SA Health

Urinary Tract Infections (adult): Empirical Treatment Clinical Guideline

Version 2.1

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Government of South Australia
SA Health

Contents

1. Name of guideline 3
2. Introduction 3
3. Background 3
4. Definitions and acronyms 3
5 Safety, quality and risk management 4
5. Priniciples of the standards 4
6. General guidance 5
   - 6.1 Diagnosis 5
   - 6.1.1 Cystitis 5
   - 6.1.2 Pyelonephritis 5
   - 6.1.3 Catheter-associated UTI (CA-UTI) 6
   - 6.1.4 Asymptomatic bacteriuria 6
   - 6.1.5 Recurrent UTI 6
   - 6.2 Treatment of UTI 6
   - 6.2.1 Empirical oral antibiotic therapy for UTI 6
   - 6.2.2 Multi-drug resistant UTI 7
   - 6.2.3 Catheter-associated UTI (CA-UTI) 7
   - 6.2.4 Recurrent UTI 7
   - 6.2.5 Urinary alkalinising agents 8
7. Associated policies / guidelines / clinical guidelines / resources 8
8. References 8
9. Document Ownership and History 9
10. Appendices 10
    - 10.1 Appendix 1. Empiric treatment recommendations for acute cystitis and pyelonephritis 10
    - 10.2 Appendix 2. Medication dose adjustment recommendations in renal impairment 11
    - 10.3 Appendix 3. Evaluation of suspected UTI for older adults in residential and community care 12
    - 10.4 Appendix 4. When to screen and treat asymptomatic bacteriuria in adults 13

1. Name of guideline

Urinary Tract Infections (adult): Empirical Treatment Clinical Guideline (v2.1)

2. Introduction

This guideline has been developed by the South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR) to assist clinicians in identifying and initiating empirical antimicrobial therapy for suspected bacterial urinary tract infections (UTI) in adult patients. The guideline includes advice on asymptomatic bacteriuria, recurrent UTI, catheter-associated UTI and pyelonephritis.

Key stewardship points

- Screening for, and treatment of, asymptomatic bacteriuria in older people is not recommended.
- Do not investigate or treat cloudy or malodourous urine in aged-care facility residents who do not have other clinical signs or symptoms of UTI.
- Prescribe only the number of days required to complete the shortest course (3-5 days for uncomplicated cystitis). Prolonged and often unnecessary use of antimicrobials is associated with increased side effects and the potential for driving resistance.
- Avoid use of norfloxacin or ciprofloxacin when other antibiotic choices are available as there is rising quinolone resistance in Gram negative bacteria. These antibiotics are the only oral antibiotics available to treat *Pseudomonas aeruginosa*.
- **Do not** use fosfomycin for uncomplicated UTIs. Fosfomycin is a last-line broad-spectrum antibiotic reserved for UTIs resistant to other agents.

3. Background

Urinary tract infections (UTI) are common in the hospital and community setting. UTIs are the fourth most common indication for prescribing antimicrobials in hospital and are responsible for a large number of presentations in general practice and frequent antibiotic prescriptions.[1,2] More than 30% of women will experience a UTI during their lifetime.[3,4]

There is a clear association between antibiotic prescribing in suspected UTI and the development of antimicrobial resistance (AMR).[5,6] In Australia, acquired resistance of *Escherichia coli* to key anti-Gram-negative antimicrobial agents continues to increase.[7] As *E. coli* is the leading causative pathogen for UTI, growing resistance can lead to increasing treatment failures and more hospital admissions.

Prudent antimicrobial prescribing is a key component of Australia's response to reduce AMR. While antibiotic therapy is usually required for symptomatic UTI, unnecessary antibiotic treatment for asymptomatic bacteriuria can increase the risk of clinical adverse events including *Clostridioides difficile* infection and the development of antibiotic resistant UTIs.

