

Guidelines for Recurrent Urinary Tract Infections in Non-pregnant women: Antibiotic Prophylaxis

Scope

This guidance is aimed at primary care clinicians to enable them to manage patients with recurrent lower urinary tract infections in non-pregnant women who do not have a catheter. The guidance does not apply to the following groups:

- Patients with catheters
- Men
- Pregnant women
- Children

**2 or more episodes of lower urinary tract infection in the last 6 months,
OR
3 or more episodes of lower urinary tract infection in the last 12 months^{1,8}.**

Definition

The symptoms of a lower urinary tract infection include frequency, dysuria, urgency, and suprapubic pain. Recurrent lower urinary tract infection (rUTI) is defined as:

It does not include bacteriuria in the absence of symptoms or in catheterised patients i.e. asymptomatic bacteriuria. Asymptomatic bacteriuria should not be screened for or treated, unless prior to urological surgery or in pregnancy (positive cultures in pregnancy should be confirmed with a second culture confirming the same organism prior to treating)².

1. Consider whether referral is required for patient with recurrent UTIs:

Consider specialist referral for the following factors^{1,3,8}:

Red flags for referral to Urology:

- Frank haematuria, even in the context of confirmed UTI
- Neurological disease e.g. spinal cord injury, spina bifida
- Pneumaturia or faecaluria
- Proteus on repeat urine cultures
- Suspected stone
- People with recurrent lower UTI when the underlying cause is unknown
- People with recurrent upper UTI
- People with suspected cancer
- Obstructive symptoms, or structural/functional abnormality, causing >200ml residual urine on bladder scan

Red flags for referral to Obstetrics:

- All recurrent UTIs in pregnancy should be discussed with the Obstetrics team.

Consider risk factors:

A sexual history and investigations for sexually transmitted infections should be performed if appropriate. In peri- and post-menopausal women, atrophic vaginitis may cause urinary symptoms and may increase the risk of bacteriuria.

Microbiological Confirmation:

Patients with rUTIs should have a mid-stream urine (MSU) sample sent for culture prior to antibiotics being initiated, in order to confirm infection and guide antibiotic therapy³. Patients should be counselled on how to provide a specimen to minimise the chance of contamination (see appendix 1).

Urine cultures sent in the absence of symptoms are unlikely to be helpful, may detect asymptomatic bacteriuria and lead to inappropriate antibiotic use. Antibiotic treatment of asymptomatic bacteriuria is more likely to be harmful than beneficial.⁴

Patients with indwelling catheters should not be treated for UTIs unless they present with physical symptoms. Urinalysis for leucocytes and nitrites is non-specific in patients with urinary catheters in situ and should not be performed as investigation for UTIs.

'Clearance' cultures are not recommended if symptoms have resolved, with the exception of pregnant women.

2. Management of Initial Presentation of Recurrent UTI in non-pregnant females

The following conservative measures should be tried prior to antibiotic prophylaxis

Conservative Measures:

- Encourage better hydration and more frequent voiding
- For sexually active women:
 - Advise post-coital voiding
 - Avoid use of contraceptive diaphragm and spermicide
- Avoid using cosmetic bath products or feminine hygiene douches.
- Perineal hygiene i.e. wiping front to back.
- Avoid using flannels. A clean non scented disposable wipe is preferable.

Intra-vaginal oestrogens:

- For post-menopausal women with recurrent UTIs, consider topical oestrogens⁴.

Antibiotic Prescribing Strategies

The relative risks and benefits of the following antibiotic prescribing strategies should be discussed with the patient. These strategies should be in addition to conservative measures. Non-pregnant patients may find products containing D- Mannose helpful. These are available as powder and tablets which can be bought. D- Mannose should not be recommended to patients with diabetes and it may increase the HbA1C. Potassium citrate may also prevent the onset of UTI which are available through pharmacies. Further information can be found on the self-care leaflet in appendix 2 or the following link [here](#)

- **Standby Antibiotics**

- If the patient is able to wait, infection should first be confirmed by MSU prior to commencing standby antibiotics.
- A patient advice sheet and boric acid container for pre-antibiotic MSU should be provided to the patient, see pages 10-12.
- A 'self-start' course of antibiotics, prescribing an agent according to previous known sensitivities and choosing the narrowest spectrum agent available⁵. Refer to Suffolk Primary Care Antibiotic Guidelines for more information.
- Safety-net with advice to seek medical attention if they develop fever, loin pain, or symptoms are not improving by 48 hours.
- This option limits antibiotic exposure and risk of resistance emerging, and may be the more suitable option for patients with <1 UTI per month.

