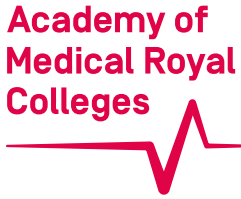


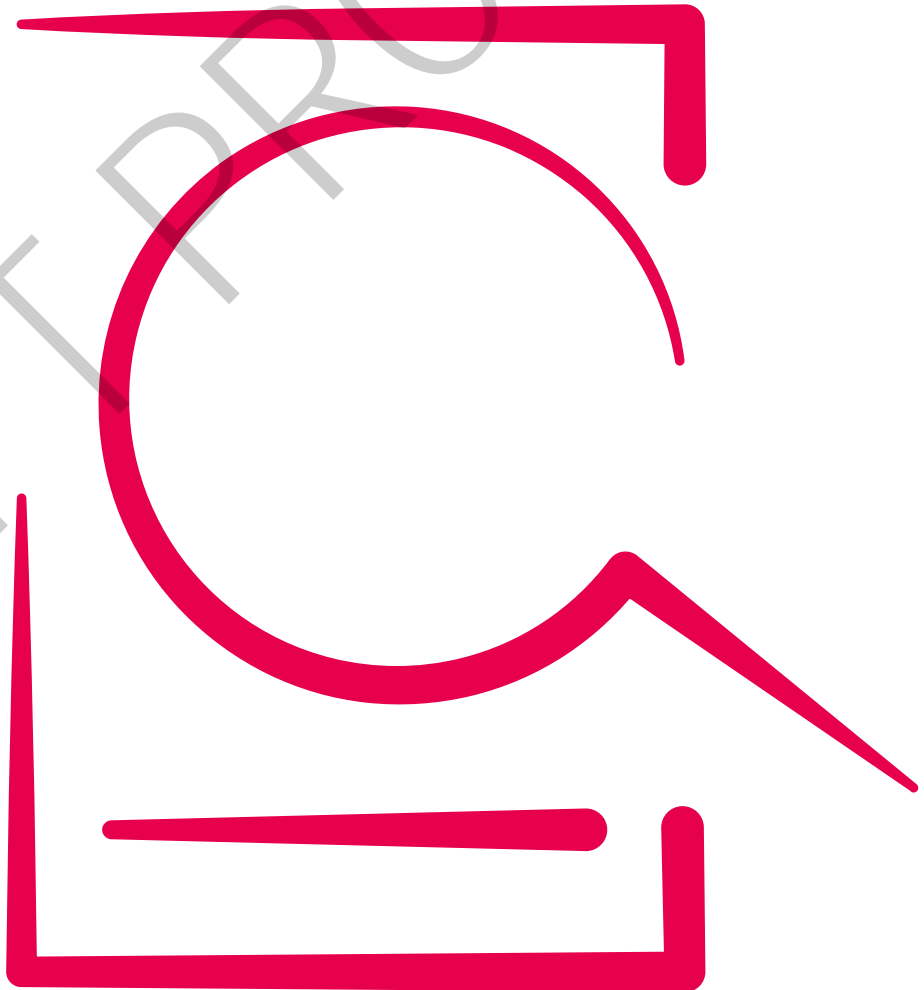
July 2023



Evidence-based Interventions

Proposed clinical guidance

Investigation and onward referral of women with recurrent urinary tract infections (rUTIs)



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Investigation and onward referral of women with recurrent urinary tract infections (rUTIs)

First published: July 2023

Prepared by: The Academy of Medical Royal Colleges on behalf of the Evidence-based Interventions Programme Board.

This information can be made available in alternative formats, such as large print, and may be available in alternative languages upon request.

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Introduction

The Evidence-based Interventions (EBI) programme is an initiative led by the Academy of Medical Royal Colleges to improve the quality of care. Since its inception in 2018, the programme has been supported by four partners: NHS England, NHS Confederation, the Patients Association and the National Institute for Health and Care Excellence (NICE).

Backed by both doctors and patients, the programme is designed to maximise the value patients get from healthcare. This might mean carrying out fewer interventions — where the benefit of certain tests, treatments and procedures is no longer supported by the evidence — but might also mean increasing activity, where the positive impact of a particular intervention for patients is compelling. And finally, it might mean changing the way a particular condition is diagnosed and then treated.

As well as improving outcomes and reducing patient harm, prioritising evidence-based care means we can improve outcomes, reduce patient harm and minimise unwarranted variation in service provision, as well as freeing up valuable resources for use elsewhere in the NHS. This is more important than ever as the NHS recovers from the impact of COVID-19 and restores services.

