

COMPASS Therapeutic Notes on the Management of Bacterial Urinary Tract Infections in Primary Care

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NEW COMPASS Therapeutic Notes now have a new author. If you have any comments or suggestions regarding this publication, please contact Michelle Bradley at the COMPASS unit – contact details on page 16

Glossary of terms	
Bacteriuria	The presence of bacteria in the urine
GFR	Glomerular Filtration Rate
LE	Leucocyte Esterase
Lower Urinary Tract Infection	Evidence of a urinary tract infection with symptoms suggestive of cystitis (dysuria or frequency without fever, chills or back pain) ¹
MSU	Mid-Stream Urine
NNT	Number Needed to Treat
Pyelitis	Inflammation of the lining of the renal pelvis of the kidney
Pyelonephritis	Inflammation of both the parenchyma of the kidney and the lining of its renal pelvis especially due to bacterial infection
Pyuria	The presence of white blood cells in the urine
RCT	Randomised Controlled Trial
Upper Urinary Tract Infection	Evidence of urinary tract infection with symptoms suggestive of pyelonephritis (loin pain, flank tenderness, fever, rigors or other manifestations of systemic inflammatory response) ¹
UTI	Urinary Tract Infection, the occurrence of pathogenic organisms in the urinary tract
VUR	Vesicoureteric reflux, the abnormal flow of urine from the bladder to the ureter
Neurogenic bladder	Lack of bladder control due to a brain, spinal cord, or nerve condition
Prostatitis	Inflammation or infection of the prostate gland. Acute bacterial prostatitis is a potentially serious bacterial infection of the prostate. It is accompanied by infection of the urinary tract. Occasionally, there may also be associated epididymitis or urethritis. Acute prostatitis is not considered a sexually transmitted infection, so partners are not at risk.
Flank pain	Pain in one side of the body, between the upper abdomen and back
SPIN and SNOUT	SPIN and SNOUT are commonly used mnemonics: a highly 'SPecific' test, when Positive, rules IN disease (SP-P-IN), and a highly 'SeNsitive' test, when Negative rules OUT disease (SN-N-OUT).

Successful completion of the assessment questions at the end of this issue will provide you with **2 hours** towards your CPD/CME requirements.

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Introduction, Background & Diagnostic Tests

What has changed since 2007?

This is an update of the 2007 Management of Bacterial Urinary Tract Infections in Primary Care. The 2012 version contains an extra section on management of urinary tract infection (UTI) in children. Updated guidance is also included for each section. New and updated information is highlighted in the text as:



Antimicrobial resistance is a huge problem and limiting the use of broad spectrum antibiotics is crucial in managing the problem. This has impacted on the management of UTI in primary care.^{1,96} The emergence of resistant bacteria in urinary tract infections further complicates treatment options. This will be discussed later in the text.

Background

UTI implies the presence of significant bacteriuria along with characteristic signs and symptoms.² This is important to bear in mind when managing the patient. UTIs are one of most common bacterial infections managed in general practice; they are the reason for between 1% and 3% of all GP consultations.³

How are UTIs classified?

UTI can be classified as either **LOWER** or **UPPER UTI**. **LOWER UTI** occurs when infection is localised to the bladder and urethra (cystitis and urethritis). LOWER UTIs are caused mostly by the ascent of organisms from the gut flora into the bladder via the urethra. Cystitis is used as a synonym for lower UTI although technically it means inflammation of the bladder and there can be non-infectious causes (e.g. radiation, chemicals). **UPPER UTI** includes pyelitis (infection of proximal part of the ureters) and

pyelonephritis (infection of the kidneys and proximal part of the ureters).²

When is a UTI termed “complicated” or “uncomplicated”?

An **uncomplicated** UTI is an infection of the urinary tract by a usual pathogen (see ‘What organisms cause UTIs?’) in a person with a normal urinary tract and with normal kidney function.²

Complicated UTI occurs when anatomic, functional, or pharmacological factors predispose the person to persistent infection, recurrent infection, or treatment failure. For example:²

- Abnormal urinary tract (e.g. calculus, vesicoureteric reflux (VUR), reflux nephropathy, neurogenic bladder, indwelling catheter, urinary obstruction, recent instrumentation)
- Virulent organism (e.g. *Staph. aureus*)
- Impaired host defences (diabetes mellitus, immune-suppressive treatment)
- Impaired renal function, or post renal transplant.

Is it an UPPER UTI or a LOWER UTI?

Clinically, differentiating between UPPER and LOWER UTI may be difficult. LOWER UTI is characterised by:⁶

- Frequency
- Dysuria
- Urgency
- Polyuria
- Strangury (a condition marked by slow, painful urination, caused by muscular spasms of the urethra and bladder)
- Haematuria
- Suprapubic pain or tenderness
- A change in the smell of the urine.

In UPPER UTI, onset of symptoms is typically rapid and include:⁶

- Fever
- Rigors
- Vomiting
- Loin/flank pain or tenderness
- Other manifestations of systemic inflammatory response.

What organisms cause UTIs?

UTI is defined by the presence of organisms in the urinary tract, which is usually sterile. Most community-acquired UTIs are caused by bacteria, although viruses, fungi and parasites can also cause infection. *Escherichia coli* (*E. coli*) is the most common uropathogen, accounting for about 80% of UTIs acquired in the community.² *Staphylococcus saprophyticus* is also common, particularly among young women. Other pathogens include *Proteus mirabilis*, *Pseudomonas species*, *Klebsiella species* or enterococci.^{2,4,5,41} *Candida albicans* rarely causes UTI in the community, but can occur in hospital patients with risk factors such as indwelling catheters, immunosuppression, diabetes mellitus, and antimicrobial treatment.²



What are ESBLs?

Extended-Spectrum Beta-Lactamases (ESBLs) are enzymes produced by bacteria that make them resistant to a range of antibiotics. ESBLs were first described in the 1980s when they were mainly confined to the hospital setting. However, a new class

of ESBL has now emerged that is widely detected in *E. coli*. These ESBLs are found most commonly in UTIs (although not simple cystitis).

Resistance – a growing problem

Most ESBL-producing *E. coli* are resistant to cephalosporins, penicillins, fluoroquinolones, trimethoprim, tetracycline and some other antibiotics, leaving very limited options for oral treatment in the community, usually only nitrofurantoin. The Health Protection Agency (HPA) hopes to extend its surveillance of *E. coli* to include ESBL-producing *E. coli* as a cause of UTIs in the community.¹⁰²

How significant is asymptomatic bacteriuria?

Bacteriuria alone is rarely an indication for antimicrobial treatment. The diagnosis of a UTI is primarily based on symptoms and signs.¹ In people less than 65 years of age bacteriuria is **abnormal** in the sense that most people do not acquire this. Bacteriuria is common in some populations of institutionalised women and people with long term indwelling urinary catheters.¹ Although treatment of asymptomatic bacteriuria in pregnant women is recommended, studies show no benefit from doing so in institutionalised elderly people.⁷



Resistance^{1,2,92}

► Unnecessary antibiotic treatment of asymptomatic bacteriuria is associated with *Clostridium difficile* (CDI) Infection, methicillin-resistant *Staphylococcus aureus* (MRSA) infection, and the development of antibiotic-resistant UTIs.^{1,96}

► Resistance is increasing to all antibiotics used to treat UTI and there is no clear alternative to trimethoprim or nitrofurantoin. A prudent evidence-based antibiotic policy is therefore required.⁹⁶

► Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) increase risk of CDI, MRSA and resistant UTI - avoid for uncomplicated UTI.^{16,90}

► Amoxicillin resistance is common in UTIs – use only if culture and sensitivity testing indicates.^{16,30}

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

► Fosfomycin is an unlicensed drug that may be used under the supervision of a Microbiologist in multi-resistant UTI.

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

► Strategy for Tackling Antimicrobial Resistance (STAR) 2012-2017 has recently been published by the Department of Health (DOH). This document outlines key areas of work in addressing antimicrobial resistance. This can be accessed on the DOH website: www.dhsspsni.gov.uk

In suspected UTI, which urine dipstick tests can be used?

