



Public Health
England

Protecting and improving the nation's health

DRAFT FOR REVIEW: Diagnosis of urinary tract infections (UTIs)

Quick reference guide for primary care:
For consultation and local adaptation

This document is currently being reviewed,
and should not be used in isolation.

**We are seeking comments by 30 May
2018. Email feedback to:**

TARGETAntibiotics@phe.gov.uk

Questions and responses specific to this
consultation may be made public.

About Public Health England

Public Health England (PHE) exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through world-leading science, knowledge and intelligence, advocacy, partnerships, and the delivery of specialist public health services. PHE is an executive agency of the Department of Health, and is a distinct delivery organisation with operational autonomy to advise and support government, local authorities, and the NHS, in a professionally independent manner.

Public Health England
Wellington House
133-155 Waterloo Road
London SE1 8UG
Tel: 020 7654 8000
www.gov.uk/phe
Twitter: [@PHE_uk](https://twitter.com/PHE_uk)
Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Professor Cliodna McNulty
For queries relating to this document, please contact TARGETAntibiotics@phe.gov.uk

© Crown copyright 2018

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government License v3.0. To view this license, visit [OGL](https://www.ogil.io) or email psi@nationalarchives.gsi.gov.uk. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned. Any enquiries regarding this publication should be sent to TARGETAntibiotics@phe.gov.uk

Published for external review: May 2018
PHE publications gateway number: 2018087

This document is available in other formats on request. Please call 0300 422 5068 or email TARGETAntibiotics@phe.gov.uk.



Contents

About Public Health England	2
Contents	3
Foreword – Aims and adaptations	4
References	10
Women under 65 years with uncomplicated UTI flow chart and table key points	10
Older person (over the age of 65 years) with suspected UTI:	14
Review need for urine culture:	20
Sampling technique in men and women:	21
Interpretation of culture results in adults:	22
Infants or children under 16 years with suspected UTI:	24
Acknowledgements	26
Abbreviations	26

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 covering acute uncomplicated infections in women, older patients with urinary symptoms, and children
- the flow chart for older patients may be suitable for some younger frail patients with or without catheter, especially with those with high incidence of asymptomatic bacteriuria. In contrast some older healthy patients will fit the younger flow chart.

Aims

- to provide a simple, effective, economical and empirical approach to the diagnosis and treatment of urinary tract infections
- to minimise the emergence of antibiotic resistance in the community

Implications

- the guidance should lead to more appropriate antibiotic use
- use of this guidance may influence laboratory workload, which may have financial implications for laboratories and primary care commissioners

Production

- the guidance has been produced in consultation with the Association of Medical Microbiologists, general practitioners, nurses, specialists, and patient representatives
- the guidance is in agreement with other publications, including **CKS**, **SIGN** and **NICE**
- the guidance is fully referenced and graded
- the guidance is not all-encompassing, as it is meant to be 'quick reference', clinicians should ultimately rely on their clinical judgement
- if more detail is required we suggest referral to the websites and references cited
- the guidance will be updated every three years; or more frequently if there are significant developments in the field

Poster Presentation of Guidance

- the summary table is designed to be printed out as a poster for use in practice
- the RATIONALE and evidence is 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 guidance, but the format allows minor changes to suit local service delivery and sampling protocols
- to create ownership agreement on the guidance 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 email any evidence or references that support your requests for change so that we may consider them at our annual review. Comments should be submitted to Professor Cliodna McNulty, Head of PHE Primary Care Unit, Microbiology Laboratory, Gloucestershire Royal Hospital, Great Western Road, Gloucester GL1 3NN.

Email: TARGETAntibiotics@phe.gov.uk

Woman (under 65 years) with suspected UTI

URINARY SYMPTOMS (e.g. dysuria, frequency, urgency) IN ADULT WOMEN under 65

This guide excludes patients with recurrent UTI (2 episodes in last 6 months, or 3 episodes in last 12 months)^{1D,2D}

↓ YES

Consider other causes of urinary symptoms:

- vaginal symptoms or discharge - only 15-20% with discharge have UTI^{3A+,4A+}
- urethritis - Urinary symptoms may be due to urethral inflammation post sexual intercourse, irritants, or can be related to a sexually transmitted infection^{5C}
- sexually transmitted infections - including Chlamydia and gonorrhoea in sexually active^{4A+,5C}
- genitourinary symptoms of menopause/atrophic vaginitis/vaginal atrophy^{5C,6D,7B+}

YES →

Follow relevant diagnostic guide and safety netting

↓ NO

- Any moderate risk of sepsis? (*see box at bottom of page) or if National Early Warning Score overall is 5: using respiration, pulse oximetry, blood pressure, pulse, consciousness, temperature
- Any new sign of pyelonephritis or systemic infection?
**see box at bottom of page

YES →

Consider Upper UTI/pyelonephritis or possible sepsis:
Consider admission if required
Send urine for culture.
Immediately start antibiotic for upper UTI/sepsis using local guidelines

↓ NO

How many of the 3 key diagnostic symptoms/signs do they have?^{8B+}

- dysuria (burning pain when passing urine)^{3A+,4A+,8B+,9B+,10B+}
- new nocturia (passing urine more often at night)^{3A+,8B+}
- urine cloudy to the naked eye^{8B+}

2 or 3 symptoms

1 symptom

no symptoms

YES

YES

YES

Perform Urine Dipstick Test

Nitrite positive
OR BOTH WBC
and RBC positive^{8B+}

WBC positive
Nitrite negative^{8B+}

ALL Nitrite, WBC, RBC
negative^{8B+}

NO

UTI likely

UTI equally likely to other diagnosis

UTI LESS likely

Offer immediate antibiotic for lower UTI
Consider self-care with back-up antibiotic if mild symptoms that do not interfere with quality of life
Consider need for urine culture

Review time of specimen (morning is most reliable)
Send urine for culture
Use Immediate or back-up antibiotic depending on symptom severity

Consider other diagnosis
Reassure and give self-care and safety netting advice

Give and discuss TARGET UTI leaflet with safety netting advice

Offer **ALL** self-care advice: e.g. hydration, taking regular paracetamol (or ibuprofen, if with back-up antibiotic)^{12C,13D,14D,15B+}

*** Signs/symptoms of moderate risk of sepsis**^{16C,17A,18C:}

- new alteration in mental state or decreased functional ability
- new heart rate above 90 beats/min at rest or dysthymia
- new dyspnoea or respiratory rate above 20 breaths/min
- new low blood pressure (systolic <100mm Hg)
- no urine passed in 12 hours (≤0.5-1ml/kg urine per hour if catheter)
- tympanic temperature 36°C or below
- impaired immune system (except if chemotherapy)

****Signs of pyelonephritis or systemic infection**^{19C:}

- kidney pain/tenderness in back under ribs
- new/different myalgia, flu like illness
- shaking chills (rigors) or temperature 38°C or above
- nausea/vomiting