These recommendations aim to reduce variation in care delivery for women with recurrent urinary tract infections, limiting harm while ensuring those in need of specialist input are investigated appropriately.

The recommendations have been drafted by a panel of senior specialist clinicians. The panel is overseen by an Expert Advisory Committee (EAC) which evaluates the evidence and ensures only those proposals which meet strict criteria are progressed. This committee in turn reports to a Programme Board which makes the ultimate decision on whether a change to the clinical guidance can be made. Their decision is based on feedback from all key stakeholders including patient groups, clinical commissioners, and clinicians. You can find out more about EBI [on our website](#).

We are [keen to hear](#) from individuals and organisations with views on this proposal. The engagement period closes on 1 September 2023. These proposals and any views received will be considered by the Programme Board who will reach a conclusion on the practicality and appropriateness of the proposed changes to clinical guidance in Winter 2023.

Summary of current practice

Urinary tract infections (UTI) are extremely common in women with over half experiencing at least one UTI in their lifetime¹. Many women experience recurrent infection, defined as at least 3 UTIs in one year or 2 UTIs in six months^{2,3}. Recurrent UTIs affect approximately 1 in 1,000 women under the age of 65⁴ and can significantly impact quality of life^{5,6}.

Urinary infections can affect the lower urinary tract (cystitis) or the upper urinary tract (pyelonephritis). Recurrent upper tract infections are uncommon, and these individuals should be reviewed in secondary care. For the remainder of this proposal, we use recurrent UTI (rUTI) to refer to recurrent cystitis only.

In the UK, most women with rUTIs present initially to primary care. Recommendations covering the primary care management of rUTIs are outlined in NICE guideline NG112³. This also specifies when clinicians should refer or seek specialist advice; in those patients where malignancy is suspected or where 'the underlying cause of rUTI is unknown'.

Specialist urological input is important for identifying and treating women with structural or functional abnormalities of the urinary tract that predispose to bacterial persistence (so-called 'complicated' rUTIs). These abnormalities are often identified through specialist tests, including cystoscopy, which allows direct visualisation of the lower urinary tract. Other tests performed in secondary care include urodynamic studies and imaging such as computed tomography or ultrasound.

Women with 'complicated' UTIs only make up a small fraction of those with recurrent infection and most will not benefit from additional investigations and could even experience harm, including new infection and bleeding, from invasive tests⁷. Identifying the subset of individuals that will benefit from specialist referral is critical in maximising patient benefit while ensuring resources are used judiciously. NICE guideline NG112³ does not define the clinical features that suggest a complicated aetiology, which are included in other international guidelines. In addition, it does not define the findings on renal tract ultrasound — a test commonly performed in primary care in the work-up of rUTI — that should prompt specialist referral.

These recommendations aim to complement NICE guideline NG112³ by providing guidance for primary care clinicians on when to refer women with rUTIs to specialist urology services and the investigations that should be performed prior to referral.

A list of important definitions used in this guideline is provided below.

- Urinary tract infection (UTI) is defined as:
 - Typical symptoms of infection (such as dysuria, nocturia, change in urine appearance or odour) with a clinical response to antibiotics, even in the absence of microbiological confirmation.
 - Typical symptoms of infection with a positive urine dipstick (positive for nitrite or leukocyte and red blood cells).
 - Typical symptoms of infection with a positive urine culture.
- Recurrent lower urinary tract infection (rUTI) — 2 or more symptomatic lower UTIs in six months or 3 or more symptomatic lower UTIs in one year.
- Relapsed urinary tract infection — where the same organism is identified in the urine within two weeks of appropriate antimicrobial treatment. Relapsed infections should not be counted as 'new' infections when defining woman with rUTIs. If the same organism is identified more than two weeks after completion of antibiotic therapy, this should be counted as a new infection.
- Asymptomatic bacteriuria — the presence of bacteria in the urine of a person without signs or symptoms of UTI. It should not be routinely screened for, or treated, in women who are not pregnant⁸. It does not count as a urinary tract infection.
- Complicated urinary tract infection — a UTI that occurs in an individual with predisposing structural or functional abnormalities of the genitourinary tract or host factors that put them at increased risk of pyelonephritis or urosepsis⁹.

Recommendations

Scope

These recommendations provide referral guidance for primary care clinicians when **managing non-pregnant women over the age of 18 with recurrent lower UTI.**

The recommendations do not cover the management of:

- Suspected malignancy ([gynaecological cancer](#); [urological cancer](#)).
- Acute UTI, which is covered by NICE guideline NG109⁸.
- Recurrent or persistent asymptomatic bacteriuria. This is common¹⁰ and should not prompt further investigation or treatment, unless it is a persistent finding in pre-menopausal women.

