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SIGN 88 • Management of suspected bacterial urinary tract infection in adults

A national clinical guideline

Updated July 2012

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 ⁺⁺	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1 ⁺	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review, or RCT rated as 1 ⁺⁺ , and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ⁺

GOOD PRACTICE POINTS

- ✓ Recommended best practice based on the clinical experience of the guideline development group



NHS Evidence has accredited the process used by **Scottish Intercollegiate Guidelines Network** to produce guidelines. Accreditation is valid for three years from 2009 and is applicable to guidance produced using the processes described in SIGN 50: a guideline developer's handbook, 2008 edition (www.sign.ac.uk/guidelines/fulltext/50/index.html). More information on accreditation can be viewed at www.evidence.nhs.uk

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SIGN guidelines are produced using a standard methodology that has been **equality impact assessed** to ensure that these equality aims are addressed in every guideline. This methodology is set out in the current version of SIGN 50, our guideline manual, which can be found at www.sign.ac.uk/guidelines/fulltext/50/index.html. The EQIA assessment of the manual can be seen at www.sign.ac.uk/pdf/sign50eqia.pdf. The full report in paper form and/or alternative format is available on request from the NHS QIS Equality and Diversity Officer.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site www.sign.ac.uk.



Scottish Intercollegiate Guidelines Network

**Management of suspected bacterial
urinary tract infection in adults**

A national clinical guideline



July 2012

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1 Introduction

1.1 THE NEED FOR A GUIDELINE

Urinary tract infection (UTI) is the second most common clinical indication for empirical antimicrobial treatment in primary and secondary care, and urine samples constitute the largest single category of specimens examined in most medical microbiology laboratories.¹ Healthcare practitioners regularly have to make decisions about prescription of antibiotics for urinary tract infection. Criteria for the diagnosis of urinary tract infection vary greatly in the UK, depending on the patient and the context. There is considerable evidence of practice variation in use of diagnostic tests, interpretation of signs or symptoms and initiation of antibiotic treatment,²⁻⁵ with continuing debate regarding the most appropriate diagnosis and management.^{1,6}

The diagnosis of UTI is particularly difficult in elderly patients, who are more likely to have asymptomatic bacteriuria as they get older.⁷ The prevalence of bacteriuria may be so high that urine culture ceases to be a diagnostic test.⁸ Elderly institutionalised patients frequently receive unnecessary antibiotic treatment for asymptomatic bacteriuria despite clear evidence of adverse effects with no compensating clinical benefit.^{9,10}

Existing evidence based guidelines tend to focus on issues of antibiotic treatment (drug selection, dose, duration and route of administration) with less emphasis on clinical diagnosis or the use of near patient tests or are limited to adult, non-pregnant women with uncomplicated, symptomatic UTI.^{11,12}

For patients with symptoms of urinary tract infection and bacteriuria the main aim of treatment is relief of symptoms. Secondary outcomes are adverse effects of treatment or recurrence of symptoms. For asymptomatic patients the main outcome from treatment is prevention of future symptomatic episodes.

Unnecessary use of tests and antibiotic treatment may be minimised by developing simple decision rules, diagnostic guidelines or other educational interventions.¹³⁻¹⁶ Prudent antibiotic prescribing is a key component of the UK's action plans for reducing antimicrobial resistance.^{17,18} Unnecessary antibiotic treatment of asymptomatic bacteriuria is associated with significantly increased risk of clinical adverse events¹⁹⁻²¹ including *Clostridium difficile* infection (CDI) or methicillin resistant *Staphylococcus aureus* (MRSA) infection, and the development of antibiotic-resistant UTIs. In people aged over 65 years asymptomatic bacteriuria is common but is not associated with increased morbidity.²¹ In patients with an indwelling urethral catheter, antibiotics do not generally eradicate asymptomatic bacteriuria.²¹

1.1.1 UPDATING THE EVIDENCE

This guideline updates SIGN 88: Management of suspected bacterial urinary tract infection in adults, published in 2006. The update replaces recommendations on prescribing with reference to local prescribing protocols. The risks of CDI and MRSA are also discussed.

This update has not addressed any new questions, but has set the existing recommendations more clearly in the context of the need to minimise the risk of antibiotic-resistant organisms developing greater resistance.

The original supporting evidence was not re-appraised by the current guideline development group and no new evidence has been assessed. Some policy related references have been updated.

1.2 REMIT OF THE GUIDELINE

1.2.1 OVERALL OBJECTIVES

This guideline provides recommendations based on current evidence for best practice in the management of adults with community acquired urinary tract infection. It includes adult women (including pregnant women) and men of all ages, patients with indwelling catheters and patients with comorbidities such as diabetes. It excludes children and patients with hospital acquired infection. The guideline does not address prophylaxis to prevent UTI after instrumentation or surgery, or treatment of recurrent UTI.

1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to healthcare professionals in primary and secondary care, officers in charge of residential and care homes, antibiotic policy makers, clinical effectiveness leads, carers and patients.

Additional epidemiological and statistical information, and proposed treatment pathways to accompany this guideline are available on the SIGN website www.sign.ac.uk

1.2.3 SUMMARY OF UPDATES TO THE GUIDELINE, BY SECTION

2	Key recommendations	New
3	Management of bacterial UTI in adult women	Antibiotic treatment section updated
4	Management of bacterial UTI in pregnant women	Antibiotic treatment section updated
5	Management of bacterial UTI in adult men	Antibiotic treatment section updated
6	Management of bacterial UTI in patients with catheters	Antibiotic prophylaxis and treatment sections updated
7	Provision of information	Minor update
8	Implementing the guideline	Updated

1.3 DEFINITIONS

<i>asymptomatic bacteriuria</i>	presence of bacteriuria in urine revealed by quantitative culture or microscopy in a sample taken from a patient without any typical symptoms of lower or upper urinary tract infection. In contrast with symptomatic bacteriuria, the presence of asymptomatic bacteriuria should be confirmed by two consecutive urine samples. ²²
<i>bacteraemia</i>	presence of bacteria in the blood diagnosed by blood culture.
<i>bacteriuria</i>	presence of bacteria in urine revealed by quantitative culture or microscopy.
<i>classic symptoms of urinary tract infection (UTI)</i>	dysuria, frequency of urination, suprapubic tenderness, urgency, polyuria, haematuria
<i>empirical treatment</i>	treatment based on clinical symptoms or signs unconfirmed by urine culture.
<i>haematuria</i>	blood in the urine either visible (macroscopic haematuria) or invisible (microscopic haematuria).
<i>long term catheter</i>	an indwelling catheter left in place for over 28 days.
<i>lower urinary tract infection (LUTI)</i>	evidence of urinary tract infection with symptoms suggestive of cystitis (dysuria or frequency without fever, chills or back pain).
<i>medium term catheter</i>	an indwelling catheter left in place for 7-28 days.
<i>mild urinary tract infection</i>	less than three of the classical symptoms of UTI. ²³
<i>near patient testing</i>	tests that are done at the point of consultation and do not have to be sent to a laboratory.

<i>pyuria</i>	occurrence of $\geq 10^4$ white blood cells (WBC)/ml in a freshly voided specimen of urine. Higher numbers of WBC are often found in healthy asymptomatic women. Pyuria is present in 96% of symptomatic patients with bacteriuria of $>10^5$ colony forming units (cfu)/ml, but only in $<1\%$ of asymptomatic, abacteriuric patients. ²³ Pyuria in the absence of bacteriuria may be caused by the presence of a foreign body, for example, a urinary catheter, urinary stones or neoplasms, lower genital tract infection or, rarely, renal tuberculosis.
<i>severe urinary tract infection</i>	Three or more of the classical symptoms of UTI. ²³
<i>short term catheter</i>	an indwelling catheter left in place for 1-7 days.
<i>significant bacteriuria</i>	For laboratory purposes the widely applied definition in the UK is 10^4 cfu/ml. For some specific patient groups there is evidence for lower thresholds: <ul style="list-style-type: none"> • women with symptomatic UTI $\geq 10^2$ cfu/ml • men $\geq 10^3$ cfu/ml (if 80% of the growth is due to a single organism).
<i>symptomatic bacteriuria</i>	presence of bacteriuria in urine revealed by quantitative culture or microscopy in a sample taken from a patient, or the typical symptoms of lower or upper urinary tract infection. The presence of symptomatic bacteriuria can be established with a single urine sample.
<i>upper urinary tract infection (UUTI)</i>	evidence of urinary tract infection with symptoms suggestive of pyelonephritis (loin pain, flank tenderness, fever, rigors or other manifestations of systemic inflammatory response).

1.4 KEY MESSAGES ABOUT BACTERIAL UTI

Bacteriuria is not a disease

- The normal flora of the human body are extremely important as a key part of host defences against infection and because of their influence on nutrition.²⁴
- Prevalence of bacteriuria is uncommon in those aged under 65 years but prevalence increases with increasing age in those over 65 years (*see Table 1*). Bacteriuria is common in some populations of institutionalised women²⁵ and people with long term indwelling urinary catheters (*see section 6*).

Tests for bacteriuria or pyuria do not establish the diagnosis of UTI

- The diagnosis of UTI is primarily based on symptoms and signs (*see section 3.1*).
- Tests that suggest or prove the presence of bacteria or white cells in the urine may contribute additional information to inform management but rarely have important implications for diagnosis (*see sections 3.2, 4.2, 5.1, 6.2*).

Bacteriuria alone is rarely an indication for antibiotic treatment

- Bacteriuria can only be an absolute indication for antibiotic treatment when there is convincing evidence that eradication of bacteriuria results in meaningful health gain at acceptable risk (*see sections 3.4, 6.3, 6.4*). In particular, in elderly patients, asymptomatic bacteriuria is common and there is evidence that treatment is more harmful than beneficial.^{9,10} In contrast, during pregnancy there is evidence that treatment of bacteriuria does more good than harm.²⁶
- The main value of urine culture is to identify bacteria and their sensitivity to antibiotics (*see sections 3.3, 4.1.2, 5.1, 6.1*).
- Indirect indicators of the presence of bacteria (for example, urinary nitrites) are likely to be much less valuable than urine culture (*see sections 3.2.3, 4.2, 6.2.2*).

There is a risk of false positive results in all tests for diagnosis of bacteriuria other than the gold standard

- The gold standard test for diagnosis of bacteriuria is culture of bladder urine obtained by needle aspiration of the bladder as it minimises the risk of contamination of the urine specimen (*see section 4.1.2*).
- All other techniques (urethral catheter and midstream specimens of urine) carry a higher risk of contamination and therefore produce some false positive results (*see section 4.1.2*).
- The significance of false positive results is greatest when testing for bacteriuria in people with low pre-test probability (for example, screening for asymptomatic bacteriuria in the first trimester of pregnancy, *see section 4.1.2*).

Routine urine culture is not required to manage LUTI in women

- Women with symptomatic LUTI should receive empirical antibiotic treatment (*see section 3.4.1*).
- All urine samples taken for culture will be from patients who are not responding to treatment and will bias the results of surveillance for antibiotic resistance (*see section 8.4*).

