AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

14 Antimicrobial stewardship in the care of children

Antimicrobial Stewardship in Australian Health Care

2020

Contents

Acronyms and Abbreviations

Abbreviation	*Definition*
ACSQHC	Australian Commission on Safety and Quality in Health Care
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
ANZPID-ASAP	Australia and New Zealand Paediatric Infectious Diseases Group - Australasian Stewardship of Antimicrobials in Paediatrics
AURA	Antimicrobial Use and Resistance in Australia
CAR	critical antimicrobial resistance
CARAlert	National Alert System for Critical Antimicrobial Resistances
CPE	Carbapenemase-producing Enterobacterales
DDD	defined daily dose
DOT	days of therapy
GP	general practitioner
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAPS	National Antimicrobial Prescribing Survey
NSQHS Standards	National Safety and Quality Health Service Standards
OECD	Organisation for Economic Co-operation and Development
OPAT	outpatient parenteral antimicrobial therapy
PBS	Pharmaceutical Benefits Scheme
PCT	procalcitonin
POC	point of care
RACGP	Royal Australian College of General Practitioners
TDM	therapeutic drug monitoring

Key Points

- Antimicrobial resistance affecting children is a growing health problem, resulting in increasing duration and severity of infective illness and limiting the therapeutic options available to treat these infections.
- Antimicrobial resistance patterns for children are different to those of adults. Organisms of particular concern for children are carbapenemase-producing Enterobacterales (CPE) and ceftriaxone non-susceptible *Salmonella* species.
- Antimicrobial use promotes bacterial resistance in children.
- Pharmaceutical Benefits Scheme (PBS) data show that in all patients aged less than 65 years, the highest rate of antibiotic dispensing is for children aged 2 to 4 years.
- Antibiotic use in children is often unnecessary. Many childhood infections are caused by viruses, and some uncomplicated bacterial infections do not require treatment with antibiotics. Determining if antibiotic therapy is indicated is an important initial step in the appropriate prescribing of antimicrobials in children.
- Antimicrobials are over-prescribed for children that receive care in Australian hospital, outpatient and general practice settings.
- There is a growing body of evidence that antibiotic exposure in very young children disrupts the developing gut microbiota, which is associated with increased risk of necrotising enterocolitis, fungal infections, childhood asthma, allergy, dermatitis and obesity later in life.
- Paediatric antimicrobial stewardship (AMS) programs have been found to:
  - decrease antimicrobial use
  - reduce antimicrobial resistance
  - decrease prescribing errors
  - improve patient outcomes
  - decrease medication costs.
- When prescribing antimicrobials for children, it is important to recognise their unique needs with respect to age, size, weight, development, pattern of antimicrobial resistance, antimicrobial risk of harm, suitability of formulations and dose effectiveness.
- Key paediatric AMS strategies include:
  - improved focus on appropriateness of antimicrobial prescribing
  - reduced duration of treatment
  - use of oral therapy where clinically feasible (including intravenous to oral switch)
  - dose optimisation.
- Antimicrobial stewardship programs in health care settings that provide paediatric care should include:
  - a multidisciplinary team that specifically comprise members with a range of paediatric expertise
  - access to evidence-based prescribing guidance that is appropriate for children (including neonates and infants)
  - systems that facilitate and audit adherence to evidence-based treatment
  - approaches that target areas of inappropriate antimicrobial use in children
  - paediatric specific education for staff
  - education support for parents and carers.
- Smaller services that provide paediatric care, including those located in rural and remote areas, should consider entering into a formalised network arrangement with tertiary paediatric care providers to access additional AMS program support and expertise specific to the care of children.
- General practice has a critical role in reducing childhood antimicrobial use and preventing antimicrobial resistance by:
  - achieving high rates of childhood immunisation
  - continuous improvement in appropriateness of antimicrobial prescribing
  - educating parents and carers in appropriate antimicrobial use
  - providing advice on alternative treatment options when antibiotic use is not indicated.
- Paediatric AMS programs measure performance differently to adult AMS programs. The standard measurement of rate of antimicrobial use in adults (defined daily dose [DDD] per 1,000 occupied-bed days) is not suitable for paediatric settings because of weight differences with age. Increased uptake of electronic medicines management systems in Australian paediatric hospitals in the future should facilitate the collection of data required to monitor paediatric antimicrobial usage using the preferred method of days of therapy (DOT).
- Other methods of monitoring AMS programs may include alternative antimicrobial usage measures, appropriateness of use measures and outcome measure such as infection rates.

