

Urinary tract infections (UTIs) – an overview of lower UTI management in adults

Lower urinary tract infection (UTI) is one of the most common community-acquired infections, with more than half of all females experiencing at least one episode during their lifetime. In the absence of complicating factors, initial empiric antibiotic treatment is usually sufficient in otherwise healthy, non-pregnant, pre-menopausal females with an acute or intermittent UTI, without the need for laboratory sensitivity testing.

KEY PRACTICE POINTS:

- In most cases, the diagnosis of an uncomplicated lower UTI is guided by clinical symptoms and signs, along with urine dipstick analysis if required
- Empiric antibiotics should be prescribed for females with an uncomplicated UTI
- Obtaining a midstream urine sample for microscopy, culture and sensitivity analysis is generally only recommended in people with UTIs who are at higher risk of complications, e.g. males, pregnant females and people with diabetes, recurrent infections, renal failure or a urinary catheter
- Self-care strategies should be discussed with all patients who have a UTI to help reduce the risk of future infections, e.g. sufficient fluid intake, improving hygiene and toileting practices and voiding after sexual intercourse
- Non-antibiotic prophylactic strategies can be considered in patients who experience recurrent UTIs but are not routinely recommended in current guidelines due to low-quality evidence of benefit
- Antibiotic prophylaxis is highly effective at preventing recurrent UTIs, however, this should usually only be considered as a "last resort" if other strategies are unsuccessful – primarily due to the risk of antibiotic resistance
- Patients with asymptomatic UTIs should generally not be treated with antibiotics; the exception is pregnant females, who should be screened at the first antenatal appointment (via urine culture) and subsequently treated if an infection is identified, regardless of whether symptoms are present

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Distinguishing "uncomplicated" and "complicated" UTIs

Urinary tract infections (UTIs) are one of the most common reasons for antibiotic prescribing in New Zealand.1 The lower urinary tract is most often affected due to bacteria, usually from the gastrointestinal tract, entering the urethra and proliferating in the bladder.1 When this occurs as a one-off or intermittent infection and remains confined to the urethra and bladder in an otherwise healthy, non-pregnant, premenopausal female or male with normal anatomy, it is broadly referred to as an uncomplicated lower UTI (or cystitis).²⁻⁴ In contrast, "complicated UTIs" include infections in people with risk factors that increase the probability of bacterial colonisation, or that decrease the potential efficacy of antibiotic treatment, e.g. indwelling catheters, pregnancy, renal calculi, immunosuppressive conditions or anatomical abnormalities.^{2,3} Despite this terminology, the criteria for distinguishing UTIs as being "uncomplicated" or "complicated" varies across the medical literature, and the significance of risk factors – and the potential need for a referral - differs according to the specific person and their clinical history. Ultimately, the focus of UTI management in any patient is to promptly resolve the infection before it ascends via the ureters to involve one or both of the kidneys (pyelonephritis), which is associated with an increased risk of sepsis and multiorgan involvement.^{2,3}

Females have an increased risk of UTI

Females have an increased UTI risk compared with males, predominantly due to the shorter length of their urethra and the shorter distance between their urethra and anus.⁵ It is estimated that one-third of females have a UTI before age 24 years, and more than 50% have one during their lifetime.⁶ In females, the risk of experiencing UTIs can be greater due to a number of factors, including:^{5,7}

- Personal hygiene practices, e.g. wiping back to front
- Sexual activity, e.g. high frequency, spermicide or diaphragm use
- Incomplete voiding, urinary retention or other urinary issues
- Vaginal wall prolapse, e.g. cystocoele
- Vulvovaginal atrophy
- Other anatomical abnormalities
- A personal or family history of UTIs (particularly in first-degree female family members, i.e. mothers, sisters, daughters)

The cause of uncomplicated lower UTIs is highly predictable

Escherichia coli is the cause in 70 – 95% of all uncomplicated UTIs;³ other possible causative species include *Staphylococcus* saprophyticus, *Proteus spp.*, *Klebsiella spp.* and *Enterococcus* spp.⁴ Complicated UTIs are also more commonly caused by *E. coli*, however, the range of possible causative species is much

broader than for uncomplicated infections.³ Although rare in the community, complicated UTIs can occur as the result of fungal infection, which is generally associated with *Candida* species, e.g. in people with an indwelling catheter.^{1,4}

