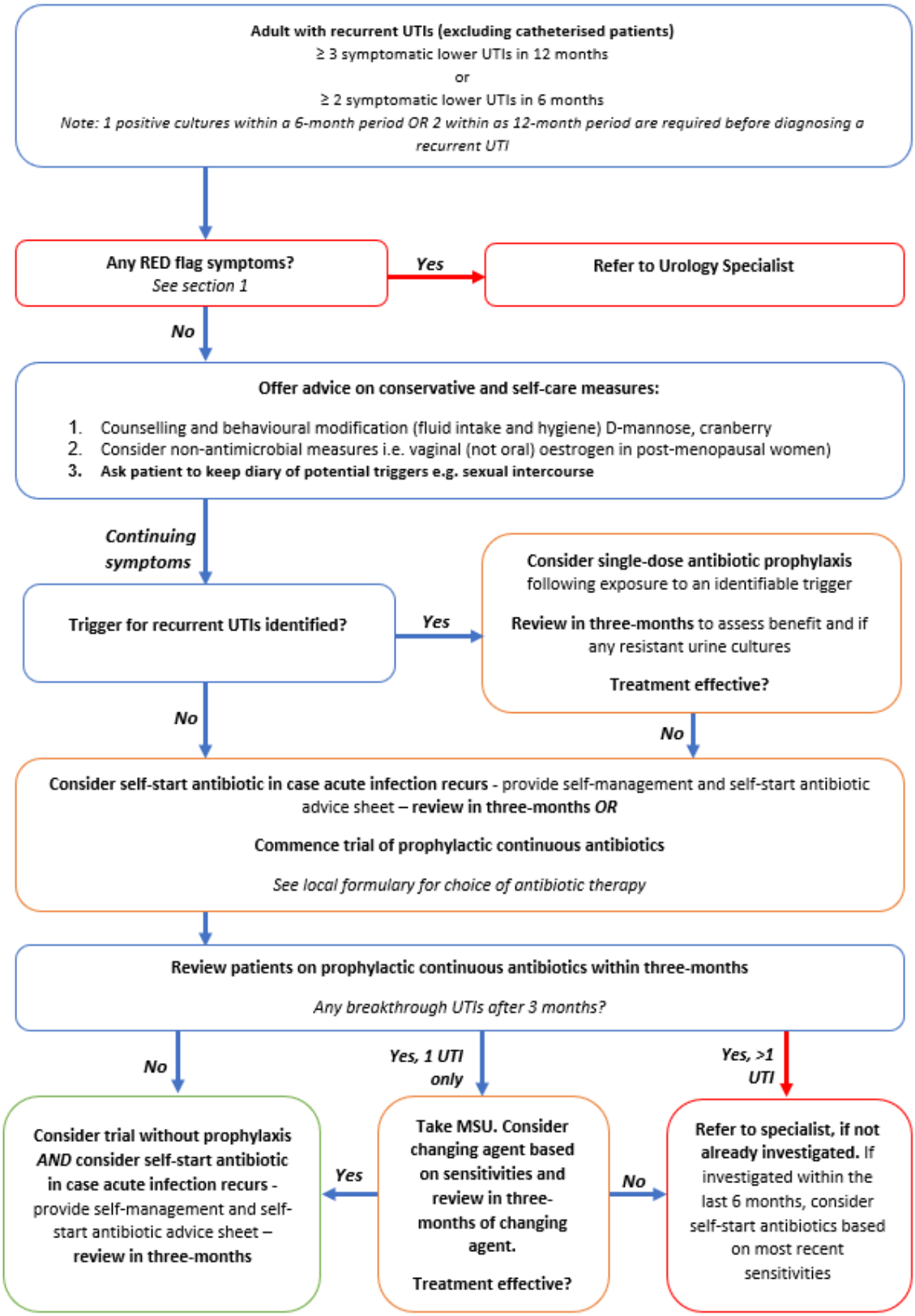
Management of Recurrent Urinary Tract Infections in Adults (aged 16 and above)



Definition of recurrent *LOWER* urinary tract infections (rUTIs)

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

≥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

NOTE 1 positive cultures within a 6-month period OR 2 positive cultures within a 12-month period are required before diagnosing a recurrent UTI

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. An immediate antibiotic prescription should be offered to pregnant women with asymptomatic bacteriuria (confirmed with a repeat sample), considering urine culture and susceptibility results and previous antibiotic use.

