Managing Common Infections

Catheter associated urinary tract infections: antimicrobial prescribing

Stakeholder comments table

08/05/2017 – 05/06/2018

ID	ORGANISATION NAME	DOCUMENT	PAGE NO.	LINE NO.	COMMENTS	DEVELOPER'S RESPONSE
1	British Infection Association	Guideline	General		The guideline includes no definition of what constitutes a 'Catheter-associated UTI'. Without such a definition the guideline would drive over-use of antibiotics for colonised rather than infected catheters. In addition without such a definition the guideline cannot be used reasonably in clinical practice as the condition referred to is unclear. It would be useful to state how a catheter associated urinary tract infection should be diagnosed i.e. based which clinical features and culture rather than by performing urinalysis on catheter urine. Dip sticking of catheter urine to 'diagnose' urinary tract infection is a significant problem nationally and drives inappropriate antibiotic usage.	Thank you for your comment. The committee have added a definition of catheter-associated UTI to the terms used in this guideline section. Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis. Providing further details on the diagnosis of catheter-associated infection is out of scope.
2	British Infection Association	Guideline	General		The antibiotic choices make no reference to local resistance rates or for come choices national data (Nottinghamshire has high co-amoxiclav resistance rates as does the recent national E coli BSI dataset) plus advises high risk antibiotics for inpatient treatment from the C difficile point of view	Thank you for your comment. The Committee has discussed your comment and has amended recommendation 1.3.1 to state that account should be taken of local resistance patterns. The committee noted that recommended broad-spectrum antibiotics, such as cephalosporins, quinolones and 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 infection 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
3	British Infection Association	Guideline	General		Treatment durations are overly long – our members would not routinely give >5 days for these except if there was evidence of an upper urinary tract infection.	Thank you for your comment. 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, This evidence base included some people with a complicated UTI, which included some people with a catheter. The duration of treatment for people with a catheter-associated UTI and upper UTI symptoms is the same as for people with acute pyelonephritis. The duration of treatment for people with a catheter-associated UTI and no upper UTI symptoms is 7 days, which is the same as for lower UTI in men and

						pregnant women. The committee agreed that 7 days rather than 3 days was required because people with a catheter are more at risk of complications and the longer course is required to ensure complete cure.
4	British Infection Association	Guideline	5	Table 1	First choice oral antibiotic if no upper UTI symptoms: Nitrofurantoin is recommended however it is not licensed for use in complicated UTI (i.e. this includes UTI associated with catheterisation regardless of whether there are upper urinary tract symptoms).	Thank you for your comment. The committee were aware that nitrofurantoin is licensed specifically for the treatment of uncomplicated lower urinary tract infections. 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.
5	British Infection Association	Guideline	5	Table 1	Trimethoprim – if low risk of resistance and not used in the past 3 months: features that imply risk of resistance need to be explicitly stated (and in line with the Public Health England guidance on 'Management and treatment of common infections')	Thank you for your comment. The committee discussed your comment and made changes to the relevant tables. The tables now include the following footnote: '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	British Infection Association	Guideline	5-6	Table 1	Second choice oral antibiotic if no upper UTI symptoms (when first choice not suitable): Neither pivmecillinam nor fosfomycin are licensed for complicated UTI (i.e. this includes UTI associated with catheterisation regardless of whether there are upper urinary tract symptoms).	Thank you for your comment. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics. The committee were aware that pivmecillinam is licensed specifically for the treatment of uncomplicated lower urinary tract infections. However, as with nitrofurantoin, they agreed that for adults with a catheter-associated UTI without upper UTI symptoms, 'lower UTI' antibiotics are an option. 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.
7	British Infection Association	Guideline	6 and 7	Table 1 and 3	First choice intravenous antibiotic (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if sepsis a concern: ceftriaxone is suitable as outpatient parenteral antibiotic therapy only (not as inpatient treatment) – this needs to be stated.	Thank you for your comment. Please note the guideline covers both primary and secondary care settings. It does not specify the care setting in which antibiotic choice is to be made in order to allow for services such as outpatient parenteral antimicrobial therapy (OPAT). The committee did not agree with the comment that ceftriaxone is not suitable for inpatient treatment. Ceftriaxone is commonly used in secondary care and has licensed indications for hospital use (such as hospital acquired pneumonia and surgical prophylaxis) where it would only be used in hospital settings.
8	British Infection Association	Guideline	6	Table 1	First choice intravenous antibiotic (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if sepsis a concern – the guidance needs to state that precise first choice stated in local antibiotic policies is ultimately determined by the local susceptibility patterns.	Thank you for your comment. The Committee has discussed your comment and has amended recommendation 1.3.1 to state that account should be taken of local resistance patterns.
9	British Infection Association	Guideline	6	Table 1	Ciprofloxacin 400 mg twice or ***three times*** a day: ciprofloxacin three times a day is not a licensed dose and is not used in this setting.	Thank you for your comment. The BNF dose indicated for urinary tract infection is 400 mg every 8–12 hours, to be given over 60 minutes. Please note that the summary of

						product characteristics does not state that this would be an unlicensed dose as it gives the dose for urinary tract infection as 400 mg twice daily to 400 mg three times a day.
10	British Infection Association	Guideline	6 and 7	Table 1, 2 and 3	Second choice intravenous antibiotic if higher risk of developing resistance – state what criteria determine whether there is a "higher risk of developing resistance".	Thank you for your comment. The committee discussed your comment and the wording in the table was changed to 'Second choice intravenous antibiotics'.
11	British Infection Association	Guideline	7	Table 3	Children aged 3 months and over First choice oral antibiotic if no upper UTI symptoms: Nitrofurantoin is not licensed for complicated UTI (i.e. this includes UTI associated with catheterisation regardless of whether there are upper urinary tract symptoms).	Thank you for your comment. The committee were aware that nitrofurantoin is licensed specifically for the treatment of uncomplicated lower urinary tract infections. 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). However, for children with a catheter-associated UTI, the committee agreed to remove nitrofurantoin from the recommended antibiotics table. This was because of its licence but also that in children with a catheter it is particularly difficult to differentiate between upper and lower UTI symptoms.
12	British Association of Urological Surgeons (BAUS)	Guideline	2	1.1.2	This recommendation may lead to clinicians' delaying antibiotics while they arrange a catheter change. This would represent a significant change to practice	Thank you for your comment. The Committee has discussed your comment and has reworded the recommendation to state 'Consider removing or, if this is not possible, 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 delay antibiotic treatment if this cannot be done straight away.'
13	Scottish Antimicrobial Prescribing Group	Visual summary	General	General	Should signs of systemic infection be included? Consider consistent reference to NEWS or a validated early warning score in the visual guidelines when assessing patients presenting with acute infection. Add information about what symptoms can indicate CaUTI e.g SAPG guidance gives a good summary. No mention of not using urinalysis in catheterised individuals. Although it is ideal to remove / change the catheter before treatment, this does not mean treatment should be delayed if this cannot be carried out immediately, as is often the case in primary care. Is there any evidence for NOT removing a catheter if in place for less than 7 days? Bacteriuria can develop as soon as 2 days post catheterisation. Applying the principles of IPC following invasive device insertion, it is possible that infection was introduced at time of insertion if all other sources of infection have been ruled out. Is removal of the catheter a 'consideration' as it currently reads, or should this be a clear direction to undertake. This is often the bit that is not done when it should in primary care so needs to be written a routine action. This statement is unclear: "Bacteriuria is more likely the longer the catheter is in place. Treatment is only needed for symptomatic UTI, and for asymptomatic bacteriuria in pregnant women (see the NICE guideline on lower UTI)" Does this refer to catheterised (as in the CAUTI pathway), un-catheterised pregnant women or both? Gentamicin and amikacin dosage should refer to local guideline rather than just giving mg/kg	Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis. Therefore, NEWS or other validated early warning scores for identifying acutely ill patients - including those with sepsis – are not referred to but the NICE guideline on sepsis is. Determining a full and accurate list of symptoms and signs predictive of systemic infection was outside the scope of the guideline and this information was not searched for. The remit of this guidance is the management of common infections not diagnosis. Providing further details on the diagnosis of catheter-associated infection is out of scope. The Committee has discussed your comment and has reworded the recommendation to state 'Consider removing or, if this is not possible, 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 delay antibiotic treatment if this cannot be done straight away.' The evidence search only found 1 RCT of catheter change for managing a UTI (Raz et al 2000), in which patients had a catheter in place for on average 31 days before infection. The recommendation about when to remove or change the catheter (if it has been in place for more than 7 days) was based on committee experience.