14.1 Introduction

Antimicrobial resistance (AMR) is a global health priority and antimicrobial stewardship (AMS) is recognised as key in the global action plan to combat this issue.[1]

Antimicrobial stewardship programs are evidence-based multi-component strategies that aim to increase judicious use of antimicrobials to improve patient outcomes and decrease AMR.[2] Initially AMS programs were largely focussed on the care of adults. Recently, AMS programs for paediatric patients have been developed to meet the needs of children, respond to high rates of antimicrobial use in children, and recognise the unique AMR patterns in children compared with adult populations.[3]

Antimicrobial Stewardship in Australian Health Care (the AMS Book) was revised in 2018 to provide an overarching resource for AMS programs in Australia. The AMS Book is available at www.safetyandquality.gov.au/our-work/healthcare-associated-infection/antimicrobialstewardship/book/.

Additional chapters of the AMS Book are added as they are completed to further support AMS in Australia.; Chapter 13: 'Role of general practice in antimicrobial stewardship' was added in 2020.

This chapter discusses AMS in the care of children, and:

- Describes the factors that influence antimicrobial prescribing for children
- Identifies key strategies to improve antimicrobial use in children
- Provides practical strategies for the implementation and evaluation of paediatric AMS programs in all healthcare settings
- Identifies approaches to measuring paediatric AMS performance.

This chapter supports implementation of an AMS program in paediatric care settings including paediatric tertiary hospitals, other hospitals that provide care to paediatric patients, and primary care providers of paediatric care such as general practice.

14.1.1 Antimicrobial use in children

Use of antimicrobial medicines in the Australian community is decreasing. However, usage continues to be higher in Australia than other comparable OECD countries.[4]

In 2017, 45% of Australian children aged 9 years and younger had at least one prescription for an antibiotic dispensed per year under the Pharmaceutical Benefits Scheme (PBS). In all patients aged less than 65 years, the highest rate of antibiotic dispensing under the PBS was for children aged 2 to 4 years.[5]

Available data show substantial geographical variation in antimicrobial use. In Australia, geographical variation in healthcare use is reported in the *Australian Atlas of Healthcare Variation* series. According to the *Australian Atlas of Healthcare Variation*, in 2016–17 there was a 16-fold difference in antimicrobial dispensing across geographical areas nationally.[6] Substantial variation prompts investigation into why this may be occurring and the potential for improvement.

Antibiotic use in children is often unnecessary. Many childhood infections are caused by viruses, and some uncomplicated bacterial infections may not require treatment with antibiotics.[7] Antibiotics should be reserved for cases in which a bacterial cause is suspected and antimicrobial treatment is recommended; this is a key area to target to reduce antibiotic prescribing.

Antimicrobials are frequently over-prescribed in Australia. A recent study of antibiotic use in children in public hospital and primary care settings found that almost 40% of antimicrobials are not prescribed in accordance with clinical practice guidelines. In some conditions, such as acute otitis media, 86% of prescribed antimicrobials are not appropriate.[8] Australian studies have also identified over-prescribing of antimicrobials in children for a range conditions including upper respiratory tract infections, bronchitis and bronchiolitis, and tonsillitis.[9]

Inappropriate use of antimicrobials also occurs in children admitted to public and private hospitals in Australia. Data from the National Antimicrobial Prescribing Survey (NAPS) identified almost 20% of antimicrobial prescriptions for admitted children were inappropriate, and 59% of prescriptions for surgical prophylaxis in children were inappropriate in NAPS contributor hospitals. The most frequently inappropriately prescribed antimicrobials in children admitted to hospital were amoxicillin and the broad-spectrum agents cefazolin and ceftriaxone.[10]

