



Public Health
England

Protecting and improving the nation's health

Diagnosis of urinary tract infections

Quick reference tool for primary care
for consultation and local adaptation

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Foreword – aims and adaptations

Audience and target group:

- primary care prescribers in general practice and out of hours settings, including doctors, nurses and pharmacists
- those giving first point of contact for urinary tract infections (UTIs) covering acute uncomplicated infections in women, older patients with urinary symptoms, and children
- incidence of asymptomatic bacteriuria is greater in care homes than in the community, and increases with age and long-term urinary catheter use
- the flow chart for women under 65 years may be more appropriate in some women over 65 years who are not in care homes
- the flow chart for older patients may be more suitable for some younger patients in care homes or who have a long-term urinary catheter

Aim

To provide a simple, effective, economical and empirical approach to the diagnosis of urinary tract infections and minimise the risk of treatment failure and emergence of antibiotic resistance so improving safe care.

Implications

The quick reference tool should lead to improved diagnosis of UTI and more appropriate antibiotic use. The tool should reduce inappropriate urine dipstick and culture tests leading to financial and time implications for laboratories and primary care commissioners and primary care staff.

Production

The quick reference tool has been produced in consultation with general practitioners, nurses, specialists, and patient representatives. The tool is in agreement with other publications, including National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summaries (CKS) and Scottish Intercollegiate Guidelines Network (SIGN).

NICE has endorsed that this quick reference tool accurately reflects recommendations in the NICE guideline on **antimicrobial stewardship, urinary tract infections** and **urinary tract infection (catheter-associated)**. It also supports statements 1 and 4 in the NICE quality standard for **urinary tract infections in adults** and statement 1 in the NICE quality standard for **urinary tract infection in children and young people**.

The quick reference tool is endorsed by:

**ROYAL
PHARMACEUTICAL
SOCIETY**



The quick reference tool is fully referenced and graded.

The tool is not all-encompassing, as it is meant to be 'quick reference'. Clinicians should ultimately rely on their clinical judgement and use with other recommended resources. If more detail is required, we suggest referral to the websites and references cited.

Updates based on new developments or user feedback will be raised to the steering group quarterly (or sooner if needed) and a change note made if an update is indicated. There will be a full review every 3 years.

Poster presentation of the quick reference tool

The summary table is designed to be printed out as a poster for use in practice.

The rationale and evidence are designed to be used as an educational tool for you, and your colleagues and trainees, to share with patients as needed.

Local adaptation

We would discourage major changes to the quick reference tool, but the format allows minor changes to suit local service delivery and sampling protocols.

To create ownership agreement on the quick reference tool locally, dissemination should be agreed and planned at the local level between primary care clinicians, laboratories and secondary care providers.

We welcome opinions on the advice given. Please send comments with corresponding evidence to Professor Clodna McNulty, 4th Floor, Twyver House, Bruton Way, Gloucester, GL1 1DQ or email: TARGETAntibiotics@phe.gov.uk

Flowchart for women (under 65 years) with suspected UTI

Excludes women with recurrent UTI (2 episodes in last 6 months, or 3 episodes in last 12 months) or urinary catheter^{1D,2D}
 This flow chart will be suitable for some women over 65 years in the community setting

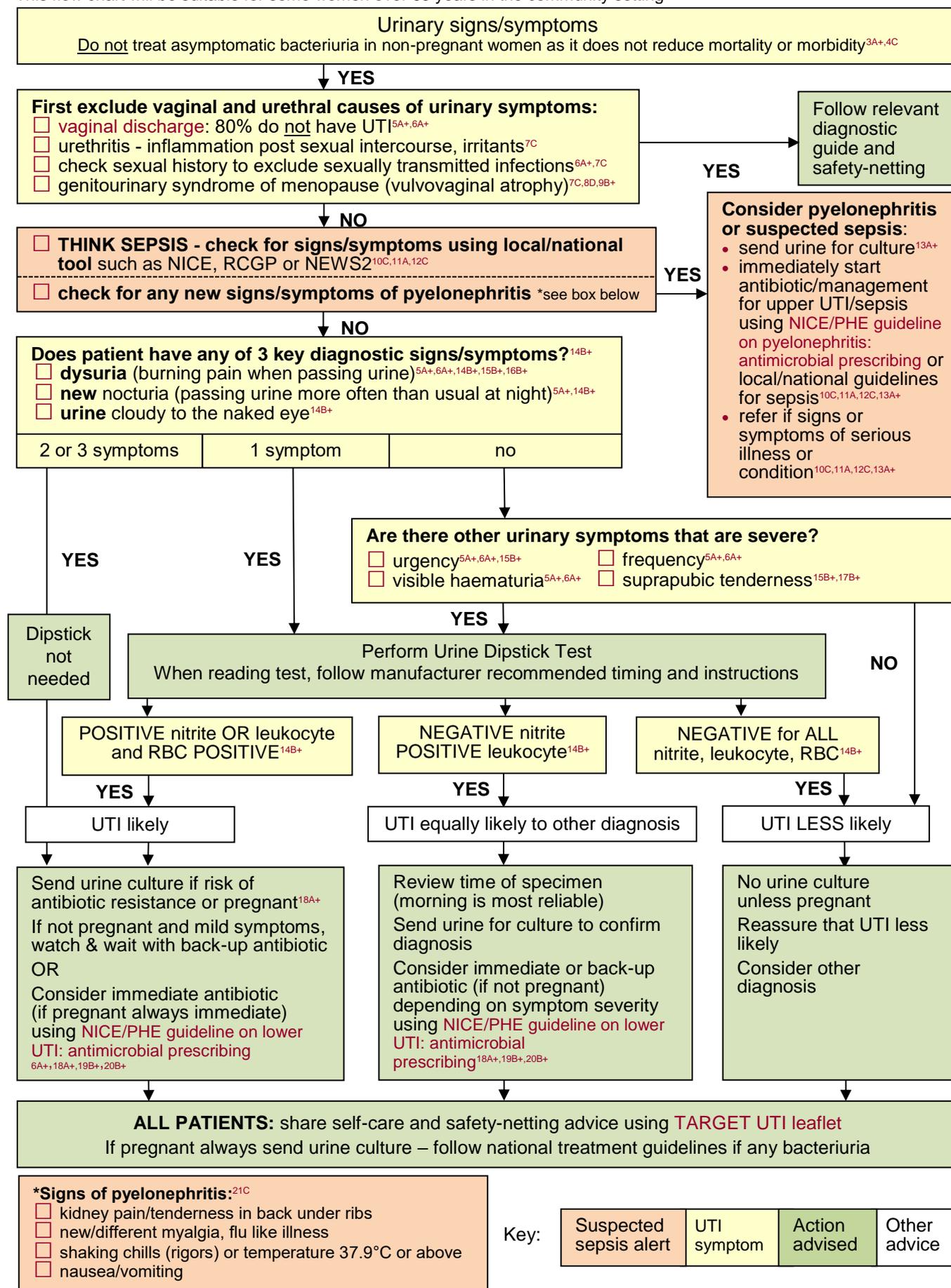


Table summary: diagnostic points for women under 65 years

Excludes women with recurrent UTI (2 episodes in last 6 months or 3 episodes in last 12 months) or urinary catheter^{1D,2D}

This flow chart will be suitable for some women over 65 years in the community setting

Using symptoms and dipsticks to help diagnose UTI: ^{5A+,6A+,14B+,15B+,16B+,17B+} no individual or combination are completely reliable in diagnosing UTI, thus severity of symptoms and safety-netting are important in all

First exclude other genitourinary causes of urinary symptoms

- 75 to 80% with vaginal discharge will not have UTI^{15A+,6A+}
- in sexually active check sexual history for STIs for example chlamydia and gonorrhoea^{6A+,7C}
- urethritis - urinary symptoms may be due to urethral inflammation post sexual intercourse, irritants, or STIs^{7C}
- genitourinary symptoms of menopause/atrophic vaginitis/vaginal atrophy^{7C,8D,9B+}

In all, check for new signs of pyelonephritis, systemic infection, or risk of suspected sepsis ^{10C,11A,12C,13A+,21C}

If pyelonephritis or suspected sepsis: send urine for culture to inform definitive treatment and immediately start antibiotic using **NICE/PHE guideline on pyelonephritis: antimicrobial prescribing** or local/national guidelines for sepsis; refer if signs or symptoms of serious illness or condition^{10C,11A,12C,13A+}

In women <65yrs use signs/symptoms of dysuria, new nocturia or cloudy urine to guide treatment ^{14B+}

- 2 or more** of these 3 signs/symptoms in general practice are likely to have a UTI: consider immediate antibiotic, or back-up if mild symptoms and woman is not pregnant^{14B+,18A+}
- 1 sign/symptom:** UTI possible as 68% will have a culture confirmed UTI ($\geq 10^6$ cfu/L) therefore use urine dipstick to increase diagnostic certainty^{14B+}
- none** of the 3: UTI less likely - use urine dipstick if other severe urinary symptoms (frequency, urgency, haematuria, suprapubic tenderness)^{14B+}

Dysuria, new nocturia or cloudy urine present ^{14B+}	% of GP patients with suspected UTI presenting with these sign/symptoms ^{14B+}	% with these symptoms who have culture confirmed UTI ($\geq 10^6$ cfu/L) ^{14B+}	Suggested management
All 3	29%	82%	Consider immediate antibiotic (if pregnant always immediate) OR back-up if mild symptoms and not pregnant ^{18A+}
≥ 2	71%	74%	
1	25%	68%	Use urine dipstick to increase diagnostic certainty ^{14B+}
None	4%	not specified	Use urine dipstick if other severe urinary symptoms

For antibiotic choice: use NICE/PHE guideline on lower UTI: antimicrobial prescribing; check history to determine resistance risk^{18A+}

Using urine dipsticks to predict UTI in women <65 years with only 0 or 1 of dysuria, new nocturia, cloudy urine increases the diagnostic certainty, and reduces unnecessary antibiotics ^{14B+}

Follow the manufacturer's guidance for accurate use of urine dipstick tests, including test timing requirements

- positive nitrite OR positive leukocyte and blood: UTI likely^{14B+} - offer empirical antibiotics for lower UTI OR if not pregnant and milder symptoms consider back-up antibiotic with self-care and safety-netting^{6A+,18A+,19B+,20B+}
- leukocyte positive but nitrite negative: UTI equally likely to other diagnosis^{14B+} - review time of specimen (morning is best); send urine for culture; use back-up (if not pregnant) or immediate antibiotic depending on symptom severity^{18A+,19B+,20B+}
- ALL nitrite, leukocyte and blood negative: UTI less likely – no urine culture unless pregnant; consider other diagnosis; reassure; give self-care and safety-netting advice^{14B+}

If pregnant and any bacteriuria: always offer immediate antibiotics and send urine culture; follow **NICE/PHE guideline on lower UTI: antimicrobial prescribing**

ALL patients: share self-care and safety-netting advice using **TARGET UTI leaflet**

For all patients please refer to the information and reference tables in joint NICE/PHE guidance: NICE guidelines on UTI (lower): antimicrobial prescribing or NICE guidelines on pyelonephritis (acute): antimicrobial prescribing

Diagnostic points for men under 65 years

Asymptomatic bacteriuria is rare in men <65yrs^{4C}

Consider other genitourinary causes of urinary symptoms

- in sexually active, check sexual history for STIs for example chlamydia and gonorrhoea^{7C,22D}
- urethritis due to urethral inflammation post sexual intercourse, irritants, or STIs^{7C}

Check for pyelonephritis, prostatitis, systemic infection, or suspected sepsis using local policy^{10C,11A,12C}

- urinary symptoms with fever or systemic symptoms in men are strongly suggestive of prostatic involvement or pyelonephritis^{1D,24B+,25D}
- acute prostatitis may present with feverish illness of sudden onset, symptoms of prostatitis (low back, suprapubic, perineal, or sometimes rectal pain), symptoms of UTI (dysuria, frequency, urgency or retention), or exquisitely tender prostate on rectal examination^{22D, 23D}
- recurrent or relapsing UTI in men should prompt referral to urology for investigation^{26D,27C}

Diagnostic points in men

- to confirm diagnosis always send a mid-stream urine sample for culture, collected before antibiotics are given^{18A+,26D}
- do not use urine dipsticks to rule out infection as they are unreliable for this^{28B+}
- a urine dipstick test with positive nitrites makes UTI more likely in men (PPV 96%). Negative for both nitrite and leucocyte makes UTI less likely, especially if symptoms are mild^{1D,28B+}
- if suspected UTI, offer immediate treatment according to [NICE/PHE guideline on lower UTI: antimicrobial prescribing](#) and review choice of antibiotic with pre-treatment culture results^{4C,18A+,24B+,26D}

For all patients please refer to the information and reference tables in joint NICE/PHE guidance: [NICE guidelines on UTI \(lower\): antimicrobial prescribing](#), [NICE guidelines on pyelonephritis \(acute\): antimicrobial prescribing](#), or [NICE guideline on prostatitis \(acute\): antimicrobial prescribing](#)

Flowchart for suspected UTI in catheterised adults or those over 65 years

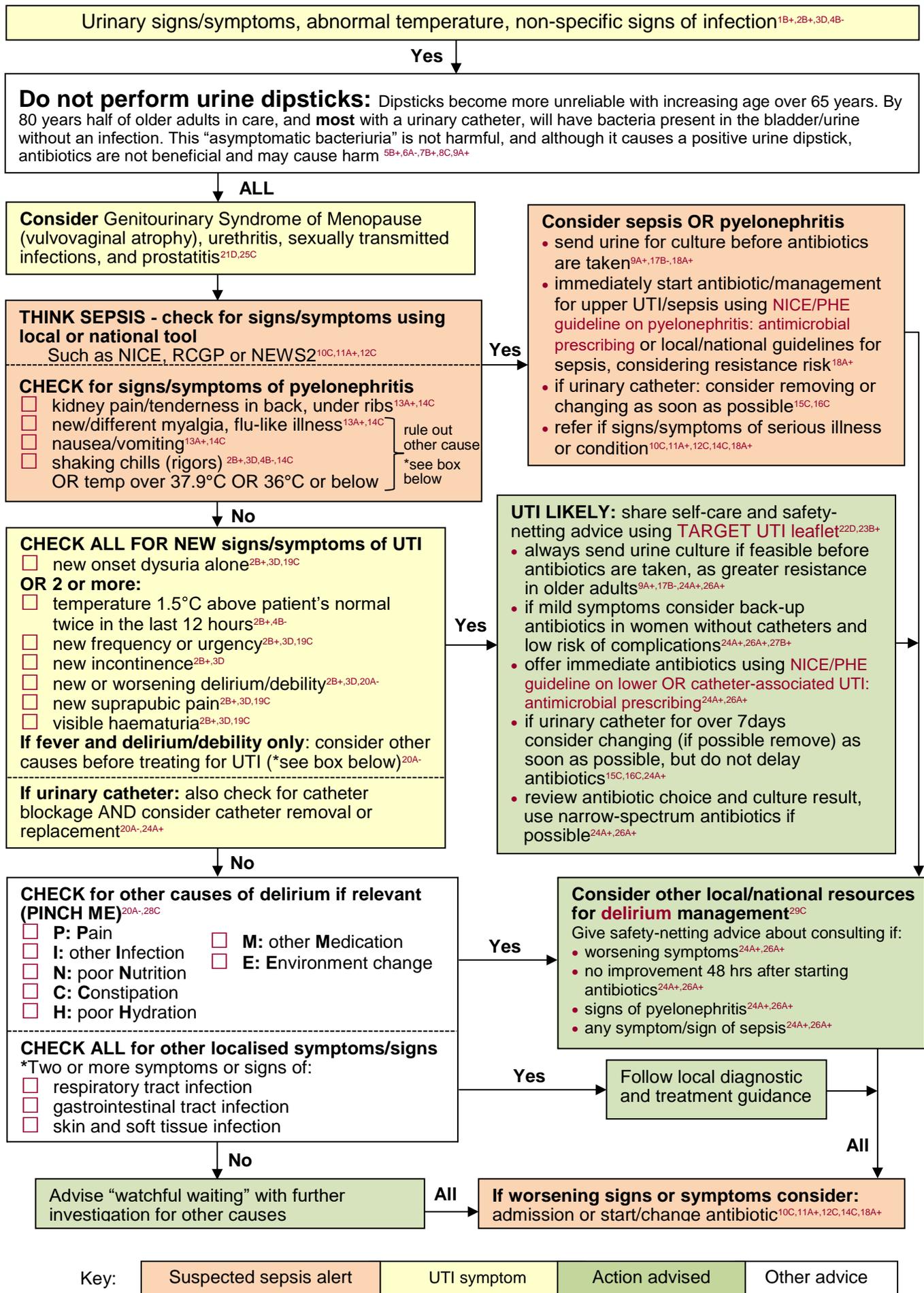


Table summary: catheterised adults or those over 65 years with suspected UTI

Men and women over 65 years may present with:

- localised signs or symptoms of a UTI including new onset dysuria; incontinence; urgency^{1B+}
- temperature: 38°C or above; 36°C or below; 1.5°C above normal twice in the last 12 hours^{2B+,3D,4B-}
- non-specific signs of infection: for example delirium; loss of diabetic control^{2B+,3D,4B-,20A-,30D,31D}

Do not perform urine dipstick as they become more unreliable with increasing age over 65 years

By 80 years half of older adults in care, and most with a urinary catheter, will have bacteria present in the bladder/urine without an infection. This “asymptomatic bacteriuria” is not harmful, and although it causes a positive urine dipstick, antibiotics are not beneficial and may cause harm^{5B+,6A-,7B+,8C,9A+}

Consider: Genitourinary Syndrome of Menopause (vulvovaginal atrophy) as can present with dysuria.^{21D}
Also consider risk of urethritis, prostatitis or STI^{13A+}

Use symptoms and signs to determine the most appropriate management

First think sepsis: check for signs using local or national tool such as NICE, RCGP or NEWS2^{10C,11A+,12C}

Exclude pyelonephritis checking for any one sign:

- kidney pain/tenderness in back, under ribs^{13A+,14C}
- new/different myalgia, or flu-like symptoms^{1B+,14C}
- nausea/vomiting^{1B+,14C}
- shaking chills (rigors) or temp over 37.9°C or 36°C or below^{2B,3D,4B,14C}

If signs of sepsis or pyelonephritis

(if no kidney pain rule out other localised infection *see symptoms of other infection box below):

- send urine for culture before antibiotics are taken^{9A+,17B-,18A+}
- assess antibiotic resistance risk and immediately start antibiotic for upper UTI/sepsis using NICE/PHE guideline on pyelonephritis: antimicrobial prescribing or local/national guidelines for sepsis^{18A+}
- if urinary catheter for more than 7 days: consider changing (if possible remove) as soon as possible but do not delay antibiotics^{15C,16C,24A+}
- refer if signs or symptoms of serious illness or condition^{10C,11A+,12C,14C,18A+}

Then check all for **NEW URINARY symptoms/signs**

- NEW onset dysuria alone^{2B,3D,19C}
- OR 2 or more new:
 - temperature: 1.5°C above normal twice in the last 12 hours^{2B+,4B-}
 - new frequency or urgency^{2B+,3D,19C}
 - new incontinence^{2B+,3D}
 - new or worsening delirium/debility^{2B+,3D,20A-}
 - new suprapubic pain^{2B+,3D,19C}
 - visible haematuria^{2B+,3D,19C}

If fever and delirium/debility only: consider other infections before treating for UTI^{20A-}

If urinary symptoms suggest UTI:

- always send urine culture if feasible before antibiotics are taken, as greater resistance in older adults^{9A+,17B-,24A+}
- if mild symptoms consider back-up antibiotics in women without catheters and low risk of complications^{24A+,25A+,26B+}
- consider immediate antibiotics for lower UTI^{24A+,25A+}
- offer immediate antibiotic in men or if urinary catheter^{24A+}
- consider antibiotic resistance risk using patient history^{24A+,25A+}
- for antibiotic choice use NICE/PHE guideline on lower UTI: antimicrobial prescribing OR NICE/PHE guideline on catheter-associated UTI: antimicrobial prescribing

If indwelling URINARY CATHETER for over 7 days: check for catheter blockage AND consider catheter removal^{20A-}