- **Post Coital Antibiotics**

- For rUTIs that are triggered by sexual intercourse, this strategy is as effective as continuous antibiotic prophylaxis⁷, and limits antibiotic exposure and risk of resistance emerging.
- Consider a single dose of nitrofurantoin 100mg within 2 hours of intercourse
- The incidence of UTIs may be increased in women who use diaphragms. Consider using alternatives if this is the case.

- **Continuous Antibiotic Prophylaxis**

Consider prophylactic drug treatment when there is unacceptable discomfort or disruption to their lives and/or if they have had 2 more episodes of lower urinary tract infection in the last 6 months, or 3 or more episodes of lower urinary tract infection in the last 12 months¹.

- Longer term antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance.
- A 6 month trial of low-dose continuous antibiotic treatment may be beneficial if rUTIs are occurring ≥ 1 per month and are not triggered by sexual intercourse.
- Urine should only be tested where a UTI develops and should be treated according to sensitivities.
- Patients should be counselled at an early stage that antibiotic prophylaxis is not usually a lifelong treatment. Documenting and triggering a review date in the patient's record, and on the repeat prescription, is strongly advised to avoid prolonged courses of antibiotics without review
- Patients should be counselled to recognise the symptoms of a UTI

Stopping continuous prophylaxis:

It is understandable for patients to be anxious about a return to frequent UTIs after stopping continuous prophylaxis. However, a prolonged period of antibiotic treatment may allow bladder epithelial healing, reducing the risk of future UTIs when antibiotics are then stopped.

- The proportion of patients who will return to suffering recurrent UTIs after stopping continuous prophylaxis may be around 50%.⁷
- This means a significant number of patients are able to stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of resistance emerging and side-effects.
- One option is to provide 'standby' antibiotics when stopping continuous prophylaxis which may give sufficient reassurance to patients for a trial off antibiotics.
- Consider referring patients who relapse after stopping continuous prophylaxis, if not already been investigated.
- Longer term prophylaxis may be helpful in those patients whose UTIs are suppressed when on prophylaxis and recur when prophylaxis is discontinued after 6 months.
- Remind the patient about behavioural and personal hygiene measures, and self-care

Choice of Agents^{5,9}:

Choice of antibiotic should be based on confirmed culture and sensitivity results (wherever possible) on the most recent active infection, and consider the patient's co-morbidities, renal function and any contra-indicating factors. Trimethoprim and nitrofurantoin are licensed for the prophylaxis of rUTIs.

The risk of adverse effects (see box below), as well as common side-effects such as rashes, oral/vaginal thrush and gastro-intestinal upset, should be discussed with the patient.

Antibiotic	Dose	Cautions and Monitoring
Trimethoprim	200 mg One dose post-coital (off label) Or 100mg nightly	<ul style="list-style-type: none"> Hyperkalaemia: caution when prescribing with drugs such as spironolactone, ACE inhibitor or angiotensin inhibitors. Renal Impairment: Avoid if eGFR <15ml/min. Discuss with renal physician Use half normal dose if eGFR <30ml/min. May increase serum creatinine. Patients should be counselled on the risk of blood disorders and advised to seek attention if fever, sore throat, purpura, mouth ulcers, bruising or bleeding occurs.
OR:		
Nitrofurantoin	100mg immediate release One dose post-coital (off label) Or 50 to 100 mg nightly	<ul style="list-style-type: none"> Avoid if renal function eGFR <45ml/min. Consider checking renal function prior to commencing continuous prophylaxis, especially in the elderly. Avoid if G6PD deficiency. Use with caution in anaemia, diabetes, vitamin B or folate deficiencies. Monitor full blood count, renal function and liver function tests every 3-6 months Advise the patient on the risk of pulmonary and hepatic fibrosis, and the symptoms to report if they develop during treatment. Reactions can develop acutely or insidiously. Advise the patient on the risk of peripheral and optic neuropathy, and the symptoms to report if they develop during treatment.

