

Therapeutic Guidelines: Antibiotic - evidence gaps

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Therapeutic Guidelines: Antibiotic is published by Therapeutic Guidelines, an independent not-for-profit organisation that aims to promote quality use of medicines. *Therapeutic Guidelines* is a leading source of independent, evidence-based, practical treatment advice to assist Australian healthcare professionals with decision making at the point-of-care.

Therapeutic Guidelines: Antibiotic provides guidance on the management of a wide range of infectious diseases. The guidelines are based on a review of the latest literature, discussed and interpreted by several multidisciplinary expert groups, with input from an extensive network of other healthcare professionals. During this review, the [Antibiotic 17 Expert Group](#) identified areas where evidence was lacking, insufficient or conflicting, warranting further research. To support the research community, these evidence gaps were collated and published in March and December 2025. In the April 2026 update, new evidence gaps have been added for melioidosis, malaria, Q fever, cytomegalovirus, febrile neutropenia and primary prophylaxis in patients with immune compromise.

The gap that was raised most often was the optimal duration of antimicrobial therapy for various infections in both adults and children, followed by the optimal duration of intravenous therapy (if it is required) before switching to oral therapy. Despite recent publications addressing these questions, additional data are required for both the implementation of the existing evidence and infections for which these questions have not been answered, including:

- endocarditis after transcatheter aortic valve replacement or implantation

- cardiac implantable electronic device infections (pocket infection or endocarditis) after device removal
- infected vascular stents customised to stent location and pathogen
- septic jugular thrombophlebitis
- mediastinitis
- exacerbations of bronchiectasis
- prophylaxis of chronic obstructive pulmonary disease exacerbations
- lung abscess when the pathogen is not identified
- complicated parapneumonic effusion or empyema after source control is achieved.

The remaining evidence gaps are grouped according to the order of topics in *Therapeutic Guidelines: Antibiotic*, rather than being listed in order of research priority. They may not represent all areas in which research is needed.

Table of Contents

Gaps that impact multiple topics	6
Cardiovascular infections	6
Infective endocarditis	6
Cardiac implantable electronic device infections	6
Septic jugular thrombophlebitis	6
<i>Clostridioides difficile</i> infection	6
Cytomegalovirus (CMV)	7
Ear, nose and throat infections	7
Otitis externa	7
Otitis media	7
Peritonsillar abscess (quinsy) and peritonsillar cellulitis	7
Retropharyngeal abscess	7
Febrile neutropenia	8
Genital and sexually transmissible infections	8
Syphilis in pregnancy and congenital syphilis	8
Intra-abdominal infections	8
Acute appendicitis	8
Diverticulitis	8
Necrotising enterocolitis in neonates	8
Mediastinitis	9
Melioidosis	9
Parasitic infections	9

Malaria	9
Perinatal infections.....	9
Intra-amniotic infection (chorioamnionitis)	9
Prevention of neonatal group B Streptococcus (GBS) disease	9
Prevention of infection.....	9
Prevention of infection in patients with asplenia or hyposplenism	9
Primary prophylaxis in patients with immune compromise	10
Assessing the need for antimicrobial prophylaxis in patients with immune compromise	10
<i>Pneumocystis jirovecii</i> pneumonia (PJP) prophylaxis in patients with immune compromise.....	10
<i>Neisseria meningitidis</i> prophylaxis in patients treated with eculizumab or ravulizumab .	10
Q fever.....	10
Surgical prophylaxis	10
Principles of surgical antibiotic prophylaxis.....	10
Abdominal procedures.....	11
Breast procedures	11
Cardiac surgical procedures.....	11
Orthopaedic procedures	11
Spinal surgery.....	11
Urological procedures.....	12
Vascular procedures.....	12
Pneumonia	12
Respiratory tract infections other than pneumonia.....	12

Bronchiectasis in adults and children.....	12
Chronic obstructive pulmonary disease (COPD) exacerbations	13
Lung abscess	13
Parapneumonic effusion and thoracic empyema	13
Sepsis and septic shock	13
Community-acquired sepsis or septic shock of uncertain source.....	13
Skin and soft tissue infections	13
Traumatic wounds.....	14
Urinary tract infections (UTI).....	14
Bacteriuria and UTI in pregnancy.....	14
Principles of aminoglycoside use.....	14
Principles of vancomycin use.....	15
Monitoring antimicrobial blood concentrations	15
Antimicrobial hypersensitivity	15

Gaps that impact multiple topics

- Optimal dosage of intravenous amoxicillin+clavulanate for children.
- Randomised controlled trial evidence of clinical efficacy of 12-hourly versus 8-hourly intravenous and/or oral metronidazole for empirical treatment of anaerobic bacterial infections.
- Optimal dosage of trimethoprim+sulfamethoxazole for people with obesity.

