or **co-amoxiclav** (only if culture results are available and bacteria are susceptible) at usual doses for acute pyelonephritis, as first-choice **oral antibiotics**.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for children and young people who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:
  – **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible); which can be given intravenously

  – **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin); which would be suitable alternatives to co-amoxiclav

  – **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some children and young people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours.

- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of children and young people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

For more information see choice of antibiotic in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing.

Rationale: 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.

For more information see antibiotics in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Rationale: choice of antibiotic for lower UTIs

- 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 the modified-release preparation of nitrofurantoin

- over the immediate-release preparation because of its twice daily dosing and, in their experience, better tolerability.

  – 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 suggest 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 NICE antimicrobial prescribing guideline on acute pyelonephritis 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 (BNF, August 2018).

  – 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 (BNF, August 2018). However, the committee acknowledged that trimethoprim is sometimes used in pregnancy when given with folic acid 5 mg daily in the first trimester (NICE clinical knowledge 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 antimicrobial prescribing guideline on acute pyelonephritis 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 NICE guideline on prostatitis (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.

For more information see choice of antibiotic in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Rationale: antibiotic course length for upper UTIs

- 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.
- Based on evidence, the committee agreed that a short course of antibiotics was generally as effective as a long course of antibiotics for acute pyelonephritis, but the definition of short and long course differed depending on the clinical trial definition and the antibiotic used.
- In line with the NICE recommendations on antimicrobial stewardship and Public Health England's Start smart – then focus, the committee agreed that the use of intravenous antibiotics should be reviewed by 48 hours (taking into account the person's response to treatment and susceptibility results from urine culture) and switched to oral treatment where possible.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that, for oral treatment, a 7-day course of ciprofloxacin was sufficient to treat acute pyelonephritis in non-pregnant women and men. However, because there was no evidence for 7-day courses of cefalexin or co-amoxiclax, a range of 7 to 10 days was recommended for these antibiotics. For trimethoprim, a 14-day course was recommended because there was no evidence for course lengths shorter than 14 days.
- For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 7 days.

Pregnant women with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that, for oral treatment, a 7- to 10-day course of cefalexin was required to treat acute pyelonephritis in pregnant women. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 7 days.

Children and young people with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that a 7- to 10-day course of oral antibiotics was required to treat acute pyelonephritis in children and young people. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 10 days.

For more information see antibiotic course length in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing.

Rationale: self-care for recurrent UTIs

- Based on their experience, and the need to minimise inappropriate use of antibiotics, the committee agreed that people should be given advice about behavioural and personal hygiene measures to reduce the risk of UTI, such as:
    - drinking enough fluids to avoid dehydration
    - not delaying habitual and post-coital urination
    - wiping from front to back after defaecation
    - not douching or wearing occlusive underwear.

Probiotics (lactobacillus)

- The committee discussed the evidence for the probiotic lactobacillus. While there was some evidence to support the use of 'effective strains', there was no information on which lactobacillus products were included in this analysis. They also noted the high drop-out rate in the study.
- Based on evidence, the committee agreed that people should be told that there is inconclusive evidence to recommend the use of lactobacillus to prevent recurrent UTIs.

Cranberry products

- The committee recognised that cranberry products are used widely and discussed the very low quality evidence showing some benefit for reducing the risk of UTIs, specifically in non-pregnant women, and children and young people. They were also aware that there was no evidence to suggest benefit in older women. The committee also noted the conflicting evidence for cranberry products in reducing the risk of antimicrobial resistance.

- Taking account of the limitations of the evidence, and the need to minimise antimicrobial resistance, the committee agreed that some women who are not pregnant and some children and young people under 16 may wish to try cranberry products as a self-care treatment. However, due to safety concerns with delayed treatment, particularly in children and young people, the committee agreed that cranberry products should only be considered in this population following advice from a paediatric specialist.
- The committee recognised that there was some evidence to suggest that cranberry juice was not significantly better than placebo in non-pregnant women, while cranberry capsules showed a significant benefit. However, due to significant limitations in the evidence the committee was not able to recommend a specific cranberry product.
- The committee discussed the sugar content of cranberry products, and based on their experience, agreed that people should be advised to take account of their daily sugar intake if using cranberry products.