Key: Sepsis alert UTI symptoms Action Advised Other advice

Older person (Over 65 years) with suspected UTI

Use symptoms/signs to guide management. Do not perform urine dipstick: not recommended if over 65 years. Up to half of older adults will have bacteria present in the bladder/urine (asymptomatic bacteriuria) and positive dipstick without an infection. This is not harmful and does not require treatment with antibiotics.^{1A-,2A-,3B+,4B+}

CHECK FOR ANY SYMPTOMS/SIGNS:

- localised symptoms or signs of UTI** e.g. new onset dysuria; incontinence; urgency^{5B+}
- temperature:** 38°C or above; 36°C or below; 1.5°C above normal twice in the last 12 hours^{6A-,7D,8B+}
- non-specific signs of infection:** e.g. increased confusion; loss of diabetic control^{16A-,7D,9B-,10A+}

YES ↓

- CHECK for moderate risk of sepsis (below) or if National Early Warning Score overall is 5:** using respiration, pulse oximetry, blood pressure, pulse, consciousness, temperature^{11C}
- acute deterioration^{11C}
 - new heart rate above 90 beats/min at rest or dysrhythmia^{12A}
 - new respiratory rate above 20 breaths/min or dyspnoea^{12A,13C}
 - new low blood pressure (systolic <100mm Hg)^{12A}
 - no urine passed in 12 hours (<1ml/kg/hr if catheter)^{12A,13C}
 - tympanic temperature below 36°C^{12A}

CHECK for any one sign of pyelonephritis:

- kidney pain/tenderness in back, under ribs^{15A+,16C}
- new/different myalgia, or flu-like symptoms^{15A+,16C}
- shaking chills (rigors) or temp over 38°C^{16C}

YES →

Consider pyelonephritis or possible sepsis:^{13C,14D}

- consider admission
- send urine for culture
- immediately start antibiotic for upper UTI/sepsis
- follow local guidelines
- If urinary catheter: change or remove immediately after starting antibiotics

NO ↓

CHECK ALL FOR symptoms/signs of UTI:

- NEW onset dysuria alone^{6A-,7D,17C}
- OR two or more new**
- frequency or new urgency^{6A-,7D,17C}
- incontinence^{6A-,7D}
- new or worsening confusion/delirium/debility^{6A-,7D} (if urinary catheter this alone can be predictive)
- suprapubic pain^{6A-,7D,17C}
- visible haematuria^{6A-,7D,17C}

If urinary catheter CHECK for blockage, and consider removal

Consider if genitourinary symptoms are atrophic vaginitis/vaginal atrophy^{18D}

YES →

UTI LIKELY:

- **consider immediate antibiotics** for lower UTI
- **if mild symptoms** consider back-up antibiotics
- **always send urine culture** if feasible, as more antibiotic resistance in older adults^{16C}
- **review antibiotic choice** with culture results
- **give paracetamol** to relieve symptoms^{19D}
- **consider non-steroidal anti-inflammatory:** if no contraindications^{20A-}
- If indwelling urinary catheter for over 7 days:**
 - change catheter as soon as possible after starting antibiotic treatment^{21C,22C}
 - assess catheter need, and remove if possible^{22C}

NO ↓

CHECK ALL for other localised symptoms/signs:

Two or more symptoms or signs in:

- respiratory tract infection:** shortness of breath; cough or sputum production; new pleuritic chest pain^{7D}
- gastrointestinal tract infection:** nausea/vomiting; new abdominal pain; new onset diarrhoea^{23C,24C}
- skin and soft tissue infection:** new redness; warmth; swelling^{7D}

CHECK ALL for other causes of confusion (PINCH ME)^{25C}:

- | | |
|--|---|
| <input type="checkbox"/> P: Pain | <input type="checkbox"/> M: other Medication |
| <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 | |

YES →

Follow local diagnostic and treatment guidance

YES →

For ALL patients:

Give TARGET UTI leaflet for older adults and discuss self-care

Give safety netting advice about consulting if:

- worsening symptoms
- signs of pyelonephritis
- any symptom/sign of sepsis

YES ↓

If worsening signs or symptoms:
consider admission or start/change antibiotic^{14D}

Key: Sepsis alert UTI symptoms Action Advised Other advice

Key Points From Flow Chart for Women under 65 years (same citations as flow chart)

Using symptoms and dipsticks to help diagnose UTI in women (under 65 years): ^{3A+,4A+,8B+,9B+,10B+,11B+} 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

- vaginal symptoms or discharge - 75-80% with discharge will not have UTI ^{3A+,4A+},
- urethritis - Urinary symptoms may be due to urethral inflammation post sexual intercourse, irritants, or can be related to a sexually transmitted infection ^{5C}
- sexually transmitted infections - including chlamydia and gonorrhoea in sexually active ^{4A+,5C}
- genitourinary symptoms of menopause/atrophic vaginitis/vaginal atrophy ^{5C,6D,7B+}

Check for new signs of pyelonephritis, systemic infection, or risk of sepsis ^{16C,17A,18C,19C}

If pyelonephritis, moderate risk of sepsis or National Early Warning Score of 5 or above: immediately start antibiotic for upper UTI/sepsis using local guidelines; consider admission, and send urine for culture to inform definitive treatment

In all patients use 3 urinary symptoms/signs of dysuria, new nocturia or cloudy urine to guide treatment ^{8B+}:

- **71% will have ≥2 symptoms/signs** ^{8B+}: UTI likely - give immediate antibiotic or consider back-up if mild symptoms
- **25% will have 1 symptom/sign** ^{8B+}: UTI possible - use urine dipstick to increase diagnostic certainty
- **4% will have 0** ^{8B+}: UTI less likely - use urine dipstick if other severe urinary symptoms (frequency, urgency, haematuria, suprapubic tenderness)

Using dipsticks are useful to help predict UTI if 0 or 1 of dysuria, nocturia, cloudy urine ^{8B+}

- **positive nitrate or positive leucocytes and blood:** UTI likely ^{8B+}: offer empirical antibiotics for lower UTI, OR consider back-up antibiotic if milder symptoms
- **leucocytes positive but Nitrite negative:** UTI equally likely to other diagnosis ^{8B+}: review time of specimen (*morning is best*); send urine for culture; use back-up or immediate antibiotic depending on symptom severity
- **ALL nitrite, leucocytes and blood negative:** UTI Less likely ^{8B+}: consider other diagnosis; reassure; give self-care and safety netting advice

REVIEW NEED FOR URINE SAMPLE FOR CULTURE

Send a urine for culture in:

- patients over 65 years if symptomatic and antibiotic given
- pregnancy: for routine antenatal tests, or if symptomatic ^{1B+}
- suspected pyelonephritis or sepsis ^{2C}
- **suspected UTI in men** ^{3C}
- failed antibiotic treatment or persistent symptoms ^{4A,5A+,6B-}
- recurrent UTI (2 episodes in 6m or 3 in 12m) ^{3C,4A}
- as advised by local microbiologist

Consider risk factors for resistance.