Cardiovascular infections

Infective endocarditis

- Clinical outcomes of partial oral therapy compared to ambulatory parenteral therapy (eg Hospital-in-the-home) for infective endocarditis, and the efficacy of individual oral antibiotics, and combinations, for directed therapy of infective endocarditis.

Cardiac implantable electronic device infections

- Pathophysiology of cardiac implantable electronic device infection after upgrade or replacement, including why the risk of infection is greater than the risk of infection after a new implant.
- Optimal timing for reimplantation of a new cardiac implantable electronic device after removal of the device because of a pocket infection.

Septic jugular thrombophlebitis

- Prospective data demonstrating the outcomes of anticoagulation versus no anticoagulation for septic jugular thrombophlebitis, with consideration of the duration of anticoagulant therapy, and resolution of thrombus or metastatic foci.

***Clostridioides difficile* infection**

- Cost-effectiveness of fidaxomicin for a first episode or first recurrence of *C. difficile* infection.
- Optimal formulations, route and dose of faecal microbiota transplantation for *C. difficile* infection (second or subsequent recurrences; ongoing refractory infection unresponsive to fidaxomicin; severe, complicated or fulminant infection).
- Cost-effectiveness of bezlotoxumab for preventing recurrence of *C. difficile* infection in the Australian healthcare setting.

Cytomegalovirus (CMV)

- Optimal threshold of CMV DNAemia at which to start antiviral therapy.
- CMV DNAemia level at which maribavir can be used first-line, without an initial induction period with another antiviral.
- Efficacy of maribavir in treating CMV disease.
- Role of maribavir in prophylaxis against CMV, including appropriate dosing.
- Optimal strategy for secondary prevention of CMV (pre-emptive prophylaxis), including duration of secondary prevention strategy.
- Optimal glomerular filtration rate cap for calculating doses in children.

Ear, nose and throat infections

Otitis externa

- Efficacy of nonantibiotic management strategies (eg aural toilet, tissue spears) to reduce the use of antibiotics for otitis externa.
- Prevalence of ototoxicity associated with the use of aminoglycoside-containing eardrops, particularly in cases of tympanic membrane perforation.

Otitis media

- Randomised controlled trial evidence of the safety and efficacy of antimicrobial eardrops for acute otitis media with perforation.

Peritonsillar abscess (quinsy) and peritonsillar cellulitis

- Optimal dose and duration of corticosteroid therapy in the treatment of peritonsillar abscess and cellulitis.

Retropharyngeal abscess

- Optimal dose and duration of corticosteroid therapy in the treatment retropharyngeal abscess.

Febrile neutropenia

- Choice of empiric therapy for febrile neutropenia in patients with a history of colonisation with multidrug-resistant gram-negative bacteria.

Genital and sexually transmissible infections

Syphilis in pregnancy and congenital syphilis

- Effectiveness of non-penicillin antibiotics for both treating syphilis in pregnant patients with severe penicillin allergies and preventing congenital syphilis.

Intra-abdominal infections

- Clinical efficacy of intravenous amoxicillin+clavulanate compared to other non-aminoglycoside antibiotics (eg ceftriaxone) for intra-abdominal infections.
- Efficacy of extended infusions of beta lactams for non-critically-ill patients with sepsis from a biliary or gastrointestinal source.

Acute appendicitis

- Optimal antibiotic regimen for nonoperative treatment of acute uncomplicated appendicitis.
- Long-term effects on microbiota and risk of multidrug-resistant (MDR) organisms with non-operative treatment of acute uncomplicated appendicitis.

Diverticulitis

- Need for any antibiotics in uncomplicated diverticulitis. (This gap is likely to be addressed; 2 large pragmatic placebo-controlled randomised controlled trials are pending.)

Necrotising enterocolitis in neonates

- Optimal antibiotic regimen for empirical treatment of necrotising enterocolitis in neonates.

Mediastinitis

- The prevalence of oesophageal colonisation with gram-negative bacteria in aged-care facility residents, to help determine the optimal antibiotic regimen for mediastinitis following oesophageal rupture in this group.

Melioidosis

- Effectiveness of granulocyte colony-stimulating factor (G-CSF) in melioidosis septic shock.

