Urinary tract infection (catheter-associated): antimicrobial prescribing

NICE guideline

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Your responsibility

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

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

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.

Contents

Overview

This guideline sets out an antimicrobial prescribing strategy for catheter-associated urinary tract infection in children, young people and adults. It aims to optimise antibiotic use and reduce antibiotic resistance.

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

NICE has also produced guidelines on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use and healthcare-associated infections: prevention and control in primary and community care.

Who is it for?

- Health professionals

- People with catheter-associated urinary tract infection, their families and carers

Recommendations

1.1 Managing catheter-associated urinary tract infection

1.1.1 Be aware that:

- a catheter-associated urinary tract infection (UTI) 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[1].

1.1.2 Give advice about managing symptoms with self-care (see the recommendations on self-care) to all people with catheter-associated UTI.

Treatment

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

1.1.4 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 (in line with the NICE guideline on 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.

1.1.5 Send the urine sample for culture and susceptibility testing, noting a

suspected catheter-associated infection and any antibiotic prescribed.

1.1.6   Offer an antibiotic (see the recommendations on choice of antibiotic) 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.

1.1.7   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.

Advice when an antibiotic prescription is given

1.1.8   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.

Reassessment

1.1.9   Reassess people with catheter-associated UTI 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.

Referral and seeking specialist advice

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

1.1.11 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.

See the evidence and committee discussion on antibiotics for managing catheter-associated UTI.

1.2 Self-care

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

1.2.2 Advise people with catheter-associated UTI about drinking enough fluids

to avoid dehydration.

See the evidence and committee discussion on self-care.

1.3 Choice of antibiotic

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

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

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

- follow table 3 for children and young people under 16 years.

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

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

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

Antibiotic[1]	Dosage and course length
First-choiceoral antibiotics if no upper UTI symptoms[2]	
Nitrofurantoin – if eGFR ≥45 ml/minute[3,4]	100 mg modified-release twice a day (or if unavailable 50 mg four times 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 antibiotics 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 antibiotics (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 antibiotics	
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] See MHRA advice for restrictions and precautions for using fluoroquinolone antibiotics due to very rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems. Warnings include: stopping treatment at first signs of a serious adverse reaction (such as tendonitis), prescribing with special caution in people over 60 years and avoiding coadministration with a corticosteroid (March 2019).

[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).

Abbreviations: BNF, British national formulary; eGFR, estimated glomerular filtration rate; UTI, urinary tract infection.

Table 2 Antibiotics for pregnant women aged 12 years and over

Antibiotic[1]	Dose 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.	

Table 3 Antibiotics for children and young people under 16 years

Antibiotic[1]	Dosage and course length[2]
Children under 3 months	
Refer to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s.	
Children aged 3 months and over	
First-choice 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 antibiotics (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 7 mg/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 table 2 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).

See the evidence and committee discussion on antibiotics for managing catheter-associated UTI.

1.4   Preventing catheter-associated urinary tract infections

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

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

See the evidence and committee discussion on antibiotic prophylaxis for preventing catheter-associated UTI and the NICE guideline on healthcare-associated infections.

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[1] See the NICE guideline on lower UTI: antimicrobial prescribing for managing asymptomatic bacteriuria in pregnant women.

Terms used in this guideline

Asymptomatic bacteriuria

The presence of significant levels of bacteria in the urine with no symptoms of urinary tract infection (UTI).

Catheter-associated urinary tract infection

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]).

Summary of the evidence

Self-care

- One randomised controlled trial (RCT; Gunnarsson et al. 2017) in adult females (n=92) who had a hip fracture and a perioperative urinary catheter with planned removal at 48 hours, compared cranberry juice concentrate (capsules) with placebo for the prevention of postoperative urinary tract infection (UTI). There were no significant differences in positive urine cultures (>10^4 colony-forming units per ml) at either 5 or 14 days after surgery (low quality evidence).

- No systematic reviews or RCTs of any other non-antimicrobial treatments were identified that met the inclusion criteria.

Committee discussion on self-care

- 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.

Antibiotics for managing catheter-associated UTI

- In most cases, managing symptomatic catheter-associated UTI will require antibiotics.