Urine dipstick tests are the most widely used near-patient tests for UTI. Dipstick testing the urine of a patient with a suspected UTI involves detecting **nitrite** and **leucocyte esterase (LE)**. See **Table ONE**. See later sections on individual patient groups for the appropriateness or otherwise of using dipstick tests in the diagnosis of UTI.¹

Table ONE: Urine Dipstick Tests for UTI. ²	
Urine dipstick test for:	Comments
Nitrite	Most urinary pathogens reduce nitrate to nitrite, and a positive test is suggestive of bacteriuria. A negative result does not rule out UTI, because some pathogens do not produce nitrate reductase, and frequent urination (which is common in cystitis) gives the enzyme less time to act. If the dipstick is exposed to air, the nitrite test can become inactive.
Leucocyte esterase (LE)	LE is an enzyme present in most white blood cells. In the absence of infection, few white blood cells are present in urine and this test is negative. When the urinary tract is infected, the number of white blood cells in urine increases significantly, and this screening test will become positive. Thus, detection of LE in urine is a marker for pyuria. However, white blood cells are present in non-infective inflammatory processes, so a positive LE test does not make a diagnosis of UTI certain. A negative LE test does not always rule out a diagnosis of UTI, because the test may not always be highly sensitive, and pyuria is not always found in UTI.

In a person with appropriate signs or symptoms, how should the results of a urine dipstick test be interpreted?

See **Table TWO**

Table TWO: Interpreting urine dipstick test* results for nitrite and leucocyte esterase in a symptomatic patient. ^{1,2,9}		
Nitrite	Leucocyte Esterase (LE)	
Positive	Positive or negative	The patient is very likely to have a UTI and antimicrobial treatment is justified. Nitrite is a 'SPecific test and therefore is good at ruling infection in. Hence the mnemonic SPin'.
Negative	Negative	The patient will likely not have a UTI and antimicrobials should not be given. However, in patients with severe or persistent symptoms – a urine culture may be appropriate. LE is a 'SeNsitive test and therefore is good at ruling infection out. Hence the mnemonic SNout'.
Negative	Positive	A positive result for LE by itself is not helpful: half of these patients will have a UTI and half will not. In this case, a culture should be performed and antimicrobial treatment delayed until the results are known.
* Note: when reading test WAIT for the time recommended by manufacturer.		

When is urine culture and sensitivity testing necessary?

Urine culture is frequently used as the "gold-standard" in diagnosing UTI. However, in most general practice cases, urine culture is not necessary for uncomplicated UTI in young women,¹⁰ and has been shown to have little impact on management.¹¹ Laboratory testing of urine for culture and sensitivity should be performed in:^{1,2}

- Pregnancy – screen for asymptomatic bacteriuria at first antenatal visit and at any stage during pregnancy if the women presents with symptoms of UTI
- Suspected pyelonephritis (temperature > 38°C more, rigors, nausea, vomiting, diarrhoea, loin tenderness)
- Suspected UTI in men
- Recurrent UTI, as resistance is more common,
- Catheterised patients – bacteriuria is common, only send a sample if there are features of systemic infection
- Failed antimicrobial treatment or persistent symptoms
- Abnormalities of the genitourinary tract
- Renal impairment or transplantation
- Children aged under 3 years of age.⁴¹

Are there any adjuvant measures that patients may undertake?

Most of these have not been evaluated in RCTs or prospective studies.⁹

- Increase fluid intake – a good fluid intake and frequent voiding may have a "flushing" effect on the urinary tract; bacterial proliferation might be hindered, owing to a shorter retention of urine in the patient's bladder. In practice, some patients find this beneficial, while others are unwilling to undertake this as voiding is painful.

NB – all patients should maintain sufficient fluid intake (at least two litres per day) to avoid dehydration.

- Micturition after sexual intercourse – this is supposed to rinse bacteria from the bladder and thus prevent UTI. However, studies show that postcoital voiding does not prevent LOWER UTI.^{12,13} Anecdotally some women do, however, find postcoital voiding helpful.
- Avoid exaggerated genital "hygiene" (deodorant sprays, vaginal lotions or douching etc.) – since damage to the physiological vaginal flora facilitates UTI.
- Avoid the use of spermicides or diaphragms in women with recurrent UTI.
- Take a cranberry product (SECTION SEVEN).

SECTION ONE: Management of UTI in Non-pregnant Women

Half of all women will suffer from at least one UTI in their lifetime.⁹ Among (non-pregnant) women under 50 years of age, with acute symptoms such as dysuria, urgency, frequency or loin pain, over 70% will have bacteriuria.¹

How should UTI be diagnosed in non-pregnant women?

No single sign or symptom accurately predicts UTI. If dysuria and frequency are both present then the probability of a UTI is increased to greater than 90% and empirical antibiotic treatment is indicated.¹ Symptoms suggesting vaginitis or cervicitis (such as vaginal irritation or discharge), reduce the likelihood of a diagnosis of LOWER UTI to about 20%.¹⁴

When is it appropriate to dipstick test the urine?

In an otherwise healthy, non-pregnant woman, UTI can be diagnosed without a dipstick test of the urine and without urine culture when there are multiple typical symptoms and signs of UTI.^{2,15} Dipstick tests are now only recommended in women who have few symptoms and signs typical of UTI; the purpose of testing is to help decide who should be treated immediately and who should have urine cultured.^{2,94} See **Tables ONE** and **TWO**.

How should acute LOWER UTI in otherwise healthy women be treated?

Otherwise healthy, non-pregnant women with symptomatic LOWER UTI should receive empirical antimicrobial treatment with:^{1,2,16}

- Trimethoprim 200mg twice daily OR
 - Nitrofurantoin 50-100mg four times daily.
- Nitrofurantoin is currently more expensive than trimethoprim.^{43,90} Immediate- and extended-release preparations are available. The extended-release preparation is designed to reduce the occurrence of nausea.⁸⁹ However, no evidence to prefer one over another has been found.²
- Patients who do not respond to trimethoprim or nitrofurantoin should have a sample of urine taken for culture to guide a change of antimicrobial.¹

Prescribing Notes

Always ask women of child-bearing age about the possibility of pregnancy; if the patient is unsure, perform a pregnancy test and treat accordingly (see later for management of UTI in pregnancy).

Antimicrobial courses – what is the recommended duration of therapy?

A **three-day course** of trimethoprim or nitrofurantoin is recommended for the treatment of simple UTI in non-pregnant women.¹ Three days of antimicrobial therapy is similar to 5 to 10 days in achieving symptomatic cure for uncomplicated UTI in non-pregnant women, while causing fewer adverse events.^{1,17-21} Compliance is also better. Compared with prolonged treatment, a 3-day course does leave a higher risk of recurrent or persistent bacteriuria. Asymptomatic bacteriuria is associated with an increased risk of symptomatic UTI in the following week, thus 7 days treatment could be recommended for a minority of women in whom bacteriological eradication is more important (e.g. women suffering from recurrent episodes, planning a pregnancy). This decision should be taken with the patient, balancing the higher bacteriological cure rate versus the increased risk for adverse events.⁹⁰

Are there any other advantages to three-day courses of antimicrobials?

Most otherwise healthy women with a UTI will not have a systemic illness and frequency and dysuria usually resolve two to three days after starting treatment. This reduces the patient's motivation to complete longer courses of treatment. Failure to complete a course can lead to an accumulation of unused medicines at home, which constitutes a hazard to children and raises the possibility of subsequent self-treatment with deteriorating or inappropriate drugs. Longer courses of antibiotics are also more expensive and associated with increased risk of adverse effects.⁹⁰

Are three day courses of trimethoprim being prescribed in Northern Ireland?

See **Table THREE**

Table THREE

Length of trimethoprim courses prescribed in Northern Ireland (Data from Pharmaceutical Department, Business Services Organisation, Belfast)

	Percentage of trimethoprim prescriptions which were for a:		
	3-day course	5-day course	7-day course
1998	3%	45%	38%
2001	9%	43%	37%
2005	17%	37%	37%
2008	25%	33%	33%
2011	29%	27%	35%

What adverse effects are associated with trimethoprim?

Gastrointestinal disturbances and **skin rashes** are occasionally experienced by people taking trimethoprim. These are usually mild and are quickly reversible when trimethoprim is stopped.

Blood dyscrasias are infrequently seen, usually in people with a predisposition to folate deficiency (pregnant women, alcoholics). Regular blood counts should be undertaken with long-term trimethoprim use. On long-term treatment, patients / carers should be told how to recognise signs of blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.

TABLE FOUR:

Drug Interactions^{31,43,92}

Antibiotic	Interactions
Trimethoprim	ACE inhibitors, warfarin, phenytoin, digoxin, antimalarials, ciclosporin, cytotoxics, methotrexate
Nitrofurantoin	Antacids
Amoxicillin and co-amoxiclav	Warfarin
Quinolones	NSAIDs, antacids, warfarin, phenytoin, ciclosporin, iron, theophylline
Cefalexin	Warfarin

NEW Oral Contraceptives (OCs) – the World Health Organisation (WHO) now recommends that no additional contraceptive precautions are required when antibacterials that *do not induce liver enzymes* are used in combination with OCs. Therefore neither nitrofurantoin nor trimethoprim are likely to interact with oral contraceptives.