Parasitic infections

Malaria

- Optimal antibiotic regimen for the treatment of delayed *Plasmodium falciparum* clearance.

Perinatal infections

Intra-amniotic infection (chorioamnionitis)

- Optimal duration of postpartum antibiotic therapy for intra-amniotic infection.

Prevention of neonatal group B Streptococcus (GBS) disease

- Optimal GBS screening strategy for the Australian setting: risk-based or universal.

Prevention of infection

Prevention of infection in patients with asplenia or hyposplenism

- Optimal antibiotic for prophylaxis against encapsulated bacteria (especially pneumococcus) in patients with asplenia or hyposplenism who have hypersensitivity to penicillins.

Primary prophylaxis in patients with immune compromise

Assessing the need for antimicrobial prophylaxis in patients with immune compromise

- Efficacy of prophylaxis against *Streptococcus pneumoniae* until 100 days after an allogeneic haematopoietic stem cell transplant.
- Optimal duration of targeted antifungal prophylaxis after liver transplant.

- Optimal drug for prevention of invasive fungal infection in liver transplant recipients with risk factors.

Pneumocystis jirovecii pneumonia (PJP) prophylaxis in patients with immune compromise

- Optimal PJP prophylaxis regimen in adults and children with immune compromise.

Neisseria meningitidis prophylaxis in patients treated with eculizumab or ravulizumab

- Optimal duration of prophylaxis against *Neisseria meningitidis* in patients treated with eculizumab or ravulizumab.

Q fever

- Optimal antibiotic regimens for the treatment of Q fever

Surgical prophylaxis

Principles of surgical antibiotic prophylaxis

- Optimal aminoglycoside dosage for procedures lasting longer than 11 hours in adults.
- Optimal aminoglycoside dosage for surgical prophylaxis in adults with kidney impairment.
- Optimal aminoglycoside dosage regimens for surgical prophylaxis in children.
- Criteria and optimal timing for preoperative MRSA screening.
- Identification of surgical procedures associated with an increased risk of postoperative MRSA infection.

Abdominal procedures

- Efficacy of oral antibiotic therapy alone (without mechanical bowel preparation) before elective colorectal resection.

Breast procedures

- Randomised controlled trial data on the efficacy and safety of antimicrobial soaking of breast implants before implantation.
- Randomised controlled trial data on the efficacy of postoperative cefalexin in breast reconstruction with implants until drain removal.

Cardiac surgical procedures

- Optimal antimicrobial dosing for procedures involving cardiopulmonary bypass.
- Optimal surgical prophylaxis regimen for transcatheter aortic valve implantation (TAVI)
- Randomised controlled trial data on the efficacy and safety of topical antibiotics (eg vancomycin paste, gentamicin-collagen sponges) for cardiac surgical procedures involving a sternotomy.

Orthopaedic procedures

- Randomised controlled trial data on the efficacy and safety of vancomycin-soaked grafts for anterior cruciate ligament reconstruction (ACL-R).
- Randomised controlled trial data on the efficacy and safety of the application of topical intrawound vancomycin powder to the surgical incision site.

Spinal surgery

- Randomised controlled trial data on the efficacy and safety of the application of topical intrawound vancomycin powder to the surgical incision site.

Urological procedures

- Risk of postoperative infection associated with newer urological procedures (eg Rezum therapy), transperineal prostate biopsy or fiducial marker insertion.

Vascular procedures

- Risk of postoperative infection associated with hybrid and endovascular procedures.

Pneumonia

- Microbiological aetiology of pneumonia in Australia.
- Whether biomarkers can help determine the need for, and optimal duration of, antibiotic therapy.
- Optimal antibiotic regimen for children with hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) or severe pneumonia.
- Whether rapid diagnostics and upper airway viral studies can identify community-acquired pneumonia (CAP) in children and the need for antibiotic therapy.
- Efficacy of linezolid compared with adequately dosed vancomycin for pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA) without intermediate resistance to vancomycin.
- Optimal antibiotic regimens for gram-negative pneumonia, considering clinical outcomes and adverse effects (including impact on microbiome and potential for resistance). Pathogens of interest include:
 - non-MDR Enterobacterales
 - non-MDR *Pseudomonas aeruginosa*
 - community-acquired *Acinetobacter baumannii*
 - hospital-acquired *Acinetobacter baumannii*.
- Optimal dosing of antibiotics for pneumonia in patients requiring intensive care support.