						The use of the word ‘consider’ reflects the strength of evidence supporting the recommendation, please see the NICE guideline manual for further detail. The Committee has discussed your comment and has reworded the recommendation to state ‘treatment is not needed for asymptomatic bacteriuria in people with a catheter (unless they are pregnant, see the NICE antimicrobial prescribing guideline on lower UTI for managing asymptomatic bacteriuria in pregnant women). The Committee has discussed your comment and has amended tables 1 and 3 to include footnotes on dose adjustment according to serum concentration of gentamicin and amikacin.
14	Scottish Antimicrobial Prescribing Group	Guideline	General	General	Catheter change – does it need to be before starting antibiotics? Current practice is to change as soon as practical when treating an infection but not to delay starting treatment until changed. Use of antibiotics for catheter change not included – should there be a statement to say not routinely required. Definition of CAUTI at start of guideline would be helpful along with signs and symptoms. Should include statement on not using urinalysis in catheterised individuals, Figures on rates of asymptomatic bacteriuria against this would be useful to back up the rationale.	Thank you for your comment. • The Committee has discussed your comment and has reworded the recommendation to state ‘Consider removing or, if this is not possible, 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 delay antibiotic treatment if this is cannot be done straight away.’ The guideline is for people with catheter associated UTI requiring treatment i.e. those who are symptomatic and does not cover routine catheter changes • The committee have added a definition of catheter-associated UTI to the terms used in this guideline section. • The remit of this guidance is the management of common infections not diagnosis. Providing further details on not using urinalysis and figures on rates of asymptomatic bacteriuria is out of scope.
15	Scottish Antimicrobial Prescribing Group	Guideline	2	1.1.1	This statement is unclear: “treatment is only needed for symptomatic catheter-associated UTI not asymptomatic bacteriuria (apart from in pregnant women with asymptomatic bacteriuria, see the NICE antimicrobial prescribing guideline on lower UTI).” Does this refer to catheterised (as in the CAUTI pathway), un-catheterised pregnant women or both?	Thank you for your comment. The Committee has discussed your comment and has reworded the recommendation to state ‘treatment is not needed for asymptomatic bacteriuria in people with a catheter (unless they are pregnant, see the NICE antimicrobial prescribing guideline on lower UTI for managing asymptomatic bacteriuria in pregnant women).
16	Scottish Antimicrobial Prescribing Group	Guideline	2	1.1.2	Is there any evidence for NOT removing a catheter if in place for less than 7 days? Bacteriuria can develop as soon as 2 days post catheterisation. Applying the principles of IPC following invasive device insertion, it is possible that infection was introduced at time of insertion if all other sources of infection have been ruled out.	Thank you for your comment. The evidence search only found 1 RCT of catheter change for managing a UTI (Raz et al 2000), in which patients had a catheter in place for on average 31 days before infection. The recommendation about when to remove or change the catheter (if it has been in place for more than 7 days) was based on committee experience.
17	Scottish Antimicrobial Prescribing Group	Guideline	6	Table 1	Nitrofurantoin is not recommended for use in upper UTI. In catheterised individuals, it is not possible to identify signs or symptoms of a lower UTI. Therefore focus is on systemic and upper signs and symptoms. Promotion of “WATCH” antibiotics over “ACCESS” antibiotics. This could have significant impact on patient outcomes in relation to CDI & resistance promotion. Co-trimoxazole is a suitable oral agent in the treatment of CAUTI and should be used over fluroquinolones.	Thank you for your comment. The committee agreed that for adults with a catheter-associated UTI without upper UTI symptoms, nitrofurantoin or pivmecillinam are 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

					Gentamicin regimes differ across regions and dosing regimes are dependant on renal function. Dependant on therapeutic monitoring dosing frequency is variable as some patients may receive 36hrly or 48hrly doses. Confusing to state “daily”. By providing a blanket statement that all patients should receive 7mg/kg is a significant patient safety risk. If there are no upper UTI symptoms, how is it proposed to diagnose CaUTI? SAPG suggests systemic symptoms are a major factor in diagnosing CaUTI. Pivmecillinam and nitrofurantoin have a site of action largely confined to the bladder – and if systemic symptoms are a part of the diagnostic process for CaUTI there would be concern about the appropriateness of this. It is poor stewardship to have levofloxacin as a first choice antibiotic where others are available. There is a body of opinion that fosfomycin should have a different dosage schedule in men with a second dose – it is only a one off dose in females – but the evidence is unclear. Co-trimoxazole should be considered in some cases as preferential to quinolones. The most likely recipients of antibiotics for CaUTI are the frail elderly whose CDI risk may well be significant. The risks / benefit profile of co-trimoxazole may well be preferable in these cases.	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 noted that use of broad-spectrum antibiotics, such as cephalosporins, quinolones and 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 infection 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 has discussed your comment and has amended tables 1 and 3 to include footnotes on dose adjustment according to serum concentration of gentamicin and amikacin. The committee discussed your comment and agreed that there was sufficient trial evidence supporting the use of quinolones to justify the inclusion of either ciprofloxacin or levofloxacin. Ciprofloxacin was chosen as it has a narrower spectrum of activity than levofloxacin. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics. Co-trimoxazole was not included because it has a BNF warning that it should only be considered for use when there is bacteriological evidence of sensitivity and good reasons to prefer this combination to a single antibiotic. Other alternatives to quinolones are recommended including co-amoxiclav and cephalosporins.
18	Scottish Antimicrobial Prescribing Group	Guideline	6	Table 2	Why choose cefalexin or cefuroxime over co-amoxiclav in pregnancy?	Thank you for your comment. The committee discussed your comment and co-amoxiclav was not recommended because of high resistance levels nationally and the risks of treatment failure in pregnancy. Resistance to co-amoxiclav is currently 19.8% of E. coli isolates reported to PHE, whereas resistance of E. coli isolates to cefalexin is 9.9% of isolates in England.
19	Scottish Antimicrobial Prescribing Group	Guideline	7	Table 3	Use of trimethoprim – considerable supply difficulties with trimethoprim liquid for the foreseeable future – would need to check the manufacturing situation before recommending trimethoprim liquid. Gentamicin is subject to different dosage schedules and dosing intervals are dependent on the results of therapeutic drug monitoring. It is not helpful to the clinician to have 5 choices as first line IV antibiotics. Unclear how CAUTI can be diagnosed without either systemic or upper GU involvement. Again, “WATCH” antibiotic promoted over “ACCESS” antibiotic. Gentamicin regimes differ across regions and dosing regimes are dependant on renal function. Dependant on therapeutic monitoring dosing frequency is	Thank you for your comment. Several antibiotics are recommended to allow for supply difficulties, which may vary over time. The committee discussed your comment but as outlined in the rationale, agreed, based on experience, that several intravenous antibiotics should be available for people with catheter-associated UTI. This enables antibiotics to be selected based on antibiotic susceptibilities from culture results when available, local resistance patterns, risk of