Send urine for culture if:

- abnormalities of genitourinary tract ^{3C}
- renal impairment ^{3C}
- care home resident ^{4A}
- hospitalisation for more than 7 days in last 6m ^{4A}
- recent travel to a country with increased resistance ^{4A}
- previous UTI resistant to trimethoprim, cephalosporins, quinolones, or broad spectrum antibiotic ^{4A,5A}

NOTE: ESBLs are multi-resistant, but often sensitive to nitrofurantoin or fosfomycin ^{7B+,8B+,9A+}

SAMPLING IN WOMEN AND MEN

Women: midstream urine and holding the labia apart may help reduce contamination but if not possible, sample can still be sent for culture ^{1B+,2A+,3B+,4D,5B} Cleansing with antiseptic leads to false negatives, as bacteria may be inhibited ^{6B}

Elderly frail: Only take a urine sample if symptomatic and it is possible to collect good sample.

Men: advise on how to take a midstream specimen (**NHS choices**) ^{1B+,4D}

People with catheters: using aseptic technique, drain a few mL of residual urine from the tubing, then collect a fresh sample from catheter sampling port ^{1B+,7A}

Refrigerate specimens to prevent bacterial overgrowth ^{1B+,4D} or use specimen pots with boric acid (fill to the line) ^{1B+}

HOW DO I INTERPRET A CULTURE RESULT IN UTI?

Culture should be interpreted in parallel with severity of signs and symptoms, as false negatives 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

- low counts $\geq 10^5$ colony forming units (CFU)/L of *Escherichia coli* or *Staphylococcus saprophyticus* ^{4B+,5B+}
- single organism $\geq 10^7$ CFU/L ^{4B+}: higher counts $\geq 10^8$ CFU/mL have even higher positive predictive value ^{4B+}
- $\geq 10^8$ /L mixed growth with one predominant organism

Epithelial cells/mixed growth:

- presence indicates perineal contamination, reducing significance of positive culture ^{4B+}

Red cells: may be present in UTI ^{6B+}

- lab red cell microscopy is less accurate than dipstick ^{6B+}
- refer patients with persistent haematuria post-UTI for investigation of bladder cancer ^{8A}

White blood cells/ leucocytes:

- white cells $\geq 10^7$ /L are considered to represent inflammation in urinary tract, this includes the urethra ^{6B+}
- 'no white cells present' indicates no inflammation and reduces culture significance ^{6B+,5B+}
- white cells can be present in elderly with asymptomatic bacteriuria as the immune system does not differentiate colonisation from infection

Sterile pyuria:

- in sterile pyuria, consider *Chlamydia trachomatis* (especially if 16-24 years), other vaginal infections, other non-culturable organisms, including TB or renal pathology ^{6B+}

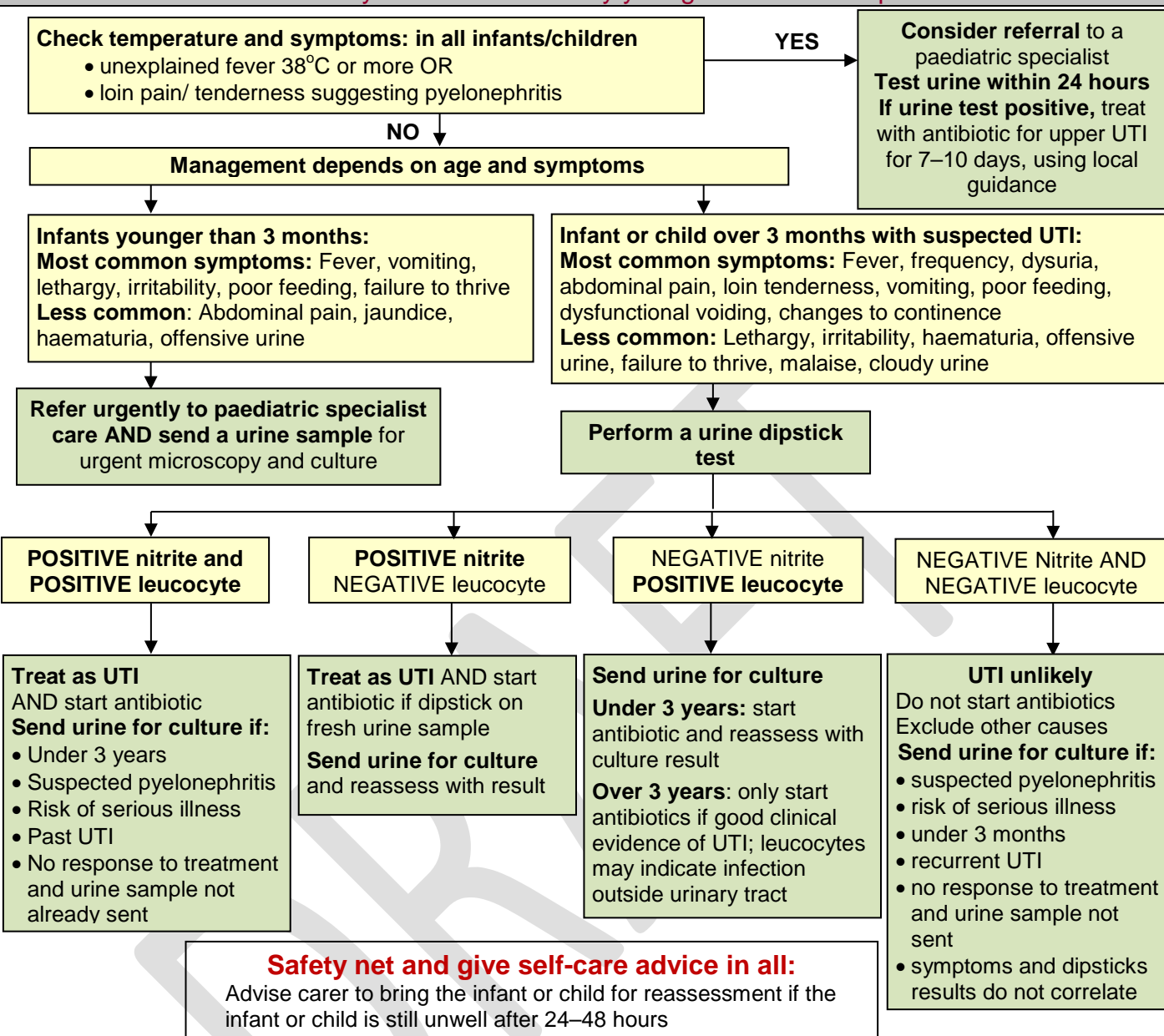
FOLLOW-UP: urine culture is usually negative at follow up if asymptomatic

Do not send follow-up urine unless pregnant, or multi-resistant organism on advice from the laboratory

Consider non-urgent referral for bladder cancer in patients ≥ 60 years with recurrent/persistent unexplained UTIs ^{8A}

Infants or children under 16 years with suspected UTI^{1B+}

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



Sampling in children^{1B+,2B+,3B,4B,5B+}:

- in toddlers, clean catch urine using potties (cleaned in hot water (60°C) with washing up liquid)
- in infants, clean catch urine recommended: urine collection pad in nappy is alternative (follow pad instructions, changing pad every 30 minutes until urine is passed). Parents found bags more distressing
- if non-invasive not possible consider: catheter sample, or suprapubic aspirate (with ultrasound guidance)
- culture urine within 4 hours, refrigerate, or use boric acid preservative (boric acid can cause false negative culture if urine not filled to correct mark on specimen bottle)

Interpretation of culture results^{1B+,5B+}:

- single organism $>10^6$ CFU/L indicates UTI; any growth from a suprapubic aspirate is significant
- white blood cells $>10^7$ /L usually indicates UTI, especially with clinical symptoms but may be absent in children, or present with fever alone

Other diagnostic tests^{1B+}:

- if child has alternative site of infection do not test urine unless remain unwell then test within 24 hours
- do not use CRP to differentiate upper UTI from lower UTI
- ultrasound all children in acute phase and undertake renal imaging in 4-6 months: 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 children within 6 weeks if: under six months and UTI not atypical, OR non-E.coli UTI, OR all ages with recurrent UTI

GRADING OF GUIDANCE 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, e.g. case reports or case series	C
Formal combination of expert opinion	D

This guidance was originally produced in 2002 by the South West GP Microbiology Laboratory Use Group, in collaboration with the Association of Medical Microbiologists, general practitioners, nurses and specialists in the field. This guidance 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 guidance with the most recent changes highlighted, please email TARGETAntibiotics@phe.gov.uk.

For detailed information regarding the search strategies implemented and full literature search results, please email TARGETAntibiotics@phe.gov.uk.

References

Women under 65 years with uncomplicated UTI flow chart and table key points

1. Grabe M, Bjerklund-Johansen TE, Cai T, Cek M, Koves B, Naber KG et al. Guidelines on urological infections. *European Association of Urology*. 2015. Available from: https://uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf
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 “At least three episodes of uncomplicated infection documented by culture in past 12 months: women only; no structural/functional abnormalities”.
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: https://www.scottishmedicines.org.uk/files/sapg1/Management_of_recurrent_lower_UTI_in_non-pregnant_women.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 three or more episodes of UTI in 12 months or two or more episodes of lower UTI in 6 months. This does not include episodes of bacteriuria without UTI symptoms (asymptomatic bacteriuria).
3. 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: <https://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. Sixteen 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 authors conclude that individual symptoms and signs have a modest ability to raise the pretest-risk of UTI. Diagnostic accuracy improves considerably when combined with dipstick tests particularly tests for nitrites.
4. 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: <https://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. The authors identified 4 symptoms and 1 sign that significantly increased the probability of a UTI (dysuria, frequency, haematuria, back pain, costovertebral tenderness). 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. Additionally, this review states that dysuria with frequency together increase the chances of UTI to 90%. This review also identifies symptoms of pyelonephritis as: fever; back pain; nausea; vomiting.
5. Michaels T, Sands J. Dysuria: Evaluation and Differential Diagnosis in Adults. *American Family Physician*. 2015;92(9). Available from: <https://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 (e.g., vaginal or urethral irritation), risk factors for a complicated urinary tract infection (e.g., male sex, pregnancy, presence of urologic obstruction, recent procedure), and symptoms of pyelonephritis. Women with dysuria who have no complicating features can be treated for cystitis without further diagnostic evaluation. Women with vulvovaginal symptoms should be evaluated for vaginitis. 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.

6. 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: <https://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 cosponsored 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 diagnostic guidance.
7. 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: <https://www.ncbi.nlm.nih.gov/pubmed/26421474>
RATIONALE: This multi-centric study was performed in order to provide nation-wide 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. Nine hundred thirteen 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 vuvular 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 VVA/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.
8. 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: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894378/>
RATIONALE: A validation study that recruited 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. 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 three of cloudy urine, dysuria of any degree, and new nocturia to any degree; 74% for two, 68% for one. The negative predictive value was 67% for none of these three features. The authors conclude that though 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 in discussion with the lead author of this paper in 2018 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 two of dysuria, cloudy urine or nocturia will have a proven UTI it is reasonable to prescribe empirically in these patients. In patients with only one 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 and severity of symptoms, then an immediate or back-up or no antibiotic strategy can be discussed with the patient.
9. Medina-Bombardó D, Seguí-Díaz B, 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: <https://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 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.

10. 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: <https://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 59.0% 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.
11. 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: <https://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 two symptoms of acute uncomplicated UTI (defined as 10^4 cfu/mL from a mid-stream urine (MSU)). 75% of those enrolled had significant bacteraemia. 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.
12. Beetz R. Mild dehydration: a risk factor of urinary tract infection? *Eur J Clin Nutr*. 2003;57 Suppl 2:S52-58. Available from: <https://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.
13. Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI). 5th Annual Report. April 2013-March 2014. 2015 Feb. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/405295/ARHAI_annual_report.pdf
RATIONALE: An ARHAI report, noting that mandatory surveillance over the past ten years has demonstrated a sustained increase in *E. coli* bacteraemia that is unexplained by improved diagnosis. The analysis demonstrates that only a small proportion of infections are related to urinary catheterisation. Other risk factors, such as repeated urinary tract infections treated by sub-optimal antibiotic prescribing, and inadequate hydration, have a significant impact. The surveillance report shows that *E. coli* bacteraemia peaks in the summer months, which may also be due to poor urine output associated with dehydration. The report

recommends that: all organisations providing care to patients with indwelling urinary catheters should ensure that the recommendations of EPIC 3 (short-term catheters) and NICE (long-term catheters) are being implemented, and provide evidence of compliance; hydration status must be a priority for those at risk of dehydration, particularly those in hospitals and long-term care facilities; treatment of UTI should be based on local antibiotic resistance patterns, and patients diagnosed with a UTI (especially those with a history of repeated infections) should be subject to a safety-netting procedure to ensure that treatment has been effective.

14. Little P. Antibiotics or NSAIDs for uncomplicated urinary tract infection? *BMJ*. 2017;359:j5037. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29117972>
RATIONALE: An editorial discussion 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.
15. 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: <https://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 NSAID. 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.
16. The UK Sepsis Trust. Do I have sepsis? 2016 Mar. Available from: <https://sepsistrust.org/news/what-is-sepsis/>
RATIONALE: A UK Sepsis Trust website with decision tools that outline amber flags of sepsis for general practice. This website defines the "flags" of sepsis as: Relatives worried about mental state/ behaviour; Acute deterioration in functional ability; Immunosuppressed (without recent chemotherapy); Trauma, surgery or procedure in last 6 weeks; Respiratory rate 21-24 OR dyspnoeic; Systolic B.P 91-100 mmHg; Heart rate 91-130 OR new dysrhythmia; Not passed urine in last 12-18 hours; Tympanic temperature $\leq 36^{\circ}\text{C}$; Clinical signs of wound, device or skin infection. The general practice guidelines also provide guidance as to action if flags are reached including the need to transfer patient to the hospital or treat in a community setting.
17. National Institute of Health and Care Excellence (NICE). Sepsis: Recognition, diagnosis and early management. 2016 Jul. Available from: <https://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 21–24 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 91–100 mmHg; not passed urine in the past 12–18 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.
18. Royal College of Physicians. National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. London:RCP2012. Available from: <https://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 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:

National Early Warning Score (NEWS2)

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO ₂ Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO ₂ Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

© Royal College of Physicians 2018



respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness, or 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; a score of 5-6 (medium clinical risk) should trigger a an urgent response; and a score of 7 (high clinical risk) should trigger an urgent or emergency response.