- consider changing (if possible remove) catheter as soon as possible but do not delay antibiotics^{15C,16C,24A+}
- **leaking or blocked long-term indwelling catheters:** offer antibiotic treatment if signs/symptoms UTI^{24A+};
- check bag positioning, constipation, see guidance for other causes^{37C}
- **at catheter change:** only consider antibiotic prophylaxis if trauma or symptomatic UTI after previous changes^{36D}

Check all for 2 or more signs or symptoms suggesting **other infection**^{20A-}

- respiratory tract infection: shortness of breath; cough or sputum production; new pleuritic chest pain^{3D}
- gastrointestinal tract infection: nausea/vomiting; new abdominal pain; new onset diarrhoea^{32C,33C}
- skin and soft tissue infection: new redness; warmth^{3D}

Follow diagnostic and treatment guidance if infection suspected

Check all for other causes of **DELIRIUM (PINCH ME)** and manage as needed^{20A-,27C}

- | | | |
|--|---|---|
| <input type="checkbox"/> P: Pain | <input type="checkbox"/> M: other Medication | <ul style="list-style-type: none"> • using PINCH ME can help identify other potential underlying causes of delirium superimposed on dementia. It can be used in different clinical settings^{28C} • consider other local/national delirium management resources^{29C} • Advise watchful waiting, with further investigation if needed |
| <input type="checkbox"/> I: other Infection | <input type="checkbox"/> E: Environment change | |
| <input type="checkbox"/> N: poor Nutrition | | |
| <input type="checkbox"/> C: Constipation | | |
| <input type="checkbox"/> H: poor Hydration | | |

Share self-care and safety-netting advice using **TARGET UTI** leaflet for older adults

Safety-netting to seek advice if:

- worsening symptoms^{24A+,25A+}
- signs of pyelonephritis^{24A+,25A+}
- signs/symptoms of sepsis^{24A+,25A+}
- no improvement after 48 hours^{24A+,25A+}

Self-care advice

- drink enough fluids to avoid feeling thirsty and to keep urine pale^{25D,34C,35C}
- take paracetamol regularly up to 4 times daily for pain/fever relief^{22D,23B+}
- ways of preventing further episodes of UTI

Please refer to the information and reference tables in joint NICE/PHE guidance: NICE guidelines on UTI (lower): antimicrobial prescribing or NICE guidelines on pyelonephritis (acute): antimicrobial prescribing or NICE/PHE guideline on catheter-associated UTI: antimicrobial prescribing

Sending urine for culture and interpreting results in ALL adults

Review need for culture when considering treatment

Send a urine for culture in:

- over 65 year olds if symptomatic and antibiotic given^{1B-}
- pregnancy: for routine antenatal tests, or if symptomatic^{2B+}
- suspected pyelonephritis or sepsis^{3C}
- suspected UTI in men^{4A+}
- failed antibiotic treatment or persistent symptoms^{5A+,6A+,7B-}
- recurrent UTI (2 episodes in 6m or 3 in 12m)^{5A+}
- if prescribing antibiotic in someone with a urinary catheter^{9A+}
- as advised by local microbiologist

Consider risk factors for resistance and send urine for culture if:

- abnormalities of genitourinary tract^{8C}
- renal impairment^{8C}
- care home resident^{5A+}
- hospitalisation for > 7 days in last 6m^{5A+}
- recent travel to a country with increased resistance^{5A+}
- previous UTI resistant^{5A+,6B-}

If prescribing an antibiotic, review choice when culture and antibiotic susceptibility results are available

Sampling in all men and women

Women: mid-stream urine (NHS choices) and holding the labia apart may help reduce contamination but if not done, sample can still be sent for culture^{1B+,2A+,3B+,4D,5B-,6A-} Do not cleanse with antiseptic, as bacteria may be inhibited^{7B-}

Elderly frail: only take urine sample if symptomatic and able to collect good sample. If incontinent, clean catch in disinfected container and condom catheters for men may be viable options but little evidence to support^{8A-}

Men: advise on how to take a mid-stream specimen (NHS choices)^{1B+,4D,7B-}

People with urinary catheters: collect from newly placed catheter using aseptic technique if changed, drain a few mL of residual urine from tubing before using sampling port, then collect a fresh sample from catheter sampling port^{1B+,9A+}

Culture urine within 4 hours of collection, refrigerate, or use boric acid preservative. Boric acid can cause false negative culture if urine not filled to correct mark on specimen bottle and can affect urine dipstick tests)^{1B+,4D,6A-}

How do I interpret a urine culture result if I suspect a UTI?

Culture should be interpreted in parallel to severity of signs/symptoms. False negatives/positives can occur Do not treat asymptomatic bacteriuria unless pregnant as it does not reduce mortality or morbidity^{1C,2D,3A+}

Urine culture results in patients with urinary symptoms that usually indicate UTI:

- many labs use growth of 10^7 - 10^8 cfu/L (10^4 - 10^5 cfu/mL) to indicate UTI^{4B+}
- lower counts can also indicate UTI if patient symptomatic:
 - strongly symptomatic women - single isolate $\geq 10^5$ cfu/L ($\geq 10^2$ cfu/mL) in voided urine^{4B+,5B+}
 - in men counts as low as 10^6 cfu/L (10^3 cfu/mL) of a pure or predominant organism^{4B+}
 - any single organism $\geq 10^7$ cfu/L ($\geq 10^4$ cfu/mL)^{4B+}
 - *Escherichia coli* or *Staphylococcus saprophyticus* $\geq 10^6$ cfu/L ($\geq 10^3$ cfu/mL)^{4B+}
 - $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) mixed growth with 1 dominant organism^{4B+}

Epithelial cells/mixed growth:

- the presence of epithelial cells is not necessarily an indicator of perineal contamination, culture result should be interpreted with symptoms and repeated if significance is uncertain^{6B-}
- mixed growth may indicate perineal contamination; however, a small proportion of UTIs may be due to genuine mixed infection. Consider a re-test if symptomatic^{4B+,7B+}

Red cells: may be present in UTI^{4B+,8D}

- chemical tests may be more sensitive than microscopy as a result of the detection of haemoglobin released by haemolysis^{4B+}
- refer patients with persistent haematuria post-UTI to urology^{9A+}

White blood cells/ leucocytes:

- white cells $\geq 10^7$ WBC/L ($\geq 10^4$ WBC/mL) are considered to represent inflammation in urinary tract, this includes the urethra^{4B+}
- white cells can be present in older people with asymptomatic bacteriuria, as the immune system does not differentiate colonisation from infection^{4B+}

Sterile pyuria:

- in sterile pyuria, consider *Chlamydia trachomatis* (especially if 16 to 24 years), other vaginal infections, other non-culturable organisms including TB or renal pathology^{4B+}
- if recurrent pyuria with UTI symptoms, discuss with local microbiologist as lower counts down to 10^5 cfu/L (10^2 cfu/mL) may be significant. Higher volume of urine may need to be cultured, including for fastidious organisms^{4B+}

Follow up: Do not send follow-up urine unless pregnant, or advised by the laboratory

If UTI recurrent, refer or seek specialist advice on further investigation/management for^{9A+,10A+}: pregnant women; men aged 16 years and over; recurrent upper UTI; recurrent lower UTI (unknown underlying cause); children under 16 years (see NICE guidance on UTI in under 16s: diagnosis and management)

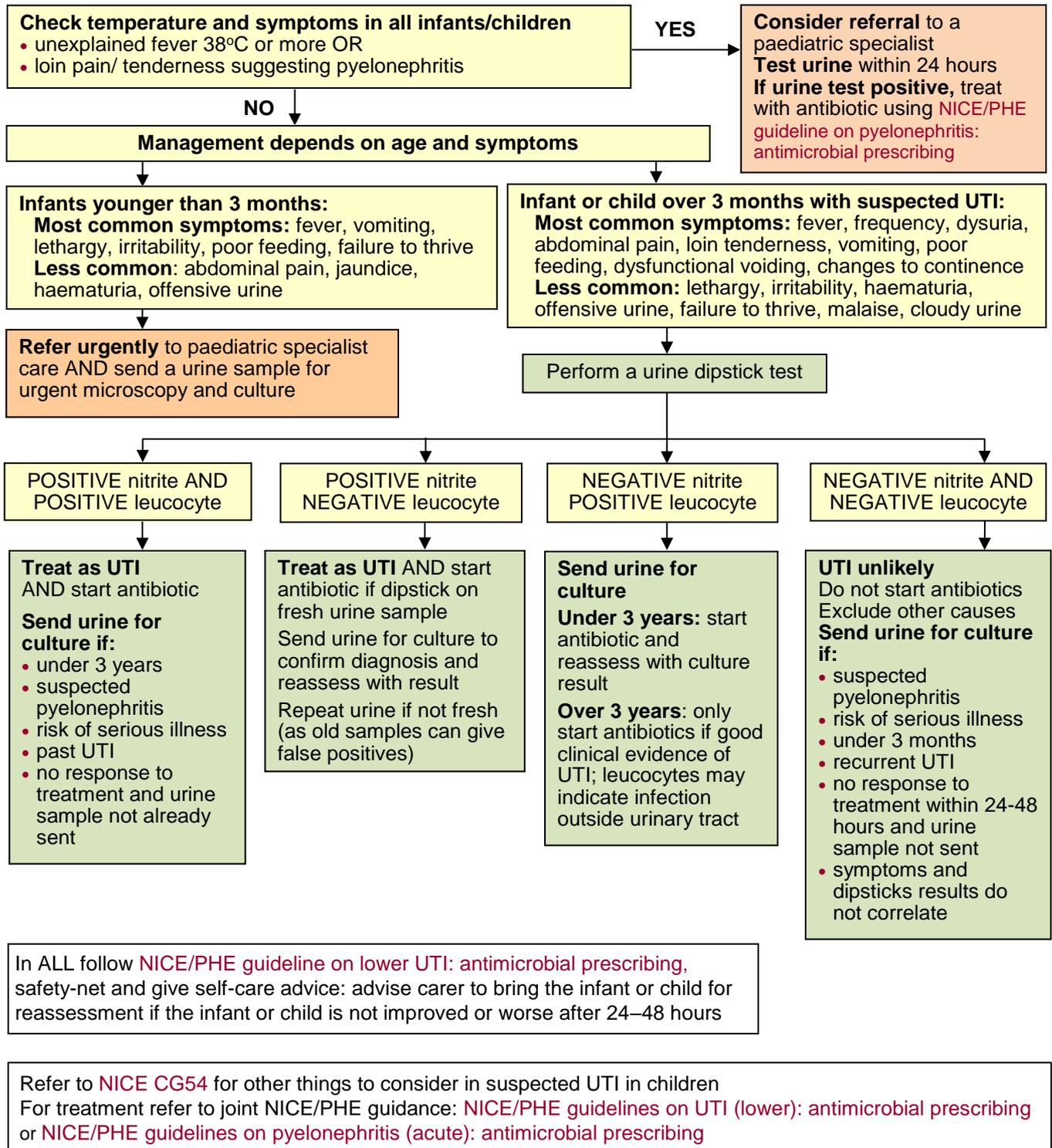
People with unexplained persistent haematuria or suspected cancer, please see NICE guideline on suspected cancer: recognition and referral for other referral criteria and considerations^{10A+}

For all patients: consider antibiotic susceptibility results and resistance when deciding on management and reviewing antibiotic treatment.

Please refer to joint NICE/PHE guidance: NICE/PHE guidelines on UTI (lower): antimicrobial prescribing; or NICE/PHE guidelines on pyelonephritis (acute): antimicrobial prescribing; or NICE/PHE guideline on catheter-associated UTI: antimicrobial prescribing

Flowchart for infants/children under 16 years with suspected UTI^{1A+}

Consider UTI in any sick child and every young child with unexplained fever



Key:

Urgent alert	UTI signs/symptoms	Action advised	Other advice
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Key points for infants/children under 16 years with suspected UTI

Sampling in children:

- if sending a urine culture, obtain sample before starting antibiotics^{2A+}
- if child has alternative site of infection do not test urine unless remains unwell - then test within 24 hours^{1A+}
- in infants/toddlers, clean catch urine advised;^{1A+,4B+,5A-} gentle suprapubic cutaneous stimulation using gauze soaked in cold fluid helps trigger voiding;^{6B+} clean catch urine using potties cleaned in hot water with washing up liquid;^{3B+} nappy pads cause more contamination, and parents find bags more distressing^{7B-}
- if non-invasive not possible consider: catheter sample, or suprapubic aspirate (with ultrasound guidance)^{1A+}
- culture urine within 4 hours of collection, if this is not possible refrigerate, or use boric acid preservative. Boric acid can cause false negative culture if urine not filled to correct mark on specimen bottle^{1A+}

Interpretation of culture results in children:

- single organism $\geq 10^6$ cfu/L (10^3 cfu/mL) may indicate UTI in voided urine^{1A+,8A-}
- any growth from a suprapubic aspirate is significant^{1A+,8A-}
- pyuria $\geq 10^7$ WBC/L (10^4 WBC/mL) usually indicate UTI, especially with clinical symptoms but may be absent^{1A+,8A-}

Other diagnostic tests: do not use CRP to differentiate upper UTI from lower UTI^{1A+}

Ultrasound:

- if proven UTI is atypical (seriously ill, poor urine flow, abdominal or bladder mass, raised creatinine, septicaemia, failure to respond to antibiotic within 48 hours, non-*E.coli* infection): ultrasound all children in acute phase and undertake renal imaging within 4-6 months if under 3 years^{1A+}
- ALL ages with recurrent UTI^{1A+}
- for children under 6 months OR those with non-*E.coli* UTI: ultrasound within 6 weeks if UTI not atypical AND responding to antibiotics^{1A+}

Refer to NICE CG54 for other things to consider in suspected UTI in children

For treatment refer to joint NICE/PHE guidance: NICE guidelines on UTI (lower): antimicrobial prescribing or NICE guidelines on pyelonephritis (acute): antimicrobial prescribing

Grading quick reference tool recommendations

The strength of each recommendation is qualified by a letter in parenthesis. This is an altered version of the grading recommendation system used by **SIGN**.

Study design	Recommendation grade
Good recent systematic review and meta-analysis of studies	A+
One or more rigorous studies; randomised controlled trials	A-
One or more prospective studies	B+
One or more retrospective studies	B-
Non-analytic studies, for example case reports or case series	C
Formal combination of expert opinion	D

This quick reference tool was originally produced in 2002 by the South West GP Microbiology Laboratory Use Group, in collaboration with the British Infection Association, general practitioners, nurses and specialists in the field. This quick reference tool was reformatted in 2017 in line with PHE recommendations. For detailed information regarding the comments provided and action taken, contact TARGETAntibiotics@phe.gov.uk. Public Health England works closely with the authors of the [Clinical Knowledge Summaries](#).

If you would like to receive a copy of this quick reference tool with the most recent changes highlighted, for detailed information regarding the search strategies implemented and full literature search results, or for any further information regarding the review process and those involved in the development of this quick reference tool, please email TARGETAntibiotics@phe.gov.uk

Public Health England is an executive agency of the Department of Health and is fully funded by the UK Government. The Primary Care and Interventions Unit does not accept funding for the development of this quick reference tool from pharmaceutical companies or other large businesses that could influence the development of the recommendations made.

Any conflicts of interest have been declared and considered prior to the development and dissemination of this quick reference tool. For any detailed information regarding declared conflicts of interest, please email TARGETAntibiotics@phe.gov.uk

References

Flow chart for women <65 years with suspected UTI and table summary for men/women

1. G. Bonkat, R. Pickard, R. Bartoletti, T. Cai, F. Bruyère, S.E. Geerlings, B. Köves, F. Wagenlehner, A. Pilatz, B. Pradere, R. Veeratterapillay; members of the EAU Urological Infections Guidelines Panel. 2018 edition of the EAU Urological Infections Guidelines. Available from: <http://uroweb.org/guideline/urological-infections/>

RATIONALE

A review of diagnosis and management guidelines for UTIs agreed upon by the Urological Infections Guidelines Panel consisting of a group of urologists, specialised in the treatment of UTIs and male genital infections. Identifies recurrent infection as “recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least 3 UTIs/year or 2 UTIs in the last 6 months. Although rUTIs include both lower tract infection (cystitis) and upper tract infection (pyelonephritis), repeated pyelonephritis should prompt consideration of a complicated aetiology.”

The guidelines also state that acute bacterial prostatitis usually presents abruptly with voiding symptoms and distressing but poorly localised pain. It is often associated with malaise and fever. The prostate may be swollen and tender on examination, but massage should be avoided as it can induce bacteraemia and sepsis. Urine dipstick testing for nitrite and leukocytes in acute prostatitis has a positive predictive value of 95% and a negative predictive value of 70% (Etienne 2008). Blood culture and complete blood count are useful. Various imaging studies can detect a suspected prostatic abscess (Lipsky 2010).

2. Scottish Antimicrobial Prescribing Group and Scottish Medicines Consortium. Guidance on management of recurrent urinary tract infection in non-pregnant women. June 2016. Available from: www.sapg.scot/media/2913/20170509_management_of_recurrent_lower_uti_in_no_n-pregnant_women_-_2016.pdf

RATIONALE

Guidance from NHS Scotland for primary care providers on the diagnosis and treatment of recurrent UTIs. This guidance indicates that the widely-accepted definitions of ‘recurrent UTI’ in women are 3 or more episodes of UTI in 12 months or 2

or more episodes of lower UTI in 6 months. This does not include episodes of bacteriuria without UTI symptoms (asymptomatic bacteriuria).

3. National Institute for Health and Care Excellence. Antenatal Care for Uncomplicated Pregnancies. Clinical guidance. Published March 2008. Available from: www.nice.org.uk/guidance/cg62/resources/antenatal-care-for-uncomplicated-pregnancies-pdf-975564597445

RATIONALE

This is national guidance that states that women should be offered routine screening for asymptomatic bacteriuria by mid-stream urine culture early in pregnancy because identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis.

4. Nicolle LE. Asymptomatic bacteriuria. *Infectious Disease Clinics of North America*. 2003;17(2):367-94. Available from: www.sciencedirect.com/science/article/pii/S0891552003000084?via%3Dihub

RATIONALE

A review of literature related to asymptomatic bacteriuria for various at-risk groups and segments of the population. Populations with structural or functional abnormalities of the genitourinary tract may have an exceedingly high prevalence of bacteriuria, but even healthy individuals frequently have positive urine cultures. Asymptomatic bacteriuria is seldom associated with adverse outcomes, though in some cases screening and treatment is recommended. For pre-menopausal non-pregnant women, it varies from 2% to 5%. These women are at increased risk for symptomatic urinary infection and recurrent asymptomatic bacteriuria. Treatment of asymptomatic bacteriuria does not decrease the frequency of symptomatic infection. Asymptomatic bacteriuria in these women is not associated with any long-term adverse outcomes. Screening for and treatment of asymptomatic bacteriuria are not recommended for healthy young women.

For young healthy adult men, asymptomatic bacteriuria is uncommon (Lipsky 1989). The author cites a study that found 0% in Japanese men under the age of 50 (Freedman 1965). One study reported a prevalence of 1.5% in 405 men aged 20 to 70 years attending a genitourinary outpatient clinic in London. On careful questioning, however, all men with bacteriuria had symptoms of dysuria (Wilson 1986). The author concludes that asymptomatic bacteriuria is not a relevant clinical issue in young healthy men, and screening for asymptomatic bacteriuria is not appropriate.

5. Giesen, L. G. et al. Predicting acute uncomplicated urinary tract infection in women: a systematic review of the diagnostic accuracy of symptoms and signs. *BMC Family Practice*. 2010;11(78). Available from: www.ncbi.nlm.nih.gov/pubmed/20969801

RATIONALE

Systematic review to determine the diagnostic accuracy of symptoms and signs in women presenting with suspected UTI. The review also examined the diagnostic value of individual symptoms and signs combined with dipstick test results in terms of clinical decision making. The authors conclude that individual symptoms and signs only have a modest ability to raise the pre-test-risk of UTI. Diagnostic accuracy improves considerably when combined with dipstick tests, particularly tests for nitrites. This supports the use in this flowchart of a stepwise approach, using symptoms initially, moving on to urine dipsticks if there are fewer discriminatory symptoms and signs.