					variable as some patients may receive 36hrly or 48hrly doses. Confusing to state “daily”. By providing a blanket statement that all patients should receive 7mg/kg is a significant patient safety risk.	resistant bacteria, and known patient factors (such as whether the person has a higher risk of developing complications). The committee noted that use of broad-spectrum antibiotics, such as cephalosporins, quinolones and 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 infection 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. In line with antimicrobial stewardship, narrower spectrum antibiotics should be used wherever possible. The committee have added a definition of catheter-associated UTI to the terms used in this guideline section. The Committee has discussed your comment and has amended tables 1 and 3 to include footnotes on dose adjustment according to serum concentration of gentamicin and amikacin.
20	Scottish Antimicrobial Prescribing Group	Guideline	9	1.4	This does not constitute advice on CAUTI prevention. Adequate hydration, catheter care, placement of catheter, frequency of bag change etc offer advice on preventing CAUTI	Thank you for your comment. The Committee has discussed your comment and added a link to the NICE guideline on Healthcare-associated infections: prevention and control in primary and community care (section 1.2), for recommendations on the general care of long-term urinary catheters.
21	Scottish Antimicrobial Prescribing Group	Guideline	11 & 13		No evidence around 7 day rule for catheter change. Bacteriuria can develop as soon as 2 days post catheterisation. Applying the principles of IPC following invasive device insertion, it is possible that infection was introduced at time of insertion if all other sources of infection have been ruled out.	Thank you for your comment. The evidence search only found 1 RCT of catheter change for managing a UTI (Raz et al 2000), in which patients had a catheter in place for on average 31 days before infection. The recommendation about when to remove or change the catheter (if it has been in place for more than 7 days) was based on committee experience.
22	Scottish Antimicrobial Prescribing Group	Guideline	12		**“**The committee noted that it is useful to add a comment to the request form to alert the laboratory to a suspected catheter-associated infection and the name of any antibiotic prescribed.” This information is essential in directing not only diagnosis but also planned therapy.	Thank you for your comment. The committee has discussed your comment and this has been added to the recommendation, which now reads ‘Send the urine sample for culture and susceptibility testing, noting a suspected catheter-associated infection and any antibiotic prescribed.’
23	Scottish Antimicrobial Prescribing Group	Guideline	13		It is ‘essential’ not ‘useful’ to add a comment to the microbiology request form that a CaUTI is suspected.	Thank you for your comment, this wording has been amended.
24	Scottish Antimicrobial Prescribing Group	Guideline	14		”if the results suggest the antibiotic given is not susceptible, the person should be contacted and if symptoms are not already improving, the antibiotic should be changed” This infers that the antibiotic should not be changed or stopped if symptoms are improving – poor stewardship.	Thank you for your comment. The committee has discussed your comment and reworded the recommendation, which now reads ‘change the antibiotic according to susceptibility results if the bacteria are resistant, using narrow spectrum antibiotics wherever possible.’

25	Scottish Antimicrobial Prescribing Group	Guideline	15		References shortages of gentamicin – shortages have applied to numerous antibiotics and are likely to continue in the future so it is inappropriate to specifically pick out gentamicin in this context.	Thank you for your comment. The Committee discussed your comment and have amended the discussion to read '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.'
26	Scottish Antimicrobial Prescribing Group	Guideline	General	General	Each guideline refers to "Allergic reactions to penicillins occur in 1-10% of people and anaphylactic reactions occur in less than 0.05%. People with a history of atopic allergy (for example, asthma, eczema and hay fever) are at a higher risk of anaphylactic reactions to penicillins" This is at odds with the British Society of Allergy and Clinical Immunology (BSACI) guidelines (published in Clinical & Experimental Allergy 45;300-327). They state "The prevalence of penicillin hypersensitivity in the general population is unknown as there are no prospective studies evaluation sensitisation rates during treatment" "Atopy does not predispose to the development of allergic reactions to penicillin, but asthma can be a risk factor for life threatening reactions"	Thank you for your comment. NICE has amended the section on penicillin allergy to reflect the advice given in the NICE guideline on drug allergy.
27	National Minor Illness Centre	Visual summary Guideline	1 5	Grey box 4	Self-care advice includes "Advise an adequate intake of fluid", but is there any evidence or rationale for this? Everyone should take 'adequate' fluid. By raising the issue under self-care, extra fluid is therefore implied. The problem is that extra fluid intake can exacerbate the frequency and associated dysuria. There could be issues with dilution of immunoglobulin / WBC in the urine. Without fever (there shouldn't be for cystitis) then there is no reason to suppose that there will be excess fluid loss that needs extra hydration to replace it. Would NICE 'Advise an adequate intake of fluid' for every infection? If not, then what is the reasoning to include it here?	Thank you for your comment. The committee have reworded the recommendation to emphasise the importance of avoiding dehydration in people with UTI.
28	National Minor Illness Centre	Visual summary Guideline	2 3 5 7	Left table 22 17	Why include standard-release form when it is associated with a higher risk of adverse symptoms and costs more than the modified-release form? Drug tariff May 2018: 50mg cap (30) £15.42; 50mg tab (28) £11.36; mr cap (14) £9.50 Liu J, Chan SY, Ho PC. Polymer-coated microparticles for the sustained release of nitrofurantoin. J Pharm Pharmacol 2002; 54(9):1205-12 Ertan G, Karasulu E, Abou-Nada M, Tosun M, Ozer A. Sustained-release dosage form of nitrofurantoin. Part 2. In vivo urinary excretion in man. J Microencapsul 1994; 11(2):137-40 Maier-Lenz H, Ringwelski L, Windorfer A. Comparative pharmacokinetics and relative bioavailability for different preparations of nitrofurantoin. Arzneimittelforschung 1979; 29(12):1898-901 There is clear incentive for a person to take medication for relief of unpleasant symptoms, so the normal concern that more than two doses daily increases the risk of missed doses is not so relevant, but there is still what is termed 'the burden of tablet taking'. Four doses daily, in addition to any other medications being taken long-term, adds to the burden for the patient. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance Clinical Therapeutics 2001; 23(8):1296-1310	Thank you for your comment. The committee discussed the comment and made changes to the relevant tables. The committee agreed to remove immediate-release nitrofurantoin from the antibiotic choice tables and recommend the modified-release preparation only, based on the twice a day dosing and, in their experience, improved tolerability.