D-mannose

- The committee was aware of the mechanism of action of D-mannose, which is also in cranberry products.
- The committee noted evidence suggesting that D-mannose was effective in reducing the risk of recurrent UTI in non-pregnant women, and noted the low NNT of 3 (range 2 to 3) over 6 months, compared with no treatment. However, this was based on 1 small RCT. The committee agreed to make a recommendation that some women who are not pregnant may wish to try D-mannose, as a self-care treatment, noting the sugar content of this product which should be considered.

For more information see self-care in the NICE guideline on urinary tract infection (recurrent): antimicrobial prescribing.

Rationale: antibiotic route of administration for upper UTIs

- Based on evidence, the committee agreed that, overall, oral antibiotics were as effective as other routes of administration for treating acute pyelonephritis in adults and children.
- The committee agreed, based on evidence and experience, that oral antibiotics should be given first line when people can take oral medicines and the severity of their condition does not require intravenous antibiotics.
- The committee agreed, based on evidence and experience, that intravenous antibiotics can be used for people who are unable to take oral antibiotics due to vomiting, or are more severely unwell, in line with Public Health England's Start Smart Then Focus.

For more information see antibiotic route of administration in the NICE guideline on pyelonephritis (acute): antimicrobial prescribing.

Rationale: antibiotic course length for lower UTIs

- 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.

For more information see antibiotic course length in the NICE guideline on urinary tract infection (lower): antimicrobial prescribing.

Rationale: antibiotic prophylaxis for recurrent UTIs

People aged 16 years and over with recurrent UTI

- Based on evidence and their experience, the committee agreed that antibiotic prophylaxis was effective in reducing the risk of recurrent UTI in non-pregnant women, although this benefit was not seen after the treatment is stopped. They noted the low NNTs for recurrent infection compared with placebo (NNT 2 [range 2 to 3]). However, they also recognised the increased risk of harms with antibiotic prophylaxis compared with placebo.
- Based on evidence, the committee agreed that antibiotic prophylaxis was also effective in a mixed population of people with recurrent UTI, including pre- and postmenopausal women, men and children (NNT 3 [3 to 4]). However, interpretation of the evidence was more difficult due to variations in the populations studied and antibiotic choice, dosage and duration.
- The committee discussed the evidence specifically in pregnant women, which found that antibiotic prophylaxis was effective in reducing the risk of recurrent asymptomatic bacteriuria in pregnant women (NNT 4 [range 3 to 13]). However, they recognised that the study had a number of limitations. The study was small and not powered to show any benefit in preterm births. The population was pregnant women who were admitted to hospital with acute pyelonephritis. The committee noted that nitrofurantoin is not an appropriate choice of antibiotic to show benefit in this population. They were also aware that UTI has been associated with developmental delay or cerebral palsy in the infant, and fetal death.
- Taking account of the benefits and harms of antibiotic prophylaxis and the need to minimise antimicrobial resistance, the committee agreed that antibiotic prophylaxis could be considered in people aged 16 years and over with recurrent UTI, but only after other management options had been unsuccessful (behavioural and personal hygiene measures, managing any triggers and using non-antimicrobial treatments), if appropriate.
- The committee recognised the importance of reviewing antibiotic prophylaxis, and considered that up to every 6 months was reasonable based on possible adverse effects of antibiotics, the risk of resistance with long-term antibiotics, the possible need for any further investigations if recurrence of UTIs continues, and to allow time to assess treatment success. People should also know to seek medical help if they experience symptoms of an acute infection despite taking prophylaxis.

- The committee discussed the importance of the review and were aware of other conditions where a specific date is included on the prescription to prompt review within 6 months.
- To reduce the risk of antimicrobial resistance, the committee agreed that at each review women should be reminded about self-care, and consideration should be given to either stopping, continuing or changing antibiotic prophylaxis (for example, from single-dose to daily prophylaxis). However the committee was not able to make specific recommendations about when to stop, continue or change antibiotic prophylaxis as it will depend on the circumstances of an individual person.
- Based on evidence that suggests antibiotic prophylaxis does not continue to be effective after stopping treatment, the committee agreed that if antibiotic prophylaxis was stopped, women should be able to access treatment rapidly if they have symptoms of an acute UTI.
- The committee recognised the limitations of the evidence on antibiotic prophylaxis in pregnant women and men, and the lack of evidence to support the use of non-antimicrobial treatments. Therefore, the committee agreed that it was appropriate to refer all pregnant women to an obstetrician if recurrent UTI is diagnosed during pregnancy. They also agreed that most men with recurrent UTI should be referred for further specialist urology investigation and management, taking an individualised approach that takes account of multimorbidity. The committee agreed that any decision to prescribe antibiotic prophylaxis in pregnant women or men should be under specialist advice.
- The committee also recognised the higher risks associated with recurrent upper UTIs (pyelonephritis), and agreed that it was appropriate to refer these people for further specialist investigation and management.
- The committee agreed that further consideration should be made for women with recurrent lower UTI if the underlying cause of recurrence was unknown or required further investigation. However, due to resource implications and the lower risk of complications for this population, the committee agreed that specialist advice should be sought, rather than specialist referral.
- The committee was aware of the recommendation in the NICE guideline on suspected cancer: recognition and referral, which states that a non-urgent referral for bladder cancer should be considered for people over 60 with recurrent unexplained UTI.
- The committee also recognised the equality considerations for managing recurrent UTI in transgender people, due to anatomical differences between women and men.