1.5 EPIDEMIOLOGY**1.5.1 PREVALENCE OF ASYMPTOMATIC BACTERIURIA**

In women, asymptomatic bacteriuria becomes increasingly common with age. The limited data about healthy men show that the prevalence of bacteriuria also increases with age, although the prevalence in men is always lower than for women of the same age (*see Table 1 and supplementary material section S2.1.2*).²⁷⁻²⁹

Table 1: Prevalence of asymptomatic bacteriuria in adult men and women

Country	Age (years)	Men (%)	Women (%)
Japan ²⁷	50-59	0.6	2.8
	60-69	1.5	7.4
	70+	3.6	10.8
Sweden ²⁸	72	6.0	16.0
	79	6.0	14.0
Scotland ²⁹	65-74	6.0	16.0
	>75	7.0	17.0

1.5.2 RISK FACTORS FOR ASYMPTOMATIC BACTERIURIA

Table 2: Risk factors for asymptomatic bacteriuria

Risk factor	Effect on prevalence of asymptomatic bacteriuria
Female sex	Increases prevalence (<i>see Table 1</i>)
Sexual activity	May increase prevalence (higher in married women than in nuns ³⁰ (<i>see supplementary material section S2.1.1</i>))
Comorbid diabetes	Increases prevalence in women less than 65 years of age with diabetes from 2-6% to 7.9-17.7% ³¹⁻³⁵
Age	Increases prevalence in women and men ^{27-29, 36-39} (<i>see Table 1 and supplementary material section S2.1.2</i>)
Institutionalisation	Increases prevalence (in people over 65 years of age) from 6-16% to 25-57% for women ^{19,40-43} and from 1-6% to 19-37% for men ⁴¹⁻⁴⁴
Presence of catheter	3-6% of people acquire bacteriuria with every day of catheterisation. All patients with long term catheters have bacteriuria ^{44,45}

1.5.3 PREVALENCE OF SYMPTOMATIC BACTERIURIA

Combined figures from nine studies show that women under 50 years of age with acute symptoms such as dysuria, urgency or frequency (suggesting lower urinary tract infection) or loin pain (suggesting upper urinary tract infection) are extremely likely to have bacteriuria (see Table 3 and supplementary material section S2.2).⁴⁶⁻⁵⁴ The prevalence of symptomatic bacteriuria in pregnant women, men and catheterised patients is discussed in sections 4.1, 5.1 and 6.1.

Table 3: Prevalence of bacteriuria in non-pregnant women under 50 years of age with acute symptoms of UTI⁴⁶⁻⁵⁴

Total number of women	Number with bacteriuria	% with bacteriuria	Lower confidence interval (CI)	Upper confidence interval (CI)
4,135	2,960	71.6%	70.2%	73.0%

1.6 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.6.1 PATIENT VERSION

A patient version of this guideline is available from the SIGN website, www.sign.ac.uk

1.6.2 PRESCRIBING OF LICENSED MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (product licence). This is known as 'off label' use. It is not unusual for medicines to be prescribed outwith their product licence and this can be necessary for a variety of reasons.

Medicines may be prescribed outwith their product licence in the following circumstances:

- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose.

"Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines."⁵⁵

Generally the off label use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.⁵⁵

Any practitioner following a SIGN recommendation and prescribing a licensed medicine outwith the product licence needs to be aware that they are responsible for this decision, and in the event of adverse outcomes, may be required to justify the actions that they have taken.

Prior to prescribing, the licensing status of a medication should be checked in the current version of the British National Formulary (BNF).⁵⁵

1.6.3 ADDITIONAL ADVICE TO NHSSCOTLAND FROM HEALTHCARE IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

Healthcare Improvement Scotland processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

No relevant advice was identified.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation. The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.

Antimicrobial resistance and healthcare associated infections such as methicillin resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infection (CDI) are a serious cause for concern across Europe. Limiting the use of broad spectrum antibiotics such as cephalosporins, quinolones, and co-amoxiclav is a key measure in addressing these problems, and this was one of the key drivers in updating this guideline.

2.1 MANAGEMENT OF BACTERIAL UTI IN ADULT WOMEN

- D** Consider the possibility of UUTI in patients presenting with symptoms or signs of UTI who have a history of fever or back pain
- B** Use dipstick tests to guide treatment decisions in otherwise healthy women under 65 years of age presenting with mild or ≤ 2 symptoms of UTI.
- D** Consider empirical treatment with an antibiotic for otherwise healthy women aged less than 65 years of age presenting with severe or ≥ 3 symptoms of UTI.
- B** Treat non-pregnant women of any age with symptoms or signs of acute LUTI with a three day course of trimethoprim or nitrofurantoin.
- ✓ Particular care should be taken when prescribing nitrofurantoin to elderly patients, who may be at increased risk of toxicity.
- D** Treat non-pregnant women with symptoms or signs of acute UUTI with a course of ciprofloxacin (7 days) or co-amoxiclav (14 days).
- A** Do not treat non-pregnant women (of any age) with asymptomatic bacteriuria with an antibiotic.

2.2 MANAGEMENT OF BACTERIAL UTI IN PREGNANT WOMEN

- B** Treat symptomatic UTI in pregnant women with an antibiotic.
- ✓ Take a single urine sample for culture before empiric antibiotic treatment is started.
- ✓ Refer to local guidance for advice on the choice of antibiotic for pregnant women.
- ✓ A seven day course of treatment is normally sufficient.
- ✓ Given the risks of symptomatic bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure.
- A** Treat asymptomatic bacteriuria detected during pregnancy with an antibiotic.

2.3 MANAGEMENT OF BACTERIAL UTI IN ADULT MEN

- B** Treat bacterial UTI empirically with a quinolone in men with symptoms suggestive of prostatitis.
- D** Refer men for urological investigation if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI.

2.4 MANAGEMENT OF BACTERIAL UTI IN PATIENTS WITH CATHETERS

- D** Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients.
- B** Do not use dipstick testing to diagnose UTI in catheterised patients.
- A** Do not routinely prescribe antibiotic prophylaxis to prevent symptomatic UTI in patients with catheters.
- B** Do not treat catheterised patients with asymptomatic bacteriuria with an antibiotic.

3 Management of bacterial UTI in adult women

An algorithm summarising the management of suspected UTI in non-pregnant women can be found on the SIGN website in the supporting material section for this guideline.

3.1 DIAGNOSIS

Symptoms suggestive of acute urinary tract infection are one of the most common reasons for women to visit healthcare professionals. Although the clinical encounter typically involves taking a history and performing a physical examination, the diagnostic accuracy of the clinical assessment for UTI remains uncertain.^{12,56}

Recommendations in this section apply to otherwise healthy women presenting with signs or symptoms of a UTI. They do not apply to frail elderly women with multiple complex pathologies who more commonly present with atypical signs and symptoms.

The prior probability of bacteriuria in otherwise healthy women who present to their general practitioner (GP) with symptoms of acute UTI is estimated at between 50-80%.¹²

If dysuria and frequency are both present, then the probability of UTI is increased to >90% and empirical treatment with antibiotic is indicated.¹²

Initiation of antibiotic treatment should be guided by the number of symptoms of UTI that are present.²¹

D Consider empirical treatment with an antibiotic for otherwise healthy women aged less than 65 years presenting with severe or ≥ 3 symptoms of UTI.

If vaginal discharge is present, the probability of bacteriuria falls. Alternative diagnoses such as sexually transmitted diseases (STDs) and vulvovaginitis, usually due to candida, are likely and pelvic examination is indicated.¹²

B Explore alternative diagnoses and consider pelvic examination for women with symptoms of vaginal itch or discharge.

The presence of back pain or fever increases the probability of UUTI and urine culture should be considered as the clinical risks associated with treatment failure are increased.²¹

D Consider the possibility of UUTI in patients presenting with symptoms or signs of UTI who have a history of fever or back pain.

3.2 NEAR PATIENT TESTING

Near patient tests may include the appearance of the urine sample, microscopy and testing by means of dipsticks.

3.2.1 APPEARANCE OF URINE

Urine turbidity has been shown to have a specificity of 66.4% and sensitivity of 90.4% for predicting symptomatic bacteriuria. When examined against a bright background, a turbid sample is positive, whereas a clear sample is negative. Visual appearance is prone to observer error and may not be a useful discriminator.

3.2.2 URINE MICROSCOPY

There is wide variation in sensitivity (60-100%) and specificity (49-100%) of urine microscopy to predict significant bacteriuria in symptomatic ambulatory women.^{57,58}

Near patient testing by microscopy raises concerns about health and safety at work, maintenance of equipment and training of staff which does not justify its use.

3.2.3 DIPSTICK TESTS

The quality of evidence for near patient testing with dipstick tests (reagent strip tests) was poor.^{12,59} The care setting varied across the studies, for example, accident and emergency, genitourinary medicine and hospital inpatients. Individual reagent responses were reported in a variable and incomplete way.

A meta-analysis of the accuracy of dipstick testing to predict UTI looked at four categories of tests: nitrite only; leucocyte esterase (LE) only; disjunctive pairing (dipstick positive if either nitrite or LE or both are positive) and conjunctive pairing (dipstick positive only if both nitrite and LE are positive).⁵⁹ The study found the disjunctive pair test to be significantly more accurate than the LE test alone ($p=0.0001$).⁵⁹ A urine sample positive for dipstick tests for LE or nitrite is less likely to predict bacteriuria than combinations of symptoms and signs, particularly combinations of confirmatory symptoms (dysuria, frequency) and absence of features that suggest alternative diagnoses (vaginal discharge and irritation).¹²

Dipstick tests are only indicated for women who have minimal signs and symptoms and whose prior probability of UTI is in the intermediate range (around 50%). Where only one symptom or sign is present, a positive dipstick test (LE or nitrite) is associated with a high probability of bacteriuria (80%) and negative tests are associated with much lower probability (around 20%).⁵⁹

Negative tests do not exclude bacteriuria. A randomised controlled trial (RCT) of near patient testing in adult women who were symptomatic but had a negative dipstick test showed that antibiotics (trimethoprim 300 mg daily for three days) improved symptoms with the median duration of constitutional symptoms being reduced by four days. Although the probability of UTI is reduced to less than 20% by a negative dipstick test, the evidence suggests that women still derive symptomatic benefit from antibiotics, number needed to treat (NNT) of 4.⁶⁰ For statistical methods see supplementary material section S1. These issues should be considered and explained to symptomatic women with a negative dipstick test. Clinical judgement should be used to decide whether to obtain urine for culture or invite the patient to return if symptoms persist or worsen.⁵⁹

B Use dipstick tests to guide treatment decisions in otherwise healthy women under 65 years of age presenting with mild or ≤ 2 symptoms of UTI.

✓ Discuss the risks and benefits of empirical treatment with the patient and manage treatment accordingly.

No robust evidence was identified describing LE or nitrite testing in elderly, institutionalised patients.