					If it is decided to keep immediate-release Nitrofurantoin in the guideline, then could it be placed after the modified-release option, to at least avoid giving prescribers a false impression of preference?	
29	National Minor Illness Centre	Visual summary Guideline	2 5	Left table 32	The dose recommended for Pivmecillinam, which includes a higher first dose than subsequent ones, concurs with BNF and PHE guideline. The committee will be aware that the dose differs from that stated in the SPC of the generic manufactured by Aurobindo Pharma - Milpharm Ltd, where all the doses are the same for the course. We have previously written to the manufacturerof Selexid (Leo), who do recommend a loading dose, to ask why this might have an advantage, as the pharmacokinetics as found in the SPC do not indicate any particular requirement (the serum half-life is 1.2 hours). We had no reply. Perhaps it would be worth checking with the MRHA on the evidence for the loading dose?	Thank you for your comment. NICE uses the BNF for dosages when making recommendations. NICE will contact the BNF about this issue. NICE antimicrobial prescribing guidelines will replace the PHE guidance as they are published.
30	National Minor Illness Centre	Visual summary Guideline	2 3 6, 7	Left table 15 3, 36	The dose of Co-amoxiclav is not as it appears in the BNF: “Prescribing and dispensing information Doses are expressed as co-amoxiclav: a mixture of amoxicillin (as the trihydrate or as the sodium salt) and clavulanic acid (as potassium clavulanate); the proportions are expressed in the form x/y where x and y are the strengths in milligrams of amoxicillin and clavulanic acid respectively.” In contrast, the suspensions are given in the BNF format.	Thank you for your comment. The Committee has discussed your comment and has amended table 1 to state 500/125 mg as it appears in the BNF.
31	National Minor Illness Centre	Visual summary Guideline	3 7	6 8	Would it be worth adding to footnote 2 that the dose calculated from a child’s weight should not exceed the adult dose? We have experience of a child discharged from hospital taking 250mg trimethoprim twice daily because he weighed 62.5kg.	Thank you for your comment. NICE uses the BNF for dosages when making recommendations.
32	National Minor Illness Centre	Visual summary Guideline	3 7	9 15	The prevalence of catheter-associated UTI in children is so low that the high price of nitrofurantoin liquid is unlikely to have significant impact on CCG/practice prescribing budgets, but the difference in price of over £400 per treatment would make it likely that a prescriber having been warned of the high price with regards to treating UTI in general, would be more inclined to skip the second choice section in this table and prescribe cefalexin if trimethoprim cannot be used. The alternative that could be included in the first choice section would be Pivmecillinam, which is licensed for children. Children over 40kg take the same dose as adults, those under 40kg can halve or quarter the tablets using a tablet cutter available from pharmacies for a cost of about £3. Children down to the age 6 years can usually swallow small divided tablets, and Bonnie Kaplan has shown the children down the age of 4 years can also swallow solid medication with simple instruction (and often they prefer it to the taste of liquid medicine). Kaplan BJ, Steiger RA, Pope J, Marsh A, Sharp M, Crawford SG (2010). Better than a spoonful of sugar: Successful treatment of pill swallowing difficulties with head posture practice. Paediatr Child Health, 15(5), e1-5. Leo Laboratories Ltd replied to our request about dosing for young children indicating that, if required, a tablet or part thereof could safely be crushed.	Thank you for your comment. The committee considered the resource implications of implementing the guideline when reviewing the evidence and producing recommendations. The committee acknowledged the current high cost of nitrofurantoin liquid. Following stakeholder comments, nitrofurantoin has been removed from table 3.
33	National Minor Illness Centre	Visual summary	3	12	To be consistent and clearer, it might be better to use the dose schedule of Cefalexin for children as it appears in the visual summary for lower UTI. In this catheter-associated visual summary the dose per kg appears after the set dose for the age range, whereas it is the other way around for trimethoprim in the same table and in the lower UTI guideline.	Thank you for your comment The committee has discussed your comment and amended the tables to give dose per kg first.

34	National Minor Illness Centre	Visual summary Guideline	3 7	15 32	To a new prescriber, it may appear odd that doses of Amoxicillin are quoted for 5-11 years and 12-17 years of age and that the dose is the same for both, and includes 17 when the table refers to young people under 16. An experienced prescriber may think nothing of this because that is how it appears in the BNFC (although in the BNFC there is a subtle difference between the two age ranges for high doses used in more serious infections). Please consider simplifying the table and just say '5 to 16 years, 500 mg three times a day for 3 days'. If this is accepted, then the other dose ranges for children and young people should also be changed from a maximum of 17 to 16 to align with that table's title.	Thank you for your comment. The committee discussed your comment and made changes to the table to reflect your comment.
35	National Minor Illness Centre	Visual summary Guideline	3	17	To aid compliance/concordance and to make dosing easier for children attending school, the twice daily option of co-amoxiclav may be preferable. Against this suggestion is that prescribers may be more familiar with the 125/31 medicine. For either three or two daily doses, it would be clearer to give the dose per kg first and only state the concentration of the medicine once. When a dose per kg is given in the BNFC, calculating a dose for a child by weight is usually preferable to using a standard dose for an age range as it should give a more appropriate dose for the individual, so long as they are not extremely obese. In view of this, it would be better to state the dose per kg first. For example, '6 to 11 years, 5 ml of 250/62 suspension or 0.15 ml/kg of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection)' would become: '6 to 11 years, 0.15 ml/kg or 5 ml of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection)'	Thank you for your comment. The committee has discussed your comment and amended the tables to give dose per kg first.
36	National Minor Illness Centre	Visual summary Guideline	3 8	25 16	The dose ranges for Ceftriaxone could be combined for 9 to 16 years. (See point 7).	Thank you for your comment. The committee has discussed your comment but the wording was not amended, because of the different weight instructions: 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.
37	NHS Bath and North East Somerset CCG	Guideline	2	1.1.2	What consideration was given to advice to treat UTI for 24 hours prior to catheter removal and replacement (where replacement is considered necessary) – this practice in some organisations is considered to reduce risk of a bacteraemia caused by catheter manipulation.	Thank you for your comment. The Committee discussed this and the rationale says 'The committee recommended considering removal or, if this was not possible, change of the catheter as soon as possible if it has been in place for more than 7 days. The committee were aware of limited evidence suggesting catheters should be removed or changed before antibiotics are given, but discussed that there were safety concerns with this approach and practical considerations about possible delays in primary care settings. The committee agreed that treatment with antibiotics should not be delayed if catheter removal or change could not be done straight away. 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 changing the catheter before starting antibiotic treatment resulted in higher cure or improvement rates and reduced mortality (from urosepsis) compared with not changing the catheter before starting antibiotics. The

						recommendation about when to remove or change the catheter (if it has been in place for more than 7 days) was based on committee experience.
38	NHS Bath and North East Somerset CCG	Guideline	2	1.1.2	Helpful to include advice to remove rather than change catheter	Thank you for your comment.
39	NHS Bath and North East Somerset CCG	Guideline	14		Why is levofloxacin included as an antibiotic option? It is reserved as a broad spectrum choice for other infections and ciprofloxacin is considered by microbiology as a more appropriate quinolone choice	Thank you for your comment. The committee discussed your comment and agreed that there was sufficient trial evidence supporting the use of quinolones to justify the inclusion of either ciprofloxacin or levofloxacin. Ciprofloxacin was chosen as it has a narrower spectrum of activity than levofloxacin.
40	NHS Bath and North East Somerset CCG	Guideline	15		It is helpful 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. This nitrofurantoin cost issue causes clinicians anxiety about appropriate treatment choices	Thank you for your comment.
41	Royal College of Physicians and Surgeons of Glasgow	Guideline	2	1.1.1	The recommendation to treat only symptomatic catheter associated UTI is consistent with local practice in most areas of the UK. This recommendation would be aided by reinforcement on the lack of utility of urine dipstick testing in frail older patients with catheters and minor functional changes. One of our other reviewers made the valid point that although it is quite clear that the guidance states that treatment should be reserved for those individuals with clinical symptoms and signs of infection, it does NOT define what these are. This is important when assessing catheter-associated infections, since many of the "normal" assessment criteria do not apply — like frequency, dysuria, and cloudy urine He recommends a simple algorithm or decision-tree at the start, indicating what symptoms and signs (and possibly laboratory investigations) should be taken as indicators of "symptomatic infection" that then require further intervention.	Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis, and further details on diagnosis or symptoms or signs of infection is out of scope.
42	Royal College of Physicians and Surgeons of Glasgow	Guideline	5	1.3	Many areas have robust local guidance on choice of antibiotics for UTI. These can differ slightly from the list produced in the recommendations list. Given that antibiotic sensitivity varies across areas, is it wise to give a single antibiotic scheme? The use of Trimethoprim for UTI for 14 days has risks in frail older patients with subtle CKD changes. Hyperkalaemia is commonly seen. Recommendations should be given to monitor U and Es and consider dose reduction. Nitrofurantoin and trimethoprim are contra indicated in some patients with connective tissue diseases (such as SLE). Trimethoprim should be avoided in patients on immunosupressants such as Methotrexate.	Thank you for your comments. • The Committee has discussed your comment and has amended recommendation 1.3.1 to state that account should be taken of local resistance patterns. • We are not sure of the context of your comment as there are 3 first choice oral antibiotics for adults (page 5). • Dose reductions may be required for several antibiotics in the guideline dependent on the individual's condition. It is expected that a prescriber would take appropriate action for example monitoring, dose adjustment or selection of therapy in the presence of contraindications or concomitant disease, where this is needed, based on the summary of product characteristics.
43	Royal College of Physicians and Surgeons of Glasgow	Guideline	General		The guideline lacks advice to prevent catheter blockage. This leads to distress and increases sepsis. While this may be outside the remit of the review, it should be considered.	Thank you for your comment. The Committee has discussed your comment and added a link to the NICE guideline on Healthcare-associated infections: prevention and control in primary and community care (section 1.2), where the general care of long-term urinary catheters is outlined.