Children and young people under 16 years with recurrent UTI

- The committee was aware that the NICE guideline on urinary tract infection in under 16s makes recommendations on referring children and young people with recurrent UTI to a paediatric specialist for assessment and investigations.
- Based on evidence, the committee noted that antibiotic prophylaxis does not appear to be effective in reducing the risk of recurrent UTI in children. However, there was considerable uncertainty in the evidence (all very low quality).
- Based on their experience, the committee agreed that most cases of recurrent UTI in children and young people are due to a functional or structural abnormality of the urinary

- tract.
- Taking account of the uncertainty in the evidence and the need to minimise antimicrobial resistance from long-term antibiotic use, the committee agreed that antibiotic prophylaxis could be considered in children and young people under 16 years, but only under specialist advice when other management options have been unsuccessful. This would be an individualised decision following an assessment of underlying causes, taking into account the severity and frequency of previous symptoms and the risk of developing complications.
- The committee recognised the importance of reviewing antibiotic prophylaxis, and considered that every 6 months was reasonable. They agreed that the same principles for the review in adults apply to children and young people.

For more information see antibiotic prophylaxis in the NICE guideline on urinary tract infection (recurrent): antimicrobial prescribing.

Antibiotics for pregnant women aged 12 years and over

When prescribing an antibiotic for acute pyelonephritis, take account of local antimicrobial resistance data and follow the table below for pregnant women aged 12 years and over.

Antibiotic[1]	Dosage and course length
First-choice oral antibiotic[2]	
Cefalexin	500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell)[2,3]	
Cefuroxime	750 mg to 1.5 g three or four times a day
Second-choice antibiotics or combining antibiotics if susceptibility or sepsis a concern	
Consult local microbiologist	

[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics.

[2] Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

[3] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Antibiotics for children and young people under 16 years

When prescribing an antibiotic for acute pyelonephritis, take account of local antimicrobial resistance data and follow the table below 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 recommendations on fever in under 5s.	
Children aged 3 months and over	
First-choice oral antibiotic[3]	
Cefalexin	3 to 11 months, 12.5 mg/kg or 125 mg twice a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 1 to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections)

	5 to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 12 to 15 years, 500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days
Co-amoxiclav (only if culture results available and susceptible)	3 to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 1 to 5 years, 0.25 ml/kg of 125/31 suspension or 5 ml of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 6 to 11 years, 0.15 ml/kg of 250/62 suspension or 5 ml of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 12 to 15 years, 250/125 mg or 500/125 mg three times a day for 7 to 10 days
First-choice intravenous antibiotics (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if susceptibility or sepsis a concern[3,4,5]	
Co-amoxiclav (only in combination or if culture results available and susceptible)	3 months to 15 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)
Cefuroxime	3 months to 15 years, 20 mg/kg three times a day (maximum 750 mg per dose), increased to 50 to 60 mg/kg three or four times a day (maximum 1.5 g per dose) for severe infections
Ceftriaxone	3 months to 11 years (up to 50 kg), 50 to 80 mg/kg once a day

	(maximum 4 g per day) 9 to 11 years (50 kg and above), 1 to 2 g once a day 12 to 15 years, 1 to 2 g once a day
Gentamicin	Initially 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration[6]
Amikacin	Initially 15 mg/kg once a day, subsequent doses adjusted according to serum amikacin concentration[6]
Second-choice intravenous antibiotic	
Consult local microbiologist	

[1] See BNF for children (BNFC) for appropriate use and dosing in specific populations, for example, hepatic and renal impairment, and administering intravenous antibiotics. See the table on choice of antibiotic for pregnant women aged 12 years and over with acute pyelonephritis [See page 34] if a young woman is pregnant.