19. Colgan R, Williams M. Diagnosis and Treatment of Acute Pyelonephritis in Women. *American Academy of Family Physicians*. 2011;84(5). Available from: <https://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. Nausea and vomiting also need to be considered. 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.

Older person (over the age of 65 years) with suspected UTI:

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: <https://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. Urinary tract infection 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.

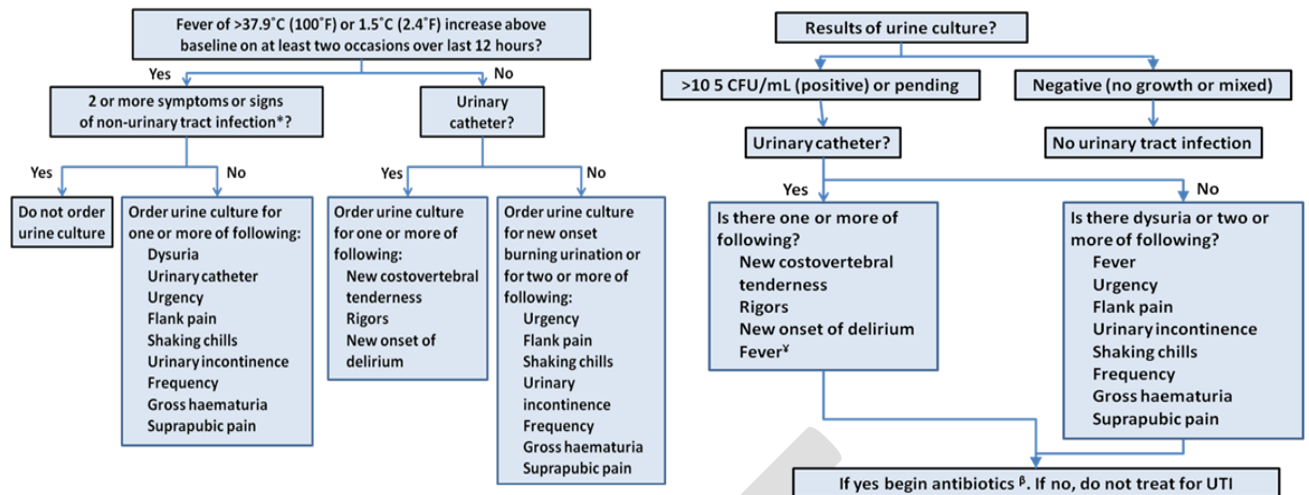
2. Nicolle LE, Mayhew WJ, Bryan L. Prospective randomized comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalized elderly women. *Am J Med*. 1987 Jul; 83(1):27-33. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/3300325>

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 one 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 percent 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

3. 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: <https://www.ncbi.nlm.nih.gov/pubmed/10724053>
RATIONALE: A prospective study of 761 newly catheterized patients in a university hospital; 82 (10.8%) developed nosocomial CAUTI (> 10(3) colony-forming units per millilitre). 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-catheterized patients with urinary tract infection. 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.
4. Sundvall PD¹, Elm M, Ulleryd P, Mölsted S, Rodhe N, Jonsson L, Andersson B, Hahn-Zoric M, Gunnarsson R. Interleukin-6 concentrations in the urine and dipstick analyses were related to bacteriuria but not symptoms in the elderly: a cross sectional study of 421 nursing home residents. *BMC Geriatr.* 2014 Aug 12;14:88. Available from: <https://bmcgeriatr.biomedcentral.com/articles/10.1186/1471-2318-14-88>
RATIONALE: In this cross sectional study, voided urine specimens for culture, urine dipstick and IL-6 analyses were collected from all nursing home residents capable of providing a voided urine sample, regardless of the presence of symptoms. Urine specimens and symptom forms were provided from 421 residents of 22 nursing homes. Residents without nonspecific symptoms had positive urine cultures as often as those with nonspecific symptoms with a duration of up to one month. Residents with positive urine cultures had higher concentrations of IL-6 in the urine (p < 0.001). However, among residents with positive urine cultures there were no differences in IL-6 concentrations or dipstick findings between those with or without nonspecific symptoms. Nonspecific symptoms among elderly residents of nursing homes are unlikely to be caused by bacteria in the urine. This study could not establish any clinical value of using dipstick urinalysis or IL-6 in the urine to verify if bacteriuria was linked to nonspecific symptoms.
5. 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: <http://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 (45-54 years, n = 102, mean age 48.14 years and over 65 years n = 94, mean age 69.21 years). Those with a confirmed UTI (>10³cfu/ml of an uropathogen in midstream 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 generalized 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 generalized symptoms that is especially important in older patients. Symptoms were grouped as voiding-related symptoms, local constant symptoms, and generalized symptoms. Local symptoms were predominated followed by voiding and generalized symptoms. In post-menopausal women predominant symptoms were storage and generalized 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 et al., 1992a) and it is not surprising that urinary symptoms of urgency, nocturia and incontinence are more common in post-menopausal women.
6. 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: <https://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 only be ordered if there is a fever of over 37.9°C, or a 1.5°C increase above baseline on at least two occasions over the previous 12 hours, and one or more of the following: dysuria; urinary catheter; urgency;

flank pain; shaking chills; urinary incontinence; frequency; gross haematuria; suprapubic pain. Advice is given on when to order a urine culture if there is a urinary catheter in situ, including: new costovertebral tenderness;



rigors; new onset of delirium; new onset burning urination, or two or more of: urgency; flank pain; shaking chills; urinary incontinence; frequency; gross haematuria; suprapubic pain. 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. It is for this reason that the clinical features referred to in this algorithm have been used in this flow chart.

7. 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: <https://www.ncbi.nlm.nih.gov/pubmed/11232875>
RATIONALE: This article describes the establishment of minimum criteria for the initiation of antibiotics in residents of 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 one of the following: new or worsening urgency, frequency, suprapubic pain, gross haematuria, costovertebral angle tenderness, or 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 one 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, or 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 two of the following: (1) 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); or (2) redness, (3) tenderness, (4) warmth, or (5) 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 one of the following: respiratory rate of over 25 breaths per minute or productive cough.
8. Berman P, Hogan DB, Fox RA. The atypical presentation of infection in old age. *Age and Ageing.* 1987;16(4). Available from: <https://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. 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 majority of patients had a temperature of at least 38 degrees 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.
9. Gorter 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: <https://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 2.0% 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.