Recommendations

1. All women with recurrent UTIs should be offered a renal ultrasound (US) in primary care. This should include measurement of a post-micturition residual volume as standard.

Specialist referral

2. Specialty urology referral should be offered to women where **ANY** of the following clinical criteria are met:
 - 2.1 Prior urinary tract surgery or trauma.
 - 2.2 Prior abdominopelvic malignancy.
 - 2.3 Visible and non-visible haematuria after resolution of infection (this should be managed as per NICE suspected cancer guidance — [gynaecological cancer](#); [urological cancer](#)).
 - 2.4 Urea-splitting bacteria on culture (e.g. Proteus, Yersinia) in the presence of a stone, or atypical infections (e.g. tuberculosis, anaerobic bacteria)

- 2.5. Bacterial persistence after sensitivity-based therapy.
- 2.6. Pneumaturia or faecaluria.
- 2.7. Obstructive symptoms (straining, weak stream, intermittency, hesitancy).

OR if any of the following features are present on renal ultrasound:

- 2.8. Hydroureter or hydronephrosis.
 - 2.9. Bladder OR ureteric OR obstructive renal stones (for non-obstructive renal stones please use advice and guidance).
 - 2.10. Post-micturition residual volume greater than 150ml.
3. Women who do not meet the above criteria for speciality referral should be managed in primary care where possible. Management will differ depending on menopausal status, may include lifestyle modifications, non-antibiotic, and antibiotic based treatments, and should follow the recommendations set out in NICE guideline NG112³.
4. If concerns persist, or symptoms remain uncontrolled despite optimal primary care management, primary care clinicians should use 'advice and guidance' to seek specialist advice in the first instance, prior to referral.

Rationale for recommendations

The panel accepted the definition of rUTI used in all the international guidelines reviewed: 2 or more symptomatic urinary tract infections in six months or 3 or more symptomatic infections in one year.

The panel considered international guidelines on rUTI¹¹. These broadly agree that most women with rUTIs do not require further investigation with cystoscopy or imaging in the absence of specific 'risk factors'^{2,12,13,14}. The panel noted that guidelines differ in what 'risk factors' they consider significant. Of the guidelines reviewed, the Canadian urological guidelines are the most detailed¹⁵ and the panel was of the opinion that this list should be adapted for use in our recommendations.

The 'risk factors' from the Canadian guidelines were discussed individually. Voiding dysfunction was discussed in detail and the panel decided that this should remain in the 'symptom list' as abnormal post-residual volume may not identify all patients with functional issues. There was a discussion about whether the presence of stones should prompt referral. The consensus view was that patients with bladder stones, or stones causing obstruction should be referred. Non-obstructive renal stones and stones <5mm are unlikely to be significant in rUTI but the panel considered that primary care should be provided with the explicit option of seeking an specialist opinion via advice and guidance in these cases. Regarding diabetes, it was agreed that this should be removed from the list as a standalone factor. In these cases, the focus should be on optimisation of diabetic control (directed by primary care, and endocrinology, where appropriate) with no added benefit provided by urology in the absence of other complicating factors.

The panel considered the evidence underpinning international recommendations relating to the utility of further investigations in women with rUTIs. The most comprehensive evidence summary is provided by a recent systematic review that includes data from seven published research studies^{16,17,18,19,20,21,22}. The panel discussions are summarised below.

Cystoscopy

In the pooled analysis from the systematic review:

- 23% of cystoscopies performed for recurrent UTI were abnormal but most abnormalities were incidental with inflammation being the main 'abnormality' found.
- Only 1 out of 656 cystoscopies performed (0.15%) revealed a potentially life-threatening finding (carcinoma).

- There were few other findings of consequence in cystoscopies performed (18 out of 656 or 2.74%). Of the findings deemed significant, 17 out of 18 could have been identified via other means such as through clinical history (colovesical fistula and suture material), by ultrasound (ureterocele), and from flow studies (stricture).

The panel noted the author's conclusions that *'there is no evidence for performing cystoscopy for recurrent UTI'*.

The panel acknowledged that cystoscopy is currently considered part of the standard work-up of rUTI in secondary care. Based on the available evidence the panel considered that most women are unlikely to derive additional benefit from cystoscopy and specialist referral should not be routinely justified so this test can be performed. It was the panel's view that women with high-risk clinical features are more likely to have significant pathology and that referral to secondary care (with the understanding that most patients will undergo cystoscopy) is still justified in these cases.