- Gram-negative bacteria, particularly *Escherichia coli (E. coli)*, are the most common

causative pathogens in UTIs. However, catheter-associated UTI can be associated with more than 1 bacterial species and is often caused by bacteria that are resistant to antibiotics (European Association of Urology guidelines on urological infections 2017).

- UTI is the most common healthcare-acquired infection, accounting for 19% of all healthcare-associated infections, with around half of these infections due to an indwelling urinary catheter (Health Protection Agency 2012). In some people, catheter-associated UTI can lead to a more serious systemic infection (urosepsis).

Efficacy of antibiotics

- One RCT (Leone et al. 2007) of adults with asymptomatic bacteriuria admitted to an intensive care unit with a short-term catheter found that a short course (3 days) of antibiotics and catheter change did not significantly reduce the proportion of patients with urosepsis (p=1, low quality evidence), or bacteraemia or severe sepsis (p>0.05, low quality evidence), compared with no antibiotics and no catheter change. Short-course antibiotics and catheter change significantly reduced the proportion of positive urine cultures (>10^5 colony-forming units/ml) at 7 days (30% versus 70%, number needed to treat [NNT] 3 [range 2 to 6], moderate quality evidence) but not at 15 days (very low quality evidence).

- One RCT (Darouiche et al. 2014) of hospitalised adults with a long-term catheter for spinal cord injury and catheter-associated UTI found that a shorter course (5 days) of antibiotics plus a catheter change was not significantly different to 10 days of antibiotics and no catheter change for clinical cure at the end of therapy (p<0.001 for non-inferiority, moderate quality evidence). However, for other outcomes (microbiological response and resolution of pyuria at the end of therapy), the short course and catheter change was not as effective as the long course and no catheter change. There were also significantly more episodes of recurrent UTI in the short course plus catheter change group compared with the long course and no catheter change group (32.1% versus 11.1%, p=0.043; low quality evidence).

Changing the catheter before antibiotics

- One prospective open-label RCT (Raz et al. 2000) in older adults in a long-stay care facility with a long-term catheter and catheter-associated UTI compared catheter change before antibiotics with no catheter change before antibiotics. Antibiotic therapy was ciprofloxacin or ofloxacin, initially intravenously then orally for 14 days.

There was a significant difference in cure or improvement, favouring catheter change at 72 hours (92.6% versus 40.7%, NNT 2 [range 2 to 4]; moderate quality evidence) and 28 days (88.9% versus 59.3%, NNT 4 [range 2 to 14]; low quality evidence), but not at 7 days. There was no significant difference in recurrence or treatment failure at either 7 or 28 days, but mortality was significantly lower in the catheter change group (0% versus 7.4% [urosepsis in 1 person on day 2 and 1 person on day 3]; very low quality evidence).

Safety of antibiotics

- The RCT on duration of antibiotics (and catheter change) for people with spinal cord injury and catheter-associated UTI (Darouiche et al. 2014) found no significant difference in adverse events between the no catheter change and 10 days of antibiotics group, and the catheter change and 5 days of antibiotics group (40.7% versus 64.3%%; low quality evidence).

- Antibiotic-associated diarrhoea occurs in 2 to 25% of people taking antibiotics, depending on the antibiotic used (NICE clinical knowledge summary on diarrhoea – antibiotic associated).

- About 10% of the general population claim to have a penicillin allergy; this is often because of a skin rash that occurred while taking a course of penicillin as a child. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the NICE guideline on drug allergy for more information.

- People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (BNF, August 2018).

- Nitrofurantoin should be used with caution in those with renal impairment. It should be avoided at term in pregnancy because it may produce neonatal haemolysis. Adults (especially older adults) and children on long-term therapy should be monitored for liver function and pulmonary symptoms (BNF, August 2018).

- Trimethoprim has a teratogenic risk in the first trimester of pregnancy (folate antagonist; BNF, August 2018). The manufacturers advise that it is contraindicated in pregnancy (trimethoprim summary of product characteristics).