Consider whether referral to specialist is required for patient with recurrent UTIs:

Consider whether the patient requires specialist referral for the following factors:

Refer or seek specialist advice from urology on further investigation and management for:

- *All men*
- *Recurrent UPPER UTI*
- *Frank haematuria, even in the context of confirmed UTI (refer to current '2 week wait' guidelines for further information)*
- *Neurological disease e.g. spinal cord injury, spina bifida*
- *Pneumaturia or faecaluria*
- *Proteus on repeat urine cultures*
- *Suspected stone*
- *Renal pathology predisposing to infections e.g. previous renal scarring*
- *Obstructive symptoms, or structural/functionality abnormality, causing>200ml residual urine on bladder scan*
- *Pregnancy – all rUTIs 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. Vaginal oestrogen should be trialed in these patients.
- Presence of cystocoele.
- History of urinary incontinence.

Microbiological confirmation:

- Primary Care investigations should include ultrasound scan (USS), bladder residual volume, HbA_{1c}, creatinine and electrolytes and renal function tests.
- Patients with rUTIs should have a mid-stream urine (MSU) sample sent for culture **prior** to antibiotics being initiated, to confirm infection and guide antibiotic therapy.
- Patients should be counselled on how to provide a specimen to minimise the chance of contamination. See patient information leaflet - **How to collect a midstream urine sample – patient information leaflet (LINK).**
- If initial sample is suspected of contamination, repeat urine culture.
- Urine culture should be repeated with each symptomatic episode to confirm diagnosis and provide susceptibility result.
- 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.

Management of initial presentation of recurrent UTI in non-pregnant females

The following conservative measures should be tried prior to antibiotic prophylaxis:

Self-care measures are first line

- Patients should be given advice about behavioural and personal hygiene measures to reduce the risk of UTI, such as:
    - Encouraging better hydration and drinking enough fluids to avoid dehydration
    - Frequent voiding and to not delay habitual and post-coital urination.
    - Wiping from front to back, including after defaecation.
    - Not douching or wearing occlusive underwear.
- Some women, who are not pregnant, may wish to try D-mannose (the evidence for D-mannose was based on a study in which it was taken as 200ml of 1% solution once daily in the evening). D-mannose is sugar that is available to buy as powder or tablets; it is not a medicine. It is not available on prescription but can be purchased over the counter.
- Some women may wish to try cranberry products. However, evidence of benefit is uncertain and there is no evidence of benefit for older women. They are not available on prescription but can be purchased over the counter.
- Advise patients taking cranberry products or D-mannose about the sugar content of these products, which should be considered as part of the person's daily sugar intake.
- Be aware that evidence is inconclusive about whether probiotics (lactuobacillus) reduce the risk of UTI in people with recurrent UTI. Therefore these products are not recommended.
- For women who are sexually active:
    - Advise post-coital voiding
    - Avoid use of contraceptive diaphragm and spermicide
- Avoid using feminine hygiene products (e.g. cosmetic bath products and feminine douches).
- Avoid using flannels. A clean non scented disposable wipe is preferable.
- Provide TARGET – Treat Your Infection Urinary Tract Infection Patient Information Leaflet.

Vaginal oestrogens for postmenopausal women:

Current NICE guidelines state that vaginal oestrogens [off-label use] such as estriol cream can be used for **postmenopausal women with recurrent UTIs** at the lowest effective dose if behavioural and personal hygiene measures alone are not effective or appropriate.