Prescribing points – Nitrofurantoin

- Urinary pH affects the activity of nitrofurantoin. Patients who are prescribed nitrofurantoin should be advised **not** to take alkalinising agents.
- Nitrofurantoin is at least as effective as trimethoprim, but it frequently causes nausea, vomiting, and loss of appetite, particularly at higher doses. Administration of nitrofurantoin **with food** will enhance absorption and possibly improve gastrointestinal tolerance.
- Nitrofurantoin may cause the urine to turn more yellow or brown than usual. Patients and/or carers should be warned of this.
- Nitrofurantoin can cause peripheral neuropathy and thus is best avoided in patients who are known to be at risk of peripheral neuropathy (e.g. renal impairment, anaemia, diabetes, electrolyte imbalance, vitamin B deficiency).
- **NEW** Chronic pulmonary reactions (including pulmonary fibrosis) can develop, and may occur commonly in elderly patients. Close monitoring in patients receiving long-term therapy is warranted.⁸⁹
- Monitor liver function if to be given for more than 6 months duration.
- Contraindicated in children under 3 months of age due to the theoretical risk of haemolytic anaemia.⁷⁵
- Caution in elderly patients – increased risk of toxicity.¹

Prescribing points – Trimethoprim

Trimethoprim is a folate antagonist and therefore folate supplementation should be considered for patients on long-term trimethoprim who are taking other folate antagonists (e.g. phenytoin).

Consider using an alternative antimicrobial for empirical treatment if trimethoprim has been taken in the past 3 months.

How should UPPER UTI in otherwise healthy women be treated?

See SECTION FIVE – Acute Pyelonephritis.

Are UTIs likely to recur?

More than 25% of women who have had a UTI will experience a recurrence.²² A patient who has three or more episodes per year of acute UTI^{2,4} or two microbiologically confirmed UTIs in 6 months is said to have “recurrent” UTIs.

Women with recurrent UTIs can accurately self-diagnose a LOWER UTI.¹⁴ When a woman who has previously had LOWER UTI has symptoms suggesting a recurrence, there is an 84-92% chance that an infection is present.^{23,24}

What are the risk factors for recurrent UTI?

In otherwise healthy, young/premenopausal women:

- Sexual intercourse
- Contraceptive use – particularly spermicides and diaphragms^{13,25-27}
- Antimicrobial use – can cause changes in the normal genital flora

In postmenopausal women:

- Oestrogen deficiency
- Urogenital surgery
- Incontinence
- High post-void residual

What strategies can be employed in an attempt to prevent recurrent UTIs?

Recurrent UTIs are a common and debilitating problem. Consider the following management options if there are three or more episodes per year:²

Imaging investigations – plain abdominal X-ray and ultrasound of kidneys, ureters and bladder

Patient-initiated antimicrobials for new episodes (“stand-by antimicrobials”) OR

Professional-initiated antimicrobials for new episodes (i.e. usual treatment when required) OR

Antimicrobial prophylaxis, (see later)

A trial of cranberry extract (see later).

How should antimicrobial prophylaxis be used?

Long-term antimicrobial prophylaxis against recurrent UTI can be given at bedtime, using nitrofurantoin 50mg at night or trimethoprim 50-100mg at night.¹⁶ Long-term prophylaxis usually entails administration for 6-12 months. Prophylaxis for recurrent urinary tract infection should not be undertaken until a negative culture 1 to 2 weeks after treatment has confirmed eradication of the urinary tract infection.¹⁰³ Future infections will require a different choice of antibiotic for treatment.

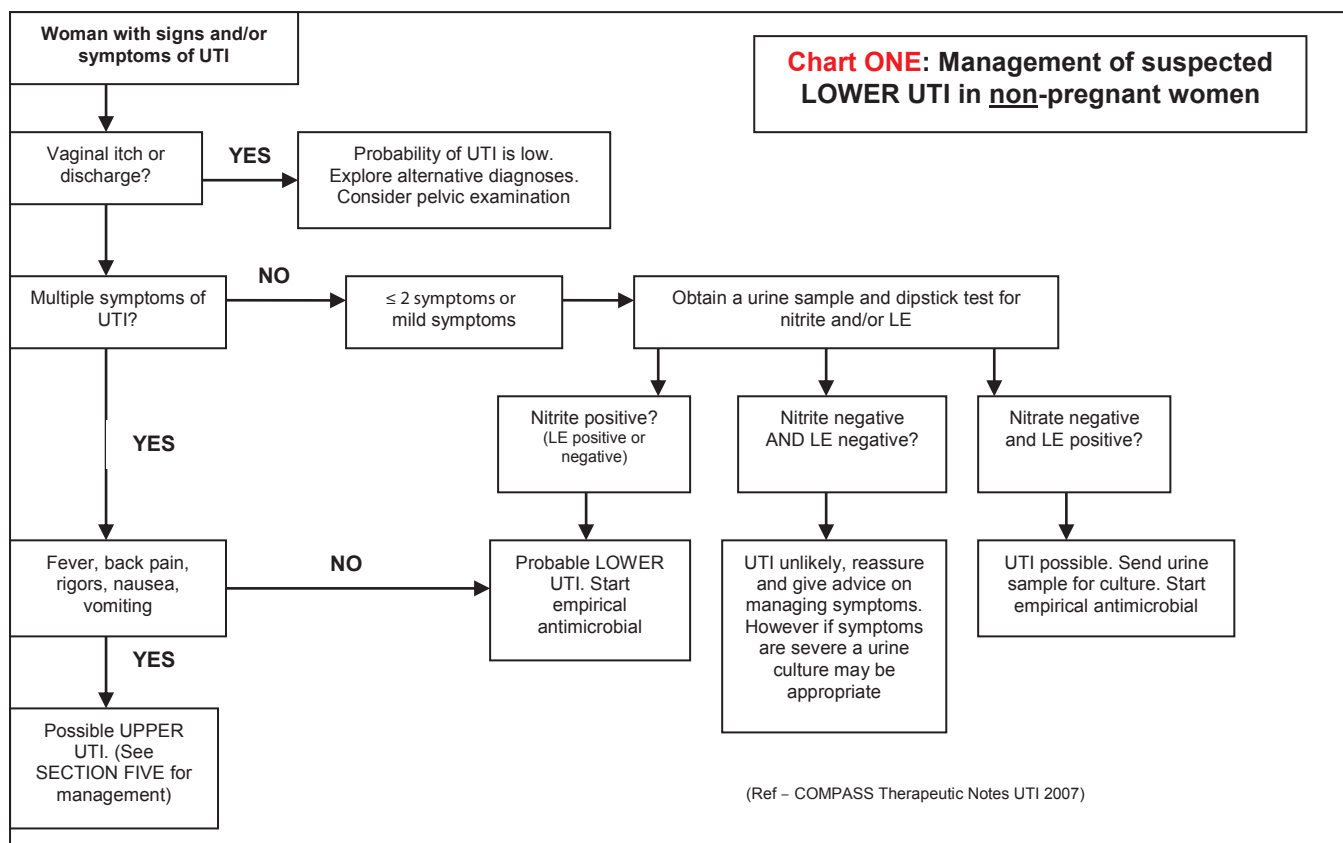
How should post-coital prophylaxis be used?

If UTI episodes occur frequently after sexual intercourse, antimicrobial prophylaxis can be prescribed. Post-coital prophylaxis is as effective as prophylaxis taken nightly.¹⁶ The following prophylactic doses can be taken every night or as a stat post-coital dose:¹⁶

Nitrofurantoin 50mg, or

Trimethoprim 100mg.

This treatment can be continued for several years if necessary.²⁸ It may be a more acceptable method of prophylaxis for some women.⁹⁸



Is there a role for topical oestrogen creams in preventing recurrent UTI?

Topical application of an oestrogen cream to prevent recurrent UTI in post-menopausal women is not recommended in the UK.² However some gynaecological specialists follow North American guidelines¹⁰³ and continue to prescribe topical oestrogens and oestrogen containing prosthetic rings for this indication. None of the available vaginal oestrogen creams are licensed for this indication.

What has been shown to have NO association with recurrent UTI?

There is no association between recurrent UTI and:⁴

- Pre- or post-coital voiding patterns
- Frequency of urination
- Delayed voiding habits

- Wiping patterns
- Douching
- Bubble baths
- Body Mass Index
- Wearing of tight clothing

However, anecdotally, some patients report that they find adopting (or avoiding as appropriate) such practice beneficial.