Urodynamics

- The panel noted that this is the area with least published literature with only two studies^{23,24} with extractable data in the systematic review and significant heterogeneity in findings.
- The data presented indicated about 50% of women with rUTI have impaired urine flow and 35% have a positive post void residual but the studies included did not consistently define what was meant by a 'positive' post-void volume.
- The pragmatic view of the panel was that all women with rUTI should have a post-void residual measured. This can be performed easily in the community as part of a standard urinary tract ultrasound without the need for additional resource. There was limited data to support the volume of the post-void residual deemed significant and a value was agreed upon based on expert opinion.
- Urodynamics require specialist equipment and given the limited data available, the panel's view was that it is reasonable to reserve further urodynamic testing for women with high-risk clinical features, particularly those with a high post-void residual or symptoms suggestive of significant voiding dysfunction.

Imaging

- Most studies included in the systematic review focussed on Intravenous urography (IVU) which is a historical test and no studies reported specifically on CT.
- Only 2 studies reported specifically on ultrasound^{19,20}. Of 785 imaging studies only 10 (1.3%) showed serious findings requiring urgent management and only 30 (3.8%) showed findings requiring some form of follow-up. Of the serious findings, most were detected on US, but missed on IVU and abdominal radiograph.
- The authors of the systematic review considered that imaging was 'unlikely to be of value in the absence of symptoms of upper tract disease or gynaecological problems'.
- The panel considered this data in the context of current UK practice, where ultrasound is commonly obtained in primary care prior to referral. The expert view of the panel was that ultrasound could serve as a valuable screening test for significant pathology and given its low cost and accessibility, should form part of the standard work-up of all women with rUTI prior to specialist referral. The fact that ultrasound does not use ionizing radiation or intravenous contrast was considered to further support its use as a screening tool over other imaging modalities.
- In the absence of robust data, the panel came to an expert consensus on what ultrasound features should warrant specialist review.

The panel discussed how specialist referral may still benefit women without high-risk features where primary care management strategies, as outlined in NICE guideline NG112³, had been exhausted, or in women who, on considering the risks and benefits associated with further tests, still want a specialist opinion/review. It was the panel's view that a specialist opinion should be sought initially through 'advice and guidance' pathways to allow referrals to be managed most effectively.

The panel discussed the recommendations on lifestyle modifications, non-antibiotic and antibiotic treatments outlined in NICE guideline NG112³. The group broadly agreed with the recommendations in NICE guideline NG112³ although noted that new evidence had emerged on the efficacy of methanamine hippurate since its publication²⁵. The panel was of the view that current NICE guidance should be reviewed in view of this trial, but that this lay outside the scope of these recommendations.

Patient information

Cystitis is a urinary tract infection (UTI) that affects the bladder. Recurrent UTIs (rUTIs) are defined as at least 3 infections in a year or 2 infections in six months. Recurrent UTIs affect approximately 1 in 1,000 women under the age of 65⁴ and can significantly impact quality of life^{5,6}.

This guidance is for non-pregnant women over 18 years old who experience rUTIs. It supports primary care clinicians (usually GPs) in deciding whether referring a patient to a hospital-based urologist is the best course of action for them. This guidance should be used alongside existing national guidance produced by the National Institute of Clinical Excellence (NICE).

We recommend that:

- Most women should be treated in primary care (usually by your GP) according to the steps set out in NICE guidance NG112³.
- All women with rUTIs should have an ultrasound scan of their kidneys, bladder, and ureters (the tubes that connect the kidneys to the bladder)
- Women should only be referred to a hospital-based specialist in kidney and urinary tract diseases (urologist) if they have symptoms, medical conditions or findings on their ultrasound that suggest a problem with the structure or function of their urinary system.

GPs always have the option of seeking advice from hospital-based urology specialists if they have additional concerns in cases that don't meet the criteria for automatic referral.

A small number of women with rUTIs will have problems with the structure and function of the urinary system. These individuals tend to have clues in their medical history and/or abnormal ultrasound findings and may therefore benefit from specialist treatments to reduce the number or severity of infections they get. Additional investigations (usually performed by hospital-based urologists) are typically needed to diagnose these conditions after someone is referred. One common test is called a flexible cystoscopy. This involves inserting a thin flexible tube called a cystoscope through the opening into the bladder to examine its lining. This procedure is relatively safe but can be painful, cause bleeding and/or a new infection (in between 1% to 10% of cases⁷). For most women with rUTIs nothing significant is found as a result of this test (less than 3% of cystoscopies). Therefore it is important that additional invasive investigations are only performed if they are likely to reveal issues or signs of disease.

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