44	Royal College of Physicians and Surgeons of Glasgow		5	1.3	Our reviewer has concerns regarding the continued inclusion Coamoxiclav and Ciprofloxacin in an antibiotic regime. Clostridium Difficile associated Disease is a problem for most Trusts and Health Boards. The inclusion of these antibiotics does not help local initiatives to reduce the incidence of this disease.	Thank you for your comment. The committee noted that use of broad-spectrum antibiotics, such as cephalosporins, quinolones and 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 infection 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. In line with antimicrobial stewardship, narrower spectrum antibiotics should be used wherever possible.
45	Royal College of Physicians and Surgeons of Glasgow	Guideline	General		Our Surgical reviewer also recommended simple methods for maintaining catheter cleanliness. His management principles of CAUTI are as follows: 1) If patient has a urethral catheter, consider changing to a suprapubic catheter for long term management. This is important in females to prevent the development of traumatic megaurethra and in males to prevent traumatic hypospadias. In males it may also decrease the incidence of prostate related infections but I suspect there is no good evidence for this. 2) Exclude upper tract causes of UTI such as stones, PUJ obstruction etc. 3) use urinary acidifiers such as high dose vitamin C (1-2g/day) 4) use regular mechanical bladder washout 5) use Hipprex (methenamine) as a urinary antiseptic 6) Have a low threshold for suggesting cystoscopy. A good washout even when no debris is seen, is very effective. Cystoscopy will also identify stones, inflammation and tumours which may be contributing to UTI. Squamous carcinoma is common in patients with long term catheters.	Thank you for your comment. • The remit of this guidance is the management of common infections, and further details on route of catheterisation or diagnosis is out of scope. • No evidence on urinary acidifiers, such as high dose vitamin C met the inclusion criteria for this guideline on catheter-associated UTI. High dose vitamin C (ascorbic acid), was not specifically included in the search terms because this is not a widely used or licensed intervention • NICE guidelines have previously recommended that bladder instillations or washouts must not be used to prevent catheter-associated infections. Please see the NICE guideline on Healthcare-associated infections: prevention and control in primary and community care (recommendations 1.2.5.11). • No evidence on methenamine met the inclusion criteria for this guideline on catheter-associated UTI. Methenamine was specifically included as a search term. • The use of cystoscopy in relation to treating or preventing catheter associated urinary tract infection was out of scope for this guideline.
46	UK Clinical Pharmacy Association	Visual summary	General	General	There should be more emphasis on only treating symptomatic patients – including definition of asymptomatic bacteriuria and what symptoms warrant treatment	Thank you for your comment. The visual summary reflects the guideline recommendations, which state 'a catheter-associated UTI is a symptomatic UTI of the bladder or kidneys in a person with a catheter' and provides a definition that 'Catheter-associated UTI in people with a catheter is defined as the presence of symptoms or signs compatible with a UTI with no other identified source of infection plus significant levels of bacteria in a catheter urine specimen or a midstream urine specimen from a person whose catheter has been removed within the previous 48 hours.'
47	UK Clinical Pharmacy Association	Visual summary	General	General	In box on left hand side background should come before treatment advice	Thank you for your comment. The background section has been moved above.
48	UK Clinical Pharmacy Association	Visual summary	General	General	The referral box should clearly separate when in-patient referral is required versus out-patient	Thank you for your comment. The visual summary is a summary of the recommendation, which states '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)'. It does not provide further detail.

49	UK Clinical Pharmacy Association	Visual summary	General	General	Why is the self-care box separate from the advice box makes sense to put them together	Thank you for your comment. The visual summaries follow a standard format and the self-care section is within the grey box on the right hand side in all visual summaries.
50	UK Clinical Pharmacy Association	Visual summary	General	General	Doesn't make clear that pregnant patients should always be treated even if asymptomatic	Thank you for your comment. The visual summary reflects the guideline recommendations, which state 'treatment is not needed for asymptomatic bacteriuria in people with a catheter (unless they are pregnant, see the NICE antimicrobial prescribing guideline on lower UTI for managing asymptomatic bacteriuria in pregnant women).'
51	UK Clinical Pharmacy Association	Visual summary	General	General	Is it possible to fit more info on sampling on the flow chart?	Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis, and further details on diagnosis is out of scope.
52	UK Clinical Pharmacy Association	Visual summary	General	General	Should the guidance have info on recognition of sepsis?	Thank you for your comment. The remit of this guidance is the management of catheter-associated urinary tract infection. Safety netting advice to reassess any symptoms or signs suggesting a more serious illness or condition, such as sepsis, and refer people with symptoms or signs suggesting a more serious illness or condition (for example sepsis) to hospital are given, but further guidance on the recognition of sepsis is out of scope.
53	UK Clinical Pharmacy Association	Visual summary + Guideline	General	General	Abx treatment options are all for a 7 day course except fosfomcyin, which is a single dose and will provide 3 days treatment at best. There is evidence that single dose fosfomycin is inferior to 5 days nitrofurantoin in uncomplicated UTIs (Huttner A, Kowalczyk A, Turjeman E et al, JAMA 2018) so advising single dose for CA-UTIs doesn't seem sensible.	Thank you for your comment. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics.
54	UK Clinical Pharmacy Association	Visual summary	General	General	Would it be worth having a comment about reviewing recent antibiotic prescriptions in past 3 months before prescribing an empiric choice	Thank you for your comment. The antibiotic table in the visual summary has a footnote to 'check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.'
55	UK Clinical Pharmacy Association	General	General	General	Nitrofurantoin suspension is ~ £450 per bottle. In secondary care we tend to reserve this as a second line option for treatment. Although we want to encourage the use of narrow spectrum agents such as trimethoprim / nitrofurantoin in reality cefalexin may be prescribed in preference to nitrofurantoin if the child cannot swallow tablets / capsules due to cost pressure – although less of an issue for short term treatment. However appreciate that cephalosporins now classed as Watch antibacterials whereas nitrofurantoin classed as Access.	Thank you for your comment. The committee considered the resource implications of implementing the guideline when reviewing the evidence and producing recommendations. The committee acknowledged the current high cost of nitrofurantoin liquid. Following stakeholder comment, nitrofurantoin has been removed from the recommended antibiotics table for children.
56	UK Clinical Pharmacy Association	General	General	General	Antibiotic dosing table for amoxicillin – perhaps state 3-11months for first age bracket for consistency (under 3 months referral to paediatric specialist).	Thank you for your comment. This has been amended to 3 to 11 months.
57	UK Clinical Pharmacy Association	General	General	General	Since antimicrobials listed have wide therapeutic ranges in practice it is preferable to use the dose banding rather than the ml/kg dosing in most cases even if children are considered small for their age, this allows for ease of administration and improves adherence. We need to try to avoid unnecessarily complex dosing such as 2.6ml.	Thank you for your comment. NICE uses the doses and scheduling set out in the BNFc, and both dose banding and ml/kg are given where these are available
58	UK Clinical Pharmacy Association	General	General	General	Usual dosing for cefotaxime in > 3 months is 50mg/kg 6-8hourly rather than 12hourly.	Thank you for your comment. The committee discussed your comment and subsequently agreed to remove cefotaxime from the table of recommended antibiotics.
59	UK Clinical Pharmacy Association	General	General	General	Ceftriaxone dosing – although the BNF-C states to dose as per adults in children 9-11 years (50kg and above) and over 12 years – in practice many paediatric centres often continue to prescribe on a mg/kg basis with a max dose of 4g/day.	Thank you for your comment. NICE uses the doses and scheduling set out in the BNFc.
60	UK Clinical Pharmacy Association	General	General	General	Should maximum doses be added for aminoglycosides as per other antibiotics?	Thank you for your comment. The Committee has discussed your comment and has amended tables 1 and 3 to include