4. Definitions and acronyms

CA-UTI	Catheter-associated urinary tract infection
CFU	Colony forming unit (viable microbial cell)

CrCl	Creatinine clearance
Cystitis	Inflammation of the bladder usually associated with infection
GFR	Glomerular filtration rate
ID	Infectious diseases
M, C & S	Microscopy, culture and sensitivity
MSU	'Mid-stream' urine – procedure for obtaining a urine sample which aims to minimise the risk of contamination with skin or urethral bacteria[19]
Pyelonephritis	Inflammation of the kidney and renal pelvis as a result of infection
Pyuria	Presence of / increased numbers of white blood cells in the urine; either alone or frequently associated with presence of bacteria
SAAGAR	South Australian expert Advisory Group on Antimicrobial Resistance
UTI	Urinary tract infection

5 Safety, quality and risk management

National Safety and Quality Health Service Standards

Clinical Governance	Partnering with Consumers	Preventing and Controlling Infections	Medication Safety	Comprehensive Care	Communicating for Safety	Blood Management	Recognising and Responding to Acute Deterioration
☐	☐	☒	☒	☐	☐	☐	☐

The following actions of the relevant standards are applicable:

Standard 3 – Preventing and Controlling Infections

- Actions 3.18, 3.19: Antimicrobial stewardship – The health service organisation has systems for the safe and appropriate prescribing and use of antimicrobials as part of an antimicrobial stewardship program.

Standard 4 – Medication Safety

- Action 4.01: Integrating clinical governance – Clinicians use the safety and quality systems from the Clinical Governance Standard when implementing policies and procedures for medication management, managing risks associated with medication management, and identifying training requirements for medication management.

5. Priniciples of the standards

National standard 3, *Preventing and Controlling Infections,* aims to reduce the risk to patients, consumers and members of the workforce of acquiring preventable infections; effectively manage infections, if they occur; prevent and contain antimicrobial resistance; promote appropriate prescribing and use of antimicrobials as part of antimicrobial stewardship; and promote appropriate and sustainable use of infection prevention and control resources.

National standard 4, *Medication Safety,* aims to ensure clinicians are competent to safely prescribe, dispense and administer appropriate medicines and to monitor medicine use. To ensure consumers are informed about medicines and understand their individual medicine needs and risk.

6. General guidance

6.1 Diagnosis

Microscopy, culture, and antibiotic sensitivity analysis of a mid-stream clean-catch urine specimen is the gold standard diagnostic test for all suspected symptomatic UTI. A detailed patient history is important to inform a differential diagnosis and exclude other causes (e.g., a sexually transmitted infection that may present with urinary symptoms alone).

Contamination should be considered for urine specimens with:

1. Greater than 20 epithelial cells with no signs or symptoms; OR
2. Bacteria but no leucocytes; OR
3. Growth of multiple organisms (with or without leucocytosis).

Staphylococcus aureus is an unusual cause of bacteriuria in the absence of catheterisation or instrumentation. This culture may therefore be indicative of *S. aureus* bacteraemia. Blood cultures and consultation with Infectious Diseases (ID)/Microbiology may be indicated.

6.1.1 Cystitis

Cystitis is an infection of the bladder associated with the presence of a positive urine culture with an organism known to cause UTIs and at least one urinary symptom (e.g. frequency, painful urination, urgency and sometimes suprapubic tenderness).[8] Note: there is no specific defined threshold concentration (CFU/mL) for diagnosis.

- **Uncomplicated** – symptomatic infection in a structurally and functionally normal urinary tract in non-pregnant women. Most commonly caused by *E. coli* (approximately 70% of cases).[9]
- **Complicated** – symptomatic infection associated with factors that increase the risk of serious complications or treatment failure. This includes all men, pregnant women, patients with structural or functional abnormalities of the urinary tract (e.g. neurogenic bladder, nephrolithiasis) or other concomitant immunocompromising diseases (e.g. diabetes).[10] Associated with a wider range of pathogens including *E. coli, Klebsiella, Proteus, Pseudomonas* species.[9]

Cystitis is less common in men than women; prevalence increases with age and is often associated with prostatic enlargement or other abnormalities of the urinary tract.[11] Consider prostatitis, particularly in men with fever (38°C or higher), obstructive urinary symptoms or prostate tenderness on gentle digital rectal examination.