Respiratory tract infections other than pneumonia

Bronchiectasis in adults and children

- Microbiological aetiology of bronchiectasis exacerbations in Australia.
- Randomised controlled trial evidence for the optimal antibiotic regimen for bronchiectasis exacerbations, particularly in children.
- Efficacy and safety of inhaled antibiotics, particularly their long-term impact on antibiotic resistance, and how this compares to antibiotics administered orally or intravenously for people with frequent exacerbations.
- Optimal antibiotic regimen to eradicate *Pseudomonas aeruginosa*, including efficacy of monotherapy versus dual therapy, and the impact of treatment on long-term outcomes for patients.

Chronic obstructive pulmonary disease (COPD) exacerbations

- Efficacy and potential harms (including development of antibiotic resistance) of azithromycin and erythromycin for long-term prophylaxis of COPD exacerbations.

Lung abscess

- Whether percutaneous biopsy in lung abscess without a microbiological diagnosis can direct antibiotic therapy or identify complications.

Parapneumonic effusion and thoracic empyema

- Utility and yield of pleural biopsy in determining a microbiological diagnosis of parapneumonic effusion or empyema, and directing antibiotic therapy.

Sepsis and septic shock

Community-acquired sepsis or septic shock of uncertain source in adults

- Head-to-head studies to determine the optimal antibiotic regimen for the empiric treatment of community-acquired sepsis of unknown source in adults.

Skin and soft tissue infections

- Whether shorter courses of antibiotic therapy can be used to treat boils and carbuncles, cellulitis and erysipelas, and, if they can, which patients would be suitable.
- Data supporting the efficacy of doxycycline for skin and soft tissue infections in patients who are at an increased risk of methicillin-resistant *Staphylococcus aureus* (MRSA).

Traumatic wounds

- Optimal duration of prophylaxis for traumatic wounds (excluding open fractures).

Urinary tract infections (UTI)

- Clinical definition, diagnosis and management of chronic UTI.

Bacteriuria and UTI in pregnancy

- Optimal timing and frequency of antenatal screening for asymptomatic bacteriuria.
- Requirement for routine screening and treatment of asymptomatic bacteriuria in low-risk pregnant patients, considering the relative harms, benefits and cost-effectiveness.

Principles of aminoglycoside use

- Optimal aminoglycoside area under the concentration-time curve (AUC) target for pathogens with a low minimum inhibitory concentration (MIC).
- Maximum doses of gentamicin, tobramycin and amikacin are provided in the guidelines - data are needed to inform whether higher doses can be used and the toxicity threshold.
- Optimal amikacin dosage regimens in adults.
- Optimal weight descriptor to calculate aminoglycoside dose in adults (eg lean bodyweight, actual bodyweight, ideal bodyweight).
- Optimal aminoglycoside dose and method for monitoring in patients undergoing haemodialysis.
- In neonates and children, the optimal aminoglycoside dose for empirical and directed therapy.
- In neonates and children, the role of aminoglycoside trough plasma concentration monitoring to avoid toxicity.

Principles of vancomycin use

- Optimal vancomycin trough plasma concentration in children aged between 3 months and 2 years.
- Optimal vancomycin loading and maintenance dosage regimens in adults with obesity.
- Role of Bayesian *a priori* dosing of vancomycin to optimise vancomycin dosing.

Monitoring antimicrobial blood concentrations

- Whether trough plasma concentration or area under the concentration-time curve (AUC) is superior for fluconazole therapeutic drug monitoring.

- Optimal method for monitoring itraconazole plasma concentrations, in particular whether the target concentration should be the sum of the concentrations of drug and its active metabolites.
- Whether monitoring beta-lactam plasma concentrations in patients outside of the intensive care unit setting improves outcomes.
- Whether CYP2C19 genotype testing can guide initial voriconazole dosing and inform therapeutic drug monitoring targets.
- Whether posaconazole plasma concentration monitoring is required for patients using posaconazole tablets for prophylaxis to ensure that the patient has adequate plasma concentrations.
- The concentration above which posaconazole causes toxicity.

Antimicrobial hypersensitivity

- Management of hypersensitivity to antimicrobials other than penicillins (eg cephalosporins, macrolides, tetracyclines, antituberculosis drugs).
- Safety of delabeling antimicrobial allergies in primary care.
- Whether cephalosporins can be safely used in patients with a severe cutaneous adverse reaction (SCAR) to penicillin.
- Required frequency of benzathine benzylpenicillin desensitisation in patients with syphilis, in particular whether desensitisation needs to be repeated before each dose.