✓ In elderly patients (over 65 years of age), diagnosis should be based on a full clinical assessment, including vital signs.

3.3 URINE CULTURE

The quality of a urine sample will affect the ability to detect bacteria and confirm a diagnosis of UTI. Specimens can be divided into those with high risk of contamination (clean catch, CSU or midstream urine samples; MSU), or low risk (suprapubic aspirate; SPA or operatively obtained urine from ureter or kidney). Standard laboratory processing of urine samples is confined to a single initial specimen per patient, which detects conventional aerobic bacteria, normally at a value of $\geq 10^5$ cfu/ml. There is no bacterial count that can be taken as an absolute 'gold standard' for the diagnosis of UTI.

The criterion for the presence of significant bacteria was established from early work comparing SPA against MSU specimens in women suffering either from acute UUTI or who had asymptomatic UTI during pregnancy. A single positive MSU reliably determined the presence of a UTI at 10^5 cfu/ml in 80% of cases studied with two samples improving this to 95%.⁶¹⁻⁶³

For women experiencing symptoms of urinary tract infection lower numbers of colony forming units may also reflect significant bacteria. A study comparing SPA against MSU specimens found that the best diagnostic criterion in women was $\geq 10^2$ cfu/ml (sensitivity 95%, specificity 85%).⁶⁴

The laboratory interpretation of a urine culture depends upon a combination of factors. These include the number of isolates cultured and their predominance, the specimen type, the clinical details, the presence or absence of pyuria and the numbers of organisms present. Conventional laboratory practice in the UK detects aerobic bacteria at a value of $\geq 10^4$ cfu/ml.²¹

3.4 ANTIBIOTIC TREATMENT

Until recently antimicrobial resistance and healthcare associated infections such as methicillin resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infection (CDI) were increasing. Scotland, in common with other European countries, has developed antimicrobial stewardship programmes to address these issues. The introduction of measures to restrict the use of antibiotics associated with a higher risk of CDI has been successful in reducing CDI rates.^{65,66} This has led to reduced use of cephalosporins, quinolones and co-amoxiclav in antibiotic policies and guidance across hospital and primary care settings and this is reflected within this guideline.

Broad spectrum antibiotics (eg co-amoxiclav, quinolones and cephalosporins) should be avoided as they increase the risk of *Clostridium difficile* infection, MRSA and resistant UTIs. Guidance from the Health Protection Agency (HPA) suggests considering narrow spectrum antibiotics such as trimethoprim or nitrofurantoin as first line treatments.²¹ For second line treatment, performing urine culture in all patients whose first line treatment has failed and prescribing against the urine culture results and any patient hypersensitivity or adverse event history is recommended.²¹

4

3.4.1 SYMPTOMATIC BACTERIURIA, LUTI

Two weeks after completion of treatment, 94% of women on a three day course of trimethoprim achieved bacteriological cure compared with 97% of those on a 10 day course of trimethoprim (n=135).⁶⁷ No difference in outcome between three day, five day or 10 day antibiotic treatment courses for uncomplicated LUTI in women (RR 1.06; 95% CI 0.88 to 1.28; 32 trials, n = 9,605).⁶⁸

1++

Another trial comparing antibiotic treatment with placebo enrolled non-pregnant women aged 15-54 with dysuria and frequency, and detected pyuria (method not specified) but no symptoms or signs of UUTI and no significant comorbidity. A three day regimen of nitrofurantoin significantly shortened time to resolution of symptoms.⁶⁹

1++

Three to six days of antibiotic treatment for uncomplicated LUTI in women aged 60 or over is as effective as treatment for 7-14 days.^{70,71}

1++

Guidelines from the Infectious Diseases Society of America (IDSA)⁷² and Health Protection Agency (HPA)²¹ recommend three days treatment with trimethoprim for LUTI. There is more direct evidence for three days treatment with co-trimoxazole (trimethoprim/sulphamethoxazole) but trimethoprim alone is considered to be as effective as co-trimoxazole in treatment of LUTI.⁷²

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Three days of treatment with nitrofurantoin has been shown to be effective in non-pregnant adult women with uncomplicated UTI.⁶⁹ The IDSA recommends seven days treatment with nitrofurantoin.⁷² There is no direct evidence comparing three days nitrofurantoin with seven days nitrofurantoin.

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4

B Treat non-pregnant women of any age with symptoms or signs of acute LUTI with a three day course of trimethoprim or nitrofurantoin.

✓ Particular care should be taken when prescribing nitrofurantoin in the elderly, who may be at increased risk of toxicity.

✓ Investigate other potential causes in women who remain symptomatic after a single course of treatment.

Nitrofurantoin is contraindicated in the presence of significant renal impairment. The British National Formulary advises against its use in patients with GFR<60.⁷³

Urinary pH affects the activity of nitrofurantoin. Nitrofurantoin is effective against *E. coli* at a concentration of 100 mg/l as the concentration of antibiotic greatly exceeds the minimum inhibitory concentration (MIC or lowest concentration of antibiotic that regularly inhibits growth of the bacterium in vitro). The MIC increases twenty fold from pH5.5 to pH8.0 (see Table 4)⁷⁴ and at pH8.0 bacterial growth occurs with 25 mg/l of nitrofurantoin. A similar situation is seen with *P. mirabilis* although it has a higher MIC than most strains of *E. coli*.

4

D Advise women with LUTI, who are prescribed nitrofurantoin, not to take alkalinising agents (such as potassium citrate).

Table 4: The effect of pH on the MIC of nitrofurantoin on *E. coli* and *P. mirabilis*⁷⁴

	Minimum inhibitory concentration of nitrofurantoin (mg/l)		
	pH 5.5	pH 7.0	pH 8.0
<i>E. coli</i>	2.5	10.0	50.0
<i>P. mirabilis</i>	15.0	50.0	100.0

Resistance is increasing to all of the antibiotics used to treat UTI and there is no clear first choice alternative to trimethoprim or nitrofurantoin.¹¹

1+

D Take urine for culture to guide change of antibiotic for patients who do not respond to trimethoprim or nitrofurantoin.

Infections due to multiresistant organisms including extended-spectrum beta-lactamase (ESBL) *E. coli* are increasing in the community.⁷⁵⁻⁷⁷ Susceptibility results are essential to guide treatment. Oral antibiotics such as nitrofurantoin, pivmecillinam and occasionally trimethoprim are often effective.⁷⁵⁻⁷⁷

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Fosfomycin is effective in treatment of UTI due to multiresistant organisms but is currently unlicensed in the UK.⁷⁸ In cases such as this, however, where a medicine offers specific advantages over licensed alternatives, it may be available on the advice of a microbiologist.

1++

3.4.2 SYMPTOMATIC BACTERIURIA, UUTI

Upper urinary tract infection can be accompanied by bacteraemia, making it a life threatening infection.¹¹ The Health Protection Agency and the Association of Medical Microbiologists recommend hospitalisation of patients with acute pyelonephritis if there is no response to antibiotics within 24 hours, due to the risk of antibiotic resistance.²¹

4

✓ Consider hospitalisation for patients unable to take fluids and medication or showing signs of sepsis.

D Where hospital admission is not required, take a midstream urine sample for culture and begin a course of antibiotics. Admit the patient to hospital if there is no response to the antibiotic within 24 hours.

The Health Protection Agency and the Association of Medical Microbiologists recommend ciprofloxacin or co-amoxiclav for the empirical treatment of acute pyelonephritis. This is based on the need to cover the broad spectrum of pathogens that cause acute pyelonephritis, and their excellent kidney penetration. Although they are associated with an increased risk of *Clostridium difficile*, MRSA, and other antibiotic-resistant infections, this has to be balanced against the risk of treatment failure and consequent serious complications that can arise from acute pyelonephritis.²¹

4

Nitrofurantoin is not recommended for UUTI because it does not achieve effective concentrations in the blood.⁷⁹ Resistance to trimethoprim is too common to recommend this drug for empirical treatment of a life threatening infection.²¹

4

One week of treatment with ciprofloxacin is as effective as two weeks treatment with cotrimoxazole.⁸⁰ | 1⁺⁺

D Treat non-pregnant women with symptoms or signs of acute UUTI with ciprofloxacin (7 days) or co-amoxiclav (14 days).

✓ A 14 day course of trimethoprim can be considered where the organism is known to be sensitive to the antibiotic.

3.4.3 ASYMPTOMATIC BACTERIURIA

There is no evidence that treatment of asymptomatic bacteriuria in adult women significantly reduces the risk of symptomatic episodes, either in women without comorbidity or with underlying diabetes or primary biliary cirrhosis.^{20, 81, 82} | 1⁺⁺
1⁺

In women with diabetes, antibiotic treatment of asymptomatic bacteriuria significantly increases the risk of adverse events without significant clinical benefit, and also increases resistance.²⁰ | 1⁺

In elderly women (over 65 years of age), treatment of asymptomatic bacteriuria does not reduce mortality or significantly reduce symptomatic episodes.^{19, 83} Antibiotic treatment significantly increases the risk of adverse events, such as rashes and gastrointestinal symptoms (number needed to harm; NNTH 3; confidence interval; CI 2 to 10. *For statistical methods see supplementary material section S1*).¹⁹ | 1⁺⁺

A Do not treat non-pregnant women (of any age) with asymptomatic bacteriuria with an antibiotic.

3.5 NON-ANTIBIOTIC TREATMENT

Recurrent UTIs are a common and debilitating problem. Repeated or prolonged treatment with antibiotics is likely to contribute to the problem of antimicrobial resistance. Effective alternatives to antibiotics have the potential to improve public health.

Alternatives to antibiotics offer an opportunity for patients to self manage the prevention of recurrent UTIs, which may improve their quality of life.

3.5.1 CRANBERRY PRODUCTS

Cranberry products (juice, tablets, capsules) are not regulated and the concentration of active ingredients is not known. Concentrations may also fluctuate between batches of the same product.

Most of the high strength preparations (tablet/capsule form) in the UK quote 200 mg of cranberry extract, equivalent to 5,000 mg of fresh cranberries (25:1 concentration).

There is evidence that cranberry products significantly reduce the incidence of UTIs at 12 months (RR 0.65, 95% CI 0.46 to 0.90) compared with placebo/control. Cranberry products were more effective in reducing the incidence of UTIs in women with recurrent UTIs, than in elderly men and women or people requiring catheterisation. The optimal dose and route of administration has not been addressed.⁸⁴ | 1⁺⁺

One study has shown that trimethoprim had a very limited advantage over cranberry extract in the prevention of recurrent UTIs in older women and had more adverse effects.⁸⁵ The NNTs for cranberry products are higher than for nightly antibiotic prophylaxis for six months,⁸⁶ or postcoital antibiotic prophylaxis for six months.⁸⁷ | 1⁺⁺

A Advise women with recurrent UTI to consider using cranberry products to reduce the frequency of recurrence.

✓ Women should be advised that cranberry capsules may be more convenient than juice and that high strength capsules may be most effective.