6.1.2 Pyelonephritis

Pyelonephritis is an infection of the kidney and renal pelvis associated with the presence of a positive urine culture with an organism known to cause UTIs and systemic symptoms. Acute pyelonephritis may present with or without symptoms of acute cystitis.

- **Mild** (suitable for oral therapy/discharge) – mild systemic symptoms (low-grade fever, no nausea or vomiting), loin pain
- **Severe** (suitable for intravenous therapy/admission) – systemic symptoms (fever, nausea, vomiting, severe pain, or suprapubic tenderness), acute renal injury

Pyelonephritis in men can indicate the presence of lower urinary tract abnormalities and referral for urological investigations is recommended.

6.1.3 Catheter-associated UTI (CA-UTI)

Catheter-associated UTI (CA-UTI) is a symptomatic infection occurring in a patient who is (or has been in the past 48 hours) catheterised, with no other identified source of infection and an appropriately collected urine specimen with bacterial count ≥ 10^3 CFU/mL. The need for ongoing catheterisation should be reviewed. To reduce the risk of sample contamination, either remove the catheter and obtain a mid-stream urine (MSU) or collect a sample via a new catheter if ongoing catheterisation is required. If the catheter cannot be removed or replaced, collect the urine sample from the port in the drainage system, not from the drainage bag.[12]

6.1.4 Asymptomatic bacteriuria

Asymptomatic bacteriuria is a positive urine culture with a bacteria count of ≥ 10^5 CFU/mL, with or without pyuria, but with no signs or symptoms of infection.[13]

With the exception of pregnant women and patients undergoing urological procedures, screening for, and treating, asymptomatic bacteriuria is not recommended. This includes those patients with indwelling catheters, patients residing in residential aged-care facilities, women after menopause, patients with diabetes or a spinal injury, or men with increased post-void residual volumes.[12]

Asymptomatic bacteriuria is common in older persons, however there is no evidence to support routine screening and treatment.[8,14] Refer to Appendix 2 for a flowchart for the evaluation of suspected UTI in residential care facility residents.

Do not investigate or treat cloudy or malodourous urine in aged-care facility residents who do not have other signs or symptoms of UTI.

6.1.5 Recurrent UTI

A UTI can be classified as recurrent if ≥ 2 episodes have occurred within six months or ≥ 3 episodes within 12 months.

Recurrent UTI may be due to relapse or reinfection.

- Relapse is recurrent UTI with the same strain of organism. Relapse is the likely cause if UTI recurs (or fails to be eradicated) within a short period (within two weeks) after sensitivity-adjusted treatment.
- Reinfection is recurrent UTI with a different strain or species of organism or the same organism more than two weeks after successful treatment course.

6.2 Treatment of UTI

Considerations for selection of empiric therapy for UTI include:

- The susceptibility of organisms recently identified in samples from the patient (if available);
- If previous patient samples are unavailable, consider the most likely pathogen/s and susceptibilities based on community and site-specific resistance data (in particular the rate of *E. coli* resistance). Consider local antibiogram data;
- **Recent overseas travel** (past 6 months) to a region **with high rates of antibiotic resistance** (e.g., Southeast Asia/South Asia) particularly if associated with antibiotic use or medical care: consult ID/Microbiology for advice;
- **Recent use of antimicrobials** (e.g., trimethoprim +/- sulfamethoxazole) or lack of response to previous antibiotic therapy. Prior use is a risk factor for resistance to these agents.