If resistance to both first line agents, other agents may be considered after discussion with Urology and/or Microbiology. Broader spectrum agents such as cefalexin, ciprofloxacin and co-amoxiclav have a higher risk of C.difficile diarrhoea and should not be routinely used for prophylaxis. Rotating between different agents for prophylaxis should be avoided as it may increase the risk of antimicrobial resistance.

Methenamine

A Cochrane review in 2007 assessed the benefits of a urinary antiseptic agent, methenamine hippurate⁸. This is converted to formaldehyde in the acidic urine environment, which is directly toxic to bacteria. It concluded that in a sub-group of women without urinary tract abnormalities or neuropathic bladder, it may be of benefit in preventing rUTIs in the short-term but long-term benefit was not demonstrated. The studies were of poor quality and there was insufficient evidence to recommend its routine use.

If there are no suitable alternative therapies, due to:

- Multi-resistant organisms
- Allergies, contraindications, or side-effects with prophylactic antibiotics.
- High-risk patients for whom prophylactic antibiotics are not appropriate e.g.C.difficile carriage

A 3 month trial of Methenamine may be advised by a Urologist or Microbiologist at the following doses (as per BNF)

- Prophylaxis: 1g every 12 hours
- Prophylaxis in patients with catheters: 1g every 8-12 hours

Methenamine should be avoided in patients with eGFR<10ml/min

Treatment should stop after 6 months and advice should be sought from the specialist if relapses or side-effects occur

3. Managing 'breakthrough' UTIs in patients on antibiotic prophylaxis:

- The first breakthrough infection should be treated according to culture and sensitivity results, with the original prophylaxis being re-started once the infection has resolved if the culture confirms it is still sensitive to the prophylactic agent in the breakthrough infection
- If the culture shows resistance to the prophylactic agent, or multiple breakthrough UTIs occur (≥ 2 UTIs in 6 months), prophylaxis has therefore proved ineffective and should be stopped.
- Consider referral to Urology or Gynaecology for pregnant patients at this point if not already been investigated.