There is no evidence to support the effectiveness of cranberry products for treating symptomatic episodes of UTI.⁸⁸

No serious adverse effects to cranberry products were reported, although the high drop-out rate in clinical trials suggests that long term treatment with cranberry products may not be well tolerated. The mechanism of action of cranberry products is unclear.

By 2003 the Committee on Safety of Medicines (CSM) received 12 reports of suspected interactions involving warfarin and cranberry juice. In eight of these cases there was an increase in International Normalized Ratio (INR) of the prothrombin time.

In October 2004 the CSM advised that patients taking warfarin should avoid taking cranberry products unless the health benefits are considered to outweigh any risks.⁸⁹

D Advise patients taking warfarin to avoid taking cranberry products unless the health benefits are considered to outweigh any risks.

✓ Consider increased medical supervision and INR monitoring for any patient taking warfarin with a regular intake of cranberry products.

One clinical trial addressed the cost effectiveness of cranberry products for preventing UTI in non-pregnant women (*see supplementary material section S4.1*).⁸⁷

✓ Advise women with recurrent UTI that cranberry products are not available on the NHS, but are readily available from pharmacies, health food shops, herbalists and supermarkets.

3.5.2 METHENAMINE HIPPURATE

A systematic review of methenamine hippurate identified considerable heterogeneity between trials and concluded that interpretation of these data should be done cautiously, due to the small sample sizes and poor methodology of the studies involved.⁹⁰

Methenamine hippurate may be effective at preventing UTI in patients without known upper renal tract abnormalities. Adverse events caused by methenamine were rare.⁹⁰

B Consider the use of methenamine hippurate to prevent symptomatic UTI in patients without known upper renal tract abnormalities.

3.5.3 OESTROGEN

Genitourinary atrophy may increase the risk of bacteriuria and the role of oestrogen therapy in reducing the risk of symptomatic UTI has been investigated.

Evidence for the efficacy of oestrogen in comparison with placebo is inconsistent. There is good evidence that this treatment is less effective than antibiotic prophylaxis. A trial comparing nine months treatment with oral nitrofurantoin versus estriol pessaries in postmenopausal women reported a significantly reduced risk of symptomatic UTI with nitrofurantoin.⁹¹ Two systematic reviews of vaginal oestrogen administration both reported considerable unexplained heterogeneity of results with some studies reporting significant reduction in risk of recurrent UTI while others report no significant effect or even a trend towards harmful effects.^{92,93}

A Do not use oestrogens for routine prevention of recurrent UTI in postmenopausal women.

Treatment with oestrogens may still be appropriate for some women.

3.5.4 ANALGESIA

No evidence was found for the use of analgesics for symptomatic relief of uncomplicated UTIs.

✓ Advise women with uncomplicated UTIs that they may use over-the-counter remedies such as paracetamol or ibuprofen to relieve pain.

3.6 REFERRAL

Recurrent UTI is a common reason for referral of women to urologists but no evidence was found describing criteria for referral or about which investigations to undertake.

There is good evidence to support prevention of recurrent bacterial UTI in women with antibiotics⁹⁴ and cranberry products (*see section 3.5.1*). These strategies should be explored before referral for specialist investigation.

3.7 COST-EFFECTIVE TREATMENT IN PRIMARY CARE

There are two key issues in the economic evaluation of strategies for managing suspected UTI:

- Antibiotics account for only 13% of the total primary care costs for patients with lower urinary tract infection and only 2-8% of the costs for patients with upper urinary tract infection. Visits to the GP account for the majority of costs.⁹⁵
- Management strategies that minimise healthcare costs may transfer costs to the patient. A decision analysis of management strategies for acute uncomplicated lower urinary tract infection in primary care concluded that empiric antibiotic treatment without urine culture was the preferred strategy.⁹⁶ This strategy, however, prolongs the average duration of symptoms because it takes longer to identify women whose infections are caused by antibiotic-resistant bacteria.⁹⁵

3.7.1 GP CONSULTATION

Three decision analyses comparing empiric antibiotic treatment with or without urine culture concluded that taking a urine culture routinely for all patients will cost more but is likely to reduce symptom days by between 0.04 and 0.32 days.⁹⁶ This is achieved through a combination of reducing risk of adverse effects, by stopping treatment if the culture is negative and early identification of infections caused by antibiotic-resistant bacteria. There is considerable variation in the estimates of the incremental cost effectiveness of urine culture.

One study estimated the cost per symptom day prevented as £215. The estimated cost per QALY (quality adjusted life year) gained was £215,000.⁹⁷ It is unlikely that routine culture of urine will be cost effective unless the prevalence of bacteriuria in symptomatic women is <30%.⁹⁷ This is well below the lowest figure reported in epidemiology studies (*see Table 3*).

Dipstick testing was shown to save fewer symptom days at greater cost than urine culture.^{98,97} Dipstick strategies only became cost effective if both the sensitivity of the test and the risk of antibiotic side effects were maximised to unrealistic levels.^{97,98} Dipstick testing is only likely to be cost effective in symptomatic women with low probability of bacteriuria (<50%, for example, with only one symptom) and urine culture is only likely to be cost effective in women with very low probability (<20%, for example, with only one symptom and negative dipstick test).

3.7.2 TELEPHONE CONSULTATION

Evidence from a controlled before and after study (CBA) and an RCT showed that telephone consultation by nurse practitioners is as effective and safe as standard consultation in a medical practitioner's office, is preferred by a majority of women and is likely to be cost saving.^{15,99} Implementation of telephone consultation in an American population with 147,000 women aged 18 to 55 years was estimated to save one health plan \$367,000 per year.¹⁵ There was a marked trend towards increase in return visits for STDs (relative risk of return visit for STD after nurse telephone consultation 1.79, CI 0.92 to 3.50).¹⁵

Although telephone consultation and antibiotic prescribing by nurse practitioners could be a cost-effective alternative to a general practitioner visit it goes against one of four key recommendations made to primary care by the Department of Health: Standing Medical Advisory Committee, which was to "limit antibiotic prescribing over the telephone".¹⁰⁰ The available evidence also raises serious questions about the safety of telephone consultations for excluding STDs. Telephone consultation cannot be recommended as an alternative to a standard consultation.

4 Management of bacterial UTI in pregnant women

An algorithm summarising the management of suspected LUTI in pregnant women can be found on the SIGN website in the supporting material section for this guideline.

4.1 DIAGNOSIS

4.1.1 SYMPTOMATIC BACTERIURIA

Symptomatic bacteriuria occurs in 17–20% of pregnancies.²⁶ There are pathophysiological grounds to support a link to pre-labour, premature rupture of membranes (PPROM) and pre-term labour.⁷⁸ Untreated upper urinary tract infection in pregnancy also carries well documented risks of morbidity, and rarely, mortality to the pregnant woman.⁷⁸

Two to nine per cent of pregnant women are bacteriuric in the first trimester, a similar prevalence to non-pregnant women of the same age.^{22, 101} Ten to thirty per cent of women with bacteriuria in the first trimester develop upper urinary tract infection in the second or third trimester.

4.1.2 THE GOLD STANDARD FOR DIAGNOSIS IN PREGNANCY

The gold standard method for diagnosis of bacteriuria is culture of urine obtained by suprapubic needle aspiration. A catheter specimen of urine is less reliable than suprapubic needle aspiration, although more reliable than two MSU samples.¹⁰² Many studies report using single MSU samples. In women with acute symptoms of UTI the presence of $\geq 10^5$ bacteria per ml of a single MSU sample has about 80% specificity in comparison with the gold standard while a single specimen (MSU or CSU) has a false positive rate of up to 40% for diagnosis of asymptomatic bacteriuria in pregnancy (*see supplementary material section S3.1*).^{102, 103}

4.2 NEAR PATIENT TESTING

A systematic review of studies comparing urine culture with near patient tests reported that no studies used the gold standard for diagnosis of asymptomatic bacteriuria in pregnancy.⁷⁸ In the only study to establish the diagnosis of bacteriuria with two consecutive urine samples at the first antenatal visit, 8.3% of pregnant women had asymptomatic bacteriuria while 12.1% had a positive dipstick test with sensitivity and specificity of 92.0% and 95.0%.¹⁰⁴ Five false negative dipstick tests were for patients who had bacteriuria with gram-positive bacteria (three group B streptococci and two enterococci) which do not cause upper UTI, but are implicated in causing premature delivery.

Dipstick testing (LE or nitrate) is not sufficiently sensitive to be used as a screening test. Urine culture should be the investigation of choice.

A Standard quantitative urine culture should be performed routinely at first antenatal visit.

A Confirm the presence of bacteriuria in urine with a second urine culture.

A Do not use dipstick testing to screen for bacterial UTI at the first or subsequent antenatal visits.

1++

4.3 ANTIBIOTIC TREATMENT

RCTs addressing treatment of UTI in pregnant women frequently include patients with asymptomatic bacteriuria and symptomatic bacteriuria, upper and lower UTI. There is often poor definition of long term outcomes.

4.3.1 SYMPTOMATIC BACTERIURIA

In pregnant women with symptoms of both UUTI and LUTI there is evidence that a range of antibiotic regimens achieve cure.¹⁰⁵⁻¹⁰⁹ There is no clear evidence of benefit by reduction of long term renal damage or pre-term labour as most studies are heterogeneous with respect to LUTI and UUTI and did not specifically address these outcomes. | 1++
1+
2+

There is no clear evidence that any particular antibiotic or dosage regimen has any advantage.²⁵ None of the studies addressed the risk of treatment, but apart from the hazards of adverse reactions or anaphylaxis caused by an inappropriate antibiotic, the risks are likely to be small compared to the proven benefit.²⁶ | 1+

B Treat symptomatic UTI in pregnant women with an antibiotic.

- ✓ Take a single urine sample for culture before empiric antibiotic treatment is started.
- ✓ Refer to local guidance for advice on the choice of antibiotic for pregnant women.
- ✓ A seven day course of treatment is normally sufficient.
- ✓ Given the risks of symptomatic bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure.

4.3.2 ASYMPTOMATIC BACTERIURIA

A systematic review concluded that antibiotic treatment of asymptomatic bacteriuria in pregnancy reduces the risk of upper urinary tract infection, pre-term delivery and low birth weight babies (*see supplementary material section S3.1*).¹¹⁰

Most of the trials in this review were of continuous antibiotic therapy from diagnosis of asymptomatic bacteriuria until the end of pregnancy.¹¹⁰ This is not standard care in the NHS in Scotland, where asymptomatic bacteriuria is usually treated with a short course (3-7 days) of antibiotics. The evidence suggests that 3-7 days treatment is as effective as continuous antibiotic therapy.¹¹⁰ | 1+

There is insufficient evidence to compare the effectiveness of single dose treatment with a 3-7 day course¹¹¹ or a three day with a seven day course.

A Treat asymptomatic bacteriuria detected during pregnancy with an antibiotic.

- ✓ Refer to local guidance for advice on the choice of antibiotic for pregnant women.
- ✓ A seven day course of treatment is normally sufficient.