- Fluoroquinolones are generally not recommended in children or young people who are still growing (BNF, August 2018). The manufacturers advise to avoid in pregnancy (ciprofloxacin summary of product characteristics). Tendon damage (including rupture)

has been reported rarely in people receiving fluoroquinolones (BNF, August 2018), and the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (press release October 2018) has recommended restricting the use of these antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. Fluoroquinolones remain an option in catheter-associated UTI with upper UTI symptoms, which is a severe infection.

- Aminoglycosides doses are based on weight and renal function and whenever possible treatment should not exceed 7 days (BNF, August 2018).

- See the summaries of product characteristics for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on 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 either the modified-release preparation of nitrofurantoin or the immediate-release preparation. However, because of its twice-daily dosing and, in their experience, better tolerability the committee was keen to point out that the modified-release preparation was preferred unless it was unavailable. The committee also discussed that, in their experience, immediate-release preparations containing nitrofurantoin in a macrocrystalline form may be better tolerated than those containing nitrofurantoin in a microcrystalline form.

— Trimethoprim 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: antimicrobial prescribing).
>
> - For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible.

Antibiotic prophylaxis for preventing catheter-associated UTI

Antibiotic prophylaxis for people with a long-term (indwelling or intermittent) catheter

- One systematic review (Niël-Weise et al. 2012) found that antibiotic prophylaxis for adults using intermittent self-catheterisation was associated with fewer episodes of either asymptomatic or symptomatic bacteriuria (incidence density rate [IDR] 0.61, 95% confidence interval [CI] 0.44 to 0.87, with significant heterogeneity, using a fixed-effect model; low quality evidence) compared with antibiotics only when microbiologically indicated. Another RCT (not included in the systematic review by Niël-Weise et al. 2012) also favoured antibiotic prophylaxis for a similar population (incidence rate ratio [IRR] 0.34, 95% CI 0.156 to 0.74; moderate quality evidence). However, 1 additional RCT included in the systematic review found no significant benefit of antibiotic prophylaxis compared with antibiotics when microbiologically indicated for the number of episodes of bacteriuria.

- Two RCTs in the systematic review (Niël-Weise et al. 2012) showed inconsistent results for antibiotic prophylaxis for symptomatic bacteriuria in adults using intermittent catheterisation compared with antibiotics when microbiologically indicated. In 1 RCT, fewer participants had at least 1 episode of symptomatic bacteriuria with antibiotic prophylaxis compared with antibiotics when microbiologically indicated (6.1% versus 31.7%, NNT 4 [range 3 to 8]; moderate quality

evidence). In the other RCT, there was no significant difference in the rate of symptomatic bacteriuria between groups.

- One RCT in the systematic review (Niël-Weise et al. 2012) compared antibiotic prophylaxis with antibiotics when clinically indicated in older adults in nursing homes with indwelling urinary catheters. There were no statistically significant differences between groups for episodes of symptomatic UTI, rates of visual encrustation, or catheter obstructions (very low to low quality evidence). The prophylaxis group had a higher number of participants with improved general condition (52.2% versus 4.3%, NNT 3 [range 2 to 4]; very low quality evidence).

- Evidence from 2 RCTs in the systematic review (Niël-Weise et al. 2012) included children with neurogenic bladder using intermittent catheterisation and found no significant difference between antibiotic prophylaxis and antibiotics only when clinically indicated for symptomatic UTI.

- Evidence from 1 RCT in the systematic review (Niël-Weise et al. 2012) included children with spina bifida using intermittent catheterisation and found no significant difference in the risk of febrile symptomatic UTI when antibiotic prophylaxis was discontinued at 6 months compared with continued prophylaxis. However, there were significantly fewer afebrile symptomatic UTIs in the group continuing antibiotic prophylaxis (IDR 0.69, 95% CI 0.55 to 0.87; low quality evidence).

- The systematic review (Niël-Weise et al. 2012) found no significant difference in adverse events between antibiotic prophylaxis and antibiotics when microbiologically indicated in adults using intermittent catheterisation. There was also no significant difference between antibiotic prophylaxis and antibiotics when clinically indicated in the rates of adverse events in older people in nursing homes (low quality evidence).