Antibiotic overuse has also been identified in very young children. A large Victorian study found half of all infants are exposed to at least one antibiotic before one year of age. The number of antibiotic prescriptions and the cumulative antibiotic exposure of infants in this Australian study was markedly higher than other high-income countries. Amoxicillin– clavulanic acid was identified as the most commonly prescribed antibiotic, despite clinical guideline recommendations that amoxicillin alone is the first-line agent for most common early childhood infections in Australia.[11]

Overuse of antimicrobials in neonatal intensive care units is an issue of significant concern. Antimicrobial medicine consumption in intensive care settings can be almost ten times general

hospital wards.[12] International and Australian data indicates a lack of consistency in antimicrobial use across neonatal intensive care units.[13,14] A recent Australian study identified only 4% of antimicrobial prescriptions for the treatment of sepsis in neonates were for microbiologically confirmed infections. Further, more than 20% of antibiotics were prescribed for greater than 48 hours, despite identification of most potential pathogens in neonatal sepsis occurring within 36 to 48 hours. Due to the unique risks associated with serious bacterial infection, risk of sepsis in neonates generally requires commencement of antibiotic therapy, despite the fact that most will not have culture-confirmed infection.[15]

Most antimicrobial prescribing for children occurs in the outpatient setting, predominantly in primary care and, to a lesser extent, in hospital clinics and emergency departments. There is also increasing use of outpatient parenteral antimicrobial therapy (OPAT) for home-based systemic treatment of serious infections in children.[16] The 2017 Australian OPAT NAPS pilot study evaluated the appropriateness of antimicrobial use in OPAT in children and adults. This study found that less than half of antimicrobial prescriptions were compliant with guidelines.[17]

14.1.2 Antimicrobial resistance and children

The overuse and misuse of antimicrobials, particularly broad-spectrum antibiotics in healthcare settings, is a key contributor to AMR. Antimicrobial resistance reduces the number of therapeutic options for treating infection; this is of particular concern in paediatric care, as therapeutic options in children are already limited compared to options available for adult patients. For children, AMR may increase the duration and severity of infective illness. Children infected with extended spectrum β-lactamase-producing organisms have, on average, a longer length of hospital stay, require more intensive care unit days and have a higher risk of death than those without such infection.[18]

The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System monitors AMR and antimicrobial use in Australia.[19] This system, which is coordinated by the Australian Commission on Safety and Quality in Health Care (the Commission), provides national data on antimicrobial use across a range of Australian healthcare settings. Data collected through the National Alert System for Critical Antimicrobial Resistances (CARAlert) show critical antimicrobial resistances (CARs) have been isolated in patients of all ages in Australia. The CARs more frequently isolated from Australian children include carbapenemase-producing Enterobacterales (CPE) and ceftriaxone non-susceptible *Salmonella* species.[20]

Antimicrobial use promotes bacterial resistance through direct selection pressure that is advantageous to bacteria expressing resistance genes.[21] Longer duration of antibiotic use and multiple courses are associated with higher rates of bacterial resistance in an individual.[22] Antibiotic resistance genes have also been identified without antimicrobial exposure.[23] This finding suggests community transmission of AMR may occur and children may be important recipients and transmitters of resistant bacteria in the community.[24]

14.1.3 Antimicrobial stewardship in paediatric care

Antimicrobial stewardship is a core component of the National Safety and Quality Health Service (NSQHS) Standards. The NSQHS Standards support hospitals and health services to ensure nationally expected levels of quality and safety are met. The NSQHS Preventing and Controlling Healthcare-Associated Infection Standard aims to improve the measures designed to help prevent infections and the spread of AMR, through appropriate prescribing and use of antimicrobials.[25] Antimicrobial stewardship components are also included in the Royal Australian College of General Practitioners (RACGP) Standards for General Practice[26] and the Aged Care Quality and Safety Commission (ACQSC) Aged Care Quality Standards.[27]