Which women should be referred for assessment by a specialist?

Consider referring women with recurrent UTI for specialist assessment after prophylaxis with an antimicrobial or cranberry product (see later) have failed.¹

SECTION TWO: Management of UTI in Pregnant women

UTIs are among the most common health problems during pregnancy. They occur in 17% to 20% of pregnancies³³ and have been associated with premature labour and delivery, clinical or subclinical chorioamnionitis (inflammation of the foetal membranes), postpartum fever in the mother and neonatal infection. UTI in pregnancy may lead to maternal complications such as septic shock, respiratory insufficiency, fluid balance disorders, and chronic renal insufficiency. Foetal complications include developmental delays, cerebral palsy and death.²

Is asymptomatic bacteriuria significant in pregnancy?

Asymptomatic bacteriuria (persistent bacterial colonisation of the urinary tract in the absence of specific symptoms) occurs in 5-10% of all pregnancies.³⁴ *E. coli* is the most common pathogen associated with asymptomatic bacteriuria.³⁵ Other organisms include other gram negative bacteria and group B streptococci.

While asymptomatic bacteriuria in non-pregnant women is generally benign, obstruction to the flow of urine in pregnancy leads to stasis and increases the likelihood that pyelonephritis will complicate asymptomatic bacteriuria. 10-30% of women with bacteriuria in the first trimester develop UPPER UTI in the second or third trimester.¹

In contrast to other patient groups, treatment of asymptomatic bacteriuria in pregnancy does more good than harm.

Who should be screened for asymptomatic bacteriuria in pregnancy?

All pregnant women should be screened for bacteriuria at their first antenatal visit.^{1,2}

How should asymptomatic bacteriuria in pregnancy be screened for?

The performance of dipstick testing (leucocyte esterase or nitrite) is **not** sufficiently sensitive to be used as a screening test for bacteriuria in pregnancy. Quantitative urine culture remains the gold standard for diagnosis of bacteriuria in pregnancy.^{1,36-38}

Which dipstick tests are appropriate in pregnancy?

Dipstick testing for UTI (LE or nitrate) is not sufficiently sensitive to be used as a screening test. Urine culture should be the investigation of choice.¹

How should asymptomatic bacteriuria in pregnancy be treated?

If bacteriuria is found, confirm its presence with a second urine culture.² **Treat confirmed asymptomatic bacteriuria for 7 days** with an antimicrobial to which the organism is sensitive² (first-line choices when sensitivities are known are shown in **Table FIVE**).^{2,88} **Repeat urine cultures 7 days after completion of treatment, and then at every antenatal visit** for the rest of the pregnancy.² Women who do not have bacteriuria in their first trimester do not need repeated urine cultures.¹

How should symptomatic bacteriuria in pregnancy be treated?

At any stage of pregnancy, women with symptomatic UTI should be treated with an antimicrobial. A single urine sample should be taken before empiric antimicrobial treatment is started.¹ **TABLE FIVE** shows possible antimicrobial choices and doses. In Northern Ireland, cefalexin is used as empiric therapy for UTI in pregnancy. Once the result of urine culture and sensitivity testing are known, the antimicrobial can be changed to one to which the organism is sensitive (if not found to be sensitive to cefalexin).²

Table FIVE: Antimicrobial choices for the management of UTI in pregnancy (asymptomatic and symptomatic bacteriuria) when sensitivities are known.

Agent	Dose	Duration
Cefalexin	500mg three times daily	7 days
Nitrofurantoin*	50 to 100mg four times daily	7 days
Trimethoprim (Plus folic acid in 1 st trimester)	200mg twice daily	7 days
Amoxicillin [#]	500mg three times daily	7 days

* Nitrofurantoin is **not** an effective treatment for UPPER UTI because it does not achieve effective concentrations in the blood and upper urinary tract.¹⁶

[#] Amoxicillin is not suitable as empirical treatment; only use where sensitivity has been confirmed.⁷⁷

A Cochrane review was unable to determine if any particular antimicrobial was more effective for symptomatic UTI during pregnancy in terms of cure rates, recurrent infection, preterm delivery, premature rupture of membranes, admission to neonatal intensive care, need for change of antimicrobial and incidence of prolonged pyrexia.³³

Given the risks of bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antimicrobial treatment as a test of cure, and then at every antenatal visit for the rest of the pregnancy.^{1,2}

NEW Northern Ireland Antimicrobial Guidelines for Primary Care recommend cefalexin as first choice treatment of UTI in pregnancy. When sensitivities are available, de-escalation to a more narrow spectrum agent is encouraged to minimise cephalosporin selective pressure for *C.difficile*.⁷⁷

Is nitrofurantoin safe in pregnancy?

Data indicate that the use of nitrofurantoin during pregnancy has not been associated with an increased risk of congenital malformations. Retrospective reviews and a large number of case reports suggest that there is no significant increase in the risk of congenital malformations or other adverse pregnancy outcomes associated with use of nitrofurantoin during

pregnancy.³⁹ Nitrofurantoin can cause haemolysis in patients with G6PD deficiency leading to a theoretical risk of intrauterine haemolysis, particularly following third trimester exposure.³⁹

Is trimethoprim safe in pregnancy? UPDATED

The BNF and the manufacturers of trimethoprim warn against its use in pregnancy.^{32,43} This is based on the knowledge that as a folate antagonist, trimethoprim may limit the availability of folic acid to the foetus and impair normal development. The National Teratology Information Service, however, indicates that trimethoprim need only be avoided in women with low folate status (i.e. women with established folic acid deficiency or low dietary intake, or in those already taking known folate antagonists)⁴⁴ and that in women with normal folate status, short-term use of trimethoprim is unlikely to induce folate deficiency. However, folate supplementation is recommended in all women treated with trimethoprim during the first trimester as a precautionary measure.⁴⁴

NEW Should any other measures be recommended in pregnancy?

- Paracetamol may be given for symptomatic relief.
- Urine alkalinizing products should not be used as there is insufficient evidence on their effectiveness.²

SECTION THREE: Management of UTI in Men

In men, issues such as pathogenesis, risk factors, investigations, follow-up, choice of antimicrobial and duration of treatment of UTI have received little attention in the medical literature. There is a lack of studies of well-defined groups of men with specified types of UTI.⁴⁵⁻⁴⁷

UTIs in men are usually viewed as complicated because they result from an anatomical or functional anomaly or instrumentation of the genitourinary tract.⁴⁶ Additionally, between 52-90% of men with a UTI have prostatic involvement,^{48,49} which may lead to complications such as prostatic abscess or chronic bacterial prostatitis.

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.

In this discussion, the term "LOWER UTI" implies infection of the bladder and possibly the urethra with no clinical evidence of prostatitis, epididymitis, or orchitis. "UPPER UTI" includes pyelitis and pyelonephritis. In patients with a history of fever or back pain the possibility of UPPER UTI should be considered.

How common is UTI in men?

UTI is considerably less common in men than in women (except in the elderly and in men with long-term indwelling urinary catheters).⁴⁶ In men, as in women, the incidence of UTI increases substantially with advancing age, co-existing illnesses, and institutional care.⁸ UTI is very **uncommon** in otherwise healthy young and middle-aged men.⁵⁰

What are the risk factors for UTI in men?

Most UTIs in men are not associated with any risk factor. However, the following risk factors need to be excluded or managed, especially in recurrent UTI:

- Incomplete bladder emptying (e.g. caused by obstruction with prostatic enlargement, blocked or misplaced indwelling catheter)
- Abnormalities of urinary tract function or structure (e.g. indwelling catheter, neurogenic bladder, vesicoureteric reflux, anatomical abnormalities)
- Previous urinary tract surgery
- Immunocompromised state.

How does UTI present in men?

UTI is likely to present "typically" if the man is **not** frail and elderly, institutionalised, or with a long-term indwelling urinary catheter. Typical features of UTI in men include:⁸

- Dysuria, frequency, urgency, nocturia, and suprapubic discomfort are usually present; pain in the flank, loin, or lower back is sometimes present.
- Fever, cloudy or foul-smelling urine may be present.

Can UTI present otherwise in men?

UTI is likely to present "atypically" if the man is frail and elderly, is institutionalised, or has a long-term indwelling catheter. There is a lack of evidence to support suggested criteria for diagnosing UTI in such patients.⁸ Accurate diagnosis is difficult and requires considerable clinical judgement. Diagnose UTI based on a comprehensive assessment that includes:⁸

- Changes in signs or symptoms
- Fever
- New or worsening urinary incontinence
- Suprapubic discomfort and flank or loin tenderness
- Signs of septicæmia and generalised illness.