10. Renko M, Tapanainen P, Tossavainen P, Pokka T, Uhari M. Meta-analysis of the significance of asymptomatic bacteriuria in diabetes. *Diabetes Care*. 2011;34(1):230-235. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/20937688>

RATIONALE: A systematic review and meta-analysis of published data since 1966. Twenty-two studies fulfilled the inclusion criteria of the meta-analysis. Results showed that asymptomatic bacteriuria was present in 439 of 3,579 (12.2%) patients with diabetes and in 121 of 2,702 (4.5%) healthy control subjects. Asymptomatic bacteriuria was more common both in patients with type 1 diabetes (odds ratio 3.0 [95% CI 1.1–8.0]) and type 2 diabetes (3.2 [2.0–5.2]) than in control subjects. History of urinary tract infections was associated with asymptomatic bacteriuria (1.6 [1.1–2.3]). Overall, the prevalence of asymptomatic bacteriuria is higher in all patients with diabetes compared with control subjects. Studies showed that diabetic subjects with asymptomatic bacteriuria more often had symptomatic urinary tract infections. This study did not focus on older adults but the findings may be generalizable to older adults. The findings only show associations between diabetes and UTI, and therefore do not show cause and effect.

11. Royal College of Physicians. National Early Warning Score (NEWS): Standardising the assessment of acute-illness severity in the NHS. London: RCP2012. Available from: <https://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 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:

National Early Warning Score (NEWS2)

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO ₂ Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO ₂ Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

© Royal College of Physicians 2018



respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness, or 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; a score of 5-6 (medium clinical risk) should trigger a an urgent response; and a score of 7 (high clinical risk) should trigger an urgent or emergency response.

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

RATIONALE: A NICE guideline for health care staff, 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 along with objective evidence of new altered mental state, respiratory rate of 21-24 breaths per minute or above, heart rate of 91-

130 beats per minute, systolic blood pressure of 91-100 mmHg or less, not passed urine in previous 18 hours (for catheterised patients, passed less than 0.5 ml/kg/hour).

13. The UK Sepsis Trust. Do I have sepsis? 2016 Mar. Available from: <https://sepsistrust.org/news/what-is-sepsis/>
RATIONALE: A UK Sepsis Trust website. The website states that if someone has early signs of a flu-like illness, chest infection, diarrhoea and vomiting, or an inability to eat and drink, together with one of the symptoms of sepsis, immediate medical advice should be sought. This website defines the symptoms of sepsis as: slurred speech; extreme shivering or muscle pain; passing no urine (in a day); severe breathlessness; skin mottled or discoloured.
14. Grabe M, Bjerklund-Johansen TE, Cai T, Cek M, Koves B, Naber KG et al. Guidelines on urological infections. *European Association of Urology*. 2015. Available from: http://uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf
RATIONALE: An expert guideline suggesting that admission should be arranged for more severe cases of acute uncomplicated pyelonephritis (dehydration; inability to take oral medication; pregnancy; patients with diabetes mellitus), if complicating factors cannot be ruled out by available diagnostic procedures, and/or the patient has clinical signs and symptoms of sepsis. This guideline also recommends that advice should be sought for people with acute pyelonephritis if there is no response to antibiotics within 24 hours, as the complications of acute pyelonephritis can be life-threatening. Lack of response to treatment is likely to be due to antibiotic resistance.
15. 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: <https://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; vomiting. 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.
16. Colgan R, Williams M. Diagnosis and Treatment of Acute Pyelonephritis in Women. *American Academy of Family Physicians*. 2011;84(5). Available from: <https://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. Flank pain is nearly universal, and its absence should raise suspicion of an alternative diagnosis. Nausea and vomiting also need to be considered. 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.
17. Chu CM. Diagnosis and Treatment of Urinary Tract Infections Across Age Groups. *American Journal of Obstetrics and Gynaecology*. 2018. Available from: [http://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 urinary tract infections include change in frequency, dysuria, urgency, and presence or absence of vaginal discharge, but suggest that urinary tract infections 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.
18. 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: <https://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 cosponsored 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 diagnostic guidance.

19. Little P. Antibiotics or NSAIDs for uncomplicated urinary tract infection? *BMJ*. 2017;359:j5037. Available from: <https://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.
20. Gagyor I, Bleidorn J, Kochen MM, Schmiemann G, Wegscheider K, Hummers-Pradier E. Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. *BMJ*. 2015 Dec; 23(351):1-11. Available from: <http://www.bmj.com/content/bmj/351/bmj.h6544.full.pdf>
RATIONALE: A randomised controlled trial across 42 German general practices, aiming to determine if treatment of symptoms of uncomplicated UTI with ibuprofen can reduce the rate of antibiotic prescriptions without a significant increase in symptoms, recurrences, or complications. 494 women aged between 18 and 65 with typical symptoms of uncomplicated UTI were included and randomly assigned to one of two treatment arms: a single dose of fosfomycin 3g for three days (n=246), or ibuprofen 3 x 400mg for three days (n=248). In both groups, additional antibiotic treatment was subsequently prescribed as necessary for persistent, worsening, or recurrent symptoms. Results indicated that, out of the 248 women in the ibuprofen group, two thirds treated symptomatically recovered without any antibiotics. Recurrent urinary tract infections were more common in the fosfomycin group. This trial also indicated that mild to moderate urinary symptoms given an anti-inflammatory agent and not treated with empirical therapy can last for a mean average of 5.6 days. The authors conclude that, although they cannot generally recommend ibuprofen as first-line treatment for uncomplicated UTI in women, the treatment option can be discussed with women with mild to moderate symptoms in a shared decision making approach, or within a strategy of delayed prescribing.
21. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. 2012 Jul. Available from: <http://www.sign.ac.uk/assets/sign88.pdf>
RATIONALE: A SIGN guideline, providing advice on how to manage suspected bacterial urinary tract infections in the elderly and people with catheters. Catheter change before treating symptomatic infection: expert opinion, based on one 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.
22. 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: <https://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 seven days) before the therapy of symptomatic catheter-associated bacteriuria.
23. 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: [http://www.gastrojournal.org/article/0016-5085\(92\)90175-X/pdf](http://www.gastrojournal.org/article/0016-5085(92)90175-X/pdf)
RATIONALE: An age- and sex-stratified random sample of noninstitutionalized Olmsted County, Minnesota, residents aged 65-93 years were mailed a valid questionnaire; 77% responded (n = 328). The age- and sex-adjusted prevalence (per 100 persons) of frequent abdominal pain was 24.3 [95% confidence interval (CI), 19.3-29.2]. 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.
24. 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: [http://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.
25. 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.