The symptoms and signs of an uncomplicated UTI

Uncomplicated lower UTIs can be diagnosed with a high level of confidence in people with a focused history of lower urinary tract symptoms in the absence of complicating factors or red flags (Figure 1). Although subtle or atypical presentations are possible, the combination of two or more "classic" features of a UTI – without vaginal irritation or discharge in females – generally indicates that a UTI is likely.² The classic features of UTI are:²

- New onset dysuria
- Increased urinary frequency
- Increased urinary urgency
- Suprapubic abdominal pain

For example, nine out of ten young females with a history of new onset dysuria and polyuria, without vaginal irritation or discharge, will have a UTI.³ Less commonly, people with a UTI may present with other features such as odorous, discoloured or cloudy urine, however, this can also occur due to non-infectious causes, e.g. dehydration, diet or renal calculi.² In addition, a UTI cannot be ruled out completely if only a single symptom or sign is present, and further investigation may be required depending on individual clinical circumstances and history (see: "Urinalysis: indications and conclusions").

Physical examination is not required but can help exclude differential diagnoses

A physical examination is not required to clinically diagnose an uncomplicated lower UTI but can be helpful to ensure systemic features are not present, e.g. measuring temperature and other baseline observations, as well as an assessment of the abdomen and flank, primarily checking for renal tenderness on palpation that may indicate the infection has spread to the kidneys (Figure 1). Pelvic examination is generally unnecessary in females if an uncomplicated UTI is suspected; this should only be performed if the patient's suprapubic pain is significant, or if an alternative diagnosis is suspected, such as vaginitis, urethritis associated with sexually transmitted infections (STI) or pelvic inflammatory disease or anatomical abnormalities.^{2,8}

Other demographic-specific considerations



Males. UTIs are rare in males aged less than 50 years, but the risk increases with age.⁹ Although the symptoms and signs are generally similar to those observed in females, UTIs in males are commonly associated with genitourinary tract

abnormalities such as prostatic enlargement.⁹ As a result, it is important to ask about any prostate symptoms, features indicative of epididymo-orchitis or a STI, alongside an abdominal examination (and bedside ultrasound, if available) to check for urinary retention.⁹ If there is a family history of prostate cancer or relevant symptoms, e.g. a weak or altered urine flow, a prostate examination should be performed.⁹ A referral is not usually required for males experiencing their first uncomplicated UTI, but if they have a subsequent infection then a renal/bladder ultrasound and a non-acute urology assessment should be arranged.⁹



People at risk of a sexually transmitted infection.

A STI check may be considered in people with an increased STI risk to exclude conditions such as chlamydia or gonorrhoea as a possible cause of symptoms, particularly if vaginal or urethral discharge is reported.³ Risk factors include having a partner with a STI, having two or more concurrent sexual partners or a new sexual partner within three months.⁵



Older people. Diagnosing a UTI in older people can be challenging due to the presence of co-morbidities or the use of multiple medicines, which can obscure or resemble UTI symptoms and signs. While classic UTI symptoms can often be present, atypical features such as acute confusion (delirium), fatigue and anorexia may also occur. Urinary incontinence and other non-specific urinary symptoms are relatively common in older people, but alone this is not predictive of a UTI.

For further information on the diagnosis and management treatment of UTIs in older people, see: bpac.org.nz/BT/2015/July/guide.aspx

Red flags for a complicated UTI

Most UTIs can be managed in primary care. However, the presence of red flags may indicate a more serious situation requiring secondary care advice or referral (Figure 1).^{3, 8} In particular, pregnant females with suspected pyelonephritis (e.g. systemic symptoms, fever > 38°C, significant flank, back or suprapubic abdominal pain) should be immediately referred for an acute obstetric appointment, and their lead maternity carer contacted due to the increased risk of maternal and fetal complications.¹¹ In addition, people with suspected pyelonephritis and signs of sepsis (e.g. tachycardia, lower than normal blood pressure, increased respiratory rate) usually require referral to secondary care for intravenous antibiotics and fluids.

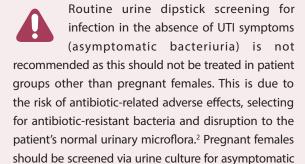
Urinalysis: indications and interpretation

Dipstick testing can strengthen diagnostic certainty in symptomatic patients

In most females aged less than 65 years without complicating factors, a lower UTI can be reliably diagnosed according to the clinical presentation alone, without additional urinalysis. However, if there are atypical features, complicating factors or diagnostic uncertainty, then urine dipstick testing can be useful to indicate if an infection is the likely cause of their symptoms.^{2,8} The key aspects to consider are:^{2,12}

- Nitrite status sterile urine generally should not contain detectable traces of nitrite. Most UTIs are caused by bacteria belonging to the Enterobacteriaceae family, which can metabolise nitrates to nitrites.
- Leukocyte esterase status leukocyte esterase is an enzyme produced by white blood cells. If the test is positive, it may indicate that white blood cells have been generated by the body in response to infection, and that they are present in the urine (pyuria).