Whilst much of the evidence for AMS is based on research pertaining to adult care, there is a growing evidence base for paediatric AMS programs. Studies of AMS programs for paediatric inpatient care in high-income countries demonstrate paediatric AMS programs:

- Decrease antimicrobial use
- Decrease prescribing errors
- Improve patient outcomes
- Decrease medication costs.[28, 29]

Recent research has also identified that paediatric AMS programs reduce AMR in inpatient and outpatient settings.[30]

A small number of studies provide evidence on the effectiveness of paediatric AMS interventions in the primary care setting. Interventions aimed at changing prescriber behaviour and educating caregivers have been found to improve prescribing in accordance with guidelines, decrease the number of antibiotics dispensed per-child per-year and decrease the prescribing of broad-spectrum agents.[31] For example, antibiotic consumption in children aged 0-6 years was halved in Sweden from the years 2000 to 2014 supported by the development, public

dissemination, and health professional uptake of new guidelines for the treatment of childhood illnesses such as otitis media.[32] These significant reductions in antimicrobial use that can be achieved in primary care are an important component of comprehensive, whole of system responses to AMR.

14.2 Factors that influence antimicrobial prescribing in children

Although many of the core principles of AMS apply to both adults and children, there are some aspects of AMS that are unique to children.

14.2.1 Anatomical and physiological factors

Children differ anatomically and physiologically from adults. Babies are born with an immature immune system, which matures and acquires memory as they grow. Early protection is provided by transplacental transfer of immunoglobulin, and also from breastmilk.[33] Despite this early protection, children have high rates of infection. It is understood that viral infections and nonspecific syndromic presentations are more common in paediatrics than in adult medicine.[34]

Different microorganisms from those often seen in adult patients may cause infectious diseases in children. For example, group B streptococci and *Escherichia coli* are the most common bacterial causes of meningitis in neonates, but *Streptococcus pneumoniae* and *Neisseria meningitidis* are the predominant causes in infants and older children. This influences empirical and targeted antimicrobial choices.[35] Patterns of AMR in children also vary significantly by age, requiring age-specific antimicrobial guidance for selected infections.[36]

Age- and development-appropriate dosing can be challenging when prescribing antimicrobials for children. An accurate body weight, and sometimes height (to determine body surface area), is required to calculate dosage. This may not always be possible (for example in critically ill children). Although age-based weight estimation formulas exist, the accuracy of these formulas is variable, which can increase the risk of inaccurate dosing.[37] Inappropriately low dosing of antimicrobials can contribute to AMR.[38]

As children grow, body composition changes (for example water, fat, protein) and the absorption, distribution, metabolism and excretion of medications change. As a result, the pharmacokinetic and pharmacodynamic properties of medications such as antimicrobials can be variable during childhood.[39] This precludes the use of a one-dose-fits-all approach to dosing. Evidence of the pharmacokinetic and pharmacodynamic properties of many antimicrobials in children is lacking; often data from *in vitro* or animal models, confirmed in adult patients have not been corroborated in paediatric patients. Where evidence exists, the appropriate duration of antimicrobial therapy is often shorter than for the same infection in adults.[40]

In addition, standard dosing schedules may not be appropriate in specific populations with altered pharmacokinetics such as neonates and children with: burns, cystic fibrosis; immunocompromise; or obesity.[41,42] Almost one-quarter of Australian children are overweight (17%) or obese (7.7%).[43] Obese children differ in body composition and physiology from children who are not obese. Dosing by actual body weight may result in either sub-therapeutic levels or drug toxicity. For example, aminoglycoside doses are usually calculated based on ideal body weight rather than actual total body weight to prevent toxicity, whilst doses for other medications are based on adjusted body weight. Little data is available to guide antibiotic dosing in obese children.[44]

Children can respond differently to antimicrobials compared to adults. The likelihood of adverse reactions to antimicrobials can increase or decrease with age and development. Lower toxicity for some antimicrobials in children (for example aminoglycoside nephrotoxicity) may mean that these antimicrobials have greater usefulness in children. Conversely, some irreversible side effects that might be tolerated in an elderly patient (for example significant ototoxicity) could be unacceptable in an infant. [45] These different side effect profiles could necessitate the use of alternative antimicrobials that would not be commonly used in adults, for example the preferential use of cefotaxime rather than ceftriaxone to avoid ceftriaxone-related cholelithiasis, which is more prevalent in infants than adults.[46]