There is no need for empirical treatment in this group of patients as all women have urine culture before treatment.

The benefits and risks of antibiotic treatment of symptomatic bacteriuria in pregnant women apply equally to pregnant women with asymptomatic bacteriuria.

4.3.3 TERATOGENICITY

Given that some antibiotics may be toxic in pregnancy,¹¹² a risk analysis should be carried out before prescribing. There is no evidence to suggest that penicillin or cephalosporins are associated with an increased risk of congenital malformations. Neither is there evidence of an increased risk of congenital malformations from use of nitrofurantoin, though it has been associated with a very low risk of haemolysis in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Trimethoprim is unlikely to cause problems in women with normal folate status, but may cause problems in women who have a folate deficiency or low folate intake.²¹

4

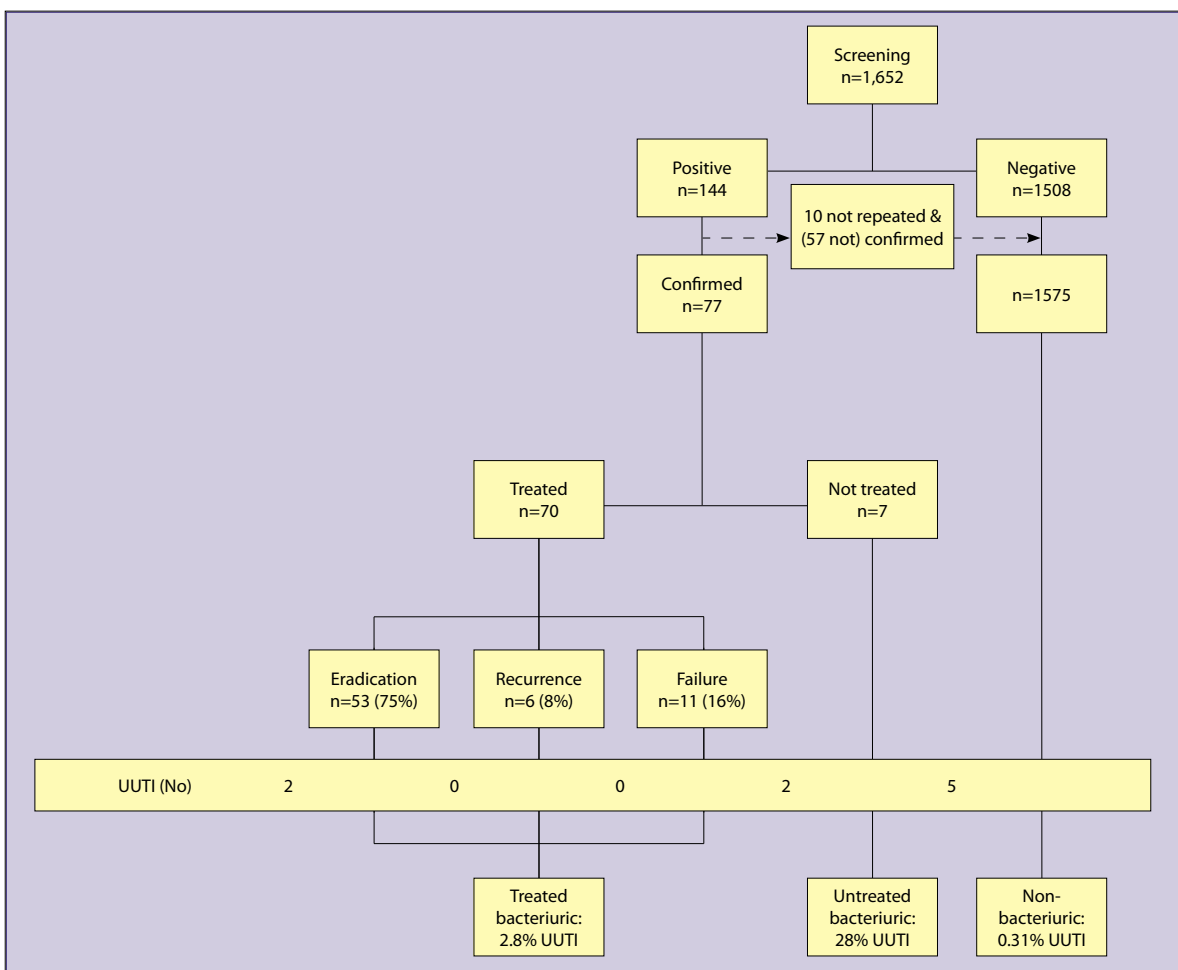
D Do not prescribe trimethoprim for pregnant women with established folate deficiency, low dietary folate intake, or women taking other folate antagonists.

4.4 SCREENING DURING PREGNANCY

A large observational study demonstrated the effectiveness of a screening programme based on diagnosis of asymptomatic bacteriuria with two urine cultures in the first trimester. (see Figure 1).¹⁰³

2+

Figure 1: Frequency of asymptomatic bacteriuria, response to treatment and subsequent development of upper urinary tract infection. Adapted from Gratacos et al 1994¹⁰³



C Women with bacteriuria confirmed by a second urine culture should be treated and have repeat urine culture at each antenatal visit until delivery.

✓ Women who do not have bacteriuria in the first trimester should not have repeat urine cultures.

There is inconsistent evidence regarding the cost effectiveness of screening pregnant women for asymptomatic bacteriuria (see supplementary material section S4.2).^{103, 113-115}

2+

5 Management of bacterial UTI in adult men

An algorithm summarising the management of suspected LUTI in men can be found on the SIGN website in the supporting material section for this guideline.

5.1 DIAGNOSIS

Urinary tract infections in men are generally viewed as complicated because they result from an anatomic or functional anomaly or instrumentation of the genitourinary tract.¹¹⁶

Conditions like prostatitis, chlamydial infection and epididymitis should be considered in the differential diagnosis of men with acute dysuria or frequency and appropriate diagnostic tests should be considered.

There is no evidence to suggest the best method of diagnosing bacterial UTI in men. Evidence from studies of women cannot be extrapolated.

- ✓ Urine microscopy should not be undertaken in clinical settings in primary or secondary care.
- ✓ In all men with symptoms of UTI a urine sample should be taken for culture.
- ✓ In patients with a history of fever or back pain the possibility of UUTI should be considered.

Obtaining a clean-catch sample of urine in men is easier than in women and a colony count of $\geq 10^3$ cfu/ml may be sufficient to diagnose UTI in a man with signs and symptoms as long as 80% of the growth is of one organism.¹¹⁷

A threshold of $\geq 10^3$ cfu/ml for diagnosing UTI is below the threshold of detection for some commonly used laboratory methods, which only detect between 10^4 and 10^5 cfu/ml.

The culture of expressed prostatic secretion and semen has no clinical benefit and is no longer common practice.¹¹⁸

5.2 ANTIBIOTIC TREATMENT

No high quality evidence for the treatment of bacterial UTI in men was identified.

Until recently antimicrobial resistance and healthcare associated infections such as methicillin resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infection (CDI) were increasing. Scotland, in common with other European countries, has developed antimicrobial stewardship programmes to address these issues. The introduction of measures to restrict the use of antibiotics associated with a higher risk of CDI has been successful in reducing CDI rates.^{65,66} This has led to reduced use of cephalosporins, quinolones and co-amoxiclav in antibiotic policies and guidance across hospital and primary care settings and this is reflected within this guideline.

Broad spectrum antibiotics (eg co-amoxiclav, quinolones and cephalosporins) should be avoided as they increase the risk of *Clostridium difficile* infection, MRSA and resistant UTIs. Guidance from the Health Protection Agency (HPA) suggests considering narrow spectrum antibiotics such as trimethoprim or nitrofurantoin as first line treatments.²¹ For second line treatment, performing urine culture in all patients whose first line treatment has failed and prescribing against the urine culture results and any patient hypersensitivity or adverse event history is recommended.²¹

The HPA suggests that a seven day course of trimethoprim or nitrofurantoin may be considered for those with symptoms of uncomplicated lower UTI.²¹

- ✓ Particular care should be taken when using nitrofurantoin in the elderly, who may be at increased risk of toxicity.

Nitrofurantoin is contraindicated in the presence of significant renal impairment. The British National Formulary advises against its use in patients with $GFR < 60$.⁷³

At least 50% of men with recurrent UTI¹¹⁹ and over 90% of men with febrile UTI¹²⁰ have prostate involvement, which may lead to complications such as prostatic abscess or chronic bacterial prostatitis.

Due to their ability to penetrate prostatic fluid, quinolones rather than nitrofurantoin or cephalosporins are indicated.¹²⁰ | 1+

B Treat bacterial UTI empirically with a quinolone in men with symptoms suggestive of prostatitis.

There is no good evidence indicating the optimum length of treatment, but the consensus between HPA and other UK bodies is that a four week course is appropriate for men with symptoms suggestive of prostatitis.²¹ | 4

5.3 REFERRAL

Recurrent UTI is a common reason for referral to urologists. There are no trials about the effectiveness of antibiotics or cranberry products for preventing recurrent UTI in men. There are no evidence based guidelines for referral or about which investigations to undertake.

Expert opinion suggests that men should be investigated if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI (two or more episodes in three months).¹²¹ | 4

D Refer men for urological investigation if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI.

Urodynamic techniques, such as pressure/flow videocystography revealed significant underlying lower urinary tract abnormalities (mainly involving bladder outflow obstruction) in 80% of adult males presenting with simple or recurrent urinary tract infections, but without prior urinary symptoms or disorders.¹²² | 2+

✓ Consider renal and post-void bladder ultrasound and a kidneys, ureters and bladder (KUB) plain X-ray of the abdomen to look for abnormalities.

6 Management of bacterial UTI in patients with catheters

An algorithm summarising the management of suspected bacterial UTI in older people can be found on the SIGN website in the supporting material section for this guideline.

6.1 DIAGNOSIS

Between two and seven per cent of patients with indwelling urethral catheters acquire bacteriuria each day, even with the application of best practice for insertion and care of the catheter.¹²³ All patients with a long term indwelling catheter are bacteriuric, often with two or more organisms.^{124,125} The catheter provides a focus for bacterial biofilm formation. The majority of data comes from studies in elderly patients with long term indwelling catheters. There is no evidence to suggest that the prevalence in younger short- or long term catheterised patients, such as those with multiple sclerosis or spinal cord injury, is any different.¹²⁶

Duration of catheterisation is strongly associated with the risk of infection. The longer the catheter is in place the greater the likelihood of infection.¹²⁷ Intermittent catheterisation is associated with a lower incidence of asymptomatic bacteriuria.¹²⁶

The presence of a short- or long term indwelling catheter is associated with a greater incidence of fever of urinary tract origin. Fever without any localising signs is a common occurrence in catheterised patients and urinary tract infection accounts for about a third of these episodes.^{126,128,129} In patients with short- or long-term catheters fever is associated with a higher occurrence of local urinary tract and systemic complications such as bacteraemia.^{126,128,130}

Although mortality appears to be higher in patients with long term indwelling catheters, there is no causative link with catheterisation or urinary tract infection.¹³¹

Urinary tract infection is the most common hospital acquired infection in the UK, accounting for 23% of all infections and the majority of these are associated with catheters.¹³² Catheter-associated UTI is the source for 8% of hospital acquired bacteraemia.¹⁸

In catheterised patients the common occurrence of fever, the consistent presence of bacteriuria, and the variable presence of a broad range of other associated clinical manifestations (new onset confusion, renal angle tenderness or suprapubic pain, chills/rigors etc) makes the diagnosis of symptomatic UTI difficult.^{25, 133,134}

Current suggested criteria for diagnosing UTI in catheterised patients are not evidence based.¹³³ A clinical algorithm for suspected UTI in catheterised and non-catheterised residents in nursing homes suggests that the presence of one of the following symptoms should stimulate antibiotic therapy.¹³⁵

- new costovertebral tenderness
- rigors
- new onset delirium
- fever greater than 37.9°C or 1.5°C above baseline on two occasions during 12 hours.