6.2.1 Empirical oral antibiotic therapy for UTI

State-wide 2020 antibiogram data from SA Pathology® indicates that 79% of *E. coli* isolates are susceptible to trimethoprim and 93% to cefalexin. All of the common causative organisms continue to have high rates of susceptibility to nitrofurantoin (99% of *E. coli*, 97% *Enterococcus spp.*).[9]

Trimethoprim continues to be recommended for empirical therapy for acute cystitis because the risk of adverse outcomes from treatment failure is low. Trimethoprim is no longer recommended as empirical therapy for non-severe pyelonephritis because it is a more serious infection than cystitis with a higher risk of adverse outcomes from treatment failure. Amoxicillin-clavulanic acid has an unnecessarily broad spectrum of activity for empirical therapy of cystitis. The use of broad-spectrum antibiotics selects for antibiotic resistant organisms and increases the risk of *C. difficile* infection. Do not use oral fosfomycin, nitrofurantoin, or norfloxacin to treat pyelonephritis, as these drugs do not reach adequate concentrations in kidney tissue.

6.2.2 Multi-drug resistant UTI

The incidence of UTIs and associated bacteraemias caused by organisms resistant to most first-line antibiotics is increasing. Multi-drug resistant *E. coli,* particularly extended-spectrum beta-lactamase (ESBL)-producing strains, have been identified in approximately 8% of blood culture isolates.[9]

Oral treatment for resistant organisms should always be directed by susceptibility testing. Increasingly, nitrofurantoin or fosfomycin may be the only oral options available for multi-drug resistant UTIs. If susceptible to nitrofurantoin, use in preference to fosfomycin.[15] Fosfomycin is a last-line broad-spectrum antibiotic and should be reserved for treatment of UTIs resistant to other antibiotics. Refer to SAAGAR position statement – Multi-drug resistant UTI for more information.

6.2.3 Catheter-associated UTI (CA-UTI)

Routine screening and treatment of catheterised patients with bacteriuria is not recommended in the absence of symptoms.[8]

Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients. Pyuria alone is not diagnostic of catheter-associated infection.[8] Pyuria and bacteriuria are common in catheterised patients and are not indicators for antibiotic treatment unless the patient is symptomatic.[16]

In catheterised patients who present with fever, exclude other potential sources of infection. Look for associated localised (loin or suprapubic tenderness) or other systemic features such as rigors, chills, vomiting or confusion. Where treatment is indicated, change the catheter prior to commencing antibiotic treatment for symptomatic UTI. If the catheter is not removed or replaced, the risk of treatment failure is increased as most antibiotics penetrate poorly into catheter biofilm. Treatment without catheter removal can lead to superinfection with resistant organisms.[12] Treat according to culture and sensitivities for seven days, or 10-14 days if response to treatment is delayed.[8] Permanent removal of the catheter is preferred.

6.2.4 Recurrent UTI

Treat relapsed UTI as for pyelonephritis (10-14 days) and investigate for urological abnormalities. If reinfection, treat as for acute cystitis or pyelonephritis, as appropriate.[12]

Reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of commencing the antibiotic, taking account of:

- Other possible diagnoses
- Any symptoms or signs suggesting more serious illness or condition, such as pyelonephritis
- Previous antibiotic use, which may have led to resistant bacteria.

Send a urine sample for culture and susceptibility testing if this has not already been done and review treatment when results are available.

6.2.5 Urinary alkalinising agents

The safety and efficacy of urinary alkalinisers for the symptomatic treatment of uncomplicated UTIs is unclear.[17] Urinary alkalinising agents significantly reduce the antimicrobial effect of nitrofurantoin[18], and should not be used with quinolones due to the increased risk of crystalluria.[12] Cranberry products, ascorbic acid and methenamine hippurate are not effective for the treatment of acute UTI.[12]

7. Associated policies / guidelines / clinical guidelines / resources

- For advice on the management of UTI in children, refer to SA Paediatric Clinical Practice Guideline "Urinary Tract Infection in Children".
- For further advice on the management of UTI in pregnant women, refer to SA Perinatal Practice Guideline "Urinary Tract Infection in Pregnancy".
- IV to Oral Switch Clinical Guideline for Adult Patients: Can Antibiotics S.T.O.P.
- SAAGAR position statement – Multi-drug resistant UTI.