A positive result for either nitrites or leukocyte esterase, in the presence of lower UTI symptoms, is sufficient to confirm a lower UTI diagnosis and proceed with treatment.8 However, negative results from urine dipstick testing may not reliably exclude the possibility of a UTI, e.g. some UTIs caused by bacterial species that are unable to produce nitrites, and early pyelonephritis may not produce positive results.8 Haematuria on dipstick can also be an informative finding as this is commonly associated with a UTI but not urethritis.2, 3 However, if microscopic haematuria is persistently present in patients with recurrent or ongoing lower urinary tract symptoms, or if gross haematuria is observed (i.e. visible blood in the urine sample), then other diagnoses should be strongly considered, e.g. renal calculi or urinary tract malignancy.2,3



For further information on urine dipstick testing, see: bpac. org.nz/bt/2013/june/urine-tests.aspx

bacteriuria, at their first antenatal appointment.

For further information on UTIs and asymptomatic bacteriuria in pregnancy, see: bpac.org.nz/2019/pregnancy-care.aspx

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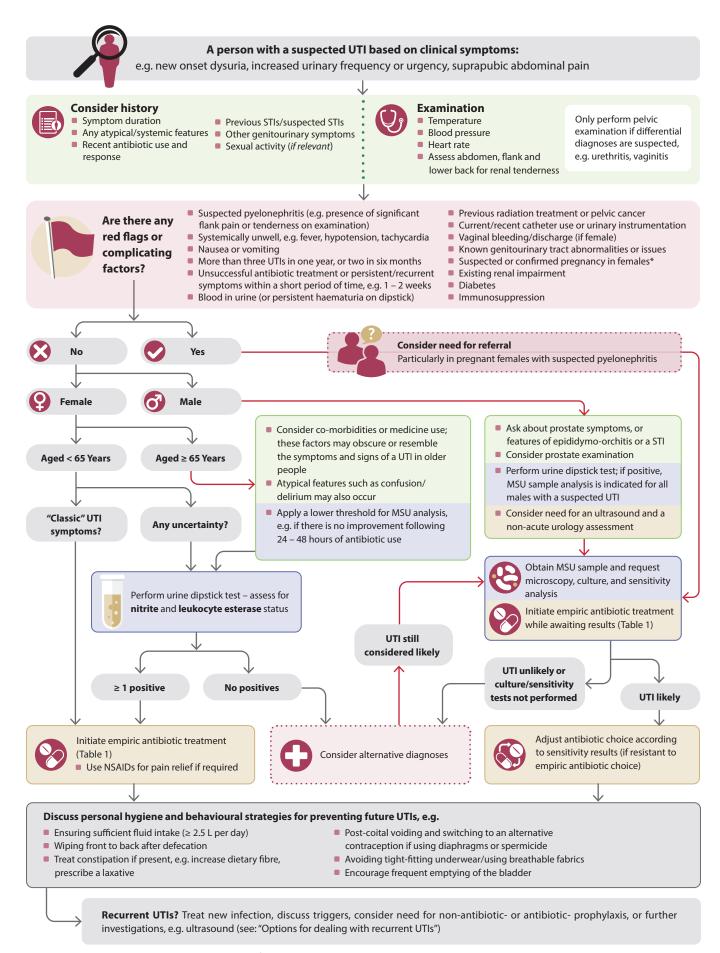


Figure 1. The diagnosis and management of symptomatic lower UTIs in adults.^{2,8}

* A midstream urine (MSU) sample should be obtained, and sent for laboratory analysis in all pregnant females, ideally as part of the first antenatal check; asymptomatic bacteriuria should be treated in this group due to the risk of complications

MSU, midstream urine; STI, sexually transmitted infection; UTI, urinary tract infection

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Requesting analysis of a MSU sample is not routinely recommended

For females with uncomplicated cystitis, the causative bacteria and antibiotic sensitivity profile are often predictable. As such, requesting microscopy, culture and sensitivity testing is not necessary as it is unlikely to influence treatment decisions (see: "Empiric antibiotic selection").² Obtaining a urine sample – ideally mid-stream urine (MSU) – and requesting laboratory analysis is only indicated in certain circumstances if there is clinical suspicion of a UTI based on symptoms (Figure 1), including:^{2,8,13}