No particular constellation of symptoms or clinical signs, for example, fever or chills, new flank or suprapubic tenderness, change in character of urine or worsening of mental or functional status, appears to increase the likelihood of a symptomatic urinary tract infection in catheterised patients. The positive predictive value (PPV) of bacteriuria for febrile urinary tract infection identified by clinical criteria has been measured as 11%.¹²⁸ The most common symptom, fever, is a non-specific presenting symptom in symptomatic urinary tract infection. The absence of fever does not appear to exclude urinary tract infection.^{126,128,130}

D Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients.

1++
3

Signs and symptoms compatible with catheter-associated UTI include new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; costo-vertebral angle tenderness; acute haematuria; pelvic discomfort; and in those whose catheters have been removed, dysuria, urgent or frequent urination, or supra-pubic pain or tenderness.⁷²

In patients with spinal cord injury, increased spasticity, autonomic dysreflexia, or sense of unease are also compatible with catheter-associated UTI.⁷²

- ✓ In catheterised patients who present with fever:
 - look for associated localising (loin or supra-pubic tenderness) or systemic features
 - exclude other potential sources of infection
 - send off an appropriately taken urine sample for culture to determine the infecting organism and susceptibility to antibiotics
 - consider antibiotic therapy taking into account the severity of the presentation and any comorbid factors.
- ✓ Only send urine samples for laboratory culture if the patient has clinical sepsis, not because the appearance or smell of the urine suggests that bacteriuria is present.

6.2 NEAR PATIENT TESTING

6.2.1 URINE MICROSCOPY

The value of microscopy of urine samples from catheterised patients is limited in diagnosing symptomatic UTI as all patients will have bacteriuria. There is no relationship between the level of pyuria and infection in patients with indwelling catheters, since the presence of the catheter invariably induces pyuria without the presence of infection.¹³⁶

2+

C Do not use laboratory microscopy to diagnose UTI in patients with catheters.

6.2.2 DIPSTICK TESTS

Symptomatic UTI cannot be differentiated from asymptomatic bacteriuria on the basis of urine analysis with dipstick tests. Pyuria is common in catheterised patients and its level has no predictive value.^{136,137}

2++

2+

There is no evidence to suggest that detecting pyuria by urine analysis is of any value in differentiating symptomatic UTI from asymptomatic UTI (bacteriuria) in catheterised patients.¹³⁶⁻¹³⁸

3

B Do not use dipstick testing to diagnose UTI in patients with catheters.

6.3 ANTIBIOTIC PROPHYLAXIS TO PREVENT CATHETER-RELATED UTI

A meta-analysis of antimicrobial prophylaxis for UTI in catheterised patients with spinal cord dysfunction included patients with acute (less than 90 days after spinal cord injury) and non-acute (greater than 90 days after spinal cord injury) spinal cord dysfunction and neurogenic bladder.¹³⁹ The majority of patients had intermittent catheterisation. Antimicrobial prophylaxis did not significantly decrease symptomatic infections. Prophylaxis was associated with the reduction of asymptomatic bacteriuria among acute patients ($p < 0.05$). There was no significant reduction among non-acute patients. On average 3.57 weeks of treatment were required to prevent one episode of asymptomatic bacteriuria in a patient with acute spinal cord injury. Overall there was an approximately twofold increase in antimicrobial-resistant bacteria except in the group who received methenamine.

1++

1+

This agrees with a systematic review of antibiotic prophylaxis in multiple sclerosis and spinal cord injury patients with neurogenic bladder.¹²⁶

There is insufficient evidence to determine whether or not administration of prophylactic antimicrobials to such patients reduces bacteremia.⁷²

A Do not routinely prescribe antibiotic prophylaxis to prevent symptomatic UTI in patients with catheters.

Prophylactic antibiotics are not routinely required when changing catheters in patients at increased risk of endocarditis such as those with a heart valve lesion, septal defect, patent ductus, or prosthetic valve.¹⁴⁰

Routine use of antimicrobial prophylaxis during catheter change should be avoided.⁷²

✓ Consider antibiotic prophylaxis in patients for whom the number of infections are of such frequency or severity that they chronically impinge on function and well-being.

✓ When changing catheters, antibiotic prophylaxis should only be used for people with a history of catheter-associated urinary tract infection following catheter change.

There is evidence that there is a higher risk of *C. difficile* infection associated with the use of fluoroquinolones, broad spectrum penicillins, or cephalosporins than with other antibiotic options.^{141,142} | 2+
3

C In a hospital setting, when prophylaxis for catheter change is required, consider using a narrow spectrum agent such as gentamicin rather than ciprofloxacin to minimise the risk of *C. difficile* infection.

6.4 ANTIBIOTIC TREATMENT

6.4.1 SYMPTOMATIC BACTERIURIA

Symptoms that may suggest UTI in patients with catheters include fever, flank or suprapubic discomfort, change in voiding patterns, nausea, vomiting, malaise or confusion.^{133,135}

No studies were identified that evaluated the prognostic value of individual or combinations of signs or symptoms, with the exception of fever. The occurrence of febrile episodes in patients with long term indwelling catheters is associated with the development of abnormalities such as calculi and kidney complications.¹⁴³

✓ Patients should be admitted to hospital if systemic symptoms, such as fever, rigors, chills, vomiting or confusion appear.

Patients with long term indwelling catheters, who have the catheter changed before starting antibiotic treatment for symptomatic UTI, have a decreased duration of fever, are more likely to be cured or improved after three days and are less likely to have recurrence of acute symptoms within one month of treatment.^{72,144} | 1+
4

B Change long term indwelling catheters before starting antibiotic treatment for symptomatic UTI.

IDSA guidelines recommend a seven day course of antibiotic treatment for patients with symptomatic catheter-associated UTI who have prompt resolution of symptoms, or 10-14 days where there is a delayed response, regardless of whether or not the catheter is withdrawn during that time.⁷² For women aged <65 years who develop a catheter-associated infection without upper UTI symptoms following removal of an indwelling catheter, a three day course of antibiotics may be sufficient.⁷² | 4

✓ Choice of empirical treatment should be guided by symptoms and follow local antibiotic policy.

6.4.2 ASYMPTOMATIC BACTERIURIA

Single dose antibiotic treatment of women with asymptomatic bacteriuria after short term catheterisation significantly reduces the risk of symptomatic episodes in the following two weeks (number needed to benefit; NNTB 7, CI 4 to 25.²⁰ *For statistical methods see supplementary material section S1*). Given that the prevalence of bacteriuria should be <20%,¹⁴⁵ this means that more than 100 women may need to be screened to prevent one symptomatic episode through treatment. Several studies addressed the cost effectiveness of screening for asymptomatic bacteriuria in catheterised patients (*see supplementary material section S4.3*).^{97, 145-147}

1+

B Do not screen women with asymptomatic bacteriuria after short term catheterisation.

There is inconsistent evidence of benefit from repeated treatment of asymptomatic bacteriuria in patients with long term catheters.^{124,148,149} There is evidence that repeated treatment of asymptomatic bacteriuria increases the risk of colonisation by antimicrobial-resistant bacteria.¹⁴⁹

1++

1+

1-

B Do not treat catheterised patients with asymptomatic bacteriuria with an antibiotic.

6.5 MANAGEMENT OF BACTERIAL UTI IN PATIENTS WITH URINARY STOMAS

There is no evidence to support the management of bacterial UTI in patients with urinary stomas but issues that affect catheterised patients are likely to apply. The prevalence of bacteriuria is likely to be 100% in patients with urinary stomas. Culture of urine from patients with symptoms suggestive of UTI should only be carried out to test the susceptibility of potential pathogens.

✓ Only send urine samples for laboratory culture if the patient has clinical sepsis, not because the appearance or smell of the urine suggests that bacteriuria is present.

7 Provision of information

This section reflects the issues most likely to be of concern to patients and carers following a diagnosis of suspected bacterial urinary tract infection in adult non-pregnant women. These points are provided for use by health professionals when discussing bacterial UTI with patients and in guiding the production of locally produced patient information materials.

7.1 SOURCES OF FURTHER INFORMATION

Age Scotland Helpline

Tel: 0845 833 0200

Website: www.ageuk.org.uk/scotland/

Association for Continence Advice – for professionals

Tel: 01506 811077

Website: www.aca.uk.com

Bladder and Bowel Foundation

SATRA Innovation Park, Rockingham Rd, Kettering, NN16 9JH

Helpline: 0845 345 0165 • Tel: 01536 533 255

www.bladderandbowelfoundation.org • Email: information.officer@bladderandbowelfoundation.org

The Bladder and Bowel Foundation is the UK wide charity for people with bladder and bowel control problems. It provides information and support services, including a confidential helpline, for anyone affected by these conditions as well as their families, carers and healthcare professionals.

Bladder Pain Syndrome Association

Tel: 020 8310 8729

Website: www.self-help.org.uk/directory/incontinence/?entryid54=30294

Provides information and support to sufferers of bladder pain syndromes (including interstitial cystitis and other related disorders/syndromes).

Cystitis and Overactive Bladder Foundation

Telephone: 0121 702 0820

Website: www.cobfoundation.org

Provides information, leaflets and support to people with all forms of lower urinary tract infection and overactive bladders.

Family Planning and Reproductive Health Care

The Sandyford Initiative, 6 Sandyford Place, Sauchiehall Street, Glasgow G3 7NB

Tel: 0141 211 8130

www.sandyford.org

Family Planning Association

www.fpa.org.uk

National Childbirth Trust

Enquiries Line 0300 330 0770, 9am–5pm, Monday to Friday - For any query not covered by the numbers listed on the website.

Website: www.nctpregnancyandbabycare.com/contact-us

National Kidney Federation

Helpline: 0845 601 02 09

Website: www.kidney.org.uk

A charity run by kidney patients for kidney patients, it provides patient support services to patients and their families.