Difficulties associated with AMR can affect risk-benefit considerations when selecting antimicrobials. Historically, use of antimicrobials such as tetracyclines and fluoroquinolones has been contraindicated due to concerns about adverse effects in children. Despite this, there is increasing use of these agents in the treatment of multidrug-resistant pathogens, where there is no safe or effective alternative, and where the benefit is considered to exceed the risk.[47]

14.2.2 Antimicrobial access and safety factors

Fewer antimicrobials are available for use in children than in adults, which may limit the ability of clinicians to treat resistant organisms. Formulations suitable for use in neonates, infants

and children are often unavailable, or have not been sufficiently assessed for safety or efficacy in children. Although formal evaluation of new antimicrobials in children is now an international regulatory requirement, the lack of clinical studies for older products means many antimicrobials are used off-label in children.[48,49] Off-label use of medications in children can limit affordable access to antimicrobials as this type of use is not subsidised under the PBS.[50]

When selecting an antimicrobial product, formulation factors are important. Considerations such as the taste of a liquid formulation, the volume of liquid required, or the ability of the child to swallow tablets can affect adherence. Modifying adult formulations such as crushing a tablet or opening a capsule is not always appropriate.[51] Small errors in volume or dose can result in underdosing or overdosing, leading to adverse outcomes, particularly in neonates.[52] The excipients present within adult formulations also require consideration. Some formulations include excipients that can be potentially harmful to neonates and children.[53] Solvents such as ethanol and propylene glycol can cause toxicity. Further, some preservatives can cause adverse effects in children; for example, benzyl alcohol can cause potentially fatal gasping syndrome in neonates, and benzoic acid is associated with increased rates of jaundice in neonates, which can result in brain dysfunction (kernicterus).[54]

Increasingly, evidence suggests antimicrobial use in very young children may cause long term harm through alteration of the microbiome of the gut.[55] The microbiota acquired by infants, mainly at birth, mature in early childhood up to the age of approximately 3 years, by which time the microbiota are mostly adult-like.[56] Microbiota have an important role in immune system development in infants. There is a growing body of evidence that antibiotic exposure early in life can change the microbiota temporarily or permanently.[57] Changes to the microbiome due to early exposure to antibiotics are associated with an increased risk of early adverse outcomes such as necrotising enterocolitis and fungal infections. Studies indicate certain probiotic strains appear to reduce the prevalence of necrotising enterocolitis in premature infants, although further research is required to determine the optimal formulation, dosage and treatment duration.[58] In addition, early antibiotic exposure is associated with increased risk of chronic disease later in life such as allergy, atopic dermatitis, celiac disease, diabetes and obesity. [59,60,61]

The potential short-term and long-term risks of neonatal antimicrobial exposure have caused Australian researchers to question the risk-benefit considerations of intrapartum antibiotic prophylaxis to prevent early-onset group B *Streptococcus* infection in neonates.[62] National Health Service clinical guidelines used in England and Wales, do not recommend routine antenatal screening for group B *Streptococcus* because evidence of its clinical and cost-effectiveness remains uncertain.[63] Further research into the clinical risks and benefits of intrapartum antibiotic prophylaxis for the prevention of early-onset group B streptococcal infection is required.

14.2.3 Other factors

Prescribers may have a lower threshold for prescribing antibiotics in children due to their perceptions of uncertainty and risk. Non-specific syndromic and viral presentations can cause diagnostic uncertainty and drive antimicrobial prescribing, especially when there are no positive microbiology results to guide therapy.[64] Children may have difficulty in communicating their symptoms, which can make assessment difficult.