						footnotes on dose adjustment according to serum concentration of gentamicin and amikacin with maximum dose specified where stated in the BNF.
61	Royal College of Pathologists	Guideline	General	General	Although the guideline sets out to provide recommendations for preventing catheter associated urinary tract infections, there is little in the guideline around prevention. In particular, there is no guidance on indications for catheterisation (and, more importantly, when catheters should not be used, or when alternative such as convene catheters should be preferred), the use of aseptic non-touch technique for catheter insertion, catheter care, and indications for catheter removal. A discussion on the choice of catheter material is also missing	Thank you for your comment. The Committee has discussed your comment and added a link to the NICE guideline on Healthcare-associated infections: prevention and control in primary and community care (section 1.2), where more general recommendations on catheter use are given.
62	Royal College of Pathologists	Guideline	General	General	All five guidelines have insufficient discussion on the diagnosis of urinary tract infections. All five guidelines start with an assumption that a correct clinical diagnosis of UTI has been made. In practice, this aspect of UTI management is probably the most problematic. This is certainly the case for catheter associated UTI and the uncertainty around the diagnosis leads to over-treatment. Section 1.1.4 of this guideline starts with the assumption that a urine sample should be collected but doesn't specify under what circumstances. This will not help with managing over-treatment.	Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis, and further information on diagnosis is out of scope.
63	Royal College of Pathologists	Guideline	3	1.1.5	This section advises waiting for urine culture and susceptibility results to be available. There are laboratories that either do not culture catheter specimens of urine or do not provide susceptibilities because of the low specificity of CSU samples for diagnosing UTIs. Consequently, this section should provide a caveat about this.	Thank you for your comment. The committee has discussed your comment and a recommendation has been added to 'Send the urine sample for culture and susceptibility testing, noting a suspected catheter-associated infection and any antibiotic prescribed.'
64	Royal College of Pathologists	Guideline	4	1.1.11	An additional reason for referring to hospital is for a patient with a multi-drug resistant infection with no oral treatment options to receive intravenous antibiotic therapy	Thank you for your comment. The Committee discussed your comment and have amended the recommendation (last bullet) to state 'have bacteria that are resistant to oral antibiotics'.
65	Royal College of Pathologists	Guideline	5	Table 1	The reference to choosing trimethoprim if there is a low risk of resistance is practically difficult to interpret. "Low" is not quantified, and even if it was, it is virtually impossible for prescribers to guess the probability that a particular urine isolate will be trimethoprim sensitive	Thank you for your comment. The committee discussed your comment and made changes to the relevant tables. The tables now include the following footnote: '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'.
66	Royal College of Pathologists	Guideline	6	Table 1	The entries for gentamicin and amikacin need to include the requirement for therapeutic drug monitoring. (Also table 3, page 8)	Thank you for your comment. The Committee has discussed your comment and has amended tables 1 and 3 to include footnotes on dose adjustment according to serum concentration of gentamicin and amikacin.
67	British Society for Antimicrobial Chemotherapy	Guideline	2	1.1.1 bullet point 1	catheter-associated UTI occurs when bacteria in a catheter bypass the body's defence mechanisms (such as the urethra and the passing of urine) and enter the bladder This statement is not true and conflicts with bullet point 3 – needs rewording	Thank you for your comment. The committee has discussed your comment and amended this statement.
68	British Society for Antimicrobial Chemotherapy	Guideline	2	1.1.2	Recommend this is reworded to "Consider removing or changing the catheter before treating the infection, particularly if it has been in place for more than 7 days."	Thank you for your comment. The Committee have discussed your comment and reworded the recommendation to 'Consider removing or, if this is not possible, 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 delay antibiotic treatment if this cannot be done straight away.'
69	British Society for Antimicrobial Chemotherapy	Guideline	5	Table 1	Recommendation to use nitrofurantoin – it is a vexed question among microbiologists whether nitrofurantoin should be used for catheter UTI – at the very least this recommendation should be accompanied by an acknowledgement of that and an explanation	Thank you for your comment. The committee were aware that nitrofurantoin is licensed specifically for the treatment of uncomplicated lower urinary tract infections. 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. This is outlined in the committee discussion section of the guideline.
70	British Society for Antimicrobial Chemotherapy	Guideline	6	Table 1/General	Should there be a warning that co-amoxiclav/quinolones/ceftriaxone are high C difficile risk compared with trimethoprim and gentamicin?	Thank you for your comment. As outlined in the committee discussion section of the guideline, the committee noted that use of broad-spectrum antibiotics, such as cephalosporins, quinolones and 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* infection 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. In line with antimicrobial stewardship, narrower spectrum antibiotics should be used wherever possible.
71	British Society for Antimicrobial Chemotherapy	Guideline	6	Table 2	Why do the recommendations for pregnant women differ so much from those for non-pregnant women? The principles should be the same, the differences should reflect nothing other than safety in pregnancy.	Thank you for your comment. The antibiotic choices for pregnant women with catheter-associated UTI are the same as those for pregnant women with acute pyelonephritis. Pregnant women are a high-risk group for complications from UTI and the committee agreed that cefalexin (oral) or cefuroxime (IV) were appropriate for empirical treatment where coverage of more resistant strains of common bacterial pathogens is required.
72	British Society for Antimicrobial Chemotherapy	Guideline	General	General	General concern is the antibiotic choices make no reference to local resistance rates or for come choices national data (we have a high co-amoxiclav resistance rates as does the recent national E coli BSI dataset) plus advises high risk antibiotics for inpatient treatment from the C difficile point of view	Thank you for your comment. The Committee has discussed your comment and has amended recommendation 1.3.1 to state that account should be taken of local resistance patterns. As outlined in the committee discussion section of the guideline, the committee noted that use of broad-spectrum antibiotics, such as cephalosporins, quinolones and 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* infection 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. In line with antimicrobial stewardship, narrower spectrum antibiotics should be used wherever possible.
73	British Society for Antimicrobial Chemotherapy	Guideline	General	General	No definition of what constitutes 'Catheter-associated UTI' as without upper symptoms drives over-use of antibiotics for just colonised catheters (dark , cloudy or smelly urine, dipstick positive urine , symptoms due to the catheter etc.)	Thank you for your comment. The committee have added a definition of catheter-associated UTI to the terms used in this guideline section. The remit of this guidance is the management of common infections not diagnosis. Providing further details on the diagnosis of catheter-associated infection is out of scope.
74	Royal College of General Practitioners	Comments form questions	Q1		For the past 2 years the RCGP, NHS England and GPs across the UK having been working to increase the appropriate use of nitrofurantoin as first-line choice for the empirical management of UTI in primary care settings, and support reduction in inappropriate prescribing of trimethoprim which is reported to have a significantly higher rate of non-susceptibility in "at-risk" groups'. The RCGP Target toolkit, which stands for: Treat Antibiotics Responsibly, Guidance, Education, Tools, helps influence prescribers' and patients' personal attitudes, social norms and perceived barriers to optimal antibiotic prescribing. It includes a range of resources that can each be used to support prescribers' and patients' responsible antibiotic use, helping to fulfil CPD and revalidation requirements. http://www.rcgp.org.uk/clinical-and-research/resources/toolkits/target-antibiotic-toolkit.aspx	Thank you for your comment. NICE have endorsed the TARGET toolkit resource for UTI this will be linked to from the resources section of the guideline webpage.
75	Royal College of General Practitioners	Comments form questions	Q2		There is a need for investment in training resources for Gps, their staff as well as community district nurses who they collaborate closely over the care of patients with a catheter in the community. Increased investment in district nursing services	Thank you for your comment. Unfortunately resources for training is not in scope for this guideline.
76	Royal College of General Practitioners	Comments form questions	Q3		Access to full patient health information at the time of assessment in the community. Increased investment in district nursing services	Thank you for your comment. Unfortunately access to health information and resources for training is not in scope for this guideline.
77	Royal College of General Practitioners	Comments form questions	Q4		Overall reduction in use of antibiotics and increase in the use relative use of nitrofurantoin to trimethoprim. Course of antibiotic treatment is 7 days rather than the usual course length of 3 days for someone without a catheter	Thank you for your comment. The duration of treatment for people with a catheter-associated UTI and upper UTI symptoms is the same as for people with acute pyelonephritis. The duration of treatment for people with a catheter-associated UTI and no upper UTI symptoms is 7 days, which is the same as for lower UTI in men and pregnant women. The committee agreed that 7 days rather than 3 days was required because people with a catheter are more at risk of complications and the longer course is required to ensure complete cure.
78	Royal College of General Practitioners	Visual summary	1		"See a 3-page visual summary of the recommendations, including tables to support prescribing decisions." This has not been included to review	Thank you for your comment. NICE has not received any other instances of stakeholders being unable to access the visual summary, we apologise for any inconvenience.
79	Royal College of General Practitioners	Guideline	2	1.1.4	Not all catheters have a sampling port	Thank you for your comment. The Committee has discussed your comment and amended the recommendation to state 'Obtain a urine sample from the catheter, via a sampling port where provided, using an aseptic technique (in line with the NICE guideline on healthcare-associated infection) and send for culture and susceptibility testing.
80	Royal College of General Practitioners	Guideline	3	1.1.6	Could a delayed prescription be also offered so that the person and their family or paid carers have to struggle to get an antibiotic if the symptoms deteriorate particularly out of hours and at weekends?	Thank you for your comment. NICE found no evidence for the intervention of back-up (delayed) prescription in people with urinary catheters for any outcomes including those of effectiveness or safety.
81	Royal College of General Practitioners	Guideline	4	1.1.10	Could the triggers and thresholds for the National Early Warning Score (NEWS) 2 be included here as this is becoming the standard method of the assessment of acute-illness	Thank you for your comment. The remit of this guidance is the management of common infections not diagnosis. Therefore, NEWS or other validated early warning scores for