In the review: 16 studies incorporating 3,711 patients are included. Six symptoms are identified as useful diagnostic symptoms when a threshold of $\geq 10^2$ CFU/mL is the reference standard. Presence of dysuria (+LR 1.30 95% CI 1.20-1.41), frequency (+LR 1.10 95% CI 1.04-1.16), haematuria (+LR 1.72 95%CI 1.30-2.27), nocturia (+LR 1.30 95% CI 1.08-1.56) and urgency (+LR 1.22 95% CI 1.11-1.34) all increase the probability of UTI. The presence of vaginal discharge combined with a negative result for combined nitrites and leucocyte-esterase dipstick test reduces the post-test probability further to 15%. Presence of haematuria has the highest diagnostic utility, raising the post-test probability of UTI to 75.8% at $\geq 10^2$ CFU/mL and 67.4% at $\geq 10^3$ CFU/ml. Subgroup analysis shows improved diagnostic accuracy using lower reference standards $\geq 10^2$ CFU/mL and $\geq 10^3$ CFU/ml. The presence of vaginal discharge decreases the probability of a UTI.

6. Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002 May;287(20):2701-2710. Available from: www.ncbi.nlm.nih.gov/pubmed/12020306

RATIONALE

A systematic review of diagnostic studies, aiming to review the accuracy and precision of history taking and physical examination for the diagnosis of UTI in women. Results indicated that the presence of vaginal discharge or vaginal irritation substantially reduced the probability of UTI to around 20%. Vaginal infections and sexually transmitted diseases such as Chlamydia and Gonorrhoea can mimic the symptoms of a UTI but should be considered separately. This review also identifies symptoms of pyelonephritis as: fever; back pain; nausea; vomiting.

7. Michaels T, Sands J. Dysuria: Evaluation and Differential Diagnosis in Adults. *American Family Physician*. 2015;92(9). Available from: www.ncbi.nlm.nih.gov/pubmed/26554471

RATIONALE

A review of evidence-based approaches for the evaluation of adult patients with dysuria. The authors state that the most common cause of acute dysuria is infection, especially cystitis. Other infectious causes include urethritis, sexually transmitted infections, and vaginitis. Non-infectious inflammatory causes include a foreign body in the urinary tract and dermatologic conditions. Non-inflammatory causes of dysuria include medication use, urethral anatomic abnormalities, local trauma, and interstitial cystitis/bladder pain syndrome. An initial targeted history includes features of a local cause (for example, vaginal or urethral irritation), risk factors for a complicated urinary tract infection (for example, men, pregnancy, presence of urologic obstruction, recent procedure), and symptoms of pyelonephritis.

Often the most relevant findings on physical examination are sex-specific, including inspecting for infectious or atrophic vaginitis and STIs in women, and prostatitis and STIs in men. Women with vulvovaginal symptoms should be evaluated for vaginitis. Urethritis should be suspected in younger, sexually active patients with dysuria and pyuria without bacteriuria; in men, urethral inflammation and discharge is typically present. In patients with suspected urethritis, a urethral, vaginal, endocervical, or urine nucleic acid amplification test for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is indicated. Any complicating features or recurrent symptoms warrant a history, physical examination, urinalysis, and urine culture. Findings from the secondary evaluation, selected laboratory tests, and directed imaging studies enable physicians to progress through a logical evaluation and determine the cause of dysuria or make an appropriate referral.

8. Portman DJ, Gass ML. Vulvovaginal Atrophy Terminology Consensus Conference P. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas*. 2014;79(3):349-54.
Available from: www.ncbi.nlm.nih.gov/pubmed/25179577

RATIONALE

Consensus report from 2012. The Board of Directors of the International Society for the Study of Women's Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) acknowledged the need to review current terminology associated with genitourinary tract symptoms related to menopause. To do this, they co-sponsored a terminology consensus conference, which was held in May 2013 and agreed that the term genitourinary syndrome of menopause (GSM) is a more medically accurate, all-encompassing, and more publicly acceptable term than vulvovaginal atrophy.

Symptoms of GSM are associated with a decrease in oestrogen and other sex steroids involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra and bladder. The syndrome may include but is not limited to genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, discomfort or pain, and impaired function; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all of the signs and symptoms. The term was presented and discussed at the annual meeting of each society. GSM is commonly used as a term to cover both atrophic vaginitis and vaginal atrophy in more recent references found during the review for the UTI diagnostic quick reference tool.

9. Palma F, Volpe A, Villa P, Cagnacci A, Writing group of As. Vaginal atrophy of women in post-menopause. Results from a multicentric observational study: The AGATA study. *Maturitas*. 2016;83:40-4. Available from: www.ncbi.nlm.nih.gov/pubmed/26421474

RATIONALE

This multi-centric study was performed in order to provide nationwide data on the prevalence and management of genitourinary signs of menopause (GSM) conducted by the Atrophy of the vaGina in womAn in posT-menopause in itAly (AGATA) group – 913 females, 59.3 ± 7.4 years old asking for a routine gynaecological examination were recruited. Diagnosis of GSM was based on patient sensation of vaginal dryness, any objective sign of vulvar vaginal atrophy and a pH > 5. 722/913 (79.1%) women were diagnosed with GSM with a prevalence ranging from 64.7% to 84.2%, starting from 1 to 6 years after menopause. Recent vaginal infection was more likely in women with GSM (OR 2.48, 95% CI: 1.33-4.62; p = 0.0041).

Symptoms reported by women with GSM were vaginal dryness (100%), dyspareunia (77.6%), burning (56.9%), itching (56.6%) and dysuria (36.1%). Signs detected by gynaecologists were mucosal dryness (99%), thinning of vaginal rugae (92.1%), pallor of the mucosa (90.7%), mucosal fragility (71.9%) and petechiae (46.7%). Only 274 (30%) of women had had a previous diagnosis of vaginal atrophy/GSM. These were treated either with no therapy (9.8%), systemic hormone (9.2%), local hormone (44.5%) or local non-hormonal (36.5%) therapy, and at the time of investigation 266 of them (97.1%) still had the disorder. GSM is a common, under-diagnosed and under-treated disorder. Measures to improve its early detection and its appropriate management are needed.

10. Royal Collage of General Practitioners. Sepsis toolkit. Accessed July 2018. Available from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/sepsis-toolkit.aspx

RATIONALE

The Royal Collage of General Practitioners is a professional membership body for GPs in the UK, with the purpose of encouraging, fostering and maintaining the highest possible standards in medical practice. The clinical toolkits on their website have been developed in partnership between the RCGP Clinical Innovation, Research Centre (CIRC) and other funding and delivery partners. The resources have been created for primary healthcare professionals, patients and carers. These toolkits can be used to assist in the delivery of safe and effective care to patients. The Sepsis toolkit provides a collection of tools, knowledge, and current guidance to support the identifying and appropriate management of patients with sepsis. The toolkit is aimed at GPs and healthcare professionals assessing people in the community with acute infection. The resources also include information for patients and those close to them to look for when concerned about a sudden deterioration in a person's health in the presence of infection.

11. National Institute of Health and Care Excellence (NICE). Sepsis: Recognition, diagnosis and early management. 2016 Jul. Available from:
www.nice.org.uk/guidance/ng51/resources/sepsis-recognition-diagnosis-and-early-management-1837508256709

RATIONALE

A NICE guideline, stating that people with sepsis may have non-specific, non-localised presentations, such as feeling generally unwell without a high temperature of over 38°C. This guideline presents a risk stratification tool for adults, children and young people aged 12 years and over with suspected sepsis. Where high temperature is recognised as a cause for concern, this guideline also lists a tympanic temperature of less than 36°C as a moderate to high risk criteria for sepsis. Symptoms that indicate someone is at a moderate risk of having sepsis include: history of new-onset changed behaviour or change in mental state, as reported by:

- the person, a friend or relative
- history of acute deterioration of functional ability
- impaired immune system (illness or drugs, including oral steroids) trauma
- surgery or invasive procedure in the past 6 weeks
- respiratory rate of 21 to 24 breaths per minute
- heart rate of 91 to 130 beats per minute or new-onset arrhythmia, or if pregnant heart rate of 100 to 130 beats per minute
- systolic blood pressure of 91 to 100 mmHg
- not passed urine in the past 12 to 18 hours (for catheterised patients, passed 0.5-1 mL/ kg/hour)
- tympanic temperature less than 36°C

- signs of potential infection, including increased redness, swelling or discharge at a surgical site, or breakdown of a wound

The document also provides guidance on considerations for treatment.

For an algorithm endorsed for use with this guidance, please use the following link:
<https://www.nice.org.uk/guidance/ng51/resources/algorithm-for-managing-suspected-sepsis-in-adults-and-young-people-aged-18-years-and-over-outside-an-acute-hospital-setting-pdf-2551485716>

12. Royal College of Physicians. National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. Updated report of a working party. London: RCP, 2017 Available from:
www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2

RATIONALE

The Royal College of Physicians (RCP) has led the development of a new National Early Warning Score (NEWS) report, which advocates standardising the use of a NEWS system across the NHS in order to drive the 'step change' required in the assessment and response to acute illness. The report was recently updated (NEWS2). Whilst the tool has not been validated in primary care, some authorities are looking to adapt it for use in this area, allowing it to aid the communication of assessment and response across multiple providers.

The report also states that subgroups of patients who are more likely to be at risk of sepsis include patients:

- who have recently had surgery or those with burns, blisters or cuts to the skin
- who are immunocompromised, including those receiving cancer chemotherapy, immunosuppressive biologics and long-term steroids
- post-splenectomy
- with indwelling cannulas or catheters

Feedback from a subgroup of the Cross-System Sepsis Programme board including both National Clinical Advisors for Sepsis, the National Medical Director's Clinical Fellow and Programme Leads also indicated that there is increased risk for younger women who are pregnant or postpartum and those who have had recent antibiotics or are currently on antibiotics. The NEWS is based on a simple aggregate scoring system in which a score is allocated to physiological measurements, already recorded in routine practice, when patients present to, or are being monitored in hospital.

Six simple physiological parameters form the basis of the scoring system:

- respiration rate
- oxygen saturation
- systolic blood pressure
- pulse rate
- level of consciousness
- new confusion, temperature

Allowance is also made for individuals with respiratory problems who are on oxygen. Thresholds and triggers indicate that a score of 0 to 4 (low clinical risk) should include a ward based response; a score of 3 (low-medium clinical risk) in any individual parameter should indicate an urgent ward based response; an aggregate NEW score of 5 to 6 is a key threshold that should trigger an urgent clinical review/response; a NEW score of 7 or more should trigger a high-level clinical alert that is an emergency clinical review.

13. National Institute for Health and Care Excellence. Pyelonephritis (acute): antimicrobial prescribing. Nice guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng111

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for acute pyelonephritis (upper urinary tract infection). It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The recommendations state that advice should be given on self-care to all those with expected pyelonephritis. Mid-stream urine specimens should be sent.

Advice is given on antibiotic choice and administration and to reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of:

- other possible diagnoses
- any symptoms or signs suggesting a more serious illness or condition, (such as sepsis)
- previous antibiotic use, which may have led to resistant bacteria

Admission should be considered in those aged 16 years and over with acute pyelonephritis if they are significantly dehydrated or unable to take oral fluids and medicines, or are pregnant, or have a higher risk of developing complications. Self-care advice includes the use of paracetamol for pain relief and drinking enough fluids to avoid dehydration.

14. Little, P., et al. Validating the prediction of lower urinary tract infection in primary care: sensitivity and specificity of urinary dipsticks and clinical scores in women. *Br J Gen Pract.* 2010; 60(576): 495-500. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC2894378/

RATIONALE

A validation study to determine the value of using urinary symptoms and signs and urine dipsticks for diagnosis of confirmed UTI. The study individuals included 434 women with at least 2 urinary symptoms of UTI and no vaginal discharge from across 62 different practices in England. Clinical symptoms and dipstick results were assessed against laboratory cultures. 66% of women had a confirmed UTI. No symptoms or signs or combination was able to confirm UTI with absolute certainty. The negative predictive value when nitrite, leukocytes, and blood are all negative was 76%. The positive predictive value for having nitrite and either blood or leukocytes was 92%.

When clinical variables were examined, the positive predictive value was 82% for women with all 3 of cloudy urine, dysuria of any degree, and new nocturia to any degree – 74% for 2, 68% for 1. The negative predictive value was 67% for none of these 3 features. The authors conclude that although dipsticks can moderately improve diagnostic precision, they are poor at ruling out infection. Clinical strategies need to take into account poor negative predictive values. Therefore, the steering group discussed and agreed that a strategy of using a combination of clinical score and urine dipstick will optimise correct use of antibiotics. As at least 74% with 2 of dysuria, cloudy urine or nocturia will have a proven UTI, it is reasonable to prescribe empirically in these patients. In patients with only 1 of dysuria, cloudy urine or nocturia, or none of these symptoms but they have other severe urinary symptoms a urine dipstick will help determine who should be given empirical antibiotics: if nitrite is positive or both WBC and RBC are positive, UTI is likely, if nitrite is negative and WBC positive only half will have UTI, if all dipstick results are negative, UTI is much less likely. Depending on the likelihood of UTI and severity of symptoms, then an immediate or back-up or no antibiotic strategy can be discussed with the patient.

15. Medina-Bombardó D, Seguí-Díaz M, Roca-Fusalbac C, Lloberad J, the dysuria team. What is the predictive value of urinary symptoms for diagnosing urinary tract infection in women? *Family Practice.* 2003;20(2):103-7. Available from: www.ncbi.nlm.nih.gov/pubmed/12651780

RATIONALE

An epidemiological analysis with a diagnostic and clinical orientation was carried out in a primary health care setting. The subjects comprised 343 women 14 years of age or older who consulted their family physician for incident urinary tract symptoms. A guided medical

examination was carried out using a check-list formulary, reactive strip test, urine culture and the clinical course of all patients. The pre-test probability of having UTI among patients with incident urinary symptoms is 0.484 [95% confidence interval (CI) 0.431–0.536]. Positive LR_s for UTI are: painful voiding 1.31 (95% CI 1.12–1.54), urgency 1.29 (95% CI 1.12–1.50), urinary frequency 1.16 (95% CI 1.06–1.28) and tenesmus 1.16 (95% CI 1.02–1.32). The probability of UTI is reduced by the presence of genital discomfort, dyspareunia, vaginal discharge, positive lumbar fist percussion and perineal discomfort. Nitrites on the urine reactive strip test increase the probability of UTI. In women with urinary symptoms, a thorough clinical examination, together with performance of a reactive strip test during the office visit, improves the chances of detecting UTI.

16. McIsaac WJ, Moineddin R, Ross S. Validation of a Decision Aid to Assist Physicians in Reducing Unnecessary Antibiotic Drug Use for Acute Cystitis. *Archives of internal medicine*. 2007;167(20):2201-6. Available from:
www.ncbi.nlm.nih.gov/pubmed/17998492

RATIONALE

Between 2002 and 2003, general practitioners recorded clinical findings, dipstick results and treatment decisions (based on a decision aid) for 331 women with suspected UTI. The decision aid took into account 4 diagnostic criteria:

- the presence of burning or pain on urination
- symptoms present for 1 day
- the presence of leukocytes (greater than a trace amount)
- and the presence of nitrites (any positive, including trace amounts)

Total antibiotic prescriptions, unnecessary prescriptions and recommendations for urine culture results were determined and compared with management. Three of the original decision aid variables (dysuria, the presence of leukocytes [greater than a trace amount], and the presence of nitrites [any positive]) were associated with having a positive urine culture result, but 1 variable (symptoms for 1 day) was not.

A simplified decision aid incorporating the 3 significant variables had a sensitivity of 80.3% (167/208) and a specificity of 53.7% (66/123). Following decision aid recommendations would have reduced antibiotic prescriptions by 23.5%, unnecessary prescriptions by 40.2%, and urine cultures by 59% compared with physician care. The authors conclude that a simple 3-item decision aid could significantly reduce unnecessary antibiotic drug prescriptions and urine culture testing in females with symptoms of acute cystitis. This study shows the importance of using decision aids when looking to improve antibiotic prescribing.

17. McNulty CA, Richards J, Livermore DM, Little P, Charlett A, Freeman E, et al. Clinical relevance of laboratory-reported antibiotic resistance in acute

uncomplicated urinary tract infection in primary care. *J Antimicrob Chemother.* 2006;58(5):1000-8. Available from: www.ncbi.nlm.nih.gov/pubmed/16998209

RATIONALE

Prospective cohort study of clinical outcome. Included 497 women (18–70 years) presenting to general practitioner surgeries in Norwich and Gloucester with at least 2 symptoms of acute uncomplicated UTI (defined as 10^4 cfu/mL from a mid-stream urine (MSU)). 75% of those enrolled had significant bacteriuria. Half of patients re-consulting in the first week had a resistant organism. Patients with uncomplicated UTI caused by trimethoprim-resistant organisms had significantly worse clinical outcomes than those with trimethoprim-susceptible organisms. Authors discuss treatment options based on findings. Of the women who presented with a UTI, 67% reported abdominal pain as a symptom.

18. National Institute for Health and Care Excellence. Urinary tract infection (lower): antimicrobial prescribing. Nice guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng109

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for lower urinary tract infection. It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The recommendations state that advice should be given on self-care to all those with expected a lower UTI. This includes paracetamol for pain, adequate intake of fluids, and no evidence was found on cranberry products to treat a lower UTI.

Obtain a mid-stream urine sample before prescribing antibiotics for pregnant women and men with lower UTI and send for culture and susceptibility testing. This should happen before antibiotics are taken. Consider a back-up antibiotic prescription or an immediate antibiotic prescription for women with lower UTI who are not pregnant. Take account of:

- the severity of symptoms
- the risk of developing complications
- previous urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria
- preferences of the woman for antibiotic use.

If a urine sample has been sent for culture and susceptibility testing and an antibiotic prescription has been given: review the choice of antibiotic when microbiological results are available, and change the antibiotic according to susceptibility results if bacteria are

resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible.

19. Kronenberg A, Butikofer L, Odutayo A, et al. Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial. *BMJ*. 2017;359:j4784. Available from: www.ncbi.nlm.nih.gov/pubmed/29113968

RATIONALE

PHE decided to not include Ibuprofen alone without a back-up antibiotic prescription as a recommended self-care treatment for older adults with UTI, due to the increased risk of pyelonephritis in this study with non-steroidal anti-inflammatory drugs (NSAIDs). However, there may be a place for the use of NSAIDs for pain relief with antibiotics, but more studies are needed to establish any risks from this. This study is a randomised, double blind, non-inferiority trial in 17 general practices in Switzerland. 253 women with uncomplicated lower UTI were randomly assigned 1:1 to symptomatic treatment with the NSAID diclofenac (n=133) or antibiotic treatment with norfloxacin (n=120). The primary outcome was resolution of symptoms at day 3 (72 hours after randomisation and 12 hours after intake of the last study drug). The pre-specified principal secondary outcome was the use of any antibiotic (including norfloxacin and fosfomycin as trial drugs) up to day 30. Analysis was by intention to treat. Six women in the diclofenac group (5%) but none in the norfloxacin group received a clinical diagnosis of pyelonephritis (P=0.03). Diclofenac is inferior to norfloxacin for symptom relief of UTI and is likely to be associated with an increased risk of pyelonephritis, even though it reduces antibiotic use in women with uncomplicated lower UTI. This study did not offer a back-up / delayed antibiotic with the NSAID or pain relief; giving a back-up antibiotic prescription, allows patients to have control of their symptoms.

20. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, et al. Effectiveness of 5 different approaches in management of urinary tract infection: randomised controlled trial. *BMJ*. 2010;340:c199. Available from: www.ncbi.nlm.nih.gov/pubmed/20139214

RATIONALE

Randomised controlled trial to assess the impact of different management strategies in urinary tract infections in primary care. The study included 309 non-pregnant women aged 18 to 70 presenting with suspected urinary tract infection who were randomised to 5 management approaches:

- empirical antibiotics
- empirical delayed (by 48 hours) antibiotics

- targeted antibiotics based on a symptom score (2 or more of urine cloudiness, urine smell, nocturia, or dysuria)
- a dipstick result (nitrite or both leucocytes and blood)
- a positive result on mid-stream urine analysis

Self-help advice was controlled in each group. The outcomes of symptom severity (days 2 to 4) and duration, and use of antibiotics were assessed. Patients had three-and-a-half days of moderately bad symptoms if they took antibiotics immediately. There were no significant differences in duration or severity of symptoms. There were differences in antibiotic use (immediate antibiotics 97%, mid-stream urine 81%, dipstick 80%, symptom score 90%, delayed antibiotics 77%; $P=0.011$) and in sending mid-stream urine samples (immediate antibiotics 23%, mid-stream urine 89%, dipstick 36%, symptom score 33%, delayed antibiotics 15%; $P<0.001$).

Patients who waited at least 48 hours to start taking antibiotics re-consulted less (hazard ratio 0.57 (95% confidence interval 0.36 to 0.89), $P=0.014$) but on average had symptoms for 37% longer than those taking immediate antibiotics (incident rate ratio 1.37 (1.11 to 1.68), $P=0.003$), particularly the mid-stream urine group (73% longer, 22% to 140%; none of the other groups had more than 22% longer duration). The authors concluded that all management strategies achieve similar symptom control. There is no advantage in routinely sending mid-stream urine samples for testing, and antibiotics targeted with dipstick tests with a delayed prescription as backup, or empirical delayed prescription, can help to reduce antibiotic use.

21. Colgan R, Williams M. Diagnosis and Treatment of Acute Pyelonephritis in Women. *American Academy of Family Physicians*. 2011;84(5). Available from: www.aafp.org/afp/2011/0901/p519.pdf

RATIONALE

A review of the evidence for diagnosis and treatment of acute pyelonephritis in women. Authors state that history and physical examination are the most useful tools for diagnosis. Most patients have fever, although it may be absent early in the illness. Flank pain is nearly universal, and its absence should raise suspicion of an alternative diagnosis. The authors also list tachycardia, hypotension, possible abdominal or suprapubic tenderness, constitutional symptoms (for example fever, chills, malaise) and gastrointestinal symptoms (for example nausea, vomiting, anorexia, abdominal pain) as possible signs/symptoms. A positive urinalysis confirms the diagnosis in patients with a compatible history and physical examination. Urine culture should be obtained in all patients to guide antibiotic therapy if the patient does not respond to initial empiric antibiotic regimens. Outpatient treatment is appropriate for most patients. Inpatient therapy is recommended for patients who have severe illness or in whom a complication is suspected.

22. Coker TJ, Dierfeldt D. Acute Bacterial Prostatitis: Diagnosis and Management. *Am Fam Physician*. 2016;93(2):114-120. Available from: www.aafp.org/afp/2016/0115/p114.pdf

RATIONALE

A review to highlight advances in research on UTI and bacterial prostatitis in men. Patients often present with acute onset of irritative (for example dysuria, urinary frequency, urinary urgency) or obstructive (for example hesitancy, incomplete voiding, straining to urinate, weak stream) voiding symptoms. Suprapubic, rectal, or perineal pain, painful ejaculation, hematospermia, and painful defecation may be present as well. Systemic symptoms, such as fever, chills, nausea, emesis, and malaise, commonly occur and should indicate the need to consider sepsis. The condition is most frequently caused by *Escherichia coli*, followed by *Pseudomonas aeruginosa*, and *Klebsiella*, *Enterococcus*, *Enterobacter*, *Proteus*, and *Serratia* species.

In sexually active men, *Neisseria gonorrhoeae* and *Chlamydia trachomatis* should be considered. The physical examination should include abdominal, genital, and digital rectal examination to assess for a tender, enlarged, or boggy prostate. Diagnosis is predominantly made based on history and physical examination, but may be aided by urinalysis. Management of acute bacterial prostatitis should be based on severity of symptoms, risk factors, and local antibiotic resistance patterns. Urine cultures should be obtained in all patients who are suspected of having acute bacterial prostatitis to determine the responsible bacteria and its antibiotic sensitivity pattern.

23. National Institute for Health and Care Excellence. Acute prostatitis: antimicrobial prescribing - evidence review. Nice guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng110

RATIONALE

This guideline sets out an antimicrobial prescribing strategy for acute bacterial prostatitis. It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The evidence review for the prostatitis guidelines summarizes some of the more recent evidence around the diagnosis of prostatitis. It cites evidence from the NICE CKS 2014 prostatitis guidelines, the BASH 2001 National guidelines on the management of prostatitis, and RCGP/BASHH 2013 Sexually transmitted infections in primary care. Signs/symptoms include: feverish illness of sudden onset, low back pain, suprapubic pain, and perineal, penile or sometimes rectal pain, symptoms of urinary tract infection

including dysuria, frequency, or urgency, or acute urinary retention, or exquisitely tender prostate on rectal examination.

Diagnostics for acute bacterial prostatitis include a mid-stream urine sample for dipstick testing, then culture for bacteria and antibiotic sensitivity. The review cites a study from 2008 suggesting that urine dipstick testing (for nitrites and leukocytes) in acute prostatitis has a positive predictive value of approximately 95%, but a negative predictive value of approximately 70%. Therefore, other conditions with similar presentations should also be considered when making a diagnosis of acute prostatitis. It is recommended not to collect prostatic secretions because prostatic massage could lead to septicaemia or a prostatic abscess, and may be very painful. Prostatic secretions are not needed for the diagnosis because infection is confirmed with urine culture.

24. Wagenlehner FM, Weidner W, Pilatz A, Naber KG. Urinary tract infections and bacterial prostatitis in men. *Curr Opin Infect Dis.* 2014;27(1):97-101. Available from: www.ncbi.nlm.nih.gov/pubmed/24253463

RATIONALE

A review with the aim of highlighting advances in research on UTIs in men over the previous year. Pub Med was searched according to Boolean principles looking for clinical trials published in 2012 to 2013 focusing on UTI and prostatitis in men. Findings included that most men with a febrile UTI and without signs of pyelonephritis show an involvement of the prostate. They also noted that there is a significant increase of antibiotic resistance complicating the clinical management of UTI and bacterial prostatitis in men. We need to develop novel strategies to combat this problem.

25. Ulleryd P. Febrile urinary tract infection in men. *International journal of antimicrobial agents.* 2003;22:89-93. Available from: [www.ijaaonline.com/article/S0924-8579\(03\)00228-0/pdf](http://www.ijaaonline.com/article/S0924-8579(03)00228-0/pdf)

RATIONALE

A multidisciplinary project, where infectious disease specialists, urologists and microbiologists studied the host/parasite interaction in men from Gothenburg, Sweden with community-acquired febrile UTI. They define a febrile UTI in men as a fever $\geq 38.0^{\circ}\text{C}$ and at least 1 symptom or sign referable to the urinary tract (frequency, dysuria, flank pain or costovertebral angle tenderness).

It is unknown to what extent the prostate is co-infected in men with UTI. A prospective study of 70 men with febrile UTI detected prostatic involvement as measured by transient increases in serum prostate-specific antigen and/ or the prostate volume in more than 90% of the patients (Ulleryd 1999). Men with fever and infection within the

urinary tract have similar findings of prostatic involvement, irrespective of prostatic tenderness. This indicates that infection is solely or also taking place within the prostate itself, unrelated to a preliminary diagnosis of acute pyelonephritis or acute prostatitis. Febrile UTI may merely be seen as a continuum between these 2 poles. The specialist discussed the findings in the light of other similar studies and related to findings in women. They found that men and women with febrile UTI have very similar infecting bacterial species, host predispositions and treatment results. Virulence expression differs in the infecting *Escherichia coli* in both sexes, besides the overt anatomical distinction including having a prostate.

26. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. 2012 Jul. Available from: www.sign.ac.uk/assets/sign88.pdf

RATIONALE

A SIGN guideline, providing advice on how to manage suspected bacterial urinary tract infections in patient groups including adult men. The authors state that there is no good evidence to suggest the best method of diagnosing bacterial UTI in men as evidence from studies that focus on women can't be extrapolated. Consensus concludes that a urine culture should be sent for all men who present with a suspected UTI. Obtaining a clean-catch sample of urine in men is easier than in women and a colony count of $\geq 10^3$ cfu/mL may be sufficient to diagnose UTI in a man with signs and symptoms as long as 80% of the growth is of 1 organism (Lipsky 1987). The guidance also states that you should refer men for urological investigation if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI.

27. Ulleryd P, Zackrisson B, Aus G, Bergdahl S, Huggosson J, and Sandberg T. Selective urological evaluation in men with febrile urinary tract infection. *BJU Int.* 2001;88:15-20. Available from: www.ncbi.nlm.nih.gov/pubmed/11446838

RATIONALE

A prospective study to investigate the prevalence and clinical importance of urological abnormalities in men with community-acquired febrile urinary tract infection (UTI). The authors assessed 85 men (median age 63 years, range 18 to 86) for 1 year after an episode of febrile UTI. They were investigated by excretory urography, cysto-urethroscopy, uroflowmetry, digital rectal examination and measurement of post-void residual urine volume by abdominal ultrasonography. The lower urinary tract investigation disclosed 46 findings in 35 men. In all, surgically correctable disorders were found in 20 patients, of whom 15 had previously unrecognised abnormalities.

All patients who required surgery were identified either by a history of voiding difficulties, acute urinary retention at the time of infection, the presence of microscopic haematuria at follow-up after 1 month, or early recurrent symptomatic UTI. Routine imaging studies of the upper urinary tract seem dispensable in men with febrile UTI. To reveal abnormalities of clinical importance, any urological evaluation should primarily be focused on the lower urinary tract.

28. Koeijers JJ, Kessels AG, Nys S, Bartelds A, Donker G, Stobberingh EE, et al. Evaluation of the nitrite and leukocyte esterase activity tests for the diagnosis of acute symptomatic urinary tract infection in men. *Clin Infect Dis.* 2007;45(7):894-6. Available from: www.ncbi.nlm.nih.gov/pubmed/17806056

RATIONALE

This prospective study assessed 422 male patients with symptoms indicative of a urinary tract infection. Nitrite and leukocyte esterase activity dipstick test results were compared with results of culture of urine samples ($\geq 10^3$ CFU/mL considered a positive culture). The mean age was 57 years. Two-hundred-and-thirty-six men (56%) had a positive urine culture result. The study was limited by the fact that, for 45 patients (12%), no nitrite and/or leucocyte test results could be obtained. The missing nitrite and leucocyte test data may be secondary to the fact that, according to the general practitioner guidelines in the Netherlands, the leucocyte test should not be performed when results of the nitrite test are positive.

Findings indicated that for all patients for whom both the nitrite test and the leucocyte test were performed, the sensitivity of the nitrite test was 47%, and the specificity was 98%. The sensitivity of the leucocyte test was 78%, and the specificity was 59%. When these parameters were calculated for all patients who underwent either test, the values changed only marginally. The positive predictive value of a positive nitrite test result was 96%. In the instance of a negative nitrite test result, the probability of disease was 41% – the addition of a negative leucocyte test result decreased this probability to 27%, and a positive result increased it to 55%. The authors conclude that for this group a positive nitrite test result should be considered to be indicative of a UTI, and the patient should be treated empirically, pending culture results. However, when the nitrite test yields negative results, a UTI cannot be excluded, and urine samples should be further investigated by culture, without start of empirical therapy.

Flowchart and table summary for men/women >65 years with suspected UTI

1. Arinzon Z, Shabat S, Peisakh A, Berner Y. Clinical presentation of urinary tract infection (UTI) differs with aging in women. *Archives of Gerontology and Geriatrics*. 2011 Oct; 55(2012:) 145–147. Available from:
www.sciencedirect.com/science/article/pii/S0167494311002202?via%3Dihub

RATIONALE

An observational study of women over the age of 45 from a community clinic with confirmed UTI. Women who presented with urinary symptoms were divided into 2 age groups (45 to 54 years, n = 102, mean age 48.14 years and over 65 years n = 94, mean age 69.2one years). Those with a confirmed UTI ($>10^3$ cfu/mL of an uropathogen in mid-stream urine culture) were asked questions related to demographics, behaviours, medical history and symptoms. There was a positive correlation between being older and reporting urine urgency, painful voiding (dysuria), incontinence, low back-pain, and lower abdominal pain. Frequency, painful and burning urination and bladder pain was reported less with the older age group (though still reported). Older women reported more generalised unspecific symptoms (lower abdominal pain, lower back pain, chills, constipation, and diarrhoea) and incontinence issues.

The study indicates that clinical presentation of UTI in older and younger (study specified pre-and post-menopausal) women is slightly different. The differences are presented not only by the voiding itself and by local symptoms but also by unspecified generalised symptoms that is especially important in older patients. Symptoms were grouped as voiding-related symptoms, local constant symptoms, and generalised symptoms. Local symptoms were predominated followed by voiding and generalised symptoms. In post-menopausal women, predominant symptoms were storage and generalised unspecific symptoms. This study shows that unspecified symptoms such as complaints on low abdomen pain, low-back pain, constipation, cold chills and nausea significantly correlated with age. UTI may itself cause incontinence symptoms (Ouslander, 1992). Menopause itself is a risk factor for incontinence (Rekers 1992a) and it is not surprising that urinary symptoms of urgency, nocturia and incontinence are more common in post-menopausal women.

2. Loeb M, Brazil K, Lohfeld L, McGeer A, Simor A, Stevenson K et al. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: a cluster randomised controlled trial. *BMJ*. 2005 Sep; 331(7518):669. Available from:
www.ncbi.nlm.nih.gov/pmc/articles/PMC1226247/

RATIONALE

A cluster randomised controlled trial in 24 nursing homes in Ontario, Canada, and Idaho, United States, with 12 allocated to a multifaceted intervention, and 12 allocated to usual care. A diagnostic and treatment algorithm was implemented in the multifaceted intervention, suggesting that urine cultures should be ordered if there is a fever of over 37.9°C, or a 1.5°C increase above baseline on at least 2 occasions over the previous 12 hours, and 1 or more of the following:

- dysuria
- urinary catheter
- urgency
- flank pain
- shaking chills
- urinary incontinence
- frequency
- gross haematuria
- suprapubic pain

If there is no fever at onset, a culture should be ordered if there is dysuria or 2 or more of:

- urgency
- flank pain
- shaking chills
- incontinence
- frequency
- haematuria
- suprapubic pain (if urinary catheter 1 or more of: rigors, delirium, or costovertebral tenderness)

If the culture is positive or pending, antibiotics were recommended in those without a urinary catheter if there was 2 or more of:

- fever
- urgency
- flank pain
- incontinence
- rigors
- frequency
- haematuria
- suprapubic pain

If urinary catheter – 1 or more of:

- costovertebral tenderness
- rigors
- new delirium
- fever

Antibiotics should only be prescribed in cases of systemic symptoms of infection with an in-situ catheter. Fewer courses of antimicrobials were prescribed in the intervention nursing homes than in the usual care homes (weighted mean difference -0.49; 95% CI -0.93 to -0.06). This algorithm is widely used and is a generally accepted tool for diagnosing and treating UTI in older adult care home settings.

3. Loeb M, Bentley DW, Bradley S, Crossley K, Garibaldi R, Gantz N et al. Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. *Infect Control Hosp Epidemiol.* 2001 Feb; 22(2):120-124. Available from: www.ncbi.nlm.nih.gov/pubmed/11232875

RATIONALE

This article describes the establishment of minimum criteria for the initiation of antibiotics in residents of long-term care facilities (LTCFs). Experts in this area were invited to participate in a consensus conference. Using a modified delphi approach, a questionnaire and selected relevant articles were sent to participants who were asked to rank individual signs and symptoms with respect to their relative importance. Using the results of the weighting by participants, a modification of the nominal group process was used to achieve consensus.

Urinary tract infections: for residents who do not have an indwelling catheter, minimum criteria for initiating antibiotics included acute dysuria alone or fever (over 37.9°C [100°F] or 1.5°C [2.4°F] increase above baseline temperature) and at least 1 of the following:

- new or worsening urgency
- frequency
- suprapubic pain
- gross haematuria
- costovertebral angle tenderness
- urinary incontinence

For residents who have a chronic indwelling catheter (either an indwelling Foley catheter or a suprapubic catheter), minimum criteria for initiating antibiotics include the presence of at least 1 of the following:

- fever (over 37.9°C [100°F] or 1.5°C [2.4°F] increase above baseline temperature)
- new costovertebral tenderness
- rigors (shaking chills) with or without identified cause
- new onset of delirium

Skin and soft-tissue infections: minimum criteria for initiating antibiotic therapy for a suspected skin or soft-tissue infection in a resident of an LTCF include either new or increasing purulent drainage at a wound, skin, or soft-tissue site – or at least 2 of:

- fever (temperature over 37.9°C [100°F] or an increase of 1.5°C [2.4°F] above baseline temperatures taken at any site)
- redness
- tenderness
- warmth
- swelling that was new or increasing at the affected site

Respiratory infections: if the resident is febrile with a temperature over 38.9°C [102°F], 24 minimum criteria for initiating antibiotics for a suspected lower respiratory infection include at least 1 of the following: respiratory rate of over 25 breaths per minute or productive cough.

4. Berman P, Hogan DB, Fox RA. The atypical presentation of infection in old age. *Age and Ageing*. 1987;16(4). Available from: www.ncbi.nlm.nih.gov/pubmed/3630842

RATIONALE

A study was designed to determine the incidence of atypical or geriatric presentation of infection in a long-term-care-hospital population of aged veterans in Canada. During the 6-month period of surveillance there were 65 instances of functional decline among the 143 veterans, with 50 episodes of infection. Although the symptoms and signs of infection were attenuated in many patients, a diagnosis was reached by careful examination and investigation. The most common infections were RTI, pneumonia then UTI, and skin/wound infections. UTI was defined by the presence of more than 100 thousand cfu/mL and 7 residents were diagnosed with a UTI. Because the residents were not able to communicate effectively, diagnosis was initiated by non-specific deterioration with confusion.

They also all exhibited a fever and had some collecting device that provided clear clinical pointers to the diagnosis. Overall, the majority of patients had a temperature of at least 38°C in the presence of infection and it is concluded that the afebrile response to infection is rare in this population. During the course of this study the death rate in this institution dropped to about half of what was anticipated, and returned to previous levels following completion of the study. Infection can be recognized at a very early stage despite an atypical geriatric presentation, and early treatment reduces morbidity and mortality.

5. Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women? *Ann Intern Med*. 1994 May;120(10):827-833. Available from: www.ncbi.nlm.nih.gov/pubmed/7818631

RATIONALE

A cohort study and a controlled clinical trial of non-catheterised older women examining the effect of antimicrobial treatment, conducted in a geriatric centre and 21 continuing care retirement communities. Urine cultures were taken every 6 months and comorbidity and mortality were monitored. Infected residents (n = 318) were older, and sicker, and had higher mortality (18.7 per 100 000 resident-days) than uninfected residents (n = 1173; 10.1 per 100 000 resident-days). However, infection was not related to mortality whereas age at entry and self-rated health were strong predictors. UTI was not an independent risk factor for mortality, and its treatment did not lower the mortality rate. Authors concluded that screening and treatment of asymptomatic bacteriuria in ambulatory elderly women to decrease mortality does not appear to be warranted. Because of this the use of urine dipsticks is not recommended in the diagnostic pathway for UTI in older adults. However, urine cultures are recommended if there is a suspected UTI in order to check for resistance.

6. Nicolle LE, Mayhew WJ, Bryan L. Prospective randomised comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalised elderly women. *Am J Med.* 1987 Jul; 83(1):27-33. Available from: www.ncbi.nlm.nih.gov/pubmed/3300325

RATIONALE

Fifty older institutionalised women with asymptomatic bacteriuria were randomly assigned either to receive therapy for treatment of all episodes of bacteriuria identified on monthly culture or to receive no therapy unless symptoms developed. Subjects were followed for 1 year. The therapy group had a mean monthly prevalence of bacteriuria 31 ± 15 percent lower than those in the no-therapy group. For residents receiving no therapy, 71% showed persistent infection with the same organism(s). Antimicrobial therapy was associated with an increased incidence of reinfection and adverse antimicrobial drug effects as well as isolation of increasingly resistant organisms in recurrent infection when compared with no therapy.