[2] The 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.

[3] Check 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.

[4] Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total of 10 days.

[5] If intravenous treatment is not possible, consider intramuscular treatment if suitable.

[6] Therapeutic drug monitoring and assessment of renal function is required (BNFC, August 2018).

Rationale: choice of antibiotic prophylaxis for recurrent UTIs

- Based on evidence of no major differences in clinical effectiveness between classes of antibiotics, the committee agreed that the choice of antibiotic prophylaxis 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 for UTI, should be checked and antibiotics chosen accordingly.
- Based on their experience and resistance data, the committee agreed that a different antibiotic should be selected for antibiotic prophylaxis if an acute UTI is being treated. They also recognised that rotational use of antibiotics may be needed, based on local policies.
- The committee discussed that, if antibiotic prophylaxis is needed to prevent 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*. Broad-spectrum antibiotics need to be reserved for second-choice treatment of non-life-threatening infections when narrow-spectrum antibiotics are ineffective.
- Based on evidence, their experience and resistance data, the committee agreed to recommend **trimethoprim** or **nitrofurantoin** (based on culture and susceptibility results) as first-choice antibiotics for prophylaxis. These antibiotics have less effect on the normal intestinal microflora in gastrointestinal tract, which is particularly improrant when continuous antibiotic prophylaxis is used.
    - 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 and in older people in residential facilities. Trimethoprim is contraindicated in pregnant women.
    - Nitrofurantoin is not recommended for people with an eGFR <45 ml/minute. With long-term use, there is a lower risk of resistance of nitrofurantoin compared with trimethoprim, but this needs to be balanced against the increased harms, such as pulmonary fibrosis.
    - 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, their experience and resistance data, the committee agreed to recommend **cefalexin** or **amoxicillin** (based on culture and susceptibility results) as second-choice antibiotics for prophylaxis.
  - Amoxicillin and cefalexin are broad spectrum antibiotics that have a similar spectrum of activity and can be used if bacteria are susceptible.
- Based on evidence that methenamine hippurate was less effective than antibiotic prophylaxis with nitrofurantoin, the committee was not able to make a recommendation on its use. They were also aware that methenamine hippurate is a medicine that is considered less suitable for prescribing (BNF, August 2018).

For more information see choice of antibiotic prophylaxis in the NICE guideline on urinary tract infection (recurrent): antimicrobial prescribing.

Antibiotics for pregnant women aged 12 years and over

When prescribing antibiotic treatment for lower UTI, take account of local antimicrobial resistance data and follow the table below for pregnant women aged 12 years and over.

Antibiotic[1]	Dosage and course length[2]
Treatment of lower UTI	
First-choice[3]	
Nitrofurantoin (avoid at term) – if eGFR ≥45 ml/minute[4,5]	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)[3,6]	
Amoxicillin (only if culture results 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, choose antibiotics based on culture and susceptibility results
Treatment of asymptomatic bacteriuria	
Choose from nitrofurantoin[4,5], amoxicillin or cefalexin based on recent culture and susceptibility results	

[1] See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment.

[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] Avoid at term in pregnancy; may produce neonatal haemolysis (BNF, August 2018).

[5] May be used with caution if eGFR 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).

[6] If there are symptoms of 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), see antibiotic treatment in the NICE recommendations on acute pyelonephritis.

Rationale: antibiotic dosing and course length for recurrent UTIs

- Based on evidence, the committee was aware that a range of doses and course lengths were used for daily antibiotic prophylaxis. The committee agreed that usual BNF doses for daily prophylaxis should be used. The duration of treatment needs to be determined on an

- individual basis with a review of treatment success within 6 months, to include discussion of a trial of stopping antibiotic prophylaxis as appropriate.
- The committee discussed the evidence for using single-dose antibiotic prophylaxis (including post-coital single-dose antibiotics) in non-pregnant women. The committee agreed that the single dose used when exposed to an identifiable trigger would be the same as a single treatment dose for a UTI.
- Based on evidence, their experience and antimicrobial resistance data, the committee agreed that single-dose prophylaxis was as effective as continuous prophylaxis, with fewer adverse effects in non-pregnant women with an identifiable trigger, and should be considered as the first option for antibiotic prophylaxis in this group of women. Prophylaxis needs to be tailored to an individual woman's personal triggers, and advice given about how to use the antibiotic. Antibiotics for single-dose prophylaxis would be kept at home to avoid unnecessary GP and pharmacy visits.
- No evidence from systematic reviews and RCTs was identified for using a course of antibiotics to keep at home for treating an acute UTI in people with recurrent UTIs (also known as stand-by antibiotics). The use of stand-by antibiotics could potentially lead to inappropriate antibiotic overuse in the absence of medical supervision, which would not reflect the principles of antimicrobial stewardship. Therefore, while the committee recognised that they may have a role in some specialist cases, they were not able to make a recommendation on their use.