8. References

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9. Document Ownership and History

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14/06/2022	V2	Domain Custodian, Clinical Governance, Safety and Quality Approved by SA Medicines Advisory Committee	Major review
10/10/2017	V1	Safety & Quality Strategic Governance Committee	Original

10. Appendices

10.1 Appendix 1. Empiric treatment recommendations for acute cystitis and pyelonephritis

Obtain mid-stream urine specimen and send for microscopy
If patient has a catheter, remove catheter, and obtain mid-stream specimen via fresh catheter

Acute Cystitis

Uncomplicated

1) **Trimethoprim 300mg PO daily** (at night) for 3 days; or
2) **Nitrofurantoin 100mg PO four times a day** for 5 days; or
3) **Cefalexin 500mg PO twice daily** for 5 days

Complicated

1) **Trimethoprim 300mg PO daily** (at night) for 7 days; or
2) **Nitrofurantoin 100mg PO four times a day** for 7 days; or
3) **Cefalexin 500mg PO twice daily** for 7 days

Pregnancy

1) **Nitrofurantoin 100mg PO four times a day** for 5 days (avoid using close to delivery (after 37 weeks gestation, or sooner if early delivery planned), increased risk of neonatal jaundice and haemolytic anaemia); or
2) **Cefalexin 500mg PO twice daily** for 5 days; or
3) **Trimethoprim 300mg PO daily** for 3 days (avoid in 1st trimester or if established folate deficiency)

Pyelonephritis

Mild / Moderate

Amoxicillin 875mg + clavulanic acid 125mg PO twice daily for 10-14 days

If penicillin allergy, proven resistance or intolerance to other agents, or *Pseudomonas aeruginosa*:

Ciprofloxacin 500mg PO twice daily for 7 days

Severe

Gentamicin IV 4-5mg/kg (7mg/kg for severe sepsis) ideal body weight STAT, then according to aminoglycoside dosing and monitoring guidelines

PLUS

Amoxicillin 2g IV SIX hourly

For patients with penicillin allergy: **use gentamicin alone**

If CrCl ≤ 40mL/min or if gentamicin contraindicated, use as a single agent:

Ceftriaxone 1g IV daily

Patients with high risk penicillin allergy AND CrCl ≤ 40mL/min: **consult ID for advice**

Modify based on micro & clinical response. Switch to oral when clinically appropriate.

Duration (IV + PO): 10-14 days depending on clinical response

Pregnancy

Gentamicin IV 4-5mg/kg (7mg/kg for severe sepsis) ideal body weight STAT, then according to aminoglycoside dosing and monitoring guidelines

PLUS

Amoxicillin 2g IV SIX hourly

For patients with penicillin allergy: **use gentamicin alone**

If CrCl ≤ 40mL/min or if gentamicin contraindicated, use as a single agent:

Ceftriaxone 1g IV daily

Patients with high risk penicillin allergy AND CrCl ≤ 40mL/min: **consult ID for advice**

Modify based on micro & clinical response. Switch to oral when clinically appropriate.

Duration (IV + PO): 10-14 days depending on clinical response

Switch to oral when clinically appropriate: to be guided by culture and susceptibility testing; use narrowest spectrum possible:

Amoxicillin 500mg PO three times a day; or
Cefalexin 500mg PO four times a day; or
Amoxicillin / clavulanic acid 875/125mg PO twice daily; or
Trimethoprim 300mg PO daily (avoid in 1st trimester or if established folate deficiency)

Additional information

IN ALL CASES: Tailor treatment based on microbiology and sensitivities according to clinical response using agent with narrowest spectrum of activity and switch to oral therapy as soon clinically appropriate (see IV to oral switch guidelines).

Contact an Infectious Diseases Consultant or Clinical Microbiologist for advice if: recent travel overseas, recurrent UTIs and documented resistance, or presence of ureteric stents.

For more information on multi-drug resistant UTI refer to SAAGAR position statement - Multi-drug resistant UTI

Criteria for defining UTI

Asymptomatic bacteriuria

No signs or symptoms with bacteriuria ≥10^5 CFU/mL.