No differences in genitourinary morbidity or mortality were observed between the groups. Thus, despite a lowered prevalence of bacteriuria, no short-term benefits were identified and some harmful effects were observed with treatment of asymptomatic bacteriuria. These data support current recommendations of no therapy for asymptomatic bacteriuria in this population. Because of this the use of urine dipsticks is not recommended in the diagnostic pathway for UTI in older adults. However, urine cultures are recommended if there is a suspected UTI in order to check for resistance.

7. Tambyah PA, Maki DG. The relationship between pyuria and infection in patients with indwelling urinary catheters: a prospective study of 761 patients. *Arch Intern Med.* 2000 Mar;160(5):673-677. Available from: www.ncbi.nlm.nih.gov/pubmed/10724053

RATIONALE

A prospective study of 761 newly catheterised patients in a university hospital; 82 (10.8%) developed nosocomial CAUTI (> 10(3) colony-forming units per ml). Pyuria was most strongly associated with CAUTI caused by gram-negative bacilli (white blood cell count, 121 vs 4 per microliter; P = .03); infection with coagulase-negative staphylococci and enterococci (white blood cell count, 39 vs 4 per microliter; P = .25) or yeasts (white blood cell count, 25 vs 4 per microliter; P = .15) produced much less pyuria. Pyuria with a white blood cell count greater than 10 per microliter (>5 per high-power field in a conventional urinalysis) had a specificity of 90% for predicting CAUTI with greater than 10(5) colony-forming units per millilitre but a sensitivity of only 37%. In patients with short-term indwelling urinary catheters, pyuria is less strongly correlated with CAUTI than in non-catheterised patients with UTI. Pyuria is common in catheterised patients and it has no predictive value in this population. Dipstick testing should not, therefore, be used to diagnose UTI in catheterised patients.

8. Nicolle LE. Asymptomatic bacteriuria. *Infectious Disease Clinics of North America.* 2003;17(2):367-94. Available from: <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.379.5055&rep=rep1&type=pdf>

RATIONALE

A review of evidence specific to asymptomatic bacteriuria in different cohorts of the population and recommendations on screening and treatment for these groups. The prevalence of asymptomatic bacteriuria is common in older populations living in the community ranging from 8% to 10% in women from 70 to 80 years and increasing with age regardless of sexual activity. In men this was up to 7% in those over 70. For older adults in long-term care facilities this increases to 25% to 50% of women and 15% to 40% of men. It correlates with impaired functional status, including incontinence of urine or bowel, and dementia. Asymptomatic bacteriuria is assumed to be attributed to impaired bladder voiding secondary to chronic degenerative neurologic or cerebrovascular diseases.

For men, prostatic hypertrophy and chronic relapsing prostatic infection likely contribute, and use of an external condom catheter to manage incontinence also increases the prevalence of bacteriuria. Treatment and screening for asymptomatic bacteriuria in older adults in the community or those living in care is not indicated. Individuals with a urinary catheter in situ for more than 30 days will have universal bacteriuria. Treatment of bacteriuria in patients with a chronic indwelling catheter is not

beneficial, and may be harmful. Screening is not recommended. In selected situations, such as a potential institutional outbreak, screening of bacteriuria may be appropriate to assess the extent of spread of an organism and assist in evaluating interventions for outbreak control, rather than for patient management.

9. Bonkat, R. Pickard, R. Bartoletti, T. Cai, F. Bruyère, S.E. Geerlings, B. Köves, F. Wagenlehner, A. Pilatz, B. Pradere, R. Veeratterapillay; members of the EAU Urological Infections Guidelines Panel. 2018 edition of the EAU Urological Infections Guidelines. Available from: <http://uroweb.org/guideline/urological-infections/>

RATIONALE

A review of diagnosis and management guidelines for UTIs agreed upon by the Urological Infections Guidelines Panel consisting of a group of urologists, specialised in the treatment of UTIs and male genital infections. The authors reviewed 4 RCTs comparing antibiotic treatment of asymptomatic bacteriuria in treatment and control groups in post-menopausal women (Boscia 1987, Abrutyn 1984, Abrutyn 1996, and Nicolle 1987). Women in these studies were mostly nursing home residents. 3 RCTs reported on the rate of symptomatic UTIs (average RR 0.71, 95% CI 0.49 to 1.05 – 208 women) and the resolution of bacteriuria (average RR 1.28, 95% CI 0.50 to 3.24; 203 women) (Bailey 1983, Estebanez 2009, and Lumbiganon 2009). There was no significant benefit of antibiotic treatment. The group does not recommend treatment for post-menopausal women who have asymptomatic bacteriuria.

To assess the need to address asymptomatic bacteriuria in older institutionalised patients, they evaluated 7 RCTs which compared antibiotic treatment with placebo controls or no treatment in this cohort (Boscia 1987, Abrutyn 1984, Abrutyn 1996, Nicolle 1987, Nicolle 1983, Potts 1996, Renneberg 1984). Antibiotic treatment was not significantly beneficial in reducing the rate of symptomatic UTIs compared to placebo or no treatment (average RR 0.68, 95% CI 0.46 to 1.00; n=210). There was no benefit of antibiotic treatment compared to placebo in the resolution of asymptomatic bacteriuria (average RR 1.33, 95% CI 0.63 to 2.79; n=328). One RCT compared the rates of incontinence before and after the eradication asymptomatic bacteriuria, and found no effect of antibiotic treatment (Ouslander 1995). The authors do not recommend screening or treatment for asymptomatic bacteriuria in this group. Because of this the use of urine dipsticks is not recommended in the diagnostic pathway for UTI in older adults. However, urine cultures are recommended if there is a suspected UTI in order to check for resistance.

10. Royal College of Physicians. National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. Updated report of a working party. London: RCP, 2017 Available from: www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2

RATIONALE

The Royal College of Physicians (RCP) has led the development of a new National Early Warning Score (NEWS) report, which advocates standardising the use of a NEWS system across the NHS in order to drive the 'step change' required in the assessment and response to acute illness. The report was recently updated (NEWS2). Whilst the tool has not been validated in primary care some authorities are looking to adapt it for use in this area, allowing it to aid the communication of assessment and response across multiple providers.

The report also states that subgroups of patients who are more likely to be at risk of sepsis include patients:

- who have recently had surgery or those with burns, blisters or cuts to the skin
- who are immunocompromised, including those receiving cancer chemotherapy, immunosuppressive biologics and long-term steroids
- post-splenectomy
- with indwelling cannulas or catheters

The report listed older age as a physiological consideration associated with higher clinical risk but did not apply a weighting based on current evidence. NEWS2 is based on a simple aggregate scoring system in which a score is allocated to physiological measurements, already recorded in routine practice, when patients present to, or are being monitored in hospital. Six simple physiological parameters form the basis of the scoring system:

- respiration rate
- oxygen saturation
- systolic blood pressure
- pulse rate
- level of consciousness
- new confusion temperature

Allowance is also made for individuals with respiratory problems who are on oxygen. Thresholds and triggers indicate that a score of 0-4 (low clinical risk) should include:

- a ward-based response
- a score of 3 (low-medium clinical risk) in any individual parameter should indicate an urgent ward-based response
- an aggregate NEWS score of 5 to 6 is a key threshold that should trigger an urgent clinical review/response
- a NEWS score of 7 or more should trigger a high-level clinical alert that is an emergency clinical review

Feedback from a subgroup of the Cross system Sepsis Programme board including both National Clinical Advisors for Sepsis, the National Medical Director's Clinical Fellow and Programme Leads indicated that older adults with NEWS score <5 might also

have infection and develop sepsis, and these should be considered in the presence of: altered mental state, inadequate urine output, a single NEWS parameter of 3, mottling/cyanosis/ashen skin/non-blanching rash, or Lactate >2.

11. National Institute of Health and Care Excellence (NICE). Sepsis: Recognition, diagnosis and early management. 2016 Jul. Available from: www.nice.org.uk/guidance/ng51/resources/sepsis-recognition-diagnosis-and-early-management-1837508256709

RATIONALE

A NICE guideline, stating that people with sepsis may have non-specific, non-localised presentations, such as feeling generally unwell without a high temperature of over 38°C. This guideline presents a risk stratification tool for adults, children and young people aged 12 years and over with suspected sepsis. Where high temperature is recognised as a cause for concern, this guideline also lists a tympanic temperature of less than 36°C as a moderate to high risk criteria for sepsis. Symptoms that indicate someone is at a moderate risk of having sepsis include:

- history of new-onset changed behaviour or change in mental state, as reported by the person, a friend or relative
- history of acute deterioration of functional ability; impaired immune system (illness or drugs, including oral steroids) trauma
- surgery or invasive procedure in the past 6 weeks
- respiratory rate of 21 to 24 breaths per minute; heart rate of 91–130 beats per minute or new-onset arrhythmia, or if pregnant heart rate of 100–130 beats per minute
- systolic blood pressure of 91 to 100 mmHg
- not passed urine in the past 12 to 18 hours (for catheterised patients, passed 0.5 to 1 mL/ kg/hour)
- tympanic temperature less than 36°C
- signs of potential infection, including increased redness, swelling or discharge at a surgical site, or breakdown of a wound

The document also provides guidance on considerations for treatment.

For an algorithm endorsed for use with this guidance, please use the following link: <https://www.nice.org.uk/guidance/ng51/resources/algorithm-for-managing-suspected-sepsis-in-adults-and-young-people-aged-18-years-and-over-outside-an-acute-hospital-setting-pdf-2551485716>

12. Royal Collage of General Practitioners. Sepsis toolkit. Accessed July 2018. Available from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/sepsis-toolkit.aspx

RATIONALE

The Royal Collage of General Practitioners is a professional membership body for GPs in the UK, with the purpose of encouraging, fostering and maintaining the highest possible standards in medical practice. The clinical toolkits on their website have been developed in partnership between the RCGP Clinical Innovation, Research Centre (CIRC) and other funding and delivery partners. The resources have been created for primary healthcare professionals, patients and carers. These toolkits can be used to assist in the delivery of safe and effective care to patients. The Sepsis toolkit provides a collection of tools, knowledge, and current guidance to support the identifying and appropriate management of patients with sepsis. The toolkit is aimed at GPs and healthcare professionals assessing people in the community with acute infection. The resources also include information for patients and those close to them to look for when concerned about a sudden deterioration in a person's health in the presence of infection.

13. Bent S, Nallamotheu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002 May; 287(20):2701-2710. Available from: www.ncbi.nlm.nih.gov/pubmed/12020306

RATIONALE

A systematic review of diagnostic studies, aiming to review the accuracy and precision of history taking and physical examination for the diagnosis of UTI in women. Results indicated that dysuria with frequency together increase the chances of UTI to 90%.

This review also identifies symptoms of pyelonephritis as: fever, back pain, nausea and vomiting. Vaginal infections and sexually transmitted diseases such as Chlamydia and Gonorrhoea can mimic the symptoms of a UTI but should be considered separately. This review looked at women of all ages but it is reasonable to assume that the symptoms identified are applicable to women over the age of 65.

14. Colgan R, Williams M. Diagnosis and Treatment of Acute Pyelonephritis in Women. *American Academy of Family Physicians*. 2011;84(5). Available from: www.aafp.org/afp/2011/0901/p519.pdf

RATIONALE

A review of the evidence for diagnosis and treatment of acute pyelonephritis in women. Authors state that history and physical examination are the most useful tools for diagnosis. Most patients have fever (over 38°C), although it may be absent early in the illness and in those who are frail. Fever greater than 100.4°F (38°C) is characteristic of acute pyelonephritis, but it may be absent in persons with early or mild cases. Fever

may also be absent in frail, older persons or in immunocompromised people, who also may not exhibit other classic manifestations of acute pyelonephritis.

Because of this, the authors included a temperature of below 36°C as a possibly sign of pyelonephritis. Flank pain is nearly universal, and its absence should raise suspicion of an alternative diagnosis. The authors also list tachycardia, hypotension, possible abdominal or suprapubic tenderness, constitutional symptoms (for example fever, chills, malaise) and gastrointestinal symptoms (for example, nausea, vomiting, anorexia, abdominal pain) as possible signs/symptoms. A positive culture confirms the diagnosis in patients with a compatible history and physical examination. Urine culture should be obtained in all patients to guide antibiotic therapy if the patient does not respond to initial empiric antibiotic regimens. Outpatient treatment is appropriate for most patients. Inpatient therapy is recommended for patients who have severe illness or in whom a complication is suspected.

15. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. 2012 Jul. Available from:
www.sign.ac.uk/assets/sign88.pdf

RATIONALE

A SIGN guideline, providing advice on how to manage suspected bacterial UTIs in the elderly and people with catheters. Catheter change before treating symptomatic infection: expert opinion, based on 1 small RCT, is that people with long-term indwelling catheters should have the catheter changed before starting antibiotic treatment for symptomatic UTI. Catheter change increases the likelihood of successful treatment. The guidance also states that a urine culture should be sent for all men who present with a suspected UTI.

16. Tenke P, Kovacs B, Bjerklund Johansen TE, Matsumoto T, Tambyah PA, Naber KG. European and Asian guidelines on management and prevention of catheter-associated urinary tract infections. *Int J Antimicrob Agents*. 2008 Feb; 31(1):68-78. Available from: www.ncbi.nlm.nih.gov/pubmed/18006279

RATIONALE

Catheter change before treating symptomatic infection: owing to the likelihood of bacteria sequestered in a biofilm on the catheter surface, expert opinion is that it may be reasonable to replace or remove the catheter (if the indwelling catheter has been in place for more than 7 days) before the therapy of symptomatic catheter-associated bacteriuria.

17. Rosello A, Hayward AC, Hopkins S, Horner C, Ironmonger D, Hawkey PM, et al. Impact of long-term care facility residence on the antibiotic resistance of urinary tract *Escherichia coli* and *Klebsiella*. *J Antimicrob Chemother.* 2017;72(4):1184-92. Available from: www.ncbi.nlm.nih.gov/pubmed/28077671

RATIONALE

A retrospective population-based study to compare the frequency of antibiotic resistance of urinary tract bacteria from residents of long-term care facilities for older adults and adults aged 70 years or older living in the community. Positive urine specimens reported to any diagnostic microbiology laboratory in the West Midlands region (England) from 1 April 2010 to 31 March 2014 were collected and analysed from individuals aged 70 years or older. The resistance of *E. coli* and *Klebsiella* to trimethoprim, nitrofurantoin, third-generation cephalosporins and ciprofloxacin and the rate of laboratory-confirmed *E. coli* and *Klebsiella* UTI were assessed in long-term care facility residents and in the community. In the community, 37% of samples had trimethoprim resistant *E. coli* and 26% trimethoprim resistant *Klebsiella* compared to 60% and 41% respectively in long-term care facilities. 4% of community samples and 7% in long-term care facilities had *E. coli* resistant to nitrofurantoin (35% community and 41% long-term care for *Klebsiella*).

Residents of long-term care facilities for the elderly had more than double the rate of *E. coli* and *Klebsiella* UTI and more than 4 times the rate of *E. coli* and *Klebsiella* UTI caused by antibiotic-resistant bacteria compared with those living in the community. The authors conclude that a very high proportion of *E. coli* and *Klebsiella* UTIs in the elderly living in LTCFs (and a high proportion of those living in their own homes) will not respond to trimethoprim treatment. However, resistance to nitrofurantoin remains low in UTIs caused by *E. coli* but high in UTIs caused by *Klebsiella*, demonstrating the need to understand further the mechanisms for the selection of resistance. Because of the high level of resistance demonstrated in older adults, this quick reference tool recommends that all older adults who have a suspected UTI have a urine culture sent for analysis.

18. National Institute for Health and Care Excellence. Pyelonephritis (acute): antimicrobial prescribing. Nice guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng111

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for acute pyelonephritis (upper urinary tract infection). It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany

the guidelines. The recommendations state that advice should be given on self-care to all those with expected pyelonephritis. Mid-stream urine specimens should be sent. Advice is given on antibiotic choice and administration and to reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of: other possible diagnoses, any symptoms or signs suggesting a more serious illness or condition, such as sepsis, or previous antibiotic use, which may have led to resistant bacteria. Admission should be considered in those aged 16 years and over with acute pyelonephritis if they are significantly dehydrated or unable to take oral fluids and medicines, or are pregnant, or have a higher risk of developing complications.

19. Chu CM. Diagnosis and Treatment of Urinary Tract Infections Across Age Groups. *American Journal of Obstetrics and Gynaecology*. 2018. Available from: [www.ajog.org/article/S0002-9378\(17\)32805-3/pdf](http://www.ajog.org/article/S0002-9378(17)32805-3/pdf)

RATIONALE

An expert review of diagnosis and treatments of UTIs in different age groups. Authors suggest that the most diagnostic symptoms of UTIs include change in frequency, dysuria, urgency, and presence or absence of vaginal discharge, but suggest that UTIs may present differently in older women. Other symptoms include suprapubic, vaginal, and urethral tenderness, as well as haematuria. It is important to note that systemic symptoms, such as nausea, vomiting, flank pain, upper back pain, and fevers may indicate ascension of infection to the upper urinary tract and should not be treated as uncomplicated UTI.

20. Balogun SA, Philbrick JT. Delirium, a Symptom of UTI in the Elderly: Fact or Fable? A Systematic Review. *Can Geriatr J*. 2014;17(1):22-6. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC3940475/pdf/cgj-17-22.pdf

RATIONALE

A systematic review that looked at the relationship between delirium and UTI. A search was conducted for published studies from 1966 through 2012 using the MESH terms 'urinary tract infection' and 'delirium', limited to humans, age 65 and older. Of the 11 identified studies, 5 met inclusion criteria of being primary studies that addressed the association of UTI and delirium. The studies were 4 cross-sectional observational studies and 1 case series. The methodological strength of the studies was evaluated using 6 standards adapted from a previous systematic review. Only 2 of the 5 studies adequately matched or statistically adjusted for differences in comparison groups. None of the studies evaluated subjects with equal intensity for the presence of delirium and UTI, nor did they have objective criteria for either diagnosis.

In subjects with delirium, UTI rates ranged from 25.9% to 32% compared to 13% in those without delirium. In subjects with UTI, delirium rates ranged from 30% to 35%, compared to 7.7% to 8% in those without UTI. Though the studies examined conclude that there is an association between UTI and delirium, all of them had significant methodological flaws that likely led to biased results. It is difficult to ascertain the degree to which UTIs cause delirium and more research is needed to clarify the relationship. The authors conclude that it is reasonable to assume that there is an association between delirium and sufficiently symptomatic UTI, just as there is for delirium and multiple other infections/conditions. It is also reasonable to conclude that asymptomatic bacteriuria, without dysuria, frequency, bladder discomfort, or fever, is unlikely to cause a patient to become delirious (Gau 2009) and that factors other than an abnormal urinalysis play a more dominant role in the development of delirium.

21. Portman DJ, Gass ML, Vulvovaginal Atrophy Terminology Consensus Conference P. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas*. 2014;79(3):349-54. Available from: www.ncbi.nlm.nih.gov/pubmed/25179577

RATIONALE

Consensus report from 2012. The Board of Directors of the International Society for the Study of Women's Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) acknowledged the need to review current terminology associated with genitourinary tract symptoms related to menopause. To do this they co-sponsored a terminology consensus conference, which was held in May 2013 and agreed that the term genitourinary syndrome of menopause (GSM) is a medically more accurate, all-encompassing, and publicly acceptable term than vulvovaginal atrophy. Symptoms of GSM are associated with a decrease in oestrogen and other sex steroids involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra and bladder.

The syndrome may include but is not limited to genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, discomfort or pain and impaired function; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all of the signs and symptoms. The term was presented and discussed at the annual meeting of each society. GSM is currently used as the as a term to cover both atrophic vaginitis and vaginal atrophy in more recent references found during the review for the UTI diagnostic flowcharts.

22. Little P. Antibiotics or NSAIDs for uncomplicated urinary tract infection? *BMJ*. 2017;359:j5037. Available from: www.ncbi.nlm.nih.gov/pubmed/29117972

RATIONALE

An editorial discussion around antibiotics or NSAID's for UTIs. The author suggests Paracetamol could be used more regularly as the first line analgesic in UTIs as it seems to be associated with a lower risk of adverse outcomes compared to nonsteroidal anti-inflammatories. The authors conclude however, that more evidence is needed to support the use of paracetamol in treating UTIs.

23. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, et al. Effectiveness of 5 different approaches in management of urinary tract infection: randomised controlled trial. *BMJ*. 2010;340:c199. Available from: www.ncbi.nlm.nih.gov/pubmed/20139214

RATIONALE

Randomised controlled trial to assess the impact of different management strategies in UTIs in primary care. The study included 309 non-pregnant women aged 18 to 70 presenting with suspected UTI who were randomised to 5 management approaches:

- empirical antibiotics
- empirical delayed (by 48 hours) antibiotics
- or targeted antibiotics based on a symptom score (2 or more of urine cloudiness, urine smell, nocturia, or dysuria)
- a dipstick result (nitrite or both leucocytes and blood)
- a positive result on mid-stream urine analysis

Self-help advice was controlled in each group. The outcomes of symptom severity (days 2 to 4) and duration, and use of antibiotics were assessed. Patients had three-and-a-half days of moderately bad symptoms if they took antibiotics immediately. There were no significant differences in duration or severity of symptoms. There were differences in antibiotic use (immediate antibiotics 97%, mid-stream urine 81%, dipstick 80%, symptom score 90%, delayed antibiotics 77%; $P=0.011$) and in sending mid-stream urine samples (immediate antibiotics 23%, mid-stream urine 89%, dipstick 36%, symptom score 33%, delayed antibiotics 15%; $P<0.001$).

Patients who waited at least 48 hours to start taking antibiotics re-consulted less (hazard ratio 0.57 (95% confidence interval 0.36 to 0.89), $P=0.014$) but on average had symptoms for 37% longer than those taking immediate antibiotics (incident rate ratio 1.37 (1.11 to 1.68), $P=0.003$), particularly the mid-stream urine group (73% longer, 22% to 140%; none of the other groups had more than 22% longer duration). The authors concluded that all management strategies achieve similar symptom control. There is no advantage in routinely sending mid-stream urine samples for testing, and antibiotics targeted with dipstick tests with a delayed prescription as backup, or empirical delayed prescription, can help to reduce antibiotic use.

24. National Institute for Health and Care Excellence. Urinary tract infection (catheter-associated): antimicrobial prescribing. NICE guidelines. Published Nov 2018. Available from: <https://www.nice.org.uk/guidance/ng113>

RATIONALE

This NICE/PHE guideline sets out an antimicrobial prescribing strategy for catheter-associated UTI (CAUTI). It aims to optimise antibiotic use and reduce antibiotic resistance. The guideline states that the longer a catheter is in place, the more likely bacteria will be found in the urine. Antibiotic treatment is not routinely needed for asymptomatic bacteriuria in people with a catheter (apart from in pregnant women with asymptomatic bacteriuria). Consider removing or changing the catheter as soon as possible in people with a CAUTI if it has been in place for more than 7 days, but do not allow this to delay antibiotic treatment. Obtain a urine sample before antibiotics are taken (from the new catheter if changed) or a midstream specimen of urine if catheter removed. Send the urine sample for culture and susceptibility testing, noting a suspected CAUTI infection and any antibiotic prescribed.

When 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 antibiotics wherever possible. If antibiotic prescribed give general advice on self-care, possible adverse effects of antibiotics, particularly diarrhoea and nausea, and when to seek medical help. Reassess if not improved in 48 hours of taking antibiotic or if symptoms worsen.

25. Michaels T, Sands J. Dysuria: Evaluation and Differential Diagnosis in Adults. *American Family Physician*. 2015;92(9). Available from: www.ncbi.nlm.nih.gov/pubmed/26554471

RATIONALE

A review of evidence based approaches for the evaluation of adult patients with dysuria. The authors state that the most common cause of acute dysuria is infection, especially cystitis. Other infectious causes include urethritis, sexually transmitted infections, and vaginitis. Non-infectious inflammatory causes include a foreign body in the urinary tract and dermatologic conditions. Non-inflammatory causes of dysuria include medication use, urethral anatomic abnormalities, local trauma, and interstitial cystitis/bladder pain syndrome. Prostatitis can present with dysuria. An initial targeted history includes features of a local cause (for example vaginal or urethral irritation), risk factors for a complicated UTI (for example, male sex, pregnancy, presence of urologic obstruction, recent procedure), and symptoms of pyelonephritis.

Often the most relevant findings on physical examination are sex-specific, including inspecting for infectious or atrophic vaginitis and STIs in women, and prostatitis and STIs in men. Women with vulvovaginal symptoms should be evaluated for vaginitis. Urethritis should be suspected in younger, sexually active patients with dysuria and pyuria without bacteriuria; in men, urethral inflammation and discharge is typically present. In patients with suspected urethritis, a urethral, vaginal, endocervical, or urine nucleic acid amplification test for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is indicated. Men with prostatitis may have deep perineal pain and obstructive urinary symptoms, whereas those with epididymo-orchitis may have localised testicular pain. Any complicating features or recurrent symptoms warrant a history, physical examination, urinalysis, and urine culture. Findings from the secondary evaluation, selected laboratory tests, and directed imaging studies enable physicians to progress through a logical evaluation and determine the cause of dysuria or make an appropriate referral.

26. National Institute for Health and Care Excellence. Urinary tract infection (lower): antimicrobial prescribing. Nice guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng109

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for lower urinary tract infection. It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The recommendations state that advice should be given on self-care to all those with expected a lower UTI. This includes paracetamol for pain, adequate intake of fluids, and no evidence was found on cranberry products to treat a lower UTI. Obtain a mid-stream urine sample before prescribing antibiotics for pregnant women and men with lower UTI and send for culture and susceptibility testing. Consider a back-up antibiotic prescription or an immediate antibiotic prescription for women with lower UTI who are not pregnant. Take account of:

- the severity of symptoms
- the risk of developing complications
- previous urine culture and susceptibility results
- previous antibiotic use which may have led to resistant bacteria; preferences of the woman for antibiotic use

If a urine sample has been sent for culture and susceptibility testing and an antibiotic prescription has been given: review the choice of antibiotic when microbiological results are available, and change the antibiotic according to susceptibility results if bacteria are resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible. Safety-netting advice should be provided specific to seeking

medical help if symptoms worsen rapidly or significantly at any time, do not start to improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell.

27. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, et al. Effectiveness of 5 different approaches in management of urinary tract infection: randomised controlled trial. *BMJ*. 2010;340:c199. Available from:
www.ncbi.nlm.nih.gov/pubmed/20139214

RATIONALE

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28. Pryor C, Clarke A. Nursing care for people with delirium superimposed on dementia. *Nurs Older People*. 2017;29(3):18-21. Available from:
<http://nrl.northumbria.ac.uk/30550/1/PryorAAM.pdf>

RATIONALE

This review describes a simple mnemonic called PINCH ME (Pain, Infection, Constipation, deHydration, Medication, Environment) which can help identify potential underlying causes of delirium superimposed on dementia (DSD) and considerations for care planning in patients with dementia. The mnemonic can easily be adapted to different clinical settings. This article explores the dichotomy in healthcare provision for 'physical' and 'mental' health, and the unique role nurses have when caring for people with DSD. In this article, dementia is contrasted with delirium and subtypes of delirium presentation are discussed. Nurses can recognise DSD through history gathering, implementation of appropriate care and effective communication with families and the multidisciplinary team. Several members of the steering group use the PINCH ME mnemonic in their clinical practice. Participants of the needs assessment (Carers and GP staff) reported it was very useful and reflected their own practice and experience of patients with confusion.

29. British Geriatrics Society and Royal College of Physicians. *Guidelines for the prevention, diagnosis and management of delirium in older people*. Concise guidance to good practice series, No 6. London: RCP, 2006. Available from: www.rcplondon.ac.uk/guidelines-policy/prevention-diagnosis-referral-and-management-delirium-older-people

RATIONALE

The objective of this document is to update the Guidelines for the diagnosis and management of delirium in the elderly (1997) compiled by Dr Lesley Young and Dr Jim George based on the work of the multidisciplinary working party on Confusion in Crises, Royal College of Physicians, 1995. The update was overseen by a multi-professional Guideline Development Group including representatives from nursing, care of the elderly, and old age psychiatry. It includes graded references and expert review of content. Key points related to the management of delirium include: The most important action for the management of delirium is the identification and treatment of the underlying cause.

The patient should be nursed in a good sensory environment and with a reality orientation approach, and with involvement of the multidisciplinary team. Keep the use of sedatives and major tranquillisers to a minimum. Use 1 drug only starting at the lowest possible dose and increasing in increments if necessary after an interval of 2 hours. Review all medication at least every 24 hours. One-to-one care of the patient is often required and should be provided while the dose of psychotropic medication is titrated upward in a controlled and safe manner.

30. KJ, Hak E, Zuithoff NP, Hoepelman AI, Rutten GE. Risk of recurrent acute lower urinary tract infections and prescription pattern of antibiotics in women with and without diabetes in primary care. *Fam Pract.* 2010;27(4):379-385. Available from: www.ncbi.nlm.nih.gov/pubmed/20462975

RATIONALE

This exploratory retrospective study involving 7063 women aged 30 years or over, studied the incidence of recurrent UTI (relapses and reinfection) in women with (n = 340) and without diabetes (n = 6618). Multivariable logistic regression and multilevel multinomial logistic analyses were used to determine the adjusted associations between diabetes characteristics and recurrent UTI and the influence of diabetes on the pattern of antibiotic prescriptions for UTI, respectively. Relapses and reinfections were reported in 7.1% and 15.9% of women with diabetes versus 2% and 4.1% of women without diabetes.

There was an independent higher risk of recurrent UTI in women with diabetes compared with women without diabetes (OR 2.0; 95% CI 1.4–2.9). Women taking oral blood glucose-lowering medication (OR 2.1; 95% CI 1.2–3.5) or insulin (OR 3.0; 95% CI 1.7–5.1) or who had had diabetes for over 5 years (OR 2.9; 95% CI 1.9–4.4) or who had retinopathy (OR 4.1; 95% CI 1.9–9.1) were at risk of recurrent UTI. This study was conducted in relatively younger women but it is believed that the findings can be applied to older women. It is also important to consider that this study only highlights an association rather than cause and effect.

31. Marik P, Bellomo R. Stress hyperglycemia: an essential survival response! *Critical Care* 2013; 17:305 Available from: www.ncbi.nlm.nih.gov/pubmed/20937688

RATIONALE

A review of the pathophysiology of stress hyperglycemia and insulin resistance and the protective role of stress hyperglycemia during acute illness. It summarises acute illness, the stress response, and hyperglycemia, how moderate stress hyperglycemia is protective during illness, and balancing the effects of chronic vs acute hyperglycemia. The authors also discuss their findings in light of the widespread adoption of protocols and programs for tight in-hospital glycaemic control. They suggest that hyperglycemia and insulin resistance in the setting of acute illness is an evolutionarily preserved adaptive response that increases the host's chances of survival. Although the patient group and findings for this review are not necessarily relevant for primary care, it was included in the rationale as a way to explain the pathophysiology specific to how acute illness affect blood glucose and how a loss of diabetic control could be evidence of a non-specific sign of physiological stress and infection.

32. Talley NJ, O'Keefe EA, Zinsmeister AR, Melton III LJ. Prevalence of Gastrointestinal Symptoms in the Elderly: A Population-Based Study. *Gastroenterology*. 1992;102(3):895-901 Available from: [www.gastrojournal.org/article/0016-5085\(92\)90175-X/pdf](http://www.gastrojournal.org/article/0016-5085(92)90175-X/pdf)

RATIONALE

A random sample of non-institutionalised Olmsted County, Minnesota stratified by age and sex. Residents aged 65-93 years were mailed a questionnaire; 77% responded (n = 328). The age/sex adjusted prevalence (per 100 persons) of frequent abdominal pain was 24.3 [95% confidence interval (CI), 19.3-29.21]. Chronic constipation and chronic diarrhoea had a prevalence of 24.1(95% CI, 19.1-29.0) and 14.2 (95% CI, 10.1-18.2), respectively. Faecal incontinence more than once a week was reported in 3.7 per 100 (95% CI, 1.6-5.9). It is concluded that complaints consistent with functional gastrointestinal disorders are common in the elderly, but symptoms are a poor predictor of presentation for medical care.

33. Cardemil CV, Parashar UD, Hall AJ. Norovirus Infection in Older Adults: Epidemiology, Risk Factors, and Opportunities for Prevention and Control. *Infect Dis Clin North Am*. 2017;31(4):839-870. Available from: [www.id.theclinics.com/article/S0891-5520\(17\)30066-1/pdf](http://www.id.theclinics.com/article/S0891-5520(17)30066-1/pdf)

RATIONALE

A review of the literature stating that symptoms of norovirus can include sudden onset of vomiting, abdominal cramps, and watery diarrhoea with prolonged symptoms in older adults.

34. Beetz R. Mild dehydration: a risk factor of urinary tract infection? *Eur J Clin Nutr*. 2003;57 Suppl 2:S52-58. Available from: www.ncbi.nlm.nih.gov/pubmed/14681714

RATIONALE

A review of the literature. The discussion pertains to bacterial eradication from the urinary tract being partially dependent on urine flow and voiding frequency. The authors postulate a connection between fluid intake and the risk of UTIs. However, experimental and clinical data on this subject are conflicting. Only few clinical studies producing contradictory results are available on the influence of fluid intake concerning the risk of UTI. One explanation for the inconsistency between the data might be the uncertainty about the exact amounts of fluid intake, which was mostly recorded in questionnaires.

So far, there is no definitive evidence that the susceptibility for UTI is dependent on fluid intake. Nevertheless, adequate hydration is important and may improve the results

of antimicrobial therapy in UTI. Results of experimental and clinical studies concerning urinary hydrodynamics are the basis for advice given by expert committees to patients with UTI to drink large volumes of fluid, void frequently, and completely empty the bladder. The combination of the behaviourally determined aspects of host defence and not simply increasing fluid intake is important in therapy and prophylaxis of UTI.

35. Kavouras SA. Assessing hydration status. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2002;5(5):519-524. Available from: www.ncbi.nlm.nih.gov/pubmed/12172475

RATIONALE

A literature review to examine the available techniques in assessing hydration status. The author concludes that urine colour in most circumstances reflects the level of hydration and is closely related to several urinary and plasma indices of hydration. Urine colour can be influenced by diet, drugs and illness.

36. National Institute for Health and Care Excellence. Healthcare-associated infections: prevention and control in primary and community care. Clinical guideline. Published March 2012. Available from: <https://www.nice.org.uk/guidance/cg139/resources/healthcareassociated-infections-prevention-and-control-in-primary-and-community-care-pdf-35109518767045>

RATIONALE

This guideline covers preventing and controlling healthcare-associated infections in children, young people and adults in primary and community care settings. The guidance states that you should not offer antibiotic prophylaxis routinely when changing long-term indwelling urinary catheter. Consider antibiotic prophylaxis for patients who have a history of symptomatic urinary tract infection after catheter change, or who experience trauma during catheterisation. However, the guidance states that currently there is an absence of evidence about the short-term and long-term effects of prophylactic antibiotic use during catheter change. The Guideline Development Group identified this as an important area for research to establish the benefits and harms of this practice in order to develop future guidance (the recommendation on this topic in the current guideline was based on group consensus).

37. Guidance for Maintaining Patency in Long Term Urinary Catheters. Healthcare Associated Infection & Antimicrobial Resistance & Prescribing Programme (HARP) team, Health Protection, Public Health Wales (in collaboration with Service continence leads), 25th October 2019. Available from: <https://phw.nhs.wales/services-and-teams/harp/urinary-tract-infection-uti-resources-and-tools/uti-downloads/guidance-for-maintaining-patency-in-long-term-urinary-catheters/>

RATIONALE

This guideline supports best practice when managing a non-draining or leaking long-term urinary catheter and guides the appropriate use of catheter patency solutions in order to reduce CAUTI and associated bacteraemia. It lists a number of reasons a catheter might leak or stop draining that need to be assessed for before using catheter patency solutions. These include: kinked tubing/poorly supported drainage bag/tight clothing, overfull draining system, bladder spasm, bladder stones, wrong length/size of catheter, over/under inflated catheter balloon, constipation, low fluid intake/dehydration, blood/debris, encrustation, UTI, drainage bag located above bladder, and drainage bag too low producing negative pressure causing mucosa to be sucked into outlet eyelets. Additional information is provided on the management of a blocked urinary catheter and use of catheter patency solutions.

Sending urine for culture and interpreting results in all adults table

Review need for urine culture when considering treatment

1. Rosello A, Hayward AC, Hopkins S, Horner C, Ironmonger D, Hawkey PM, et al. Impact of long-term care facility residence on the antibiotic resistance of urinary tract *Escherichia coli* and *Klebsiella*. J Antimicrob Chemother. 2017;72(4):1184-92. Available from: www.ncbi.nlm.nih.gov/pubmed/28077671

RATIONALE

A retrospective population-based study to compare the frequency of antibiotic resistance of urinary tract bacteria from residents of long-term care facilities for older adults and adults aged 70 years or older living in the community. Positive urine specimens reported to any diagnostic microbiology laboratory in the West Midlands region (England) from 1 April 2010 to 31 March 2014 were collected and analysed from individuals aged 70 years or older. The resistance of *Escherichia coli* and *Klebsiella* to trimethoprim, nitrofurantoin, third-generation cephalosporins and ciprofloxacin and the rate of laboratory-confirmed *E. coli* and *Klebsiella* urinary tract infection (UTI) were assessed in long-term care facility residents and in the community. In the community, 37% of samples had trimethoprim resistant *E. coli* and 26% trimethoprim resistant *Klebsiella* compared to 60% and 41% respectively in long-term care facilities – 4% of community samples and 7% in long-term care facilities had *E. coli* resistant to nitrofurantoin (35% community and 41% long-term care for *Klebsiella*).

Residents of long-term care facilities for the elderly had more than double the rate of *E. coli* and *Klebsiella* UTI and more than 4 times the rate of *E. coli* and *Klebsiella* UTI caused by antibiotic-resistant bacteria compared with those living in the community. The authors conclude that a very high proportion of *E. coli* and *Klebsiella* UTIs in the elderly living in LTCFs (and a high proportion of those living in their own homes) will not respond to trimethoprim treatment. However, resistance to nitrofurantoin remains low in UTIs caused by *E. coli* but high in UTIs caused by *Klebsiella*, demonstrating the need to understand further the mechanisms for the selection of resistance. Because of the high level of resistance demonstrated in older adults, the authors recommend that all older adults who have a suspected UTI have a urine culture sent for analysis.

2. National Institute for Health and Care Excellence (NICE). Antenatal care for uncomplicated pregnancies. 2008 Mar. Available from: www.nice.org.uk/guidance/CG62

RATIONALE

NICE recommend that women should be offered routine screening for bacteriuria by mid-stream urine culture early in pregnancy, because identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis and premature delivery.

3. Warrell DA, Cox TM, Firth JD. Oxford Textbook of Medicine. Oxford Medicine Online. 2017. Available from:
<http://oxfordmedicine.com/view/10.1093/med/9780199204854.001.1/med-9780199204854>

RATIONALE

A diagnosis of pyelonephritis is usually made on the basis of flank pain (usually unilateral), fever, rigors, raised C-reactive protein (or erythrocyte sedimentation rate), and evidence of urine infection on a mid-stream urine sample.

4. National Institute for Health and Care Excellence. Urinary tract infection (lower): antimicrobial prescribing NICE guidelines. Published October 2018. Available from:
www.nice.org.uk/guidance/ng109

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for lower urinary tract infection. It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The guidance states you should obtain a mid-stream urine sample before prescribing antibiotics for pregnant women and men with lower UTI and send for culture and susceptibility testing. Consider a back-up antibiotic prescription or an immediate antibiotic prescription for women with lower UTI who are not pregnant.