Is it necessary to send a urine sample for culture and sensitivity testing if UTI is suspected in a man?

Yes, prior to starting an antimicrobial, culture the urine whenever UTI is suspected in a man. The results will usually help to confirm the diagnosis and guide

treatment.^{1,8} Note however that asymptomatic bacteriuria, particularly in very elderly men with prostatic enlargement, may also give positive results.

Are urine dipstick tests helpful in diagnosing UTI in men?

Urine dipstick tests can help decide if a temporary “working” diagnosis of UTI should be made. If the dipstick test is positive for both nitrite and LE, diagnose UTI. If the dipstick test is negative or equivocal, use clinical judgement to decide if a temporary “working” diagnosis of UTI should be made while waiting for the urine culture results⁸.

UPDATED How should LOWER UTI in a man be treated?

Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones, cephalosporins) are no longer recommended first line due to antimicrobial resistance.¹ The HPA now recommends a **seven day course of trimethoprim or nitrofurantoin as first line treatments of lower UTI in men.**

UPDATED What if there is prostatitis also present?

Up to 90% of men with febrile UTI will have a concomitant infection of the prostate. Therefore the goal is not only to sterilise the urine but also to eradicate the prostatic infection. Quinolones (e.g. ciprofloxacin, norfloxacin, ofloxacin) reach free concentrations in prostatic tissue and prostatic fluid that exceed the minimum inhibitory concentrations of most of the causative bacteria.⁵⁰

What symptoms are suggestive of prostatitis?

- A feverish illness of sudden onset.
- Irritative urinary voiding symptoms or acute urinary retention.
- Perineal or suprapubic pain (low back pain, pain on ejaculation, and pain during bowel movements can also occur).
- Very tender prostate on rectal examination.¹⁰⁵

How to confirm prostatitis?

Urine dipstick tests will suggest presence of white blood cells and bacteria in the urine. However, a urine culture will be required to confirm prostatitis. Prostatic secretions should not be collected¹⁰⁵.

How to treat prostatitis?

Bacterial UTI with **symptoms suggestive of prostatitis should be treated empirically with a**

quinolone for four weeks.¹ Trimethoprim also yields good concentrations in the prostate and is an alternative to quinolones provided the causative bacteria are fully sensitive to trimethoprim. In contrast, the use of β -lactam antimicrobials and nitrofurantoin should be discouraged because of the low concentrations attained by these agents in the prostate.^{16,50} Patients who do not respond to antimicrobial treatment should be referred for investigation for prostatitis.¹

How should recurrent UTI in a man be managed?

Each episode should be treated as an acute infection. If two or more episodes of UTI occur in 3 months, look for an underlying cause such as:

- Prostatitis
- Prostatic enlargement due to cancer or benign prostatic hypertrophy
- Calculi
- Bladder carcinoma
- Vesicoureteric reflux (VUR)

Also, in sexually active men, rule out chlamydial infection.

NEW Trimethoprim is not recommended if it has been used in the past 12 months – increased risk that infection is due to a resistant organism.⁸

How should UTI in an elderly man be managed?

UTI in an elderly man should be managed similarly to that in a younger man, but the following should be taken into account:

- In elderly men, UTI may present with non-specific features, including an acute confusional state
- UTI, especially recurrent UTI, in elderly men may be due to prostatic enlargement and/or prostatitis

N.B. Asymptomatic bacteriuria in an elderly man should not be treated.⁸

Which men need specialist referral?

Referral for assessment by a specialist should be considered for men who have:^{1,8}

- Suspected UPPER UTI
- Failed to respond to appropriate antimicrobial therapy
- Frequent episodes of UTI (e.g. two or more episodes within one or two years)
- Features of urinary obstruction
- A history of pyelonephritis, calculi, or previous genitourinary tract surgery.

SECTION FOUR: Management of UTI in patients with long term indwelling catheters

NEW All patients with a long term indwelling catheter are bacteriuric, often with two or more organisms. The catheter provides a focus for bacterial biofilm formation¹. **Antibiotics should not be given to patients with indwelling catheters with bacteriuria who are asymptomatic.** Indeed there is evidence that repeated treatment of asymptomatic bacteriuria increases the risk of colonisation by drug-resistant bacteria.⁵⁵

NEW How should UTI be diagnosed in patients with indwelling catheters?

Classical UTI signs and symptoms do not always apply.¹ Symptoms that *may* suggest UTI in patients with catheters include fever, flank or suprapubic

discomfort, nausea, vomiting, malaise or confusion.^{7,51} Fever is the most common symptom of UTI in patients with catheters. However it is non-specific and its absence does not exclude UTI.¹

Should dipstick tests be used?

Dipstick tests should not be used as they will not differentiate between symptomatic and asymptomatic bacteriuria in patients with catheters.¹

Should a person with an indwelling catheter be screened routinely for asymptomatic bacteriuria?

No, people with indwelling catheters should **not** be screened for asymptomatic bacteriuria.² All persons with long-term indwelling catheters will have bacteriuria at some stage.^{52,53} SIGN guidelines recommend that:¹

- Urine be cultured only in those who become **symptomatic**
- Catheterised people with asymptomatic bacteriuria should **not** receive antimicrobial treatment.

Renal impairment

Trimethoprim

- Reduce dose in renal impairment:

GFR 15 to 30mL/min – use half the normal dose after 3 days

GFR < 15mL/min – use half the normal dose
(Monitor plasma trimethoprim concentration if GFR <10mL/min)⁴³

- Caution particularly in the elderly with chronic renal impairment – ensure a recent renal function test is performed when prescribing.

Nitrofurantoin UPDATED

- People with renal impairment (GFR <60 mL/min) should **not** be treated with nitrofurantoin as:^{1,2,43}
 - An effective concentration of antimicrobial in the urine is not achievable
 - A toxic concentration of antimicrobial can occur in the plasma.

Should antimicrobial prophylaxis be prescribed to prevent catheter-related UTI?

In general, antimicrobial prophylaxis is not recommended for the prevention of symptomatic UTI in catheterised patients. Studies have shown that antibiotic prophylaxis reduces the number of cases of asymptomatic bacteriuria but not those of symptomatic bacteriuria. Antimicrobial prophylaxis may be considered in patients for whom the number of infections are of such frequency or severity that they chronically impinge on function and well-being.¹

NEW Should antimicrobial prophylaxis be used when changing catheters?

Only if the patient has a history of catheter-associated urinary tract infection following catheter change.

Routine use of antimicrobial prophylaxis during catheter change should be avoided.¹

How should symptomatic UTI in catheterised patients be managed?

Catheter care and function should be reviewed, including checking if the catheter is blocked. The catheter will need to be changed as it is likely to be the source of the infection. However, before doing so, send a urine sample for culture.^{1,2} If practical, withhold antimicrobials until the result of urine culture is available to guide the choice of antimicrobial. However, empiric antimicrobials could be started, taking into account the severity of the presentation and any co-morbidity.²

If, following a diagnosis of UTI, the catheter is to be changed, this should be carried out under antibiotic cover.

If there is flank/loin pain or tenderness, treat as for UPPER UTI (see later, SECTION FIVE, Acute Pyelonephritis) otherwise, treat for **7-14 days** with an antimicrobial appropriate for LOWER UTI (i.e. trimethoprim or nitrofurantoin).² Take into account any previous treatments and culture results when choosing an antimicrobial for empirical treatment. Once urine cultures are available, if necessary change the antimicrobial to one to which the organism is sensitive.²

NEW When to refer to hospital?

If systematic symptoms such as fever, rigors, chills, vomiting or confusion appear.¹

NEW Intermittent catheterisation

Patients sometimes intermittently self-catheterise in order to manage urinary retention or incontinence, often due to a neuropathic or hypotonic bladder. In intermittent catheterisation the catheter is inserted into the urethra several times a day. Current evidence suggests that these patients should be managed in the same way as patients with long term indwelling catheters.¹⁰⁵

SECTION FIVE: Acute Pyelonephritis

What is pyelonephritis?

Pyelonephritis is inflammation of the UPPER urinary tract, specifically of the parenchyma of the kidney and the lining of its renal pelvis.⁵⁶ Pyelonephritis is mainly caused by bacterial infection and can be acute or chronic. The management of chronic pyelonephritis is outside the remit of this review.

Uncomplicated V complicated?