4. Managing a patient who has had a prolonged course of prophylactic antibiotics:

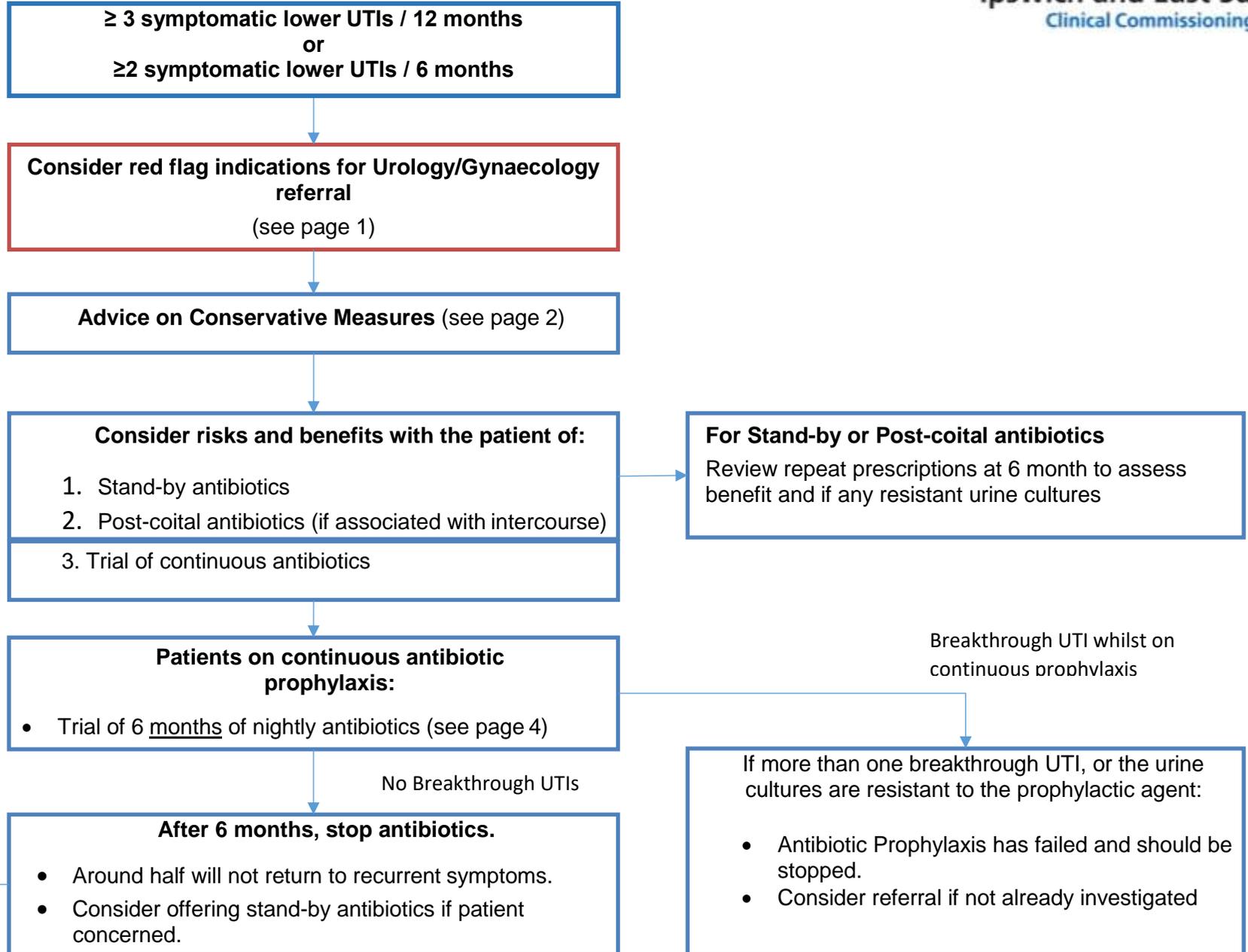
Identifying patients for review:

- Patients should be reviewed after 6 months of prophylactic antibiotics with a view to stopping (refer to 'Stopping Continuous Prophylaxis' page 4).
- 12 months is a suggested trigger for audit purposes for patients on long-term prophylaxis.
- Patients who have urine cultures confirming resistance to the prophylactic agent they are on, should have their prophylaxis stopped (exposure to antibiotic without benefit) and a clinical review to discuss ongoing management and/ or need for referral.

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Summary of Management of Recurrent Lower UTIs (in non-pregnant women):



Appendix 1: Midstream Specimen of Urine (MSU)

What is the purpose of a midstream specimen of urine (MSU) test?

- **To confirm the diagnosis of a urine infection.** The usual symptoms of a urine infection are pain when you pass urine and passing urine frequently. However, symptoms are not always typical, particularly in children and the elderly, so a urine test may be needed.
- **To decide the best antibiotic to use.** Some germs (bacteria) are resistant to some antibiotics. If the test shows that bacteria are in the urine then the bacteria are tested against various antibiotics. This finds which antibiotics will kill the bacteria in the urine.

How do I do a midstream specimen of urine (MSU)?

The aim is to obtain a sample (specimen) of urine from the middle of your bladder. Urine does not normally have any germs (bacteria) in it (urine should be sterile). If bacteria are found in the sample, it means that the urine is infected. A midstream sample is best, as the first bit of urine that you pass may be contaminated with bacteria from the skin.

Before doing an MSU, wash your hands and ideally your genitals as well.

Women - hold open the entrance to the vagina (your labia). Men - pull back your foreskin. Pass some urine into the toilet. Then, without stopping the flow of urine, catch some urine in a clean (sterile) bottle. (The bottle is usually provided by a doctor or nurse.) Once you have enough urine in the bottle, finish off passing the rest of your urine into the toilet.