- Common in the elderly
- Treatment generally NOT required (see exceptions below)
- Requires treatment in **all** pregnant women and patients undergoing urological procedures

Acute Cystitis

Presence of positive urine culture with an organism known to cause UTIs and at least one urinary symptom (e.g. frequency, painful urination, suprapubic pain, non-specific back pain)

- *Uncomplicated*

Symptomatic infection in non-pregnant women with a structurally and functionally normal urinary tract

- *Complicated*

Symptomatic infection in **men OR pregnant women** OR a urinary tract in which there is a structural or functional abnormality:

- Urinary tract obstruction
- Chronic kidney disease
- Poorly controlled type 2 diabetes
- Immunosuppression
- Urinary catheter in situ
- Neurogenic bladder
- Post-menopausal women
- History of recurrent UTIs (≥ 2 in 6 months or ≥ 3/year)
- Nephrolithiasis

Pyelonephritis

Presence of positive urine culture with an organism known to cause UTIs and systemic symptoms.

- *Mild (suitable for oral therapy/discharge)*
  - Mild systemic symptoms (low grade fever, no nausea or vomiting)
  - Loin pain
- *Severe (suitable for IV therapy/admission)*
  - Systemic symptoms (fever, nausea, vomiting, severe pain)

Catheter-associated UTI (men and women)

Bacteriuria and pyuria are common; routine screening & treating catheterised patients with bacteriuria is not recommended in the absence of symptoms - see (Page 5).

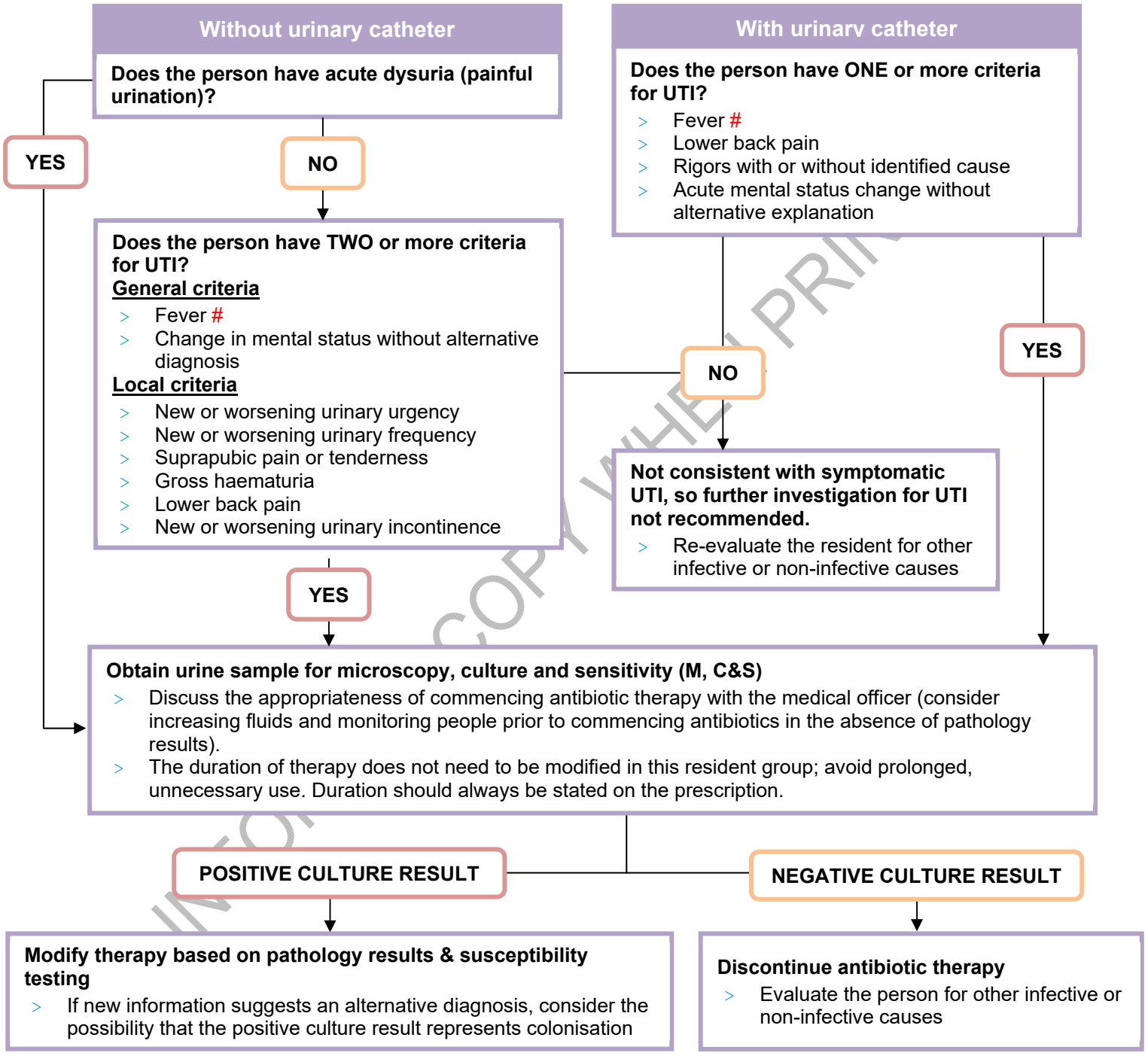
- *Symptomatic UTI*: Urine specimen ≥ 10^3 CFU/mL with at least one sign or symptom referable to the urinary tract, with no other identifiable source of infection.