Pyelonephritis is considered to be **uncomplicated** if the infection is caused by a typical pathogen in an immunocompetent person who has normal renal anatomy and renal function.⁵⁷ It is considered to be **complicated** if there are factors that increase susceptibility or reduce the person's response to infection, such as:⁵⁷

- Anatomical abnormality
- Renal stone, urinary, ureteric, or nephrostomy catheter
- Immunocompromise
- Instrumentation
- Obstruction
- Pregnancy

What are the symptoms of acute pyelonephritis?

The following symptoms can develop rapidly over a few hours or a day and include:⁵⁶

- High fever
- Rigors
- Costovertebral angle (loin) pain – usually unilateral and may worsen on micturition
- Nausea
- Vomiting
- Diarrhoea

Symptoms of LOWER UTI (e.g. frequency, dysuria) and suprapubic pain may also be present.

Because the symptoms of pyelonephritis can be minimal or even absent, silent (subclinical) pyelonephritis should be suspected in a person who presents with symptoms of LOWER UTI that has not responded to treatment. It has been suggested that silent pyelonephritis may be present in up to 30% of women with symptoms of LOWER UTI.^{56,57}

How should UPPER UTI be treated?


UPPER UTI can be accompanied by bacteraemia, making it a life-threatening infection.¹ A mid-stream urine sample should be taken for culture and empirical antibiotics commenced. The HPA and the AMM

(Association of Medical Microbiologists) recommend that men and non-pregnant women (including those with a long-term, indwelling catheter) with suspected acute UPPER UTI should be started on **ciprofloxacin (500mg twice daily) for 7 days or co-amoxiclav (500mg/125mg three times a day) for 14 days**.^{1,58,87} Hospitalisation should be considered in patients:

- unable to take fluids/medication
- showing signs of severe sepsis
- who do not respond to antibiotics within 24 hours (due to antibiotic resistance)¹

Prescribing points – treating pyelonephritis with ciprofloxacin

- ▶ Ciprofloxacin is preferably avoided in pregnancy due to the theoretical risk of arthropathy. Ciprofloxacin should be reserved for serious life threatening conditions unresponsive to standard antibiotic therapy in pregnancy.^{61,62}
- ▶ Because quinolones can lower seizure threshold, avoid ciprofloxacin in people with epilepsy or conditions that predispose to seizures.⁶²
- ▶ Concurrent NSAID and quinolone use should also be avoided due to increased risk of convulsions.⁴³
- ▶ Ciprofloxacin can rarely cause tendon damage. Treatment should be stopped if pain or inflammation of a tendon occurs.⁶²
- ▶ Ensure that the patient has an adequate fluid intake during the ciprofloxacin course as there is a risk of crystalluria.
- ▶ Risk of *C. difficile* – recent strains of *C. difficile* are resistant to quinolones, which make them a major cause of *C. difficile* infection.¹⁰⁴

 Remember to prescribe ciprofloxacin **generically**. (Ten Ciproxin[®] 500mg tablets cost £12.49 compared to £1.00 for ten non-branded ciprofloxacin 500mg tablets).⁴³

Prescribing points – UPPER UTI:

- ▶ Nitrofurantoin is an ineffective treatment for UPPER UTI because it does not achieve effective concentrations in the blood and upper renal tract.
- ▶ Resistance to trimethoprim is too common to recommend this drug for empirical treatment of suspected UPPER UTI. However, trimethoprim can be prescribed if culture results have been obtained and the uropathogens are susceptible.^{1,16}

What else should be considered if a person is being managed at home?

In a person with pyelonephritis being managed at home (having obtained a urine sample for culture and sensitivity testing and started an empirical antimicrobial).⁵⁹

- Treat pain and fever with paracetamol (ibuprofen is best avoided as NSAIDs may impair renal function).
- Encourage intake of fluids and ensure adequate hydration.
- Advise the person to seek early medical advice if their condition is deteriorating or if there is no response to treatment in 24 hours.
- If there is no response to treatment in 24 hours, consider hospital admission.
- Review within 48 hours anyway, to assess response to treatment and to ensure the person is taking an appropriate antimicrobial.

How should pyelonephritis in pregnancy be managed?

The incidence of pyelonephritis increases in pregnancy. Overall it occurs in 1-2% of all pregnancies.⁶⁰ Because of the risks to mother and child, pregnant women with pyelonephritis should be admitted to hospital.⁵⁹



SECTION SIX: Management of UTI in Children

How common are UTIs in children?

UTI is a common bacterial infection causing illness in infants and children.⁷¹ Approximately 7 to 8% of girls and 2% of boys have a urinary tract infection during the first 8 years of life.^{73,79,80}

Problems in diagnosing UTIs in children

It may be difficult to recognise UTI in children because:

- presenting symptoms and signs are non-specific, particularly in infants and children younger than 3 years⁶⁸

- young children cannot clearly articulate symptoms
- when children wear nappies, parents are not aware of the classic dysuria and frequency symptoms as experienced by adults

- obtaining an adequate urine sample can be frustrating, time consuming, and costly.⁷¹

Diagnosis of UTI is therefore often delayed and may be missed in up to 50% of children presenting to primary care.⁸¹ Sometimes symptoms are incorrectly attributed to other causes, e.g. otitis media.^{71,81}

What are the risk factors for UTI in children?

The following can be present:

- Poor urine flow
- History suggesting previous UTI or confirmed previous UTI

- Recurrent fever of uncertain origin
- Antenatally diagnosed renal abnormality
- Family history of vesicoureteric reflux (VUR) or renal disease
- Constipation
- Dysfunctional voiding (voluntary withholding of urine or faeces)
- Enlarged bladder
- Abdominal mass
- Evidence of spinal lesion
- Poor growth
- High blood pressure

Should infants under 3 months of age be managed in primary care?

No, infants under 3 months of age with a suspected UTI should be admitted urgently to a paediatric specialist for IV antibiotics.⁶⁸

Signs and symptoms of UTI in infants under 3 months include:

- Fever (without an obvious cause), vomiting, irritability, lethargy (most common presentation).
- Poor feeding, failure to thrive (intermediate presentation).

Abdominal pain, jaundice, haematuria, offensive urine (least common presentation).⁶⁹

From this point this document will cover only management of UTIs in children over 3 months of age.

When to suspect a UTI in children over 3 months of age?

Suspect a UTI with any combination of the following signs and symptoms:

- Unexplained fever of 38°C or higher (most common presentation in preverbal children).
- Frequency, dysuria (most common presentation in verbal children).
- Poor response to treatment for a presumed alternative site of infection.
- Abdominal pain, loin tenderness, vomiting, poor feeding, malaise, lethargy, irritability, haematuria, offensive urine, cloudy urine, failure to thrive.
- Dysfunctional voiding, incontinence of urine or faeces, new onset of bedwetting.⁶⁹

How to confirm a UTI in children?

- Preliminary diagnosis as per clinical symptoms PLUS
- Urine testing:
 - 3 months to 3 years: urgent microscopy (or dipstick if unavailable)
 - 3 years plus: urine dipstick for leukocyte esterase and nitrite (or microscopy if available).^{68,69}
- A urine sample should be tested after 24 hours at the latest.⁶⁸

TABLE SIX: NICE Clinical Guideline 54 – Presenting symptoms and signs in infants and children over 3 months of age with UTI⁶⁸

Symptoms and signs Most common→Least common			
Preverbal:	Fever	Abdominal pain Loin tenderness Vomiting Poor feeding	Lethargy Irritability Haematuria Offensive urine Failure to thrive
Verbal:	Frequency Dysuria	Dysfunctional voiding Changes to continence Abdominal pain Loin tenderness	Fever Malaise Vomiting Haematuria Offensive urine Cloudy urine

Table SEVEN: NICE Clinical Guideline 54 – Interpretation of microscopy results in children⁶⁸

Microscopy Results	Pyuria positive	Pyuria negative
Bacteriuria positive	The infant or child should be regarded as having UTI	The infant or child should be regarded as having UTI
Bacteriuria negative	Antibiotic treatment should be started if clinically UTI	The infant or child should be regarded as not having UTI

How to distinguish between LOWER and UPPER UTI in children?

Diagnose **UPPER UTI** (acute pyelonephritis) if:

- Fever of greater than 38°C (or history of fever) and bacteriuria
- OR
- Fever of less than 38°C (and no history of fever) with loin tenderness and bacteriuria.⁶⁹

All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered to have **LOWER UTI** (cystitis).⁶⁸

C-reactive protein alone should not be used to differentiate acute pyelonephritis/upper urinary tract infection from cystitis/lower urinary tract infection in infants and children.⁶⁸

When to refer to a paediatric specialist?