- One open-label RCT (Fisher et al. 2018) in adults using clean intermittent self-catheterisation who had recurrent UTIs found antibiotic prophylaxis reduced symptomatic UTIs requiring antibiotic treatment by 48% compared with no prophylaxis at 6 months' follow-up (IRR 0.52, 95% CI 0.44 to 0.61; moderate quality evidence). Prophylaxis also reduced the incidence of microbiologically confirmed symptomatic UTI requiring antibiotic treatment at 6 months' follow-up compared with no prophylaxis (IRR 0.49, 95% CI 0.39 to 0.6; moderate quality evidence). Prophylaxis did not reduce the incidence of febrile UTI or asymptomatic bacteriuria.

- The RCT (Fisher et al. 2018) found that antibiotic prophylaxis increased adverse events, mainly nausea, diarrhoea and Candida infection, compared with no prophylaxis

(9.4% versus 2.0%, number needed to harm 16 [95% CI 9 to 40]; low quality evidence).

- The RCT (Fisher et al. 2018) found that antibiotic prophylaxis increased antibiotic resistance to nitrofurantoin, trimethoprim and co-trimoxazole compared with no prophylaxis, but not to amoxicillin, cefalexin, ciprofloxacin, co-amoxiclav and mecillinam. There was an increasing trend towards antibiotic resistance at 12 months compared with baseline for amoxicillin, cefalexin, co-trimoxazole and trimethoprim, but not for ciprofloxacin, co-amoxiclav and nitrofurantoin. There was no increase in resistance over 12 months to any antibiotic in the 'no prophylaxis' group or in perianal swabs for *E. coli* for either the prophylaxis or 'no prophylaxis' groups.

Antibiotic prophylaxis before or during short-term catheterisation in hospital

- One systematic review (Lusardi et al. 2013) compared antibiotic prophylaxis with no prophylaxis in hospitalised adults with a short-term catheter. A meta-analysis of 3 RCTs of surgical patients showed a significant reduction in asymptomatic bacteriuria with antibiotics (8.2% versus 31.3%, NNT 5 [range 4 to 7]; moderate quality evidence). Two further RCTs of non-surgical patients could not be pooled for the outcome of asymptomatic bacteriuria because of heterogeneity. One study showed no reduction with antibiotics (low quality evidence) and the other a significant reduction with antibiotics (10% versus 53.7%, NNT 3 [range 2 to 4], moderate quality evidence). One RCT of surgical patients found significantly fewer cases of symptomatic bacteriuria with antibiotic prophylaxis (6.3% versus 31%, NNT 4 [range 3 to 11]).

- The systematic review (Lusardi et al. 2013) also found that antibiotic prophylaxis was associated with a significantly lower risk of pyuria (presence of white cells in the urine) in surgical patients (7.5% versus 32.9%, NNT 4 [range 3 to 7]; moderate quality evidence) and significantly reduced febrile (high temperature) morbidity (12.5% versus 23.2%, NNT 10 [range 6 to 52]; very low quality evidence).

- Evidence from 1 additional RCT (Dieter et al. 2014) found the risk of requiring antibiotic treatment for a UTI within 3 weeks of urinary catheterisation for pelvic organ prolapse or urinary incontinence surgery was not significantly associated with prophylactic use of nitrofurantoin compared with placebo (moderate quality evidence).

- The systematic review (Lusardi et al. 2013) found no significant difference between levofloxacin and ciprofloxacin (very low quality evidence) or between 2 different doses of ciprofloxacin (250 mg versus 1,000 mg daily; very low quality evidence) for

asymptomatic bacteriuria at follow-up.

- Evidence from 1 RCT in the systematic review (Lusardi et al. 2013) found that a single antibiotic dose at the time of catheterisation only compared with antibiotic prophylaxis throughout the entire period of catheterisation was associated with significantly fewer cases of bacteriuria (12.5% versus 42.9%, NNT 4 [range 2 to 13]; low quality evidence).

- The systematic review (Lusardi et al. 2013) included 3 RCTs that reported adverse reactions to antibiotics. One RCT reported 23 adverse reactions; none were judged to be treatment related and there were no serious adverse events. A second RCT reported no serious adverse reactions to co-trimoxazole. The third RCT reported that 3 patients taking ciprofloxacin had moderate gastrointestinal symptoms on the second day of prophylaxis and the antibiotic was discontinued (very low quality evidence).