10.2 Appendix 2. Medication dose adjustment recommendations in renal impairment[12,20]

Drug	Adjustment
Amoxicillin / clavulanic acid	*CrCl <30mL/min:* 500mg/125mg 12-hourly
Ciprofloxacin	*CrCl 10-30mL/min:* 250mg 12-hourly **OR** 500mg 24-hourly *CrCl <10mL/min:* 500mg 24-hourly
Nitrofurantoin	*CrCl 10-40mL/min:* avoid; if GFR is 30-40mL/min, may be used for 5-7 days for **multi-drug resistant infections**; monitor for adverse effects *CrCl <10mL/min:* avoid – may be ineffective due to low urinary concentrations, increased risk of adverse effects
Norfloxacin	*CrCl 10-50mL/min:* 400mg 12-hourly **OR** 400mg 24-hourly *CrCl <10mL/min:* 400mg 24-hourly
Trimethoprim	*CrCl 15-30mL/min:* normal dosing; monitor full blood count *CrCl <15mL/min:* avoid; if essential, up to 150mg 24-hourly; monitor full blood count

10.3 Appendix 3. Evaluation of suspected UTI for older adults in residential and community care

Suspected urinary tract infection (UTI)



Notes:

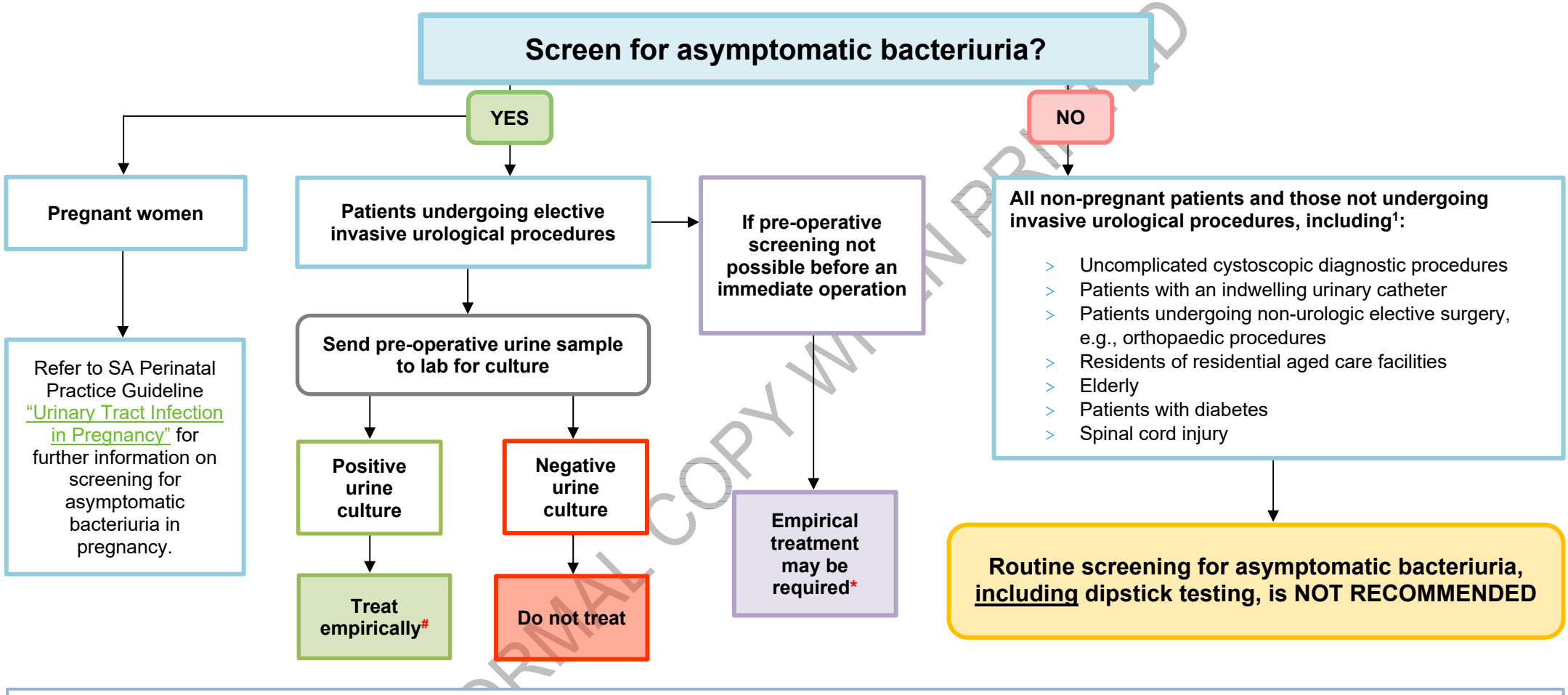
1. Do not investigate or treat cloudy or malodourous urine in older adults in residential & community care who do not have other symptoms or signs of UTI.
2. Consider whether an alternative diagnosis is likely. Consider both infective (e.g., pneumonia) and non-infective causes (e.g., medication-related adverse events).
3. Establish whether an advanced care plan is in place that may influence assessment and management (e.g., whether investigations are performed, or antibiotics given).
4. Do not routinely conduct a post-antibiotic urinalysis. If symptoms of UTI persist then discuss with medical officer.