- When dipstick testing is negative, but a UTI is still strongly suspected after considering differential diagnoses
- People with recurrent UTIs, atypical symptoms or persistent symptoms despite antibiotic treatment
- People with suspected pyelonephritis
- Females with complicating factors, e.g. pregnancy, catheterisation, urinary tract abnormalities, immunosuppression, renal impairment, diabetes
- Other high-risk groups, including males, children aged 14 years and under and people living in residential care facilities

The treatment of uncomplicated UTI

Antibiotic resistance is a global issue, primarily driven by inappropriate and excessive use.¹⁴ In response, some international guidelines now recommend that NSAIDs are considered as an alternative first-line treatment for UTIs associated with mild symptoms rather than immediate antibiotic use in females aged less than 65 years.^{2,15}

However, while uncomplicated UTIs can be self-limiting in some cases, the natural course can vary between people, and symptoms may progress instead. Therefore, it currently remains standard practice to prescribe antibiotics to most patients with uncomplicated UTIs in New Zealand primary care. A systematic review including 1,309 females with uncomplicated UTI found that the number needed to treat (NNT) with antibiotics rather than NSAIDs to achieve symptom resolution in one additional female by day 3 or 4 of treatment ranged from three to six, i.e. more females have a shorter UTI duration with antibiotic treatment versus NSAID use. In addition, antibiotic use was associated with a lower risk of pyelonephritis and other complications.

Empiric antibiotic selection

The initial antibiotic choice for patients with uncomplicated UTI should be empiric (Table 1).^{2, 18} If symptoms do not resolve, or a patient experiences a recurrent infection within a short period of time, e.g. one to two weeks, consider sending a MSU sample for microscopy, culture and sensitivity analysis

to guide the selection of an alternative choice.² If laboratory testing is performed at any time, and resistance to the empiric choice is demonstrated, an alternative antibiotic can be selected. However, MSU samples will not be cultured in some laboratories if the initial microscopy indicates that infection is unlikely, e.g. if white blood cells are absent.



Citrate sodium anhydrous + citric acid anhydrous + sodium bicarbonate + tartaric acid (Ural) is no longer routinely

recommended during the acute treatment of UTIs as it raises the urinary pH, which in turn reduces the effectiveness of some antibiotics, e.g. nitrofurantoin.⁸ Instead, NSAIDs can be considered as an add-on to antibiotic treatment for pain relief if required.⁸

Table 1. Empiric antibiotic regimens for uncomplicated UTI in adults.¹⁸

N.B. Treat for **seven days** in pregnant females and in all males, regardless of antibiotic choice.

	Antibiotic	Dose
First-line	Nitrofurantoin*†	Modified release (Macrobid): 100 mg, twice daily, for five days
		Immediate release (Nifuran): 50 mg, four times daily, for five days
Alternatives	Cefalexin	500 mg, twice daily, for three days
	Trimethoprim [‡]	300 mg, once daily, for three days

- * Contraindicated in patients with a creatine clearance < 60 mL/min due to the risk of peripheral neuropathy. Prescribe nitrofurantoin by brand name to reduce errors as there are two different formulations.¹⁹ Nitrofurantoin is not an appropriate first-line choice in patients with suspected pyelonephritis as it is associated with poor tissue penetration.¹⁸
- † Avoid after 36 weeks gestation in pregnant females
- ‡ Avoid in the first trimester of pregnancy

Discuss self-care strategies with all patients

Before the patient leaves the appointment, it is important to discuss self-care in relation to behavioural and hygiene practices. In some cases, these changes may reduce the risk of future infections, and will likely have wider health benefits.^{2, 3} Strategies include:

- Ensuring fluid intake is sufficient (at least 2.5 L per day)
- Avoid wearing tight-fitting underwear and using breathable fabrics such as cotton rather than synthetics, e.g. nylon or polyester

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- Urinating when required (i.e. not "holding on" unnecessarily)
- Post-coital voiding; this behaviour has not been proven to reduce the risk of recurrence in controlled studies, but is anecdotally supported
- Switching to an alternative contraceptive method if diaphragms or spermicide are used (these are associated with an increased risk of UTI)
- Wiping front to back after defaecation or urination to avoid perineal or urethral contamination with faecal bacteria
- Treating constipation if present, by increasing dietary fibre intake or using a pharmacological intervention, e.g. docusate sodium + sennoside B (Laxsol) or lactulose; constipation may exert pressure on the bladder, or even obstruct it, leading to incomplete voiding which increases the risk of a UTI