Do NOT offer oral oestrogens (hormone replacement therapy) specifically to reduce the risk of recurrent UTI in postmenopausal women.

Discuss the following with the woman to ensure shared decision-making:

- The severity and frequency of previous symptoms
- The risk of developing complications from recurrent UTIs
- The possible benefits of treatment, including for other related symptoms, such as vaginal dryness
- The possible adverse effects such as breast tenderness and vaginal bleeding (which should be reported because it may require investigation)
- The uncertainty of endometrial safety with long-term or repeated use
- Preferences of the woman for treatment with vaginal oestrogen.
- Consideration should be given to continuing for three months and then review effectiveness. Treatment should be reviewed at least annually or earlier, as agreed with the woman.
- As with any treatment discussed, the risks and benefits for the individual patient should be outlined.

Should vaginal oestrogens be considered, local experience and published evidence suggests applying once topically each night for two weeks followed by twice-weekly applications for 4 weeks initially.

Should be used in the smallest effective amount and for the shortest duration possible to minimise systemic effects.

Methenamine Hippurate:

Methenamine hippurate is a urinary antiseptic and non-antibiotic alternative prophylactic intervention for recurrent UTIs. It requires an acidic urine for its antimicrobial activity and has a role in the prophylaxis and treatment of chronic or recurrent uncomplicated lower urinary-tract infections.

Non-antibiotic prophylaxis treatment with methenamine hippurate may be appropriate for women with a history of recurrent episodes of UTIs. It is indicated for the prophylactic therapy for recurrent UTIs and the prevention of recurrent cystitis. Methenamine hippurate is suitable for prescribing in primary care following the recommendation of a urologist, as may have a benefit for some patients.

The dose recommended is 1g twice daily for adult patients.

Discuss the following with women to ensure shared decision-making:

- The severity and frequency of previous symptoms
- The risk of developing complications from recurrent UTIs
- The possible benefits of non-antibiotic treatment

- The possible adverse effects which are uncommon, rashes, itching, stomach irritation, bladder irritation, nausea, and vomiting
- Consideration should be given to continuing for three months and then review.
- As with any treatment discussed, the risks and benefits for the individual patient should be outlined.

Methenamine hippurate is available to be purchased over the counter from community pharmacies.

Antibiotic prescribing strategies – for women who are not pregnant

Antibiotic prophylaxis should be offered when behavioural modifications and non-antimicrobial measures have been unsuccessful.

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 and behavioural measures.

Chose antibiotics according to recent culture and susceptibility results where possible. Consideration must be given to causative organism and resistance reporting. Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) need to be reserved for second-choice treatment where narrow spectrum antibiotics are ineffective or unsuitable.

Self-start antibiotic prescription:

- If none or only one symptom of: dysuria, new nocturia, cloudy urine; the patient can wait, infection should first be confirmed by MSU prior to commencing antibiotics.
- Provide the patient with:
    - A TARGET – Treat Your Infection urinary tract infection Patient Information Leaflet.
    - A urine sample collection bottle for pre-antibiotic MSU
    - The 'self-start' course of antibiotics - prescribing an agent according to previous known sensitivities and choosing the narrowest spectrum agent available.
    - Safety advice to seek medical attention if they develop any of the following: shivering, chills and muscle pain, feel confused or very drowsy, have not passed urine all day, are vomiting, see blood in their urine, temperature above 38°C or less than 36°C, kidney pain in your back just above your ribs, loin pain, symptoms get worse or are not starting to improve within 48 hours of taking antibiotic.
- This option limits antibiotic exposure and risk of resistance emerging and may be the more suitable option for patients with <1 UTI per month.
- Patient will need to return for a review within 3 months.