For more information see antibiotic dosing and course length in the NICE guideline on urinary tract infection (recurrent): antimicrobial prescribing.

Antibiotics for children and young people under 16 years

When prescribing antibiotic treatment for lower UTI, take account of local antimicrobial resistance data and follow the table below 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 recommendations on fever in under 5s.	
Children aged 3 months and over	

First-choice[3,4]	
Trimethoprim – if low risk of resistance[5]	3 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 6 to 11 years, 4 mg/kg (maximum 200 mg per dose) or 100 mg twice a day for 3 days 12 to 15 years, 200 mg twice a day for 3 days
Nitrofurantoin – if eGFR ≥45 ml/ minute[6]	3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 to 15 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)[3,4,7]	
Nitrofurantoin – if eGFR ≥45 ml/ minute[6] and not used as first-choice	3 months to 11 years, 750 micrograms/kg four times a day for 3 days 12 to 15 years, 50 mg four times a day or 100 mg modified-release twice 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 15 years, 500 mg three times 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 15 years, 500 mg twice a day for 3 days

[1] See BNF for children (BNFC) for appropriate use and dosing in specific populations, for example, hepatic and renal impairment. See the table on choice of antibiotic for pregnant women aged 12 years and over [See page 40] if the young woman is pregnant.

[2] The 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.

[3] Check 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.

[4] If 2 or more antibiotics are appropriate, choose the antibiotic with the lowest acquisition cost. Some children may also be able to take a tablet or part-tablet, rather than a liquid formulation, if the dose is appropriate.

[5] A lower risk of resistance may be more likely if not 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 suggest resistance is low. A higher risk of resistance may be more likely with recent use and in older people in residential facilities.

[6] May be used with caution if eGFR 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).

[7] If there are symptoms of 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), see the recommendations on antibiotic treatment [See page 12] in the NICE guidance on acute pyelonephritis.

Atypical UTI

Includes seriously ill (for more information refer to NICE's recommendations on fever in under 5s), poor urine flow, abdominal or bladder mass, raised creatinine, septicaemia, failure to respond to treatment with suitable antibiotics within 48 hours, infection with non-*E. coli* organisms.

asymptomatic bacteriuria

the presence of significant levels of bacteria in the urine with no symptoms of UTI

Back-up antibiotic prescription

prescription given in a way to delay the use of an antibiotic, and with advice to only use it if symptoms worsen or don't improve within a specified time; the prescription may be given during the consultation (which may be a post-dated prescription) or left at an agreed location for collection at a later date

bacteriuria

bacteria in the urine with or without urinary tract infection

BNF

British natural formulary

BNFC

British natural formulary for children

DMSA

dimercaptosuccinic acid

eGFR

estimated glomerular filtration rate

HRT

hormone replacement therapy

MCUG

micturating cystourethrogram

NSAID

non-steroidal anti-inflammatory drug

pyuria

white cells in the urine

Recurrent UTI

2 or more episodes of UTI with acute pyelonephritis/upper urinary tract infection, or 1 episode of UTI with acute pyelonephritis/upper urinary tract infection plus 1 or more episode of UTI with cystitis/lower urinary tract infection, or 3 or more episodes of UTI with cystitis/lower urinary tract infection.

SPA

suprapubic aspiration

trigger

some people (mainly women) may be able to identify 1 or more triggers (for example, sexual intercourse) that often brings on a UTI; these triggers may vary for different people

UTI

urinary tract infection

VUR

vesicoureteric reflux

Sources

Urinary tract infection (catheter-associated): antimicrobial prescribing (2018) NICE guideline NG113

Urinary tract infection (recurrent): antimicrobial prescribing (2018) NICE guideline NG112

Pyelonephritis (acute): antimicrobial prescribing (2018) NICE guideline NG111

Urinary tract infection (lower): antimicrobial prescribing (2018) NICE guideline NG109

Urinary tract infection in under 16s: diagnosis and management (2007 updated 2018) NICE guideline CG54

Your responsibility

Guidelines

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.

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 assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so 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.

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

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to

make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

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