Some children presenting with UTI symptoms will require referral to secondary care. It is important to distinguish between those children who require referral to a General Paediatric Clinic and those that require referral to a Paediatric Nephrologist:

General Paediatric Clinic⁶⁸

- All children under 3 months of age will require an immediate referral.
- Children over 3 months of age if the UTI is recurrent OR who have abnormal imaging (if carried out at request of GP).
- Children with atypical features of UTI (see below for 'what is 'atypical' UTI in children') OR the child appears seriously unwell.
- Children presenting with dysfunctional voiding.

Paediatric Nephrologist

If child presents with any of the following refer to a nephrologist:

- Bilateral renal abnormalities
- Raised creatinine
- Raised blood pressure
- Proteinuria

What is 'atypical' UTI in children?

The following symptoms are suggestive of an atypical UTI:

- Seriously ill
- Poor urine flow
- Abdominal or bladder mass
- Raised creatinine
- Septicaemia
- Failure to respond to treatment with suitable antibiotics within 48 hours
- Infection with non-E. coli organisms.

Infants and children with atypical UTI should have ultrasound of the urinary tract during the acute infection to identify structural abnormalities of the urinary tract such as obstruction. This is to ensure prompt management.⁶⁸

How to manage LOWER UTI in children?

Accurate and timely diagnosis of UTI is important to allow appropriate treatment.⁷¹

Treatment is as follows:

- Oral antibiotic **for 3 days**.
- Choice of antibiotic will depend on locally developed multidisciplinary guidance. Avoid broad spectrum antibiotics.⁶⁹ See 'Choice of Antibiotic' later.
- Treat empirically, then on basis of sensitivity.
- Treat fever and pain with paracetamol.⁶⁹
- Encourage adequate fluid intake.⁶⁹
- Emphasise importance of not delaying voiding.⁶⁸

- Parents/carers should be advised to bring the child for reassessment if the child is still unwell after 24 to 48 hours. If an alternative diagnosis is not made, a urine sample should be sent for culture to identify the presence of bacteria and determine antibiotic sensitivity (if this has not already been carried out).⁶⁸

Choice of antibiotic

The Northern Ireland Antimicrobial Guidelines for Primary Care recommends a three day course of either trimethoprim or nitrofurantoin for uncomplicated LOWER UTI in children.⁷⁷

Trimethoprim

1 month – 12 years: 4mg/kg (max 200mg) twice daily for 3 days OR
 3 – 6 months 6–8kg 30mg (3mL) twice daily
 6 –12 months 8–10kg 40mg (4mL) twice daily
 1 – 5 years 12kg 50mg (5mL) twice daily
 6 – 12 years 25kg 100mg (10mL) twice daily⁷⁷
 Available as trimethoprim 50mg/5mL suspension.

Nitrofurantoin

3 months –12 years: 750micrograms/kg four times a day for 3 days^{43,69,75}
 Available as nitrofurantoin 25mg/5mL suspension.

Should asymptomatic bacteriuria in children be treated?

No, asymptomatic bacteriuria in infants and children should not be treated with antibiotics.

How to manage UPPER UTI in children?

Acute pyelonephritis is the most common serious bacterial infection in childhood. Most cases are readily treated, provided diagnosis is prompt, though in some children fever may take several days to abate. Oral antibiotics OR short courses of IV therapy (2 to 4 days) followed by oral therapy may be used.⁷² Parenteral antibiotic therapy and hospitalisation should be considered for children who appear to be severely ill or dehydrated, who are unable to retain oral intake. As in LOWER UTI, infants under 3 months of age will require hospitalisation.⁷³

Therefore, if treating in primary care, management is as follows:

- Oral antibiotic for 7 to 10 days^{68,69}
- Obtain urine specimen before starting antibiotics.
- Consider co-amoxiclav or a cephalosporin (depending on local sensitivity patterns)^{68,73}
- Treat fever and pain with paracetamol.⁶⁹
- Encourage adequate fluid intake.⁶⁹

Co-amoxiclav

3mths – 1 year: 0.25mL/kg of 125mg/31mg suspension TDS.
 1 – 6 years: 5mL OR 0.25mL/kg of 125mg/31mg suspension TDS.
 6 – 12 years: 5mL or 0.15mL/kg of 250mg/62mg suspension TDS.
 NB – double dose in severe infection⁷⁵
 Available as co-amoxiclav 125mg/31mg and 250mg/62mg suspensions.

What follow-up will be required?

The incidence of recurrent UTI within 12 months of an initial UTI is approximately 12 to 30%.⁸²⁻⁸⁴ Parents/carers should be counselled on the possibility of a UTI recurring, the need for vigilance, and to seek

prompt treatment from a healthcare professional for any suspected re-infection.⁶⁸

Repeated UTIs in children can result in renal scarring, which can cause long term morbidity including hypertension, chronic renal failure (early adulthood) and eclampsia (in pregnancy).⁷⁰

Long-term antibiotic prophylaxis and surgery are not routinely recommended but *may* be considered in some patients with recurrent UTIs (see later).^{68,73}

When are imaging tests indicated?

- Recurrent episodes of infection are an indication for imaging tests.⁷⁵ This is to detect any renal or urinary tract abnormalities that may predispose to repeated UTIs. The most common abnormality detected in children is vesicoureteric reflux.⁷⁰
- Dysfunctional elimination syndromes and constipation should be addressed in infants and children who have had a UTI.⁶⁸
- Children presenting with 'atypical' symptoms.

What is considered recurrent UTI in children?⁶⁸

- Two or more episodes of UTI with acute pyelonephritis/upper urinary tract infection, or
- One episode of UTI with acute pyelonephritis/upper urinary tract infection plus one or more episode of UTI with cystitis/lower urinary tract infection, or
- Three or more episodes of UTI with cystitis/lower urinary tract infection.

When to use antibiotic prophylaxis in children?

Early diagnosis and treatment are the most effective prophylactic treatment against renal scarring in every case of pyelonephritis in children.⁹⁶ Evidence is lacking that prophylactic antibiotics reduce the incidence of recurrent childhood UTI⁷⁶; prophylaxis has been shown to be effective in reducing the number of positive urine cultures, however a significant reduction in the number of symptomatic infections or new renal scarring have not been demonstrated.^{73,74,76} Therefore:

- Antibiotic prophylaxis should not be routinely recommended in infants and children following first-time UTI, but may be considered in infants and children with recurrent UTI.^{68,69}
- If an infant or child is receiving prophylactic medication and develops an infection, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.
- Choice of antibiotic for prophylaxis include: nitrofurantoin and trimethoprim.⁷⁵

Nitrofurantoin

3mths – 12 years: 1mg/kg at night.⁴³

Trimethoprim

2mg/kg (max 100mg) at night OR
 6 weeks – 6 months: 12.5mg at night
 6 months – 6 years: 25mg at night
 6 – 12 years: 50mg at night.⁴³

What risks are associated with prophylaxis?

- Inconvenient for the patient and parent/carer.
- Poor adherence.
- Adverse effects, e.g. vomiting or gastrointestinal intolerance.
- Colonisation with resistant organisms in patient.
- Important to continually ensure that the dose is appropriate as the weight of the child increases over

time. This will be particularly important in very young children.

- Bacterial resistance in wider population.^{73,74,76,96}

Any evidence for circumcision to reduce incidence of UTIs in children?

Circumcision has been shown to be associated with a reduced risk of urinary tract infection: circumcised male infants have a three to ten-fold reduced risk of UTI than

non-circumcised boys.^{85,86,97} However, clinical benefit relates only to boys at high risk for urinary tract infection or boys with high-grade vesicoureteric reflux.^{73,86} Furthermore, routine circumcision is not a recommendation in Western European countries.⁹⁷

Any evidence on the effectiveness of cranberry products reducing UTIs in children?

See SECTION SEVEN.