Single-dose antibiotic when exposed to an identifiable trigger (for example, sexual intercourse)

- For women with rUTIs who are not pregnant, ensure that any current UTI has been adequately treated then consider single-dose antibiotic prophylaxis for use when exposed to a known, identifiable trigger e.g. post-coital.
- Confirm compliance with self-care measures and where known trigger is sexual

intercourse, confirm that the patient passes urine post-coitally.

- Single dose antibiotic is as effective as continuous antibiotics in non-pregnant women with an identifiable trigger and should be considered as the first option.
- Using a single dose antibiotic limits antibiotic exposure therefore reducing the risk of resistance emerging.
- This also reduces the risk of adverse events to antibiotic treatment including gastrointestinal symptoms and vaginitis.
- Patient will need to return for a review within 3 months.

Continuous antibiotic prophylaxis

- For women with rUTI who are not pregnant and had no improvement after single-dose antibiotic prophylaxis or have no identifiable triggers, ensure that any current UTI has been adequately treated then consider a trial of daily antibiotic prophylaxis.
- **Longer term antibiotic prophylaxis is strongly associated with the development of antimicrobial resistance, which means that antibiotic may be less effective in the future.**
- A **trial** of low-dose continuous antibiotic treatment may be beneficial if rUTIs are occurring ≥1 per month and are not triggered by sexual intercourse.
- Patients should be counselled that low-dose continuous antibiotic treatment will be commenced for 3 months and a review date should be included within the patient's record to ensure that the prophylaxis is reviewed at the 3-month time interval. If antibiotic prophylaxis is added to a repeat prescription template, a review time frame and expiry date should be added to ensure that the patient is viewed timely, to prevent unnecessary prolonged use of antibiotic therapy.
- A review at 3-months should include discussing a trial of stopping antibiotic prophylaxis at that stage. Continuing antibiotic prophylaxis long-term is not evidence-based.

Resistance Patterns

Percentage resistance of *E. coli* (the main causative organism of lower UTIs) in laboratory-processed urine specimens to the following antibiotics is as follows.

Table 1 – Percentage resistance of E. coli to nitrofurantoin in laboratory-processed urine specimens for 2021- 2022

Percentage Resistant to nitrofurantoin	*2021- Quarter 1*	*2021 – Quarter 2*	*2021 – Quarter 3*	*2021 – Quarter 4*
East of England	**2.3%**	**2.0%**	**1.8%**	**2.5%**
National	2.4%	2.4%	2.3%	2.3%

Table 2 – Percentage resistance of E. coli to trimethoprim in laboratory-processed urine specimens for 2021

Percentage Resistant to trimethoprim	2021- Quarter 1	2021 – Quarter 2	2021 – Quarter 3	2021 – Quarter 4
East of England	**27.7%**	**25.7%**	**23.8%**	**25.0%**
National	26.3%	25.7%	24.8%	25.1%

Table 3 – Percentage resistance of E. coli to pivmecillinam in laboratory-processed urine specimens for 2021

Percentage Resistant to pivmecillinam	2021- Quarter 1	2021 – Quarter 2	2021 – Quarter 3	2021 – Quarter 4
East of England	**12.9%**	**10.2%**	**8.4%**	**8.8%**
National	9.7%	9.3%	8.9%	8.3%

Table 4 – Percentage resistance of E. coli to cefalexin in laboratory-processed urine specimens for 2021

Percentage Resistant to cefalexin	2021- Quarter 1	2021 – Quarter 2	2021 – Quarter 3	2021 – Quarter 4
East of England	**10.2%**	**9.5%**	**9.3%**	**8.5%**
National	10.5%	9.8%	9.5%	9.3%

(UKHSA - Antimicrobial resistance quarterly surveillance: 2021-2022).

Choice of antibiotic agents:

Choice of antibiotic should be based on **confirmed culture and sensitivity results** (wherever possible), and consider the patient's co-morbidities, renal function, and any contraindications or **allergies** that the individual patient may have.

Nitrofurantoin is the first line choice for antibiotic prophylaxis.