Options for dealing with recurrent UTIs

UTIs are considered recurrent when there are at least three symptomatic episodes within 12 months, or two or more within six months.³ In most cases, recurrent UTIs are thought to be caused by reinfection of the urinary tract rather than relapse linked to the previously treated isolate – assuming a complete antibiotic course was taken.² If the recurrence occurs within a short period of time, e.g. less than two weeks after finishing the antibiotic course, it is more likely to be caused by the same original strain. In these cases, consider obtaining a MSU sample for microscopy, culture and sensitivity testing to refine treatment selection.³

Non-antibiotic prophylactic treatments can be discussed

In all patients with recurrent UTIs, first reiterate the importance of self-care strategies, and investigate known triggers specific to the patient's history, e.g. use of spermicide-containing contraceptives. Some other non-antibiotic prophylactic strategies that have a low risk of harm can be discussed, but their use is not routinely recommended due to a lack of high-quality evidence for efficacy.²

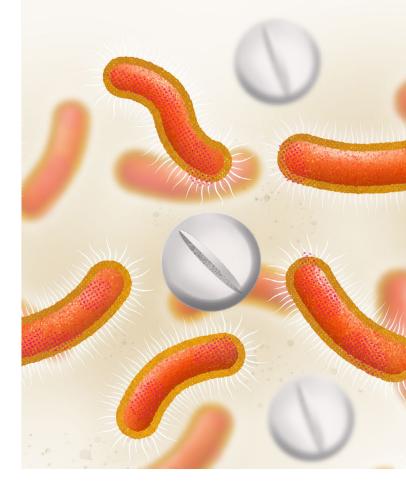
Prophylactic strategies for UTIs include:2,3

Topical vaginal oestrogen (estriol; fully funded). The use of topical vaginal oestrogen has been found to consistently reduce the risk of UTI recurrence in postmenopausal females participating in small randomised controlled trials. However, given the heterogeneity in the application method used between trials, a pooled estimate of the effect size cannot be determined. Oral oestrogen supplementation has not been found to confer a similar benefit in clinical trials.

Why is trimethoprim no longer a first-line empiric antibiotic option?

Previously, trimethoprim was considered a first-line empiric option for managing uncomplicated UTIs, and it has been commonly prescribed by clinicians in primary care. Since 2012, pharmacists who have completed a UTI training course have been able to supply trimethoprim without a prescription to females with a suspected UTI aged 16 – 65 years who are not pregnant and do not have any other complicating factors.²⁰

However, there is now evidence that trimethoprim should not be a first-choice antibiotic for managing uncomplicated lower UTIs due to a growing pattern of resistance across New Zealand.²¹ A multi-region audit of urine samples obtained between June 2016 and August 2018 demonstrated that approximately one-quarter of all *E. coli* isolates from females aged 15 – 55 years lacked trimethoprim sensitivity.²¹ In comparison, < 1% of *E. coli* tested were resistant to nitrofurantoin, and < 5% were resistant to cefalexin.²¹ Although trimethoprim is often preferred by people due to its once daily dosing, these findings suggest that nitrofurantoin and cefalexin are generally better empiric antibiotic treatment choices – unless there is recent community resistance data available to pragmatically guide such decisions.



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Consumption of cranberry products, e.g. juices or concentrated capsules (not funded). Meta-analyses have demonstrated that patients with a history of recurrent UTIs taking cranberry products have a 47% relative risk reduction for future UTIs compared with control groups.²² However, there is high variability in the "active ingredient" dose between products, inconsistent methodology and drop-out rates in clinical trials, and no standardised regimen exists. Overconsumption of cranberry products may cause gastrointestinal irritation, as well as exceed the recommended daily sugar intake.

Expert practice tip: when recommending a cranberry product, higher percentage formulations (e.g. ≥ 18%) are more likely to be effective than lower percentage formulations (e.g. 2 – 4%). Using a higher concentration product also means that a smaller volume or dose can be consumed (e.g. 200 mL of juice or two capsules, daily). Some people may find that taking cranberry products at night is more effective.

Products/supplements containing D-mannose (not funded). D-mannose has been proposed to limit the adherence of bacteria to cells in the urinary tract. There is weak evidence from unblinded randomised controlled trials that it reduces the risk of UTI recurrence. While these results are encouraging, further investigation is required to determine the optimal dose, frequency and duration of use.