Take account of: the severity of symptoms; the risk of developing complications; previous urine culture and susceptibility results; previous antibiotic use which may have led to resistant bacteria; preferences of the woman for antibiotic use. If a urine sample has been sent for culture and susceptibility testing and an antibiotic prescription has been given: review the choice of antibiotic when microbiological results are available, and change the antibiotic according to susceptibility results if bacteria are resistant and symptoms are not already improving, using a narrow spectrum antibiotic wherever possible.

5. Hawkey PM, Warren RE, Livermore DM, McNulty CAM, Enoch DA, Otter JA, et al. Treatment of infections caused by multidrug-resistant Gram-negative bacteria:

report of the British Society for Antimicrobial Chemotherapy/Healthcare Infection Society/British Infection Association Joint Working Party. *J Antimicrob Chemother.* 2018;73(suppl_3):iii2-iii78. Available from:
https://academic.oup.com/jac/article/73/suppl_3/iii2/4915406

RATIONALE

Report from Working Party making recommendations in antimicrobial prescribing for the treatment of infections caused by multidrug-resistant gram-negative bacteria. The guidance has been derived from current peer-reviewed publications and expert opinion with open consultation. Methods for systematic review were NICE compliant and in accordance with the SIGN 50 Handbook. Critical appraisal was applied using AGREE II. Published guidelines were used as part of the evidence base and to support expert consensus. The guidance includes recommendations for stakeholders (including prescribers) and antibiotic-specific recommendations.

The authors recommend no antibiotic prescriptions for treating the elderly with asymptomatic bacteriuria. The authors also list risk factors for patients with urinary tract infections caused by multi-drug resistant gram negative bacteria in the UK. Patients are at increased risk if they have:

- recurrent UTI
 - persistent urinary symptoms after an initial antibiotic
 - over 7 days hospital admission in the last 6 months
 - residence in a care home
 - recent travel and especially healthcare in a country with increased antimicrobial resistance
 - previously known UTI (within 1 year) caused by bacteria resistant to amoxicillin/clavulanate, cephalosporins or quinolone or recent treatment with these agent
6. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ.* 2010 May; 18(340):2096. Available from:
www.ncbi.nlm.nih.gov/pubmed/20483949

RATIONALE

This systematic review found that individuals prescribed an antibiotic in primary care for a respiratory or urinary infection develop bacterial resistance to that antibiotic. The effect is greatest in the month immediately after treatment, but may persist for up to 12 months. In 5 studies of urinary tract bacteria (14,348 participants), the pooled odds ratio for bacterial resistance was 2.5 (95% CI 2.1 to 2.9) within 2 months of antibiotic treatment, and 1.33 (95% CI 1.2 to 1.5) within 12 months of treatment.

7. Hawkey PM, Jones AM. The changing epidemiology of resistance. *J Antimicrob Chemother.* 2009;64 Suppl 1:i3-10. Available from: https://academic.oup.com/jac/article/64/suppl_1/i3/750430

RATIONALE

A review of the global antibiotic resistance challenge. Dispersion of successful clones of multidrug resistant (MDR) bacteria is common, often via the movement of people. β -Lactamase production is a common resistance mechanism in Gram-negative bacteria, and the rapid dissemination of novel genes reflects their evolution under the selective pressure of antibiotic usage. Antibiotic use and environmental factors all have a role in the emergence and spread of resistance. This article reviews some of the new mechanisms and recent trends in the global spread of multi drug resistant bacteria. It indicates that there are significant global resistance patterns to the bacteria most commonly responsible for UTIs.

8. Bonkat, R. Pickard, R. Bartoletti, T. Cai, F. Bruyère, S.E. Geerlings, B. Köves, F. Wagenlehner, A. Pilatz, B. Pradere, R. Veeratterapillay; members of the EAU Urological Infections Guidelines Panel. 2018 edition of the EAU Urological Infections Guidelines. Available from: <http://uroweb.org/guideline/urological-infections/>

RATIONALE

A review of diagnosis and management guidelines for UTIs agreed upon by the Urological Infections Guidelines Panel consisting of a group of urologists, specialised in the treatment of UTIs and male genital infections. A complicated UTI (cUTI) occurs in an individual in whom factors related to the host or specific anatomical or functional abnormalities related to the urinary tract (for example obstruction, incomplete voiding due to detrusor muscle dysfunction) are believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection. A cUTI is associated with clinical symptoms (for example dysuria, urgency, frequency, flank pain, costovertebral angle tenderness, suprapubic pain and fever), or symptoms may be atypical, for example.

Clinicians must also recognise that symptoms, especially lower urinary tract symptoms, are not only caused by UTIs but also by other urological disorders, such as, for example, benign prostatic hyperplasia and autonomic dysfunction in patients with spinal lesions and neurogenic bladders. Medical conditions, such as diabetes mellitus and renal failure, which can be related to urological abnormalities, are often also present in a cUTI. The authors state that laboratory urine culture is the recommended method to determine the presence or absence of clinically significant bacteriuria in patients suspected of having a cUTI.

9. National Institute for Health and Care Excellence. Urinary tract infection (catheter-associated): antimicrobial prescribing. NICE guidelines. Published Nov 2018. Available from: <https://www.nice.org.uk/guidance/ng113>

RATIONALE

This NICE/PHE guideline sets out an antimicrobial prescribing strategy for catheter-associated UTI (CAUTI). It aims to optimise antibiotic use and reduce antibiotic resistance. The guideline states that the longer a catheter is in place, the more likely bacteria will be found in the urine. Antibiotic treatment is not routinely needed for asymptomatic bacteriuria in people with a catheter (apart from in pregnant women with asymptomatic bacteriuria). When 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 antibiotics wherever possible.

Sampling in all men and women

1. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.6. www.gov.uk/government/publications/smi-b-41-investigation-of-urine

RATIONALE

UK Standards for Microbiology Investigations comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. This publication includes updates from 2018 and is NICE accredited. Standards are produced in partnership with PHE, NHS, Royal College of Pathologists and professional societies. The guidance states that mid-stream urines and clean-catch urine are recommended for routine use but cleaning the area beforehand makes little difference in contamination. A urine sample may be obtained either from a transient ('in and out') catheterisation or from an indwelling catheter. In the latter case, the specimen is obtained aseptically from a sample port in the catheter tubing or by aseptic aspiration of the tubing.

The specimen should not be obtained from the collection bag. Delays and storage at room temperature allow organisms to multiply, which may generate false positive results. Where delays in processing are unavoidable, refrigeration is recommended. Use of a boric acid preservative may also be useful. Boric acid preservative holds the bacterial population steady for 48 to 96 hours. Toxicity to some organisms has been reported, but this often reflects under filling of the container. Boric acid may be inhibitory to some organisms and may inhibit tests for leucocyte esterase, so you should not use with urine dipsticks. Carry-over contamination is a potentially problem

for devices that analyse urine and this should be assessed for during their validation and verification. One strategy to limit this is to use sample aliquots if a dipstick is required before sending it for culture.

2. Holm A, Aabenhus R. Urine sampling techniques in symptomatic primary-care patients: a diagnostic accuracy review. *BMC Fam Pract.* 2016;17:72. Available from: <https://bmcfampract.biomedcentral.com/track/pdf/10.1186/s12875-016-0465-4?site=bmcfampract.biomedcentral.com>

RATIONALE

A systematic review of clinical studies conducted in primary care to compare the result of urine culture obtained with 2 or more collection techniques in women with symptoms of urinary tract infection. Seven studies investigating urine sampling technique in 1,062 symptomatic patients in primary care were included. Mid-stream-clean-catch had a positive predictive value of 0.79 to 0.95 and a negative predictive value close to 1 compared to sterile techniques. Two randomised controlled trials found no difference in infection rate between mid-stream-clean-catch, mid-stream-urine and random samples.

Authors conclude that at present, no evidence suggests that sampling technique affects the accuracy of the microbiological diagnosis in non-pregnant women with symptoms of urinary tract infection in primary care. However, the evidence presented is in-direct and the difference between mid-stream-clean-catch, mid-stream-urine and random samples remains to be investigated in a paired design to verify the present findings. This quick reference tool continues to recommend a mid-stream sample is collected until further investigations can verify the lack of difference between the sampling techniques.

3. Lifshitz E, Kramer L. Outpatient urine culture: does collection technique matter? *Arch Intern Med.* 2000 Sep; 160(16): 2537-2540. Available from: www.ncbi.nlm.nih.gov/pubmed/10979067

RATIONALE

This randomised study of 242 women who presented with symptoms suggestive of UTI found that there was no difference in contamination rates between samples obtained with no technique (not mid-stream and no cleansing: 29%; contaminated: n=77; samples obtained mid-stream with perineal cleansing and spreading of the labia: 32% contaminated: n=84; samples obtained mid-stream with perineal cleansing and a vaginal tampon in place: 31% contaminated; n=81). Contamination rates were nearly identical and there was no significant difference between the no-cleaning and mid-stream/combined cleansing group. This suggests that encouraging use of the mid-stream clean catch method or cleaning might not be warranted. Though authors

indicate that further in study is needed. This quick reference tool continues to recommend a mid-stream sample is collected until further investigations can verify the lack of difference between the sampling techniques.

4. National Health Services Choices. How should I collect and store a urine sample? Accessed 6 April 2018. Available from: www.nhs.uk/chq/Pages/how-should-i-collect-and-store-a-urine-sample.aspx

RATIONALE

This website provides National Health Service guidance for men and women on how to collect a mid-stream urine sample. The guidance states that a sample can be collected any time during the day or night unless advised otherwise by doctor or nurse. The process includes labelling the sterile screw top container, washing hands, starting urination then catching the sample mid-stream, closing the lid and washing hands. Further information is provided on why to collect a mid-stream specimen, how to store the sample, and what it might be used for.

5. Baerheim A, Digranes A, Hunskaar S. Evaluation of urine sampling technique: bacterial contamination of samples from women students. *Br J Gen Pract.* 1992 Jun; 42(359):241-243. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC1372060/

RATIONALE

This prospective study obtained a series of urine samples (a new sample was obtained each day for 8 days, using a different set of instructions each day) from 111 healthy young women. There was no statistically significant difference in contamination rates between the following techniques:

- no precautions (31%)
- mid-stream sample (23.9%)
- mid-stream sample with perineal cleansing (20.4%)
- mid-stream and holding labia apart (21.1%)

However, holding the labia apart as the sole technique was associated with a lower contamination rate (13%) in this study.

6. LaRocco MT, Franek J, Leibach EK, Weissfeld AS, Kraft CS, Sautter RL, et al. Effectiveness of Preanalytic Practices on Contamination and Diagnostic Accuracy of Urine Cultures: a Laboratory Medicine Best Practices Systematic Review and Meta-analysis. *Clin Microbiol Rev.* 2016;29(1):105-47. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC4771218/pdf/zcm105.pdf

RATIONALE

A large systematic review to identify and evaluate preanalytic practices associated with urine specimens and to assess their impact on the accuracy of urine culture microbiology. Specific practices included collection methods for men, women, and children; preservation of urine samples in boric acid solutions; and the effect of refrigeration on stored urine. Practice efficacy and effectiveness were measured by 2 parameters:

- reduction of urine culture contamination
- increased accuracy of patient diagnosis

The CDC Laboratory Medicine Best Practices (LMBP) initiative's systematic review method for assessment of quality improvement (QI) practices was employed. Results were then translated into evidence based practice guidelines. Data from 9 studies (rated as fair in quality) suggest that boric acid and refrigeration both preserve urine specimens for up to 24 hours before processing. Data from 3 studies indicate that urine held for more than 4 hours before processing should not be used due to overgrowth of flora. However, evidence quality for this is rated as low and the panel could not make a recommendation.

If non-invasive collection is being considered for women, mid-stream collection with cleansing is recommended, but no recommendation for or against is made for mid-stream collection without cleansing. For urine specimens collected from men, there was a reduction in contamination in favour of mid-stream clean-catch over first-void specimen collection. The strength of this evidence was rated as high. However, there was no benefit to cleaning beforehand in either sex. Overall evidence quality for the studies specific to women was rated as low and for men was fair but not strong enough for the panel to make recommendations.

7. Roberts AP, Robinson RE, Beard RW. Some factors affecting bacterial colony counts in urinary infection. *Br Med J.* 1967 Feb; 1(5537):400-403. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC1841545/pdf/brmedj02123-0050.pdf

RATIONALE

Suprapubic specimens and mid-stream samples taken using perineal cleansing with chlorhexidine were both taken from a series of 20 women presenting with suspected UTI. The colony count was reduced in 12 of the mid-stream plus chlorhexidine cleaning samples compared with the suprapubic sample from the same woman. Vulvar cleansing with a 1:2,000 solution of chlorhexidine (Hibitane) was shown to result often in a marked reduction in the bacterial colony count of mid-stream urine. Cleansing with sterile water has been shown to provide a satisfactory alternative for this procedure. Urinary diuresis greatly reduces the colony count of infected urine.

8. Latour K, Plüddemann A, Thompson M, Catry B, Price CP, Heneghan C, et al. Diagnostic technology: alternative sampling methods for collection of urine specimens in older adults. *Family Medicine and Community Health*. 2013;1(2):43-9. Available from: www.ingentaconnect.com/content/cscript/fmch/2013/00000001/00000002/art00008?crawler=true&mimetype=application/pdf

RATIONALE

The authors conducted a literature search to determine the validity of alternative sampling methods compared to in and-out catheterisation and suprapubic aspiration in older adults who are unable to self-collect urine specimens and/or cooperate with the urine collection. Six studies meeting the research question criteria were identified. Three studies from the 1990s explored the validity of clean catch specimens in disinfected bed pans or bowels/caps. The majority of study participants were women (90.3%; n=204/226). The reference methods were in-and-out catheterisation, urethral catheterisation, and suprapubic aspiration. The sensitivity and specificity varied from 90% to 98% and 86% to 98%, respectively. The authors of all 3 studies concluded that the clean catch collection method is valid and that it can avert the use of more invasive methods. Urine sampling from disposable diapers for microbiological analysis was assessed in 1 study. Urine was extracted by pressing over a sterile flask using diapers without an ultra-absorbent gel.

Given the high sensitivity of 93% and the high specificity of 91% the authors considered this urine sampling technique was a fairly reliable method for use in severely incontinent elderly women, but it was noted that the results cannot be generalised to other types of diapers, such as gel-based ones. Extraction from gel-based diapers needs further exploration, as only 1 non-clinical study was available. In the late 1980s the validity of condom catheters to collect urine specimens in elderly men was explored by 2 studies. With a sensitivity of 86% to 98% and a specificity of 90% to 97% the condom catheter method can potentially replace catheterisation for urine collection. The authors listed a number of limitations with the studies they found that kept them being able to make recommendations. These included limited recent research, small sample sizes, and limited consensus on minimum colony-forming units. They conclude that larger diagnostic studies in adults are needed to confirm findings before recommendations can be made.

9. National Institute for Health and Care Excellence. Urinary tract infection (catheter-associated): antimicrobial prescribing. NICE guidelines. Published Nov 2018. Available from: <https://www.nice.org.uk/guidance/ng113>

RATIONALE

This NICE/PHE guideline sets out an antimicrobial prescribing strategy for catheter-associated UTI (CAUTI). It aims to optimise antibiotic use and reduce antibiotic

resistance. The guideline states that a clinician should obtain a urine sample before antibiotics are taken (from the new catheter if changed) or a midstream specimen of urine if catheter removed. Take the sample from the catheter, via a sampling port if provided, and use an aseptic technique.

How do I interpret a urine culture result if I suspect a UTI, and follow up patients?

1. Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women: *Ann Intern Med*. 1994 May; 120(10):827-833. Available from: www.ncbi.nlm.nih.gov/pubmed/7818631

RATIONALE

This cohort study found that asymptomatic bacteriuria occurs in 25% of women over 65 years and 10% of men over 65 years. However, it was not a risk factor for mortality in elderly women without catheters. Those with asymptomatic bacteriuria were subsequently randomised to treatment or no treatment. There was no difference in the risk of mortality between the treated and untreated groups.

2. Nicolle LE. Asymptomatic bacteriuria. *Infectious Disease Clinics of North America*. 2003;17(2):367-94.
<http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.379.5055&rep=rep1&type=pdf>

RATIONALE

Review of evidence specific to asymptomatic bacteriuria in different cohorts of the population. The prevalence of asymptomatic bacteriuria in premenopausal women varies from 2% to 5%. It increases with age and is up to 5-times higher in women who are sexually active. Though women with the condition are at higher risk for symptomatic infection, treating asymptomatic bacteriuria in healthy women does not decrease the frequency of symptomatic infection and screening isn't recommended.

3. National Institute for Health and Care Excellence. Antenatal Care for Uncomplicated Pregnancies. Clinical guidance. Published March 2008. Available from: www.nice.org.uk/guidance/cg62/resources/antenatal-care-for-uncomplicated-pregnancies-pdf-975564597445

RATIONALE

This is national guidance that states that women should be offered routine screening for asymptomatic bacteriuria by mid-stream urine culture early in pregnancy because identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis.

4. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.6. www.gov.uk/government/publications/smi-b-41-investigation-of-urine

RATIONALE

UK Standards for Microbiology Investigations comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. This publication includes updates from 2018 and is NICE accredited. Standards are produced in partnership with PHE, NHS, Royal College of Pathologists and professional societies.

The document states that significant pyuria correlates well with bacteriuria and symptoms in most patients to suggest a diagnosis of UTI. Generally, a pure growth of between 10^7 - 10^8 cfu/L (10^4 - 10^5 cfu/mL) is indicative of UTI in a carefully taken specimen.

A level of $>10^8$ WBC/L ($>10^5$ WBC/mL) has been suggested as being more appropriate in discriminating infection. Sterile pyuria (that is pyuria in the presence of no growth on routine culture media) may be the result of many factors, including:

- a result of prior treatment with antimicrobial agents
- catheterisation
- calculi (stones)
- or bladder neoplasms

Other conditions which may lead to sterile pyuria include genital tract infection and sexually transmitted diseases, for example *C. trachomatis* or an infection with a fastidious organism or renal tuberculosis. If there is no growth and symptomatic marked/persistent pyuria the guidance suggest that you can look at a culture as low as 10^2 cfu/mL. Increased inoculum sizes are also required for persistently symptomatic patients without bacteriuria if the patient has recurrent 'sterile pyuria', or for specimens where lower counts are to be expected.

When interpreting a culture, the guidance states that studies conducted in the 1950s remain the basis for interpreting urine culture results showing that bacterial counts of $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) are indicative of an infection and counts below this usually indicate contamination. The guidelines indicate that urine culture results showing that in acutely symptomatic women, UTI may be associated with counts of a single isolate as low as 10^5 cfu/L (10^2 cfu/mL) in voided urine (referencing Stamm and Kuplain). In men counts as low as 10^6 cfu/L (10^3 cfu/mL) of a pure or predominant organism have been shown to be significant in voided urine. A pure isolate with counts between 10^7 and 10^8 cfu/L (10^4 - 10^5 cfu/mL) should be evaluated based on clinical information or confirmed by repeat culture. If there are 2 isolates and each organism $\geq 10^6$ cfu/L ($\geq 10^3$ cfu/mL) including possible pathogen like *E. coli* or *S. saprophyticus* the patient might have a UTI.

Routine culture methods may not be sensitive enough to detect low bacteria levels (for example $\leq 10^7$ cfu/L / $\leq 10^4$ cfu/mL) and increased sensitivity will be achieved by increasing the inoculum size. Increased inoculum sizes are also required for persistently symptomatic patients without bacteriuria if the patient has recurrent 'sterile pyuria', or for specimens where lower counts are to be expected, such as suprapubic aspiration or other surgically obtained urine.

The guidance indicates that mixed bacterial growth is probably related to contamination but that one should consider a re-test if the patient is symptomatic. Chemical tests for the presence of blood may be more sensitive than microscopy as a result of the detection of haemoglobin released by haemolysis. When haematuria is present, finding 1 to 2 red blood cells (RBCs)/high power field is not considered to be abnormal. Haematuria may be caused by non-infective pathological conditions of the urinary tract or by renal mycobacterial infection, with or without associated pyuria. Apparent haematuria may be the result of menstruation.

5. Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. NEnglJ Med 1982;307:463-8. Available from: www.ncbi.nlm.nih.gov/pubmed/7099208

RATIONALE

A prospective study that aimed to examine the conventional criteria for diagnosing coliform infection of the lower urinary tract. The authors examined 187 sexually active young women with dysuria and urinary urgency. They excluded women who were pregnant and those with suspected complicated UTI, sexually transmitted illness or pyelonephritis. Cultures of mid-stream urine samples were compared to urine cultures obtained through suprapubic aspiration or urethral catheterisation. Enterobacteriaceae were isolated from bladder urine in 98 (52%) women. *S. saprophyticus*, *S. aureus* and enterococci were cultured in 26 (14%). The women who had 'coliform' bacteria in bladder urine were further analysed regarding the number of CFB/L. If 10^8 CFB/L

mid-stream urine was used as a cut-off for 'significant' bacteriuria, the sensitivity was 51%, and the negative predictive value was 65%.

If, on the other hand, a cut-off of 10^5 CFB/L mid-stream urine was used, the sensitivity was 95% with a negative predictive value of 94%, whereas specificity declined from 99% to 85%. Thus, low cut-off of 'coliform' bacteria in mid-stream urine more accurately predicted bladder infection in symptomatic women than in asymptomatic. Many additional studies support the observation that low bacterial concentrations of *E. coli* in particular have diagnostic relevance, even in mixed flora.

6. Mohr NM, Harland KK, Crabb V, Mutnick R, Baumgartner D, Spinosi S, et al. Urinary Squamous Epithelial Cells Do Not Accurately Predict Urine Culture Contamination, but May Predict Urinalysis Performance in Predicting Bacteriuria. *Acad Emerg Med*. 2016;23(3):323-Available from: www.ncbi.nlm.nih.gov/pubmed/26782662

RATIONALE

The authors sought to determine the value of using quantitative squamous epithelial cells as a predictor of urinalysis contamination. They conducted a retrospective cross-sectional study of adults presenting to a tertiary academic medical centre who had urinalysis with microscopy and urine culture performed. The primary analysis aimed to determine a squamous epithelial cells threshold that predicted urine culture contamination. They also explored how demographic variables (age, sex, body mass index) may modify the test performance and whether squamous epithelial cells impacted traditional urinalysis indicators of bacteriuria. A total of 19,328 records were included.

Results showed that squamous epithelial cells count was a poor predictor of urine culture contamination (area under the receiver operating characteristics curve = 0.680, 95% confidence interval [CI] = 0.671 to 0.689). In secondary analysis, the positive likelihood ratio (LR+) of predicting bacteriuria via urinalysis among non-contaminated specimens was 4.98 (95% CI = 4.59 to 5.40) in the absence of squamous epithelial cells, but the LR+ fell to 2.35 (95% CI = 2.17 to 2.54) for samples with more than 8 squamous epithelial cells /low-powered field (lpf). In an independent validation cohort, urinalysis samples with fewer than 8 squamous epithelial cells/lpf predicted bacteriuria better (sensitivity = 75%, specificity = 84%) than samples with more than 8 SECs/lpf (sensitivity = 86%, specificity = 70%; diagnostic odds ratio = 17.5 [14.9 to 20.7] vs. 8.7 [7.3 to 10.5]). The authors concluded that squamous epithelial cells are a poor predictor of urine culture contamination, but may predict poor predictive performance of traditional urinalysis measures.

7. Bartlett R, Treiber N. Clinical Significance of Mixed Bacterial Cultures of Urine. *Am J Clin Pathol*. 1984 Sep;82(3):319-22. Available from: www.ncbi.nlm.nih.gov/pubmed/6465098

RATIONALE

The authors studied 247 patients yielding mixed urine cultures in order to understand the frequency with which isolation of more than 1 bacterial species from urine signifies treatable mixed infection versus contamination or colonization occurs. Specimens were collected by clean catch from 88 and from closed drainage systems from 159. A second specimen was collected within 48 hours, and the results of the 2 cultures were compared. The percentages in which the initial mixed culture was found to represent probable, possible, and improbable treatable mixed infection were as follows: for clean catch specimens, 11%, 20%, and 67%, and for closed drainage systems specimens, 3%, 21%, and 77%.

The authors have found that empiric antibiotic therapy and reporting of mixed cultures based on culture morphology without complete identification or antibiotic susceptibilities (except for certain colony types suggesting potentially multi-drug resistant strains) with request for resubmission represents a cost-effective solution to the mixed culture problem in the diagnosis and treatment of urinary tract infection.

8. Renal Association and British Association of Urological Surgeons. Joint consensus statement on the initial assessment of haematuria. 2008 Jul. Available from: www.baus.org.uk/_userfiles/pages/files/News/haematuria_consensus_guidelines_July_2008.pdf

RATIONALE

This Joint Working Party agreed that urine testing for haematuria should only be performed for identifiable clinical reasons; there is currently no evidence to support opportunistic screening of the general population. Urine dipstick of a fresh voided urine sample, containing no preservative, is considered a sensitive means of detecting the presence of haematuria. Significant haematuria is considered to be 1+ or greater. Trace haematuria should be considered negative. Routine microscopy for confirmation of dipstick haematuria is not necessary. Significant haematuria is diagnosed if there is:

- any single episode of visible haematuria
- any single episode of non-visible haematuria (in absence of UTI or other transient causes)
- persistent (2 out of 3 dipsticks positive)
- asymptomatic non-visible haematuria (in absence of UTI or other transient causes)

Haematuria in association with UTI is not uncommon. Following treatment of UTI, a dipstick should be repeated to confirm the post-treatment absence of haematuria. Other causes of transient haematuria include exercise induced haematuria, rarely myoglobinuria and menstruation. Refer to urology: all patients with visible haematuria (any age), all patients with s-NVH (any age); all patients with a-NVH aged 40 years or over.

9. National Institute for Health and Care Excellence. Urinary tract infection (recurrent): antimicrobial prescribing. Nice guidelines. Published October 2018. Available from: <https://www.nice.org.uk/guidance/ng112>

RATIONALE

NICE guideline on the management of recurrent UTI states to refer or seek specialist advice on further investigation and management for: men aged 16 years and over, people with recurrent upper UTI, people with recurrent lower UTI when the underlying cause is unknown, pregnant women, children and young people under 16 years in line with the NICE guideline on urinary tract infection in under 16s, people with suspected cancer in line with the NICE guideline on suspected cancer: recognition and referral.

10. National Institute for Health and Care Excellence (NICE). Suspected cancer: recognition and referral. 2015 Aug. Updated 2018. Available from: www.nice.org.uk/guidance/ng12/resources/suspected-cancer-recognition-and-referral-pdf-1837268071621

RATIONALE

This guideline covers the identification of children, young people, and adults with symptoms that could be caused by cancer. It includes the investigation of cancer in primary care and when to refer people for specialist opinion. It states that you should refer people aged 45 and older with unexplained visible haematuria without urinary tract infection, those with visible haematuria that persists or recurs after treatment, or those aged 60 and over with unexplained non-visible haematuria and either dysuria or a raised white cell count on a blood test. It also says that you should consider non-urgent referral for bladder cancer in people aged 60 and over with recurrent or persistent unexplained urinary tract infection. Please see full guidance for further criteria.

Flowchart and tables for infants/children under 16 years with suspected UTI

1. National Institute for Health and Care Excellence (NICE). Urinary tract infection in under 16s: diagnosis and management. 2007 Aug. Updated 2018. Available from: www.nice.org.uk/guidance/cg54/resources/urinary-tract-infection-in-under-16s-diagnosis-and-management-pdf-975507490501

RATIONALE

This guidance aims to inform several aspects of UTI in children under 16 years, including:

- when to consider the diagnosis of UTI

- urine collection
- tests to establish or exclude UTI
- treatment
- use of prophylactic antibiotics and investigations to assess the structure and function of the urinary tract
- referral to secondary and tertiary care
- surgical intervention
- long-term follow-up
- and advice to give to parents or carers

In 2017, NICE included an update on recommendations for urine testing for infants and children under 3 years. This included:

- send a urine sample for microscopy and culture for infants under 3 months of age with suspected UTI and urgently refer for specialist care
- for infants/children over 3 months use dipstick testing for leukocyte esterase and nitrite
- only send in a sample for microscopy if 1 of the criteria listed below are met or if the dipstick is positive.

In children over the age of 3 years, dipstick testing is as useful as culture. Criteria for sending in a urine for microscopy and culture:

- in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection
- in infants and children with a high to intermediate risk of serious illness
- in infants under 3 months
- in infants and children with a positive result for leukocyte esterase or nitrite
- in infants and children with recurrent UTI
- in infants and children with an infection that does not respond to treatment within 24 to 48 hours, if no sample has already been sent
- when clinical symptoms and dipstick tests do not correlate

Atypical UTIs (seriously ill, poor urine flow, abdominal or bladder mass, raised creatinine, septicaemia, failure to respond to treatment within 48 hours, non-*E.coli* infection) should have an ultrasound in acute phase; non-*E.coli* infection ultrasound within 6 weeks. C-reactive protein alone should not be used to differentiate upper from lower UTI. Expert opinion is that if urine cannot be cultured in 4 hours of collection the sample should be refrigerated or preserved with boric acid. Also, pyuria may be absent in childhood UTI, and non-*E. coli* organisms are an atypical cause of UTI in children. NICE recommends urgent ultrasound imaging in this situation to exclude structural abnormalities of the genitourinary tract, and to guide management. However, if child with non-*E.coli* UTI is responding well to antibiotics and presents with no other features of an atypical infection, ultrasound can be requested on a non-urgent basis to take place in 6 weeks.

This guidance reviews all the evidence around sample collection in children, and suggests that clean catch method should be used to collect a sample. If this is not possible non-invasive methods should be employed according to manufactures instruction (not cotton wool, gaze or sanitary towels). Catheter or suprapubic aspiration should be used if non-invasive methods are not practical. The guidance also states that for urine that can't be cultured within 4 hours of collection, the sample should be refrigerated or preserved with boric acid, ensuring the correct specimen volume to avoid potential toxicity against bacteria in the specimen.

2. National Institute for Health and Care Excellence. Urinary tract infection (lower): antimicrobial prescribing NICE guidelines. Published October 2018. Available from: www.nice.org.uk/guidance/ng109

RATIONALE

This guideline (produced by the NICE Public Health and Social Care Guidelines Team) sets out an antimicrobial prescribing strategy for lower urinary tract infection. It aims to optimise antibiotic use and reduce antibiotic resistance. It is clearly stated which antibiotics should be used for infections in tables within the guidelines and these tables are also included in the visual summaries that accompany the guidelines. The recommendations include that advice should be given with self-care to all people with a lower UTI. For children under 16 years the guidance recommends a urine sample from children and young people with lower UTI before antibiotics are taken. Then to dipstick test or send for culture and susceptibility testing in line with the NICE guideline on urinary tract infection in under 16s: diagnosis and management.

3. Rees JC, Vernon S, Pedler SJ, Coulthard MG. Collection of urine from washed-up potties. *Lancet*. 1996 Jul; 348(9021):197. Available from: www.ncbi.nlm.nih.gov/pubmed/8684173.

RATIONALE

This study tested 4 methods of cleaning the potty to reduce faecal contamination of the sample. Washing potties using washing up liquid with hot water at 60°C before taking a urine specimen was the most effective method of reducing faecal contamination. Cleaning potties with Dettol or bleach were less successful.

4. Birnie K, Hay AD, Wootton M, Howe R, MacGowan A, Whiting P, et al. Comparison of microbiological diagnosis of urinary tract infection in young children by routine health service laboratories and a research laboratory: Diagnostic cohort study. *PLoS One*.2017;12(2):e0171113. Available from: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0171113>

RATIONALE

This prospective diagnostic cohort study in 4,808 acutely ill children aged <5 years attending UK primary health care, defining UTI as pure/predominant growth 10⁵ CFU/mL of a uropathogen (the reference standard), calculated areas under the receiver-operator curve (AUC) for UTI predicted by pre-specified symptoms, signs and dipstick test results (the index test), separately according to whether samples were obtained by clean catch or nappy (diaper) pads. 2,619 had clean catch urine specimens and 2,189 had nappy pads. 251 (5.2%) and 88 (1.8%) children were classified as UTI positive by health service and research laboratories, respectively. Agreement between laboratories was moderate (kappa = 0.36; 95% confidence interval [CI] 0.29, 0.43), and better for clean catch (0.54; 0.45, 0.63) than nappy pad samples (0.20; 0.12, 0.28). In clean catch samples, values of AUC were lower in nappy pad samples (0.65 [0.61, 0.70] and 0.79 [0.70, 0.88] for health service and research laboratory positivity, respectively) than clean catch samples.

The agreement of microbiological diagnosis of UTI comparing routine health service laboratories with a research laboratory was moderate for clean catch samples and poor for nappy pad samples and reliability is lower for nappy pad than for clean catch samples. Positive results from the research laboratory appear more likely to reflect real UTIs than those from routine health service laboratories, many of which (particularly from nappy pad samples) could be due to contamination. The researchers concluded that primary care clinicians should try to obtain clean catch samples, even in very young children.

5. LaRocco MT, Franek J, Leibach EK, Weissfeld AS, Kraft CS, Sautter RL, et al. Effectiveness of Preanalytic Practices on Contamination and Diagnostic Accuracy of Urine Cultures: a Laboratory Medicine Best Practices Systematic Review and Meta-analysis. *Clin Microbiol Rev.* 2016;29(1):105-47. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC4771218/pdf/zcm105.pdf

RATIONALE

A large systematic review to identify and evaluate preanalytic practices associated with urine specimens and to assess their impact on the accuracy of urine culture microbiology. Specific practices included:

- collection methods for men, women, and children
- preservation of urine samples in boric acid solutions
- the effect of refrigeration on stored urine

Practice efficacy and effectiveness were measured by 2 parameters:

- reduction of urine culture contamination
- increased accuracy of patient diagnosis

The Center for Disease Control Laboratory Medicine Best Practices (LMBP) initiative's systematic review method for assessment of quality improvement (QI) practices was employed. Results were then translated into evidence based practice guidelines. Data from 9 studies (rated as fair in quality) suggest that boric acid and refrigeration both preserve urine specimens for up to 24 hours before processing. Data from 3 studies indicate that urine held for more than 4 hours before processing should not be used due to overgrowth of flora. However, evidence quality for this is rated as low and the panel could not make a recommendation.

In children, mid-stream collection with cleansing is recommended and collection with sterile urine bags, from diapers, or mid-stream without cleansing is not recommended. Data from 6 studies – 2 with a quality rating of 'good' and 4 rated as 'fair' – found large reductions in contamination in mid-stream clean-catch urine specimens compared to contamination after other non-invasive methods of collection. Data from 8 studies – 2 with a quality rating of 'good' and 6 rated as 'fair' – suggest that mid-stream collection with cleansing is accurate for the diagnosis of urinary tract infections in infants and children and that mid-stream collection with cleansing has higher average accuracy than sterile urine bag collection (data for diaper collection was lacking). However, the overall strength of evidence was low, as multivariate modelling could not be performed; thus, no recommendation for or against can be made due to insufficient evidence.

6. Kaufman J, Fitzpatrick P, Tosif S, Hopper SM, Donath SM, Bryant PA, et al. Faster clean catch urine collection (Quick-Wee method) from infants: randomised controlled trial. *BMJ*. 2017; 357:j1341. Available from: www.ncbi.nlm.nih.gov/pubmed/28389435

RATIONALE

This randomised controlled trial in an emergency department of a tertiary paediatric hospital, Australia, aimed to determine if a simple stimulation method increases the rate of infant voiding for clean catch urine within 5 minutes. They recruited 354 infants (aged 1 to 12 months) requiring urine sample collection as determined by the treating clinician. Infants were randomised to either gentle suprapubic cutaneous stimulation (n=174) using gauze soaked in cold fluid (the Quick-Wee method) or standard clean catch urine with no additional stimulation (n=170), for 5 minutes. The Quick-Wee method resulted in a significantly higher rate of voiding within 5 minutes compared with standard clean catch urine (31% v12%, P<0.001), difference in proportions 19% favouring Quick-Wee (95% confidence interval for difference 11% to 28%). Quick-Wee had a higher rate of successful urine sample collection (30% v 9%, P<0.001) and greater parental and clinician satisfaction (median 2 v 3 on a 5-point Likert scale). Contamination rates were similar, but sample size was too low to evaluate this outcome.

7. Lynster LCT, Nayar DM, Pedler SJ, Coulthard MG. Home collection of urine for culture from infants by 3 methods: survey of parents' preferences and bacterial contamination rates. *BMJ*. 2000 May; 320(7245):1312-1313. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC27376/.

RATIONALE

In this series of 44 infants, parents collected 3 urine samples using a urine pad, bag, and clean-catch method (in a randomised order). Urine contamination levels were similar between pads (16%) and bags (18%), but lower with clean-catch (2%). Parents disliked the clean-catch method (requiring nursing the infant with a bottle ready until they wee, which is both time consuming and messy). Parents found pads and bags easy to use, and preferred them to clean-catch. The pad was considered comfortable. However, the bag was distressing, particularly on removal, often leaking, and leaving red marks.

8. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.5. www.gov.uk/government/publications/smi-b-41-investigation-of-urine

RATIONALE

UK Standards for Microbiology Investigations comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. They are produced in partnership with PHE, NHS, Royal College of Pathologists and professional societies. The document states that in children confirmation of UTI in children is dependent on the quality of the specimen and that UTIs are more likely if there is isolation of the same organism from 2 specimens. Colony counts of $\geq 10^6$ cfu/L (10^3 cfu/mL) of a single species may be diagnostic of UTI in voided urine.

Generally, a pure growth of between 10^7 - 10^8 cfu/L (10^4 - 10^5 cfu/mL) is indicative of UTI in a carefully taken specimen. Negative cultures or growth of $<10^7$ cfu/L ($<10^4$ cfu/mL) from bag urine may be diagnostically useful. Counts of $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) should be confirmed by culture of a more reliable specimen, either a single urethral catheter specimen or, preferably, a suprapubic aspirate. Bacteriuria usually exceeds $\geq 10^8$ cfu/L ($\geq 10^5$ cfu/mL) in suprapubic aspirate from children with acute UTI, although any growth is potentially significant. In microscopy, for adults significant pyuria is defined as the occurrence of 10^7 or more WBC/L (10^4 WBC/mL), although higher numbers of WBC are often found in healthy asymptomatic women. A level of $>10^8$ WBC/L ($>10^5$ WBC/mL) has been suggested as being more appropriate in discriminating infection.

Acknowledgements

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Abbreviations

- a-NVH:** Asymptomatic non-visible haematuria
- BMC:** British Medical Council
- BMJ:** British Medical Journal
- °C =°Centigrade**
- CAUTI:** Catheter-associated urinary tract infection
- CFB:** Colony forming bacteria
- CFU:** Colony forming units
- CI:** Confidence interval
- CIRC:** Clinical Innovation and Research Centre
- CKS:** Clinical Knowledge Summaries
- CRP:** C-reactive protein
- C. trachomatis:*** *Chlamydia trachomatis*
- cUTI:** Complicated urinary tract infection
- EAU:** European Association of Urology
- E. coli:** Escherichia coli
- GSM:** Genitourinary syndrome of menopause
- LTCF:** Long-term care facilities
- L:** Litres
- LR:** Likelihood ratio
- MDR:** Medical Devices Regulations
- MESH:** Medical subject heading
- mL:** Millilitres
- MSU:** Mid-stream urine
- NSAIDs:** Nonsteroidal anti-inflammatory drugs
- NEWS 2:** National Early Warning Score 2
- NICE:** National Institute for Health and Care Excellence
- NPV:** Negative predictive value
- PPV:** Positive predictive value
- P. aeruginosa:*** *Pseudomonas aeruginosa*

P. mirabilis: *Proteus mirabilis*

PHE: Public Health England

RBC: Red blood cell

RCGP: Royal College of General Practitioners

RCP: Royal College of Physicians

RCT: Randomised controlled trial

RTI =Respiratory tract infection

rUTI: Recurrent Urinary tract infection

SIGN: Scottish Intercollegiate Guidelines Network

s-NVH: Symptomatic non-visible haematuria

S. saprophyticus: *Staphylococcus saprophyticus*

STI: Sexually Transmitted Infection

UTI: Urinary tract infection

WBC: White blood cell