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. If resistance to trimethoprim and nitrofurantoin is confirmed, other agents may be considered after discussion with Urology, Urogynaecology 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. In addition MHRA have issued an alert restricting the use of fluoroquinolone antibiotics e.g. ciprofloxacin, advising that treatment with these antibiotics should be discontinued at the first signs of a serious adverse reaction, including tendon pain or inflammation.

Table 5 – Antibiotic Therapy Prophylactic Dose, Cautions and Monitoring

Antibiotic	Dose	Cautions and Monitoring
Nitrofurantoin **First line**	100mg immediate release, one dose when exposed to a trigger i.e., post-coital (off label) *OR* 50 to 100mg at night	Avoid if renal function eGFR <45ml/min. Consider checking renal function prior to commencing continuous prophylaxis, especially in the elderly. Avoid if G6PD deficiency. Avoid at term in pregnancy. 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 (such as chronic cough) 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.
Trimethoprim	200mg, one dose when exposed to a trigger i.e., post-coital (off label) *OR* 100mg at night	Hyperkalaemia: caution when prescribing with drugs such as spironolactone, ACE inhibitor or angiotensin inhibitors. Concurrent or sequential use of methotrexate with trimethoprim (a folate antagonist) is strongly discouraged. There is a very high risk of haematological toxicity, cases of fatal bone marrow suppression have been reported. Renal Impairment: Avoid if eGFR <15ml/min. Discuss with renal physician if eGFR <30ml/min. May increase serum potassium. Teratogenic risk in first trimester, manufacturers advise to avoid in pregnancy 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.
Amoxicillin	500mg, one dose when exposed to a trigger *OR* 250mg at night	Avoid if history of anaphylaxis, urticaria or rash immediately after previous penicillin administration.
Cefalexin	500mg, one dose when exposed to a trigger *OR* 125mg at night	Contra-indicated in patients with cephalosporin hypersensitivity. Patients with a history of immediate hypersensitivity to penicillin and other beta-lactams should not receive a cephalosporin.

Choose antibiotics according to recent culture and susceptibility results where possible. Consideration must be given to causative organism and resistance reporting. Broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) need to be reserved for second-choice treatment when narrow spectrum antibiotics are ineffective.

Managing a patient who has a prolonged course of prophylactic antibiotics

Identifying patients for review:

Review antibiotic prophylaxis for recurrent UTI **at least every 3 months** and include:

- Assessing prophylaxis success
- Reminders about behavioural and personal hygiene measures, and self-care.
- Discussing whether to change antibiotic prophylaxis or stop treatment.

Changing antibiotic prophylaxis at the 3-month review:

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, considering changing to an effective agent and/or whether a referral is required.

Stopping continuous prophylaxis at the 3-month review:

- A significant number of patients can stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of antimicrobial resistance emerging and side effects.
- Test of cure is not required in asymptomatic patients at the end of a course of prophylaxis.
- One option is to provide a 'self-start' prescription of antibiotics and a urine sample collection bottle when stopping continuous prophylaxis which may give sufficient reassurance to patients for a trial off antibiotics.

Continuing treatment for a further 3 months and stopping continuous prophylaxis at the 6-month review:

- A significant number of patients can stop continuous prophylaxis without a return of symptoms and therefore avoid the risks of antimicrobial resistance emerging and side effects.
- Half (50%) of patients who stop continuous antibiotic prophylaxis at 6-months, will not return to suffering rUTIs.
- Test of cure is not required in asymptomatic patients at the end of a course of prophylaxis.
- One option is to provide a delayed or back-up prescription of 'standby' antibiotics and a urine sample bottle 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.**

Managing breakthrough UTIs in patients on antibiotic prophylaxis

Managing a 'breakthrough' (1 only) UTI 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.
- If the culture shows resistance to the prophylactic agent, this should be switched to another agent based on sensitivities.
- Review treatment within three-months of changing agent.