Fever is defined as a single oral temperature > 37.8°C; repeated oral temperatures > 37.5°C; rectal temperature > 37.5°C or an increase of more than 1.1°C above baseline temperature (*McGeer Criteria, 2012*).

Adapted with permission from Antibiotic Expert Groups. Initial assessment and management of aged-care facility residents with suspected urinary tract infection (figure 2.13). In: eTG complete (online). Melbourne: Therapeutic Guidelines Limited.

10.4 Appendix 4. When to screen and treat asymptomatic bacteriuria in adults

Screening for and treatment of asymptomatic bacteriuria in adults is NOT recommended, except in limited circumstances



Notes:

5. Do not investigate or treat cloudy or malodourous urine in older adults in residential & community care who do not have other symptoms or signs of UTI.
6. Treatment of asymptomatic bacteriuria in healthy young women may increase the risk of future symptomatic UTI.
7. Screening and requesting a urine culture without a clear indication or failing to correctly interpret and correlate the culture result to the clinical situation, significantly contributes to antibiotic misuse.

Refer to Appendix 1 in the Urinary Tract Infections (adult): Empirical Treatment Clinical Guideline for empirical treatment recommendations. Modify empirical therapy based on microbiology and sensitivities, using agent with the narrowest spectrum of activity.

* Refer to the Therapeutic Guidelines; see *Treating pre-operative bacteriuria* for further information.

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