Do not open the sterile bottle until you are ready to take the sample. Avoid touching any part of your genitals with the bottle, as this will increase the risk of contamination. Put the cap back on the container. You do not need to fill the bottle to the top; a small amount will do. Some specimen bottles contain a powder, which helps the sample last longer for testing (a preservative). If this is the case, a mark on the bottle will indicate the ideal amount of urine. However, if that is difficult, any amount is better than none.

The sooner the sample is given in to the doctor's surgery, or to the laboratory, the better. Within two hours is best. If that is not possible, put the sample in the fridge until you take it to the doctor or laboratory.

If it is difficult to aim your urine stream into the bottle, you may use another container such as a jam jar or a disposable plastic cup. You can then pour the urine into the sterile bottle. If you do this, make sure the container you pass water into is as clean as possible. Wash it well and rinse it with boiling water. You should still pass the first part of your urine stream into the toilet. In this way, you are collecting the urine from the bladder.

The result of an MSU takes 2-7 days.

Urine specimens and children

It is not easy to get a pure midstream specimen of urine (MSU) in young children and babies. The following methods may be used:

The clean catch method

The usual way is to catch some urine in the specimen bottle whilst the child is passing urine. This is called the clean catch method. Just be ready with the open bottle as the child passes urine. (Be careful not to touch the open rim of the bottle with your fingers, as this may contaminate the specimen with germs (bacteria) from your fingers.)

For babies the following might work: take the nappy off about one hour after a feed. Tap gently with a finger (about once a second) just at the bottom of the tummy (abdomen) above the genitals. Have the open bottle ready. Quite often, within about five minutes, the baby will pass urine. Try to catch some in the bottle.

Urine pads

One method is to place a special absorbent pad in a nappy. Your doctor or nurse will provide the special pad and tell you how to use it. Basically, when you place the pad in the nappy, check the pad every 10 minutes to see if it is wet with urine. Do not leave in for longer than 30 minutes as this may increase the risk of contamination. Therefore, replace the pad with a fresh one every 30 minutes until urine has been passed. Then, use the syringe provided to suck the urine from the pad. Then, transfer the urine in the syringe into a sterile container. Do not use other type of pads, cotton wool balls or gauze as they could alter the results.

Urine collection bags
These are bags which are placed inside the nappy to collect urine. They are stuck to the skin around the genitals. When the infant passes urine, it collects in the bag. You then take off the bag, cut the corner of the bag and pour the urine into the sterile bottle. Always wash your child's genital area and dry it carefully before sticking the bag on. This is so germs from the skin are not mixed in with the urine.

Appendix 2



TREATING YOUR INFECTION - URINARY TRACT INFECTION (UTI)



For women under 65 years with suspected lower urinary tract infections (UTIs) or lower recurrent UTIs (cystitis or urethritis)