Managing 'breakthroughs' (> 1) UTI in patients on antibiotic prophylaxis:

- If multiple breakthroughs UTIs occur (>1 UTIs in 6 months), treatment has proved ineffective and should be stopped.
- If antibiotic prophylaxis is stopped, ensure that patients have rapid access to treatment if they have an acute UTI via a breakthrough or back-up (standby) antibiotic prescription.
- **Refer to Urology or Urogynaecology**

UTIs associated with urinary catheters including recurrent UTIs:

- Cloudy or offensive urine alone does not merit treatment or investigation for UTIs in patients with urinary catheters.
- A catheter-associated UTI is a symptomatic infection of the bladder or kidneys in a person with a urinary catheter, therefore, look for associated localising or systemic features of infection including flank pain and exclude other potential sources of infection in catheterised patients who present with fever.
- Do not use dipsticks to diagnose UTIs in patients with urinary catheters as symptomatic UTIs cannot be differentiated from asymptomatic bacteriuria based on dipstick urinalysis.
- Antibiotic treatment is not routinely needed for asymptomatic bacteriuria in people with a catheter.
- Where an acute infection is suspected, consider removing or, if this cannot be done, changing the catheter as soon as possible in people with a catheter-associated UTI if it has been in place for more than 7 days.
- Do not allow catheter removal or change to delay antibiotic treatment.
- Obtain a urine sample from the sampling port of the catheter using an aseptic technique (in line with the NICE guideline on healthcare-associated infection) and send for culture and susceptibility testing.
    - If the catheter has been changed, obtain the sample from the new catheter.
    - If the catheter has been removed obtain a midstream specimen of urine.
- Send the urine sample for culture and susceptibility, noting a catheter associated

infection and any antibiotic prescribed.

- Offer an antibiotic for an acute catheter associated UTI, considering:
  - Severity of symptoms
  - Risk of developing complications, which is higher in people with known or suspected structural or functional abnormality of the genitourinary tract, or immunosuppression.
- Where urine culture and susceptibility results are available:
  - Review the choice of antibiotic and
  - Change the antibiotic according to susceptibility results if the bacteria are resistant, using narrow-spectrum agents wherever possible.
- **Patients with recurrent catheter associated UTIs should be referred for specialist review.**
- **Do not routinely offer antibiotic prophylaxis to people with a short-term or long-term catheter.** Antibiotic prophylaxis does not significantly decrease symptomatic infections and increases the risk of antimicrobial resistance. It is therefore not usually recommended to reduce the frequency of UTIs in patients with urinary catheters. Seek explicit guidance from a microbiologist before commencing antibiotic prophylaxis in patients with a urinary catheter.

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Document ratification details

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Self-Management and stand-by pack advice sheet

You have been provided with a urine sample pot and a stand-by pack of antibiotics.

What to do if you experience urinary tract infection symptoms:

1. Collect a mid-stream sample of your urine in the sample pot provided.
2. Place the pot of urine in a sealed plastic bag and hand in to the GP reception straight away. If there is a delay, store in the fridge and hand in on the next working day.
3. Take the first dose of the antibiotic supplied.
4. Follow the instructions for taking the full course of antibiotics.
5. Contact your GP practice to discuss the results of the urine culture (usually available 24-72 hours after handed into the practice), and to obtain a new sample pot and stand-by pack of antibiotics. The GP will check whether the same antibiotics are still appropriate for your next stand-by pack (if the antibiotic will still work against the bacteria in the urine).

What to do if the symptoms of urinary tract infection do not improve:

Your symptoms should start to improve once you start taking the antibiotics. If you have not improved within 48 hours, or the symptoms have got worse, or you feel feverish, develop new back pain or feel generally unwell, contact the GP practice, or call 111 if the GP practice is shut.

Urinary Infections Diary

Episode	Start date of symptoms	Date urine sample provided	Start date of antibiotics (if given)	Date symptoms settled
1				
2				
3				
4				
5				
6				