Clinical uncertainty and concerns regarding risk of serious bacterial infection, particularly in neonates can also affect decisions to commence and continue antimicrobial therapy.[65] Perinatal infection remains the highest cause of Australian neonatal death and clinical signs of neonatal sepsis can be non-specific.[66] As such, empiric antibiotic therapy is commonly commenced in hospitalised neonates as prescribers seek to balance the unique risks and benefits of antimicrobial treatment associated with this vulnerable patient group. Tools to assist clinicians in determining the probability of a neonatal early-onset sepsis[67] can safely reduce neonatal blood culture screening, empirical antibiotic exposure and hospital length of stay.[68,69]

Antibiotic allergy labels are usually acquired by children because of rash presentation after antibiotic use; however, many never have a formal allergy evaluation. When formal evaluation is performed the majority are found not to have antibiotic allergy.[70]

Unevaluated childhood antibiotic allergy labels can perpetuate into adulthood, drive the use of broad-spectrum antibiotics and subsequently AMR, and lead to poorer health outcomes.[71] A recent study conducted in Western Australia identified more than 5% of children admitted to a major paediatric tertiary hospital had an antibiotic allergy label. Those with an antibiotic allergy label were treated with more broad-spectrum antimicrobials than those without an antibiotic allergy label, and had longer lengths of hospital stays.[72] Testing to prove or disprove antibiotic allergy labels can increase access to appropriate antibiotic therapy, reduce AMR and improve health outcomes.[73]

Aboriginal and Torres Strait Islander children experience a greater infectious disease burden, higher rates of invasive infections, and are more

likely to be hospitalised for infectious diseases than non-Indigenous children.[74,75] Acute rheumatic fever, caused by an immunological response to group A *Streptococcus* infection predominantly affects Aboriginal and Torres Strait Islander children aged 5-14 years. Antibiotic use in the treatment and secondary prophylaxis of acute rheumatic fever is important to minimise heart valve damage and progression to rheumatic heart disease. Prompt assessment and antibiotic treatment of superficial infections often caused by group A *Streptococcus* (such as sore throats and skin sores) is also important for the prevention of acute rheumatic fever in Aboriginal and Torres Strait Islander children.[76] See Chapter 15 of the AMS Book for additional information regarding AMS and Aboriginal and Torres Strait Islander people.

14.3 Antimicrobial Stewardship strategies for paediatric Care

Many of the strategies and tools for AMS, as described in Chapter 3 of the AMS Book, are also applicable to the paediatric care setting. In this section five key strategies are discussed that are specifically used in the care of children.

14.3.1 Reduce antimicrobial prescribing in primary care

Chapter 13: 'Role of general practice in antimicrobial stewardship', of the AMS Book contains general information about strategies to reduce antimicrobial prescribing in the general practice setting. In addition to the information provided in Chapter 13, AMS strategies for general practice also need to consider issues that are specific to children and their carers.

A meta-review of studies to reduce antibiotic prescriptions for children presenting to primary care with respiratory tract infections, identified evidence that interventions reducing clinical uncertainty, reducing clinician/parent miscommunication, eliciting parent concerns, making clear delayed or no-antibiotic recommendations and providing clinicians with alternate treatment actions have the best chance of success.[77]

Although childhood infections are often due to viral pathogens and can be managed with watchful waiting, GPs are often faced with diagnostic uncertainty, as the causative pathogen is often unknown. Fears of failing to identify a serious bacterial infection often drive a cautious approach that may include the precautionary use of antibiotics. Increasing use of point-of-care (POC) testing for biomarkers of bacterial infection and some common childhood pathogens is evident in Europe in an effort to reduce clinical uncertainty and improve targeted therapy.[78,79] Point-of-care testing uptake in Australia has been slow due to the costs associated with POC testing and regulation of POC testing.[80]

Parents often expect that antibiotics are required for mild childhood infections. In 2017, an NPS MedicineWise survey identified almost one-third of Australian parents visit their GP expecting to receive antibiotics for their child's sore throat, cough or cold.[81] Health professionals' perceptions of parental expectation can also influence prescribing practices. A systematic review of qualitative studies identified primary care clinicians may misinterpret parent requests for information as requests for antibiotic prescriptions.[82] In order to elicit patient concerns and reduce clinician-perceived pressure to prescribe antibiotics, GPs should explicitly ask parents or carers about their concerns and expectations early in the consultation.[83]