						identifying acutely ill patients - including those with sepsis – are not referred to but the NICE guideline on sepsis is.
82	Royal College of General Practitioners	Guideline	5	1.2.2	Could the recommendation be more specific about what is adequate intake of fluids in both terms of volume, number of average cups of water and types of fluid? A link to an information sheet such as that from the British Dietetic Association would be useful https://www.bda.uk.com/foodfacts/fluid.pdf	Thank you for your comment. The committee have reworded the recommendation to emphasise the importance of avoiding dehydration in people with UTI.
83	Nordic Pharma	Guideline	General		As a general comment across all of the UTI guidelines, where fosfomycin is mentioned, please ensure it is very clear whether the guidelines are referring to IV or oral fosfomycin as these are both very different treatment options. This distinction is often not made and can cause potential confusion e.g. the recent publication Hawkey P. et al. J Antimicrob Chemother 2018; 73 Suppl 3: iii2–iii78	Thank you for your comment. Please note that the tables within the guideline specify whether the antibiotic is first or second choice and whether they are oral or intravenous. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics.
84	Nordic Pharma	Guideline	General		With the recent publication of the white paper on the antibiotic supply chain by the Access to Medicine Foundation (available here) it is worth noting that since the introduction of licensed IV fosfomycin to the UK in 2014, consistent supply has been maintained, with two European manufacturing sites for security.	Thank you for your comment. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics.
85	Nordic Pharma	Guideline	General		There is no reference to treatment of biofilms such as those that may be associated with indwelling devices such as urethral stents and catheters causing blockages. Although a key aim of the guidance is to 'Consider removing or changing the catheter before treating the infection if it has been in place for more than 7 days. Catheters should be removed rather than changed where possible', biofilms may also be associated with the urothelium, prostate stones, and implanted foreign bodies. There is evidence to support the efficacy of IV fosfomycin I treating biofilms – see comment 6 below	Thank you for your comment. NICE recognise that biofilms are important in the development of catheter-associated urinary tract infection. However, the guideline is for the treatment of catheter-associated urinary tract infection not treatment of biofilms. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics.
86	Nordic Pharma	Guideline	General		In tables 1, 2 and 3, where the decision to use an IV antibiotic is made, this includes reference to patients who are severely unwell. By definition, a proportion of these patients are likely to have renal impairment and this patient group may warrant specific attention There is evidence which demonstrated IV fosfomycin has nephroprotective properties, which may be beneficial in this patient population - please see comment 6 below	Thank you for your comment. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics.
87	Nordic Pharma	Guideline	6		• By definition, catheter associate UTIs are generally considered complicated UTIs • Oral fosfomycin is not indicated for complicated UTIs If fosfomycin is to be considered, then the IV form may be appropriate as indicated for complicated urinary tract infections	Thank you for your comment. Based on stakeholder comments, the committee agreed to remove fosfomycin from the table of recommended antibiotics. While NICE appreciates that fosfomycin is a useful antibiotic in treating infection, unfortunately we found no evidence from randomised controlled trials that evaluated fosfomycin in people with catheter-associated UTI or acute pyelonephritis, and fosfomycin was specifically included by name in the NICE search strategy (see the evidence review document).
88	Nordic Pharma	Guideline	6		Within table 1. 'Antibiotics for non-pregnant women and men aged 16 years and over' and table 2. 'Antibiotics for pregnant women aged 12 years and over' IV fosfomycin should be included The evidence to support the efficacy of IV fosfomycin in complicated urinary tract infections includes: ○ K.G. Naber, Therapiewoche, 33,23, 1983 ○ Peters H.J. et al, MMW Munch Med Wochenschr. 1981 May 1;123 (18), 748-50 ○ Zeus data: ID week 2017, poster #1845 ○ Preliminary FORREST study results – presented at ECCMID 2018	Thank you for your comment. While NICE appreciates that fosfomycin is a useful antibiotic in treating infection, unfortunately we found no evidence from randomised controlled trials that evaluated fosfomycin in people with catheter associated urinary tract infection or acute pyelonephritis, and fosfomycin was specifically included by name in the NICE search strategy (see the evidence review document). In relation to the submitted articles: • Naber (1983) did not meet the criteria for inclusion as it falls outside the date range set by the committee for