Review need for urine culture:

1. National Institute for Health and Care Excellence (NICE). Antenatal care for uncomplicated pregnancies. 2008 Mar. Available from: <https://www.nice.org.uk/guidance/CG62>
RATIONALE: NICE recommend that women should be offered routine screening for bacteriuria by midstream urine culture early in pregnancy, because identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis and premature delivery.
2. 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 midstream urine sample.
3. Grabe M, Bjerklund-Johansen TE, Botto H, Cek M, Naber KG, Pickard RS et al. *Guidelines on urological infections*. 2013 Mar. Available from: https://uroweb.org/wp-content/uploads/18_Urological-infections_LR.pdf
RATIONALE: A review of diagnosis and management guidelines for UTIs. Diagnosis in men: a urine sample is recommended because UTI in men is generally regarded as complicated (it results from an anatomic or functional abnormality) and there are no studies on the predictive values of dipstick testing in men. Urinalysis is highly recommended for pregnant women with suspected cystitis. Antibiotic therapy should be guided by urine culture when possible for people with suspected UTIs due to urological disorders in order to avoid resistant strains. Recurrent UTIs need to be diagnosed by a urine culture.
4. 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 agents.
5. 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: <https://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 five 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 two months of antibiotic treatment, and 1.33 (95% CI 1.2 to 1.5) within 12 months of treatment.
6. 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.

7. Vellinga A, Cormican M, Hanahoe B, Murphy AW. Predictive value of antimicrobial susceptibility from previous urinary tract infection in the treatment of re-infection. *Br J Gen Pract.* 2010 Jul; 60(576):511-513. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/20594440>
RATIONALE: Analysis of susceptibility results from 3,413 patients who provided at least two *E. coli* positive urine samples over the study period found that, if resistance to ampicillin, trimethoprim, or ciprofloxacin was detected, a recurrent UTI within three months of this sample is likely to be associated with an organism that is still resistant. However, if resistance to nitrofurantoin was detected, a recurrent UTI within three months has only a one in five chance of being a resistant organism. If the organism was susceptible to nitrofurantoin, ciprofloxacin, or trimethoprim, then a recurrent UTI within 12 months is likely to still be susceptible.
8. Naber KG, Schito G, Botto H, Palou J, Mazzei T. Surveillance study in Europe and Brazil on clinical aspects and Antimicrobial Resistance Epidemiology in Females with Cystitis (ARESC): implications for empiric therapy. *Eur Urol.* 2008 Nov; 54(5):1164-1175. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/18511178>
RATIONALE: Prospective study investigating uncomplicated cystitis in women. This survey went on for 3 years and included 68 centres in nine European countries and in Brazil. Female patients between 18 and 65yr with symptoms of uncomplicated cystitis were included. Uropathogens were identified and their susceptibility tested for nine antimicrobials. Clinical data of 4264 eligible patients were analysed. A positive urine culture was found in 74.6%. Within the 3018 pathogens, *Escherichia coli* (*E. coli*) was most frequent (76.7%), followed by *Enterococcus faecalis* (4.0%), *Staphylococcus saprophyticus* (3.6%), *Klebsiella pneumoniae* (3.5%), and *Proteus mirabilis* (3.5%). *E. coli* showed the highest rate of susceptibility to fosfomycin (98.1%) followed by mecillinam (95.8%), nitrofurantoin (95.2%), and ciprofloxacin (91.8%). The lowest rate was found for ampicillin (45.1%). For the total spectrum the order was fosfomycin (96.4%), mecillinam (95.9%), ciprofloxacin (90.3%), and nitrofurantoin (87.0%). In all countries, susceptibility rate to *E. coli* above 90% ($p < 0.0001$) was found only for fosfomycin, mecillinam, and nitrofurantoin, indicating that they are a good options for empiric therapy for women with uncomplicated cystitis.
9. Falagas ME, Kastoris AC, Kapaskelis AM, Karageorgopoulos DE. Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum beta-lactamase producing, Enterobacteriaceae infections: a systematic review. *Lancet Infect Dis.* 2010 Jan; 10(1):43-50. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/20129148>
RATIONALE: A systematic review of studies evaluating the antimicrobial activity, or the clinical effectiveness of fosfomycin. The authors evaluated the evidence on fosfomycin as a treatment option for infections caused by members of the family Enterobacteriaceae with advanced resistance to antimicrobial drugs, including producers of extended-spectrum beta-lactamase (ESBL). Seventeen antimicrobial-susceptibility studies were found and included and 11 of the 17 studies reported that at least 90% of the isolates were susceptible to fosfomycin. 96.8% of 1657 *Escherichia coli* isolates producing ESBL were susceptible to fosfomycin. 81.3% of 748 *Klebsiella pneumoniae* isolates producing ESBL were susceptible to fosfomycin. In two clinical studies, oral treatment with fosfomycin-trometamol was clinically effective against complicated or uncomplicated lower urinary tract infections caused by ESBL-producing *E. coli* in 93.8% of patients evaluated. Findings support the use of fosfomycin for the treatment of urinary tract infections caused by these pathogens, although further research is needed.

Sampling technique in men and women:

1. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.5. <https://www.gov.uk/uk-standards-for-microbiologyinvestigations-smi-quality-and-consistency-in-clinical-laboratories>
RATIONALE: Midstream urines and clean-catch urine are recommended for routine use but cleaning the area beforehand makes little difference in contamination. 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 may also be useful. Boric acid preservative holds the bacterial population steady for 48-96 hours. Toxicity to some organisms has been reported, but this often reflects under filling of the container.
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 two or more collection techniques in women with symptoms of urinary tract infection. Seven studies investigating urine sampling technique in 1062 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 randomized 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 guidance continues to recommend a mid-stream sample is collected until further investigations can verify the lack of difference between the sampling techniques.*

2. Lifshitz E, Kramer L. Outpatient urine culture: does collection technique matter? *Arch Intern Med.* 2000 Sep; 160(16): 2537-2540. Available from: <https://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 midstream and no cleansing: 29%; contaminated: n=77; samples obtained midstream with perineal cleansing and spreading of the labia: 32% contaminated: n=84; samples obtained midstream 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 midstream/combined cleansing group. This suggests that encouraging use of the midstream clean catch method or cleaning might not be warranted. Though authors indicate that further in study is needed. *This guidance continues to recommend a mid-stream sample is collected until further investigations can verify the lack of difference between the sampling techniques.*
3. National Health Services Choices. How should I collect and store a urine sample? Accessed 6 April 2018. Available from: <https://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 midstream, 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.
4. 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: <https://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 eight 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%), midstream sample (23.9%), midstream sample with perineal cleansing (20.4%), midstream 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.
5. 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: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1841545/pdf/brmedj02123-0050.pdf>
RATIONALE: Suprapubic specimens and midstream 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 midstream 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 midstream 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.
6. National Institute for Health and Care Excellence (NICE). Infection control: prevention of healthcare-associated infection in primary and community care. 2003 Jun. Available from: <https://www.nice.org.uk/guidance/cg2>
RATIONALE: Expert opinion is that urine samples from catheters should be obtained from the catheter sampling port, to reduce the risk of contamination. Maintaining a sterile, continuously closed catheter system is central to the prevention of catheter-associated infection.