Antibiotic prophylaxis at the time of short-term catheter removal in hospital

- Evidence from a systematic review (Marschall et al. 2013) in hospitalised patients found that antibiotic prophylaxis at the time of short-term catheter removal was associated with a significantly lower risk of symptomatic UTI at 2 to 42 days' follow-up compared with placebo or other control intervention (4.7% versus 10.5%, NNT 18 [range 12 to 31]).

- In subgroup analyses, the effect was maintained for surgical patients (4.8% versus 10.3%, risk ratio [RR] 0.45, 95% CI 0.29 to 0.59; moderate quality evidence) but not for mixed hospital populations. Additional subgroup analysis of the surgical studies found significant benefit for people undergoing prostate surgery (3.57% versus 8.18%, RR 0.41, 95% CI 0.22 to 0.79; low quality evidence) but not for those undergoing other surgery (6.1% versus 14.1%, RR 0.45, 95% CI 0.18 to 1.14; low quality evidence).

- In further subgroup analyses of surgical studies without the studies of prostate surgery, there was a significant benefit of antibiotic prophylaxis with catheter duration longer than 5 days (3.8% versus 16.7%, RR 0.25, 95% CI 0.10 to 0.59; high quality evidence) but not with catheter duration less than 5 days (3.22% versus 12.3%, RR 0.41, 95% CI 0.02 to 10.96; very low quality evidence).

Antibiotic prophylaxis during short-term catheterisation for

urodynamic procedures

- A systematic review (Foon et al. 2012) in people who had short-term catheterisation during urodynamic studies found that prophylactic antibiotics did not significantly reduce episodes of symptomatic UTI (low quality evidence) but did significantly reduce bacteriuria (4.1% versus 12.5%, NNT 12 [range 9 to 21]; moderate quality evidence) compared with placebo or no treatment. In a single study of people with spinal cord injury, antibiotic prophylaxis was not significantly different to placebo or no treatment for the outcome of bacteriuria (very low quality evidence). There was a significant reduction in the number of participants with haematuria with antibiotic prophylaxis (6.3% versus 13.7%, NNT 14 [range 8 to 89]; low quality evidence) but not fever or dysuria.

- The systematic review (Foon et al. 2012) found no significant difference in adverse events between antibiotics and placebo (very low quality evidence).

Committee discussion on antibiotic prophylaxis for 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.

Other considerations

Medicines adherence

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

No systematic reviews or randomised controlled trials (RCTs) were identified that addressed medicines adherence.

Resource implications

Antibiotic prophylaxis before or during short-term catheterisation in hospital

- One RCT included in a systematic review (Lusardi et al. 2013) of hospitalised adults with a short-term catheter compared antibiotic prophylaxis (levofloxacin or ciprofloxacin) with placebo calculated hospital stay in presurgery and postsurgery phases. There was no statistically significant difference in mean presurgical or postsurgical stay between the placebo group and either the levofloxacin or ciprofloxacin groups (low quality evidence).

- In a second included RCT comparing antibiotic prophylaxis with placebo, the mean hospital stay was significantly higher in the placebo group compared with the intervention group (8 days [±1.4 days] compared with 7 days [±1.2 days], p=0.0002; low quality evidence). Febrile morbidity and urinary tract infection (UTI) prolonged hospitalisation significantly to a mean stay of 9.2 days ([±1.6 days], p<0.05).

- In a third included RCT comparing antibiotic prophylaxis with placebo, the average hospital stay was 6 days and 5.6 days for abdominal hysterectomy, and 6.1 days and 7.6 days for vaginal hysterectomy patients, in the prophylaxis group and placebo groups respectively.

- Recommended antibiotics (nitrofurantoin, trimethoprim, penicillins, cephalosporins, fluoroquinolones and aminoglycosides) are available as generic formulations, see Drug

Tariff for costs.

Update information

Minor updates since publication

September 2019: Minor wording changes were made and a footnote was updated in table 1 to reflect new restrictions and precautions for the use of fluoroquinolone antibiotics.

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

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