					○ Dinh A et all, Scand J Infect Dis 2012 Mar 44(3):182-189 In addition, the evidence for IV fosfomycin for the treatment of biofilms is particularly relevant for consideration in the treatment of catheter-associated UTIs, or other situations where biofilm formation may be a factor:. • Fosfomycin has the ability to penetrate into biofilms - there is evidence which shows it has excellent properties in eradicating a variety of biofilm-associated pathogens. Fosfomycin has the ability to break up biofilms to enhance the permeability of other antibiotics. Therefore it enhances the activity and penetration of other antibiotics inside the biofilm, which may be associated with the unique mechanism of action of fosfomycin. • Evidence to support this includes: ○ Sabir N et al. Am J Inect Control. 2017 ○ Mihaelecu Antimicrobial Agents and Chemotherapy , May 2014 Volume 58 Number 5 p. 2547–2553 ○ Corvec, Antimicrobial Agents and Chemotherapy ,March 2013 Volume 57 Number 3 p. 1421–1427 ○ Oliva et al. Antimicrobial Agents Chemotheapyr. 2014; 58(3): 1284 ○ Mikuniya, Acta Medica, vol 59, issue 5, 2005 ○ Kumon H et al. Antimicrob Agents Chemother 1995;39:1038–44 ○ Mikuniya T et al. J Infect Chemother 2007;13:285–90 ○ Monden K et al. J Infect Chemother 2002;8:218–26 ○ Marquès C, et al. J Med Microbiol 2015; 64(9): 1021-6 ○ Rodriguez-Martinez, JM, Ballesta, S, Pascual, A. Int J Antimicrob. Agents 2007; 366-376. • Combining antibiotics for patients with confirmed/suspected sepsis –IV fosfomycin should be considered as part of a combination regimen for the treatment of MDR Enterobacteriaceae in complicated urinary tract infections and sepsis ○ Evidence to support this includes: ○ Matteo Bassetti, management of MDRO enterobacteriaceae, 2016 • Several studies have shown that fosfomycin reduces aminoglycoside-induced nephrotoxicity and has nephron-protective properties which may be beneficial in 'severely unwell patients' where appropriate ○ Evidence to support this includes: ○ Inouye S, Niizato T, Komiya I, Yuda Y, Yamada Y. J Pharmacobiodyn. 1982 Dec;5(12):941-50. ○ Fujita K, Fujita HM, Aso Y. Jpn J Antibiot. 1983 Dec;36(12):3392-4. ○ Chie Yangida et al. Chemico-Biological Interactions 148 (2004) 139-147 ○ Kimio Fujita. The Journal of antibiotics apr. 1984 p408-412 ○ Yuji Yoshiyama et al. J.Infect. Chemother (2005) 11: 14-17 ○ Nakamura M, Hashimoto Y, Kokuryo T, Inui K-I. Pharm Res. 1999,51(2):227-232 ○ Bär W, Grosch H, Ahland R, Krülls-Münch J. DMW 2005, 130: 31-32 ○ Hoyer J, Winterhoff R, Fricke L, Sack K. Transplantation Proceedings. 1997, 29: 2948-2950 ○ Sirijatuphat R, Thamlikitkul V. Antimicrob Agents Chemother. 2014 Sep,58(9):5598-601 The IV fosfomycin licence covers infections in adults (including pregnant women) and children including neonates	includable studies (before 2006) and is not available in English (language) • Peters et al. (1981) did not meet the criteria for inclusion as falls outside the date range set by the committee for includable studies (before 2006) and is not available in English (language) • Zeus data (2017) did not meet the criteria for inclusion as it is a conference abstract • Dinh et al. (2012) did not meet the inclusion criteria as it is a prospective cohort study not a systematic review or randomised controlled trial Thank you for your comment. NICE recognise that biofilms are important in the development of catheter-associated urinary tract infection. However, the guideline is for the treatment of catheter-associated urinary tract infection not treatment of biofilms. Additionally: • Sabir et al. (2017) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial • Mihailescu et al. (2014) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, additionally in vivo studies were in animals (guinea pigs) not humans • Corvec et al. (2013) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, additionally in vivo studies were in animals (guinea pigs) not humans • Olivia et al. (2014) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, additionally in vivo studies were in animals (guinea pigs) not humans • Mikuniya et al. (2005) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, only in vitro tests were used • Kumon et al. (1995) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, only in vitro tests were used and falls outside the date range set by the committee for includable studies (before 2006) • Mikuniya et al. (2007) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, additionally in vivo studies were in animals (rats) not humans • Monden et al. (2002) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, only in vitro tests were used • Marquès et al. (2015) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial, only in vitro tests were used • Rodriguez-Martinez et al. (2007) did not meet the criteria for inclusion as it is not a systematic review or randomised controlled trial (letter to editor)

						• Inouye et al. (1982) did not meet the criteria for inclusion as it is an animal study (rats) and falls outside the date range set by the committee for includable studies (before 2006) • Fujita et al. (1983) did not meet the criteria for inclusion as it is an animal study (rats) and falls outside the date range set by the committee for includable studies (before 2006) • Chie Yanagida et al. (2004) did not meet the criteria for inclusion as it is an animal study (rats) and falls outside the date range set by the committee for includable studies (before 2006) • Kimio Fujita (1984) did not meet the criteria for inclusion as it is an animal study (rats) and falls outside the date range set by the committee for includable studies (before 2006) • Yuji Yoshiyama et al. (2005) did not meet the criteria for inclusion as it is an animal study (rats) • Nakamura et al. (1999 [sic] actual publication date May 1998) did not meet the criteria for inclusion as it is an animal study (rats) and falls outside the date range set by the committee for includable studies (before 2006) • Bär et al. (2005) did not meet the criteria for inclusion as it is not available in English (language) • Hoyer et al. (1997) did not meet the criteria for inclusion as it falls outside the date range set by the committee for includable studies (before 2006) and is not in the same population as the guideline (study is in people with renal transplantation) • Sirijatuphat et al. (2014) did not meet the inclusion criteria as the population of the guideline (n=94, <6% overall had a urinary tract infection and it is unclear if any had a catheter associated urinary tract infection
89	Nordic Pharma	Guideline	11		IV fosfomycin may be a suitable treatment option for patients with suspected penicillin allergy (fosfomycin disodium molecule does not contain a beta lactam ring) Refs: ○ Rosales et al., [167]; Durupt et al., [50] ○ Fomicyt IV (fosfomycin) Summary Of Product Characteristics July 2015 • Due to unique mode of action no cross-resistance and no cross-allergy has been observed during IV fosfomycin therapy ref: ○ Fomicyt IV (fosfomycin) Summary Of Product Characteristics July 2015 • With just over 40 years clinical experience, there is evidence which demonstrates IV fosfomycin is very well tolerated ref: Grabein et al., Intravenous fosfomycin-back to the future. Systematic review and meta-analysis of the clinical literature. Clinical Microbiology and Infection. Dec 2016	Thank you for your comment.