NHS24

Tel: 08454 24 24 24 • Textphone: 18001 08454 24 24 24

Website: www.nhs24.com

NHS 24 is a nurse-led helpline providing confidential healthcare advice and information.

PRODIGY

Website: www.prodigy.nhs.uk

A source of evidence based clinical knowledge about the common conditions and symptoms managed by primary healthcare professionals. Patient information leaflets form an integral part of PRODIGY.

Urostomy Association

Tel: 01889 563191

www.urostomyassociation.org.uk/home.php

Women's Health Concern Ltd.

Whitehall House, 41 Whitehall, London SW1A 2BY

Tel: 020 7451 1377

Website: www.womens-health-concern.org

7.2 KEY ISSUES

There is a need to balance the accuracy of a diagnosis with the speed in which results (and treatment, if necessary) are delivered to the patient. Patients get very frustrated waiting for "official" results to merit treatment of a painful, uncomfortable situation that is preventing normal daily activities.

Many professionals are interested in the accuracy of the assessment, in order not to prescribe inappropriate or unnecessary treatment, which can prolong symptoms.

Patients are aware that dipsticks are not always accurate and that waiting for laboratory analysis can delay time to diagnosis and treatment.

Patients know that factors such as their mood and communication of discomfort also are important in signalling infection.

Patients perceive that the best healthcare professionals are those who take factors that the patient finds signal infection into consideration.

Many patients want information and clear explanation of questions such as:

- "Why doesn't this treatment seem to be working?"
- "How long until I feel better?"
- "Can something alleviate my symptoms (and pain!) in the meantime, or at least ensure a level of comfort so that I can resume normal daily activities (for example, go to work, sleep at night)?"
- "What could happen if I don't comply fully (for example, if I forget to take the full course of treatment)?"
- "Will this drug react/interact with any other drugs/medicines/herbal medicines I am taking?"

7.3 GENERAL ADVICE

Healthcare professionals should offer:

- advice on prudent use of antibiotics as a means of reducing healthcare associated infections and development of antimicrobial resistance. The need for antibiotic treatment and the choice of antibiotic has to be balanced against the risks of *Clostridium difficile* and MRSA infection, and antibiotic resistance.
- information on cranberries. Patients should be advised that further research is required to determine the best way to take cranberries, for example, juice, tablets, or a combination; in what concentration; routinely or preventatively; and how often (see section 3.5.1).
- advice on 'complicated' versus 'uncomplicated' infections. The distinction between a 3 day and a 7 day course of pills and the reasons for using one or the other should also be explained to the patient. These issues could affect concordance.
- contraception advice. This and the role of sexual activity is a critical issue for women, and one which may affect concordance. This issue should be explicitly dealt with by healthcare professionals prescribing and dispensing treatment.
- a reminder to patients and carers that the presence of bacteriuria does not always indicate disease. Especially in elderly patients, asymptomatic bacteriuria is a normal condition and should not be treated with antibiotics.

Given that there is no conclusive association between lifestyle factors, such as diet, hydration, clothing, toileting and sexual activity, and susceptibility to bacterial UTI in adult, non-pregnant women, there is no evidence to support healthcare professionals giving routine advice to patients about lifestyle factors.¹⁵⁰⁻¹⁵³ There may be a link between a second UTI and sexual activity.¹⁵⁰

- ✓ Do not offer routine advice about adopting or discontinuing any particular lifestyle factors to patients with bacterial UTI.
- ✓ For an individual with recurrent and/or complicated urinary tract infection, consider discussing the features of the patient's own situation that may particularly contribute to the problem.

8 Implementing the guideline

8.1 IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by SIGN. The implementation strategy for this guideline encompasses the following tools and activities:

- publishing the full guideline and Quick Reference Guide on the SIGN website
- alerting the NHS in Scotland through the Scottish Antimicrobial Prescribing Group and SIGN networks
- addition to SIGN iPhone and Android mobile 'phone apps
- awareness raising through our networks and in medical journals
- audit tool (based on sections 8.2 and 8.3)
- development and implementation of a care pathway.

8.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

8.2.1 KEY AREAS FOR AUDIT IN PRIMARY CARE

The management of patients with acute urinary symptoms should be audited against the appropriate algorithm (*see the supporting material for this guideline on the SIGN website*).

8.2.2 KEY AREAS FOR AUDIT IN SECONDARY CARE

- Audit of clinical evidence of infection in patients with long term catheters who have been treated with antibiotics or had catheter urine samples sent for culture.
- Audit of elderly patients (typically confused, with a cough, who are positive for nitrite in the urine) treated with augmentin or equivalent and frusemide (so called elderly 'coamilofrus' regimen) with no documented evidence of symptoms of UUTI or LUTI.

8.3 IMPLEMENTATION AND AUDIT OF THE RECOMMENDATIONS

8.3.1		MANAGEMENT OF BACTERIAL UTI IN ADULT WOMEN	
		Recommendation	Implementation or audit
3.1	D	Consider empirical treatment with an antibiotic for otherwise healthy women aged less than 65 years presenting with severe or ≥ 3 symptoms of UTI.	Implementation of care pathways in primary and secondary care including minimum data to be recorded in assessing a woman with symptoms of LUTI.
	B	Explore alternative diagnoses and consider pelvic examination for women with symptoms of vaginal itch or discharge.	
	D	Consider the possibility of UUTI in patients presenting with symptoms or signs of UTI who have a history of fever or back pain.	
	✓	Discuss the risks and benefits of empirical treatment with patient and manage treatment accordingly.	
3.4.1	A	Treat non-pregnant women of any age with symptoms or signs of acute LUTI with a three day course of trimethoprim or nitrofurantoin.	Audit of practice against care pathway.
	✓	Particular care should be taken when using nitrofurantoin in the elderly, who may be at increased risk of toxicity.	
	✓	Investigate other potential causes in women who remain symptomatic after a single course of treatment.	
3.4.2	✓	Consider hospitalisation for patients unable to take fluids and medication, pregnant, or showing signs of sepsis.	Implementation of care pathway for UUTI in primary and secondary care with audit of practice against recommendations.
	D	Where hospital admission is not required, take a midstream urine sample for culture and begin a course of antibiotics. Admit the patient to hospital if there is no response to the antibiotic within 24 hours.	
	A	Treat non-pregnant women with symptoms or signs of acute UUTI with ciprofloxacin (7 days) or co-amoxiclav (14 days).	
3.4.3	A	Do not treat non-pregnant women (of any age) with asymptomatic bacteriuria with an antibiotic.	Percentage of women treated in secondary care for UTI with no documented evidence of symptoms of UUTI or LUTI.

8.3.2 MANAGEMENT OF BACTERIAL UTI IN PREGNANT WOMEN			
		Recommendation	Implementation or audit
4.1.3	A	Standard quantitative urine culture should be performed routinely at first antenatal visit.	Care pathway for detection and management of asymptomatic bacteriuria of pregnancy with audit against targets.
	A	Confirm the presence of bacteriuria in urine with a second urine culture.	
	A	Do not use dipstick testing to screen for bacterial UTI at first or subsequent visits.	
4.3.1	B	Treat symptomatic UTI in pregnant women with an antibiotic.	Care pathway for detection and management of asymptomatic bacteriuria of pregnancy with audit against targets.
	✓	Take a single urine sample for culture before empiric antibiotic treatment is started.	
	✓	A seven day course of treatment is normally sufficient.	
4.3.1	✓	Given the risks of symptomatic bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure.	Audit of antibiotics prescribed to pregnant women against local guidance.
	✓	Refer to local guidance for advice on the choice of antibiotic for pregnant women.	
4.3.2	A	Treat asymptomatic bacteriuria detected during pregnancy with an antibiotic.	Care pathway for detection and management of asymptomatic bacteriuria of pregnancy with audit against targets.
	✓	Refer to local guidance for advice on the choice of antibiotic for pregnant women.	
4.3	C	Women with bacteriuria confirmed by a second urine culture should be treated and have repeat urine culture at each antenatal visit until delivery.	Care pathway for detection and management of asymptomatic bacteriuria of pregnancy with audit against targets.
	✓	Women who do not have bacteriuria in the first trimester should not have repeat urine cultures.	
8.3.3 MANAGEMENT OF BACTERIAL UTI IN ADULT MEN			
		Recommendation	Implementation or audit
5.1	✓	Urine microscopy should not be undertaken in clinical settings in primary or secondary care.	Care pathway for detection and management of suspected UTI in men with audit against targets.
5.2	B	Treat bacterial UTI empirically with a quinolone in men with symptoms suggestive of prostatitis.	
5.3	D	Refer men for urological investigation if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI.	

8.3.4 MANAGEMENT OF BACTERIAL UTI IN PATIENTS WITH CATHETERS			
		Recommendation	Implementation or audit
6.1	D	Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients.	Care pathway for diagnosis of symptomatic UTI in catheterised patients with audit against practice.
	✓	In catheterised patients who present with fever: <ul style="list-style-type: none"> • look for associated localising (loin or suprapubic tenderness) or systemic features • exclude other potential sources of infection • send off an appropriately taken urine sample for culture to determine the infecting organism and susceptibilities • consider antibiotic therapy taking into account the severity of the presentation and any comorbid factors. 	
6.1 and 6.5	✓	Only send urine samples for laboratory culture if the patient has clinical sepsis, not because the appearance or smell of the urine suggests that bacteriuria is present.	Audit of clinical evidence of infection in patients with long term catheters or ureteric stomas who have been treated with antibiotics or had urine samples sent for culture.
6.2.1	C	Do not use laboratory microscopy to diagnose UTI in patients with catheters.	Care pathway for diagnosis of symptomatic UTI in catheterised patients with audit against practice.
6.2.2	B	Do not use dipstick testing to diagnose UTI in patients with catheters.	
6.3	A	Do not routinely prescribe antibiotic prophylaxis to prevent symptomatic UTI in patients with catheters.	Percentage of patients with long term catheters who receive antibiotics with no clinical evidence of symptomatic UTI.
6.3	C	In a hospital setting, when prophylaxis for catheter change is required, consider using a narrow spectrum agent such as gentamicin rather than ciprofloxacin to minimise the risk of <i>C. difficile</i> infection.	Audit as part of antimicrobial prevalence surveys.
6.4.1	✓	Choice of empirical treatment should be guided by symptoms and follow local antibiotic policy.	
6.4.1	B	Change long term indwelling catheters before starting antibiotic treatment for symptomatic UTI.	Audit of catheter change prior to commencing antibiotic.
6.4.2	B	Do not treat catheterised patients with asymptomatic bacteriuria with an antibiotic.	Audit of clinical evidence of infection in patients with long term catheters or ureteric stomas who have been treated with antibiotics or had urine samples sent for culture.

8.4 RECOMMENDATIONS FOR SURVEILLANCE

There should be routine sampling of urine for culture from all patients presenting with acute urinary symptoms in some selected practices to establish the true level of resistance in bacteria causing acute UTI in general practice. Primary research may be required to provide evidence to support details of surveillance (for example, sample sizes, frequency of surveillance studies and geographical location of practices).