Lactobacillus containing probiotics (not funded). There is a plausible scientific basis for the use of probiotics in preventing UTIs, e.g. the competitive exclusion of UTI-causing bacteria. However, efficacy has not been demonstrated in clinical trials that use oral formulations. The application of Lactobacillus using an intravaginal suppository decreased the rate of recurrent UTIs by 12% compared with placebo in a small clinical trial (N = 50).²³ However, intravaginal probiotic suppositories for the treatment of UTIs are not readily available in New Zealand. If an oral formulation is to be trialled, ensure that one containing Lactobacillus bacteria is used; although there is insufficient clinical trial evidence to guide the selection of a particular Lactobacillus strain or dose, L. rhamnosus is among the most widely used in clinical trials at doses of ≥ 108 colony forming units (CFU)/capsule.²⁴

Low-dose antibiotic prophylaxis should generally be a last resort

Females with recurrent UTIs are over six times less likely to experience another UTI if they take prophylactic antibiotics.³ However, in keeping with the principles of antibiotic stewardship, this approach is not appropriate for all patients; it should generally only be considered in non-pregnant females* if behavioural and/or personal hygiene measures

are ineffective in preventing recurrent UTIs.¹⁹ The main options include a once daily night time dose of nitrofurantoin (immediate release formulation, 50 – 100 mg[†]), trimethoprim (150 mg) or cefalexin (125 – 250 mg).^{3, 19} Single-dose antibiotic prophylaxis (unapproved indication) may also be considered for use after exposure to a known UTI trigger, e.g. taking a low-dose antibiotic (as above) two hours post-sexual intercourse.³

There is no convincing evidence on the optimal duration of long-term antibiotic prophylaxis; if it is prescribed, a review should be conducted within three to six months to consider the benefits and risks of continued use.^{2, 3} If a decision is made to stop antibiotic prophylaxis, a "back pocket" antibiotic prescription can be provided to manage any acute UTIs that subsequently develop.²

Methenamine hippurate (Hiprex) 1 g every 12 hours can be considered as an alternative form of antimicrobial prophylaxis in patients with a history of recurrent UTIs to avoid long-term antibiotic use.19 While methenamine hippurate has bacteriostatic properties, it is not considered a traditional antibiotic as its effect is non-specific; methenamine is progressively converted into formaldehyde within an acidic environment (below a pH 6), which then functions to indiscriminately denature bacterial proteins and nucleic acids.²⁵ In most cases, urine is already slightly acidic and hippurate acts to lower the pH further, thereby promoting formaldehyde production.²⁵ The use of methenamine hippurate has been shown to reduce the risk of recurrent UTIs in several small trials and it is generally well-tolerated in both females and males.^{2,25} however, there is not yet sufficient high-quality data to support routine prophylaxis.

- * Antibiotic prophylaxis may also be trialled under the supervision of a renal specialist (e.g. nephrologist, urologist) in males and pregnant females who experience recurrent UTIs¹⁹
- † Caution is required when considering nitrofurantoin for long-term antibiotic prophylaxis due to the risk of pulmonary toxicity; discontinue if any deterioration in pulmonary function is identified¹⁹

Further investigation for patients with recurrent UTIs

There is no compelling evidence for early investigation with imaging or cystoscopy in females aged less than 65 years with lower UTI symptoms unless other risk factors are present, e.g. suspected nephrolithiasis, or if differential diagnoses are strongly suspected.² Referral for non-acute urology assessment may be considered in:^{2,3,10}

- Females if they continue to present with recurrent UTIs despite sensitivity testing and prophylactic antibiotics, particularly if they have had previous radiation treatment or pelvic cancer
- Females with recurrent UTI symptoms, in addition to microscopic haematuria and/or pyuria, despite negative urine cultures; multiple courses of antibiotics should

- generally not be used if there is no other evidence of infection, e.g. nitrite/leukocyte positivity on dipstick testing
- Males who do not respond to initial treatment or who experience a second UTI; consider checking for urinary retention by examination or bedside ultrasound in older males
- Older people who do not improve with antibiotic treatment, even after requesting urine culture to confirm infection and sensitivity analysis to guide antibiotic selection
- For further information on the diagnosis and management of UTIs in other groups:
 - Pregnant females: bpac.org.nz/2019/pregnancy-care. aspx
 - Older people: bpac.org.nz/BT/2015/July/guide.aspx
 - Children: starship.org.nz/guidelines/urinary-tract-infection/

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