Summary table – managing LOWER UTI in primary care

Patient Group	Urine sample needed for culture and sensitivity testing?	Dipstick testing of urine appropriate?	Antimicrobial of choice	Length of course
Non-pregnant women	No, not if multiple typical symptoms of lower UTI reported	Only where there are few signs & symptoms of UTI	Trimethoprim 200mg twice daily, OR Nitrofurantoin 50-100mg four times daily	3 days (7 days for women who have recurrent UTIs or are planning pregnancy)
UPDATED Pregnant women	Yes, and treat both asymptomatic and symptomatic bacteriuria	No, dipstick testing for LE and/or nitrite not appropriate. (Antenatal urine dipstick testing for protein and/or glucose is appropriate)	1 st line: cefalexin 500mg three times daily ⁷⁷ 2 nd line: nitrofurantoin 50-100mg four times daily (OR amoxicillin 500mg three times daily if susceptible) 3 rd line: trimethoprim 200mg twice daily (+folic acid if 1 st trimester) Start empirically and change if required once culture results known ¹⁶	7 days
UPDATED Men	Yes	Only to decide if a "working" diagnosis of UTI should be made	Trimethoprim 200mg twice daily, OR Nitrofurantoin 50-100mg four times daily. Start empirically and change if required once culture results known. If prostatitis is suspected: ciprofloxacin 500mg twice daily for 28 days	7 days
Patients with long-term indwelling catheters	Urine should only be cultured if patient is symptomatic	No, cannot distinguish between infection and asymptomatic bacteriuria. Also, LE will often be false positive due to foreign body reaction to catheter material	Trimethoprim 200mg twice daily, OR Nitrofurantoin 50-100mg four times daily. Start empirically and change if required once culture results known	7 to 14 days
NEW Children (3mth+)	Yes, send pre-treatment MSU for all	Use positive nitrite to start antibiotics	Trimethoprim 4mg/kg twice daily OR Nitrofurantoin 3mg/kg daily in four divided doses	3 days

SECTION SEVEN: Cranberry Products

Cranberry products are a popular choice of complementary therapy for UTI. Cranberry has been used anecdotally for centuries, undergoing a revival in recent years for UTI management. Evidence is growing to support its use in the management of UTI, however, further research is still required to determine optimum benefit of cranberry.^{1,63,97}

In which patient groups have cranberry products been shown to be effective?

Cranberry products have been shown to be more effective in preventing UTI in **adult women with recurrent UTI** than in any other patient group.⁶³

The evidence is currently inconclusive in elderly men and women, patients requiring catheterisation, and in children.^{1,63,97}

Points to consider...

- ▶ Women with recurrent UTI may consider using cranberry products to **reduce frequency of recurrence**.
- ▶ There is **no** convincing published evidence to support the use of cranberry products in **treating** people with **current** UTI.^{1,64,65}



What evidence exists?

A Cochrane Review concluded that cranberries were better than placebo in preventing recurrence of UTI in menopausal women without causing severe adverse effects.⁶³

A RCT suggested beneficial results in terms of preventing symptomatic recurrences of UTI in children.⁹⁵

No evidence to support use of cranberry products for reducing UTI in men has been located.¹



Any comparison to other prophylactic therapies?

It has been reported that cranberry products are not as effective as nightly antibiotic treatment given for six months, or post-coital antibiotic prophylaxis for six months, in preventing UTI.^{100,101}

One study showed that trimethoprim had only limited advantage over cranberry in preventing recurrent UTI in older women (and had more adverse effects).⁶⁷



How does cranberry work against UTI?

No definitive mechanism has been established.⁶³ However it has been postulated that cranberry inhibits the uropathogen *E.coli* at the uroepithelium.⁹⁷ That is to say, cranberry prevents bacteria sticking to the walls of the bladder and causing infection.⁶³

What dose is recommended?

The optimal dosage and required duration for cranberry products have not yet been established.^{1,63,64}

What types of cranberry products are available?

Cranberry can be taken as tablets or capsules, juice drinks, or the fresh berries themselves.

Cranberry tablets or capsules are convenient and are available as "high strength" formulations. Most of the "high-strength" capsules and tablets are stated to contain between 200mg and 400mg of cranberry extract, equivalent to between 5 to 10 grams of fresh cranberries² (5 fresh cranberries weigh approximately 5 grams).

Cranberry juice drinks probably contain a lot less active ingredients than tablets or capsules.² In addition, juice drinks often contain a high concentration of sugar (to mask the bitter taste)² and as such should be used with caution in people with diabetes.

Cranberry products are not available on prescription, but are readily available from most health food shops, pharmacies, herbalists and supermarkets. Cranberry products are not regulated and as such, the concentration of active ingredients is not always stated, and concentrations may vary between batches of the same product.¹

Points to consider...

- ▶ Cranberry capsules may be more convenient than juice.
- ▶ High strength capsules may be more effective.¹

Are there any safety issues for people taking cranberry products?

In studies, no serious adverse effects of cranberry products were reported, but high drop-out rates suggest that they may not be well tolerated.² An unpleasant taste was often given as a reason for drop out.⁶³ Cranberry juice has been reported to interact with warfarin – see Prescribing Point.



Prescribing Point: Interaction between cranberry products and warfarin

- ▶ There have been reports of an increase in INR in patients taking warfarin and cranberry juice.^{31,66}
- ▶ In 2004 the MHRA issued a warning that patients taking warfarin should avoid cranberry products unless the health benefits are considered to outweigh any risks, and that increased INR monitoring should be carried out with concurrent use.⁶⁶
- ▶ Recent studies have shown that cranberry does not alter the pharmacokinetics of warfarin. However a pharmacodynamic mechanism has not been ruled out, e.g. salicylate in commercial cranberry juice may cause hypothermibinaemia. The studies suggest that **moderate** doses of cranberry products in otherwise healthy individuals taking warfarin may not have an adverse effect on anticoagulation control.³¹
- ▶ Patients on warfarin are still advised to be cautious if taking warfarin – avoid large quantities of cranberry, try to ensure consistency in daily amount consumed, and ensure regular monitoring of INR.

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Please note that every effort has been made to ensure that the content of the COMPASS Therapeutic Notes is accurate at the time of publication. Readers are reminded that it is their responsibility to keep up-to-date with any changes in practice.

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COMPASS THERAPEUTIC NOTES ASSESSMENT

Management of Bacterial Urinary Tract Infections in Primary Care

COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 250 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.

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- Doctors and nurses should submit their answers at: www.medicinesni.com
- Pharmacists should submit their answers at: www.nicpld.org

1 In the management of urinary tract infections in NON-pregnant women:

a	Dysuria and frequency are highly suggestive of UTI.	T	F
b	UTI in an otherwise healthy non-pregnant woman can be diagnosed without a dipstick test of the urine and without urine culture when there are multiple typical symptoms and signs of UTI.	T	F
c	A three-day course of trimethoprim or nitrofurantoin is recommended for the treatment of simple UTI in non-pregnant women.	T	F
d	A woman who has three or more episodes per year of acute UTI, or two microbiologically confirmed UTIs in 6 months, is said to have "recurrent" UTIs.	T	F

2 In pregnant women:

a	All pregnant women should be screened for bacteriuria at their first antenatal visit.	T	F
b	Asymptomatic bacteria should be treated in all pregnant women.	T	F
c	A three day course is sufficient for uncomplicated UTI in pregnant women.	T	F
d	Given the risks of bacteriuria in pregnancy, a urine culture should be performed seven days after completion of antibiotic treatment as a test of cure, and then at every antenatal visit for the rest of the pregnancy.	T	F

3 In the management of urinary tract infections in men:

a	It is not necessary to send a sample of urine for culture and sensitivity testing.	T	F
b	Co-amoxiclav should be considered as first line therapy for uncomplicated UTI in men.	T	F
c	In a man with an uncomplicated lower urinary tract infection, a three-day course of antibiotics is appropriate.	T	F
d	Failure to respond to appropriate antibiotic therapy is an indication for referral to a specialist.	T	F

4 In the management of patients with indwelling catheters:

a	Classical signs and symptoms of UTI do not always apply; fever is the most common symptom.	T	F
b	Dipstick tests may be used to differentiate between asymptomatic and symptomatic bacteriuria.	T	F
c	Patients should receive antibiotic treatment for bacteriuria regardless if clinically symptomatic or not.	T	F
d	Nitrofurantoin is a suitable choice for patients with renal impairment.	T	F

5 In the management of urinary tract infection in children:

a	Infants under three months of age may be managed in primary care.	T	F
b	A three day treatment with trimethoprim or nitrofurantoin should be used empirically in children over 3 months of age.	T	F
c	Antibiotic prophylaxis of UTI in children has been shown to be effective in reducing the incidence of recurrent UTI.	T	F
d	A higher dose of the prophylactic antibiotic should be prescribed if the child develops an infection.	T	F

6 Cranberry products:

a	There is some evidence to support the effectiveness of cranberry products in the treatment of urinary tract infections	T	F
b	Cranberry products are not regulated and as such, the concentration of active ingredients is not always stated, and concentrations may vary between batches of the same product.	T	F
c	Cranberry products have been shown to be effective for UTI prophylaxis in men.	T	F
d	Cranberry products should be used with caution in patients also taking warfarin.	T	F