There should be surveillance of catheter-associated urinary tract infection (CAUTI following the Scottish Surveillance of Healthcare Associated Infection Programme (SSHAIP) www.hps.scot.nhs.uk/haic/sshai/ssdetail.aspx?id=192

8.4.1 USEFUL SITES FOR SURVEILLANCE AND INFECTION CONTROL

Healthcare Acquired Infections Education for Infection Prevention and Control portal

www.nes.scot.nhs.uk/education-and-training/by-theme-initiative/healthcare-associated-infections.aspx

British Society for Antimicrobial Chemotherapy (BSAC)

www.bsac.org.uk

Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

www.dh.gov.uk/ab/ARHAI/index.htm

National electronic Library of Infection (NeLI)

www.neli.org.uk

9 The evidence base

9.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group.

Literature searches were initially conducted in Medline, Embase, Cinahl, and the Cochrane Library using the year range 1994-2002. The literature search was extended from 1966-2003 for RCTs and diagnostic studies. The National Economic Evaluation Database (NEED) was searched for economic studies to cover the period up to January 2004. Key websites on the internet were also searched. These searches were supplemented by the reference lists of relevant papers and group members' own files. The Medline version of the main search strategies can be found on the SIGN website.

No additional literature searching was done for this update, but references to other sources of advice and Cochrane Reviews were updated. None of these reviews had changed their conclusions.

9.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline (*see Annex 1*). The following areas for further research have been identified:

- What is the risk of misdiagnosis, including STDs, after patients with suspected UTI have telephone consultation and antibiotic prescribing by nurse practitioners?
- How effective are near patient tests when compared to a reliable method for diagnosing asymptomatic bacteriuria in pregnant women?
- Are there laboratory methods capable of detecting bacteria at densities of <104 cfu/ml that can be widely introduced?
- Which antibiotics are most effective for prevention and treatment of recurrent UTI in men?
- What is the optimum length of a course of antibiotics for recurrent UTI in men?
- Are cranberry products effective for prevention and treatment of recurrent UTI in men?
- Is methenamine prophylaxis effective for the prevention of symptomatic UTI in elderly, institutionalised, catheterised patients?
- What are the most effective ways of questioning patients to elicit the most relevant information to aid diagnosis and treatment?
- What are the most effective methods of communication between healthcare professionals and patients about symptoms and factors that relate to a potential infection?
- What is the impact of UTI and its treatment (including side effects) on patients' quality of life?
- What are patients' attitudes and expectations towards treatment and what personal strategies do they have for self care?

9.3 REVIEW AND UPDATING

This guideline was last updated in 2012 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

10 Development of the guideline

10.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at www.sign.ac.uk

10.2 THE GUIDELINE DEVELOPMENT GROUP

Professor Peter Davey (Chair)	<i>Professor of Pharmoeconomics, Medicines Monitoring Unit, Ninewells Hospital and Medical School, Dundee</i>
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Mr Robin Harbour	<i>Quality and Information Director, SIGN</i>
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Ms Brin Jardine	<i>Lay representative, Edinburgh</i>
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Ms Valerie Sillito	<i>Community Pharmacist, Woodend Hospital, Aberdeen</i>
Ms Doreen Simpson	<i>Community Staff Nurse, Green Street Surgery, Forfar</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

10.2.1 ACKNOWLEDGEMENTS

SIGN is grateful to the following former members of the guideline development group and others who contributed to the development of the original guideline.

Ms Fiona Brandt	<i>Practice Nurse, Aberlour</i>
Dr Ali El-Ghorr	<i>Programme Manager, SIGN</i>
Dr Michael Power	<i>Clinical Knowledge Author, Guideline Developer and Informatician, Prodigy Knowledge, Newcastle</i>
Dr Kate Woodman	<i>Lay representative, Edinburgh</i>

10.3 THE GUIDELINE REVIEW GROUP

Dr Jacqueline Sneddon (Chair)	<i>Project Lead, Scottish Antimicrobial Prescribing Group (SAPG)</i>
Ms Helen Cadden	<i>Public Partner, SMC and SAPG</i>
Ms Claire Colligan	<i>Antimicrobial/Clinical Governance Pharmacist, NHS Forth Valley</i>
Professor Peter Davey	<i>Lead Clinical for Quality Improvement, Medical Research Unit, University of Dundee</i>
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Mr Robin Harbour	<i>Lead Methodologist, Healthcare Improvement Scotland</i>
Ms Deirdre Harris	<i>Nurse Consultant - Infection Control, Victoria Hospital, Kirkcaldy</i>
Dr Alexander Mackenzie	<i>Consultant in Infectious Diseases, NHS Grampian</i>
Professor Robert Masterton	<i>Executive Medical Director, NHS Ayrshire and Arran</i>
Dr Andrew Seaton	<i>Consultant in Infectious Diseases and General Medicine, NHS Greater Glasgow and Clyde</i>
Dr Susan Smith	<i>Consultant Microbiologist, NHS Fife</i>

The membership of the guideline review group was made up of members of the Scottish Antimicrobial Prescribing Group, with the agreement of SIGN. All members of the guideline review group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive and SAPG secretariat. All members of the SIGN Executive make yearly declarations of interest and further details of these are available on request.

Ms Lisa Birch	<i>Distribution and Office Coordinator, SIGN</i>
Ms Karen Graham	<i>Patient Involvement Officer, SIGN</i>
Mr Stuart Neville	<i>Publications Designer, SIGN</i>
Ms Susan Paton	<i>Project Officer, SAPG</i>
Ms Gaynor Rattray	<i>Guideline Coordinator, SIGN</i>

10.4 CONSULTATION AND PEER REVIEW

10.4.1 PUBLIC CONSULTATION

The draft guideline was available on the SIGN website for a month to allow all interested parties to comment. All contributors made declarations of interest and further details of these are available on request from the SIGN Executive.

10.4.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments. All expert referees made declarations of interest and further details of these are available on request from the SIGN Executive.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Mr Graeme Bryson	<i>Prescribing Adviser, NHS Ayrshire and Arran</i>
Dr Martin Connor	<i>Consultant Microbiologist, NHS Dumfries and Galloway</i>
Dr Gail Haddock	<i>General Practitioner, NHS Highland</i>
Dr Simon Hurding	<i>GP Adviser Efficiency and Productivity Scottish Government</i>
Dr Edward James	<i>Consultant Microbiologist, NHS Borders</i>
Mr Ishtiaq Mohammed	<i>Clinical Effectiveness Pharmacist, NHS Fife</i>
Ms Carol Philip	<i>Antimicrobial Pharmacist and Prescribing Adviser, NHS Lothian</i>

10.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

<i>Dr Keith Brown</i>	<i>Chair of SIGN; Co-Editor</i>
Dr Roberta James	<i>SIGN Programme Lead; Co-Editor</i>
Dr Niketa Platt	<i>Antimicrobial Pharmacist, NHS Fife</i>
Dr Vijay Sonthalia	<i>General Practitioner</i>
Dr Sara Twaddle	<i>Director of SIGN; Co-Editor</i>

All members of the SIGN Editorial group make yearly declarations of interest and further details of these are available on request from the SIGN Executive.

Abbreviations

ARHAI	Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection
BNF	British National Formulary
BSAC	British Society for Antimicrobial Chemotherapy
CAUTI	catheter-associated urinary tract infection
CBA	controlled before and after study
CDI	Clostridium difficile infection
cfu	colony forming units
CI	confidence interval
CSM	Committee on Safety of Medicines
CSU	catheter specimen of urine
ESBL	extended-spectrum beta-lactamase
G6PD	glucose-6-phosphate dyhydrogenase
GFR	glomerular filtration rate
GP	general practitioner
HAI	healthcare associated infection
HPA	Health Protection Agency
IDSA	Infectious Diseases Society of America
INR	International Normalized Ratio
KUB	kidneys, ureters and bladder
LE	leucocyte esterase
LUTI	lower urinary tract infection
MIC	minimum inhibitory concentration
MRSA	methicillin resistant Staphylococcus aureus
MSU	midstream urine
MTA	multiple technology appraisal
NEED	The National Economic Evaluation Database
NeLI	National electronic Library of Infection

NICE	National Institute for Health and Clinical Excellence
NNT	number needed to treat
NNTB	number needed to benefit
NNTH	number needed to harm
PPROM	pre-labour, premature rupture of membranes
PPV	positive predictive value
QALY	quality adjusted life year
QRG	Quick Reference Guide
RCT	randomised controlled trial
RR	relative risk (also referred to as risk ratio)
SAPG	Scottish Antimicrobial Prescribing Group
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SPA	suprapubic aspirate
SSHAIP	Scottish Surveillance of Healthcare Associated Infection Programme
STD	sexually transmitted disease
UTI	urinary tract infection
UUTI	upper urinary tract infection
WBC	white blood cells

Annex 1

Key questions addressed in this update

The original guideline was based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk.

KEY QUESTIONS USED TO DEVELOP THE ORIGINAL GUIDELINE

Key question	See guideline section
<p>1. What evidence is there for the accuracy of:</p> <ul style="list-style-type: none"> • clinical decision-making rules • lab microscopy • near-patient testing (ie stick testing/dipsticks) <p>in diagnosing symptomatic bacteriuria in women, compared with lab cultures of urine samples?</p>	3.1, 3.2, 3.3
<p>2. What evidence is there for the accuracy of:</p> <ul style="list-style-type: none"> • clinical decision making rule • lab microscopy • near patient testing (ie stick testing/dipsticks) <p>in diagnosing symptomatic and asymptomatic bacteriuria in pregnant women, compared with lab cultures of urine samples?</p>	4.1, 4.2
<p>3. What evidence is there for the accuracy of:</p> <ul style="list-style-type: none"> • clinical decision making rules • lab microscopy • near patient testing (ie stick testing/dipsticks) <p>in diagnosing symptomatic bacteriuria in men, compared with lab cultures of urine samples?</p>	5.1
<p>4. What evidence is there for the accuracy of:</p> <ul style="list-style-type: none"> • clinical decision making rule • lab microscopy • near patient testing (ie stick testing/dipsticks) <p>in diagnosing symptomatic bacteriuria in catheterised patients, compared with lab cultures of urine samples?</p>	6.1, 6.2
<p>5. What evidence is there for the clinical effectiveness of antibiotic treatment in achieving asymptomatic status in UTI patients compared to no treatment? (Applies to all patient subgroups except asymptomatic pregnant women where outcome is bacteriological cure.)</p>	3.4, 5.2, 6.3, 6.4
<p>6. What evidence is there for the clinical effectiveness of non-antibiotic treatment in UTI compared to no treatment? (Non-antibiotic treatment includes: cranberry juice, mix potassium citrate, acidification, increased fluid intake? Applies to all patient subgroups.)</p>	3.5
<p>7. Is there any evidence for long term health benefits of early intervention with antibiotic treatment in pregnant women, ie avoiding pre-term labour, fetal loss, chronic pyelonephritis, renal damage?</p>	4.2

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