Possible urinary signs & symptoms	The outcome	Recommended care	Types of urinary tract infection (UTI)
<p>Key signs/symptoms: Dysuria: Burning pain when passing urine (wee) New nocturia: Needing to pass urine in the night Cloudy urine: Visible cloudy colour when passing urine</p> <p>Other severe signs/symptoms: Frequency: Passing urine more often than usual Urgency: Feeling the need to pass urine immediately Haematuria: Blood in your urine Suprapubic pain: Pain in your lower tummy</p> <p>Other things to consider: Recent sexual history <ul style="list-style-type: none"> • Inflammation due to sexual activity can feel similar to the symptoms of a UTI. • Some sexually transmitted infections (STIs) can have symptoms similar to those of a UTI. Changes during menopause <ul style="list-style-type: none"> • Some changes during the menopause can have symptoms similar to those of a UTI. </p>	<p>All women:</p> <p><input type="checkbox"/> If none or only one of: dysuria, new nocturia, cloudy urine; AND/OR vaginal discharge</p> <ul style="list-style-type: none"> • Antibiotics less likely to help. • Usually lasts 5 to 7 days. • You may need a urine test to check for a UTI. <p>Non-pregnant women:</p> <p><input type="checkbox"/> If 2 or more of: dysuria, new nocturia, cloudy urine; OR bacteria detected in urine; AND NO vaginal discharge</p> <ul style="list-style-type: none"> • Antibiotics are more likely to help. • You should start to improve within 48 hours • Symptoms usually last 3 days. <p>Pregnant women: Always request urine culture</p> <p><input type="checkbox"/> If suspected UTI.</p>	<p><input type="checkbox"/> Self-care and pain relief. • Symptoms may get better on their own.</p> <p><input type="checkbox"/> Delayed or backup prescription with self-care and pain relief. Start antibiotics if symptoms: • Get worse. • Do not get a little better with self-care within 48 hours.</p> <p><input type="checkbox"/> Immediate antibiotics prescription plus self-care.</p> <p><input type="checkbox"/> If mild symptoms, delayed or back-up antibiotic prescription plus self-care.</p> <p><input type="checkbox"/> Immediate antibiotic prescription.</p>	<p>UTIs are caused by bacteria getting into your urethra or bladder, usually from your gut. Infections may occur in different parts of the urinary tract.</p>  <p>Kidneys (make urine) Infection in the upper urinary tract • Pyelonephritis (pie-lo-nef-right-is). Not covered in this leaflet and always needs antibiotics.</p> <p>Bladder (stores urine) Infection in the lower urinary tract • Cystitis (sis-tight-is).</p> <p>Urethra (takes urine out of the body) Infection or inflammation in the urethra • Urethritis (your-ith-right-is).</p>
Self-care to help yourself get better more quickly	When should you get help?	Options to help prevent a UTI	Antibiotic resistance
<ul style="list-style-type: none"> • Drink enough fluids to stop you feeling thirsty. Aim to drink 6 to 8 glasses including water, decaffeinated and sugar-free drinks. • Take paracetamol or ibuprofen at regular intervals for pain relief, if you have had no previous side effects. • You could try taking cranberry capsules or cystitis sachets. These are effective for some women. There is currently no evidence to support their use. • Consider the risk factors in the 'Options to help prevent UTI' column to reduce future UTIs. 	<p>The following symptoms are possible signs of serious infection and should be assessed urgently.</p> <p>Phone for advice if you are not sure how urgent the symptoms are.</p> <ol style="list-style-type: none"> 1. You have shivering, chills and muscle pain. 2. You feel confused, or are very drowsy. 3. You have not passed urine all day. 4. You are vomiting. 5. You see blood in your urine. 6. Your temperature is above 38°C or less than 36°C. 7. You have kidney pain in your back just under the ribs. 8. Your symptoms get worse. 9. Your symptoms are not starting to improve within 48 hours of taking antibiotics. 	<p>It may help you to consider these risk factors: Stop bacteria spreading from your bowel into your bladder. Wipe from front (vagina) to back (bottom) after using the toilet. Avoid waiting to pass urine. Pass urine as a soon as you need a wee. Go for a wee after having sex to flush out any bacteria that may be near the opening to the urethra. Wash the external vagina area with water before and after sex to wash away any bacteria that may be near the opening to the urethra. Drink enough fluids to make sure you wee regularly throughout the day, especially during hot weather.</p> <p>If you have a recurrent UTI, also consider the following:</p> <ul style="list-style-type: none"> • Cranberry products and D-mannose: Some women find these effective, but there is currently poor evidence to support this. • After the menopause: You could consider topical hormonal treatment, for example, vaginal creams. 	<p>Antibiotics can be lifesaving. But antibiotics are not always needed for urinary symptoms.</p> <p>Antibiotics taken by mouth, for any reason, affect our gut bacteria making some resistant.</p> <p>Antibiotic resistance means that the antibiotics cannot kill that bacteria.</p> <p>Antibiotic resistant bacteria can remain in your gut for at least a year after taking an antibiotic.</p> <p>Common side effects to taking antibiotics include thrush, rashes, vomiting and diarrhoea. Seek medical advice if you are worried.</p> <p>Keep antibiotics working, only take them when advised by a health professional. This way they are more likely to work for a future UTI.</p>

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Keep Working