Interpretation of culture results in adults:

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: <https://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 postmenopausal women varies from 2-5%. 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 at: <https://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 midstream urine culture early in pregnancy because identification and treatment of asymptomatic bacteriuria reduces the risk of pyelonephritis.
4. European Confederation of Laboratory Medicine. European urinalysis guidelines. *Scand J Clin Lab Invest Suppl*. 2000 Jan; 231(1):1-86. Available from: http://www.hemltd.ru/publications/sections/bakteriozi/Bac_urina/medicine/Bac_urina004/article.PDF
RATIONALE: The cut-offs for symptomatic urinary tract infection caused by primary pathogens (*E. coli* and *S. saprophyticus*) are set by the European Confederation of Laboratory Medicine at $\geq 10^3$ CFU/mL in midstream urine specimens. For secondary pathogens (such as Enterobacter species, Enterococcus species, *P. mirabilis*, *P. aeruginosa* etc.) cut offs are set as $\geq 10^4$ CFU/mL for women and $\geq 10^3$ CFU/mL for men. Evaluating urine culture findings has long been dominated by Kass's criteria for significant bacteriuria. Kass found that 95% of women with pyelonephritis had $\geq 10^8$ CFB/L ($\geq 10^5$ CFU/mL) or one bacterial species in a clean-catch midstream urine, and that such a finding in two consecutive midstream urine specimens in asymptomatic women would, with 95% probability, give the same result in a third midstream urine specimen. Kass also showed that $< 10^7$ CFB/L indicated contamination during sample collection, whereas bacterial concentration in the interval of 10^7 to $< 10^8$ CFB/L was difficult to interpret. Despite the fact that the criteria were developed for acute pyelonephritis and asymptomatic bacteriuria in women, they began to be used generally, even for symptomatic lower urinary tract infection. Stamm et al examined 187 sexually active young women with dysuria and urinary urgency. Cultures of midstream 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 midstream 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 midstream 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 midstream 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. Findings of *E. coli* have been interpreted as the first phase in urethritis in an ascending infection.
5. Grabe M, Bjerklund-Johansen TE, Cai T, Cek M, Koves B, Naber KG et al. Guidelines on urological infections. *European Association of Urology*. 2015.. Available from: https://uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf
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 aim of the guidelines is to provide both urologists and physicians from other medical specialities with evidence-based guidance regarding the treatment and prophylaxis of UTI. These guidelines cover male and female UTIs, male genital infections and special fields such as UTI in paediatric urology, immunosuppression, renal insufficiency and kidney transplant recipients. The guidelines state that although the number of bacteria is considered relevant for the diagnosis of a UTI, it has recently become clear that there is no fixed bacterial count that is indicative of significant bacteriuria, which can be applied to all kinds of UTIs and in all circumstances. They highlight $> 10^3$ cfu/mL of uropathogens in a mid-stream sample of urine (MSU) as a clinically significant culture in acute uncomplicated cystitis in women, $> 10^4$ cfu/mL of uropathogens in an MSU in acute uncomplicated pyelonephritis in women, $> 10^5$ cfu/mL of uropathogens in an MSU in women, or $> 10^4$ cfu/mL uropathogens in an MSU in men, or in straight catheter urine in women, in a complicated UTI.
6. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.5. <https://www.gov.uk/uk-standards-for-microbiologyinvestigations-smi-quality-and-consistency-in-clinical-laboratories>

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. It is defined as the occurrence of 10^7 WBC/L (10^4 WBC/mL) or more, 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. Sterile pyuria (i.e. 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; sexually transmitted diseases, e.g. *C. trachomatis* or an infection with a fastidious organism or renal tuberculosis. 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. 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. 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. 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 1–2 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.

7. Renal Association and British Association of Urological Surgeons. Joint consensus statement on the initial assessment of haematuria. 2008 Jul. Available from:

http://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 (two out of three 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.

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

RATIONALE: This guidance 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. The guidance states that you should refer people aged 45 and older with unexplained visible haematuria without urinary tract infection or those with visible haematuria that persists or recurs after treatment. It also says that you should consider referral of people over the age of 60 with persistent unexplained urinary tract infection.

Infants or 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:

<https://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 three 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 one of the criteria listed below are met or if the dipstick is positive. In children over the age of three 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 24–48 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 recommend 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.

2. Rees JC, Vernon S, Pedler SJ, Coulthard MG. Collection of urine from washed-up potties. *Lancet*. 1996 Jul; 348(9021):197. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/8684173>.
RATIONALE: This study tested four 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.
3. Lynster LCT, Nayar DM, Pedler SJ, Coulthard MG. Home collection of urine for culture from infants by three methods: survey of parents' preferences and bacterial contamination rates. *BMJ*. 2000 May; 320(7245):1312-1313. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC27376/>.
RATIONALE: In this series of 44 infants, parents collected three 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.
4. Rao S, Bhatt J, Houghton C, Macfarlane P. An improved urine collection pad method: a randomised clinical trial. *Arch Dis Child*. 2004 Aug; 89(8):773-775. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/15269081>.
RATIONALE: Febrile children under the age of two were randomised to either the same urine collection pad kept in the nappy until urine was passed, or to urine collection pads to be changed every 30 minutes until urine was passed. From 80 children enrolled, a satisfactory sample was obtained from 68 of them (12 samples were unusable because of faecal soiling). Heavy mixed growth (indicating contamination) occurred in 3% of the replaced urine collection pad group (one of 31), compared with 29% (10 of 35) in the single urine collection pad group (p=0.008).
5. Public Health England. (2018). Investigation of urine. UK Standards for Microbiology Investigations. B 41 Issue 8.5. <https://www.gov.uk/uk-standards-for-microbiologyinvestigations-smi-quality-and-consistency-in-clinical-laboratories>
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 two 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, an 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

Authors

(hold)

For any further information regarding the review process and those involved in the development of this guidance, 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 Unit does not accept funding for the development of this guidance 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 guidance. For any detailed information regarding declared conflicts of interest, please email TARGETAntibiotics@phe.gov.uk.

Abbreviations

a-NVH = Asymptomatic non-visible haematuria

°C = Degrees centigrade

CFB = Colony forming bacteria

CFU = Colony forming units

CI = Confidence interval

CPE = Carbapenemase-producing enterobacteriaceae

C. trachomatis = *Chlamydia trachomatis*

E. coli = *Escherichia coli*

ESBL(s) = Extended-spectrum beta-lactamase(s)

GI = Gastrointestinal

IgA = Immunoglobulin A

L = Litres

mL = Millilitres

MSU = Midstream urine

NNH = Number needed to harm

NPV = Negative predictive value

PPV = Positive predictive value

P. aeruginosa = *Pseudomonas aeruginosa*

P. mirabilis = *Proteus mirabilis*

RCT(s) = Randomised controlled trial(s)

s-NVH = Symptomatic non-visible haematuria

S. saprophyticus = *Staphylococcus saprophyticus*

TB = Tuberculosis

UTI(s) = Urinary tract infection(s)

WBC = White blood cell

DRAFT