When antibiotic use is not warranted, prescribers should take time to discuss with parents: the likely nature of the condition; why prescribing an antimicrobial may not be the best option, and alternative options to prescribing an antimicrobial.[84] This information needs to be conveyed confidently and unambiguously. A recent Australian survey identified most consumers would accept the GP's decision not to prescribe an antibiotic if it was clearly explained.[85]

Parents also require clear guidance on the usual time to recovery and what they should do if their child's clinical condition deteriorates. The NPS survey found that parents generally expect mild respiratory tract infection symptoms to last for a shorter time than they actually do.[86] Many people presenting to a general practice simply want reassurance that the illness is not serious and does not require treatment.[87]

The decision not to prescribe an antibiotic can be perceived as creating a 'treatment vacuum.' Explicit advice regarding alternative treatment options such as over-the-counter symptomatic relief products, home care and standard safety-net advice is important to provide parents with the advice and assurance they need to appropriately care for their child.[88]

Figure 1 provides a series of evidence-based statements to change antibiotic prescribing for childhood respiratory tract infection (RTI), ordered from the strongest to weakest evidence.

Figure 1: Recommendations for interventions to change antimicrobial prescribing behaviour in childhood respiratory tract infections (RTI) [89]

An intervention to change clinician prescribing behaviour should:

1. **Give explicit antibiotic prescription recommendations**
2. **Give alternative treatment options (including for parents e.g. home care advice, and clinicians e.g. delayed scripts)**
3. **Address the treatment/no treatment distinction made by clinicians**
4. **Give information on specific symptoms**
5. **Address both clinicians and parents**
6. **Provide information on prognosis that is tailored to the child and addresses the common and/or stated (not implied) concerns of parents**
7. **Address known environmental pressures (e.g. external pressures to prescribe/consult)**
8. **Make clinicians feel more confident/experienced**
9. **Acknowledge treatment decisions in care of childhood RTIs are usually made in the absence of definitive diagnosis.**
10. **Be designed in consultation with clinicians and parents**

An intervention to change clinician prescribing behaviour should not:

1. **Work against the environment in which clinician operates**
2. **Be generic**
3. **Patronise or undermine parental or clinician decision making**
4. **Be passive (e.g. posters)**
5. **Increase anxiety or perception of risk for either party**

General practice has a key role in achieving high rates of childhood immunisation. Vaccines can reduce AMR through direct reduction of specific organisms and strains carrying resistant genes or by reduction in febrile illness, which reduces antibiotic use. Evidence shows immunisation of children with the pneumococcal conjugate vaccine reduces the number of AMR episodes in children and reduces antibiotic use. Further, children who receive influenza vaccination have fewer antibiotics prescribed compared to those that are not immunised. A large cluster-randomised trial also identified influenza vaccination of children is associated with reduced antibiotic consumption for vaccinated children, their families and community contacts.[90,91]

14.3.2 Limit duration of antimicrobial therapy

Limiting the duration of antimicrobial therapy is an important means of reducing unnecessary antimicrobial exposure in children. Prolonged exposure has been associated with the emergence of antimicrobial resistance, *Clostridioides (Clostridium) difficile* (CDI) infection and fungal infection. Evidence suggests the appropriate duration of therapy for some common infections is shorter in children than in adults. For example, in a study of community-acquired pneumonia in children aged less than five years, five days of high-dose oral amoxicillin resulted in equivalent outcomes to a 10-day course, with no treatment failures, although a three-day course had a 40% treatment failure rate.[92] A study of uncomplicated gram-negative bacteraemia in children found 10 days of intravenous antimicrobial therapy was as effective as 14 to17 days of therapy in preventing relapse.[93]

The Australia and New Zealand Paediatric Infectious Diseases Group - Australasian Stewardship of Antimicrobials in Paediatrics (ANZPID-ASAP) has developed evidence-based recommendations for duration of antibiotic treatment and intravenous to oral step down for a variety of bacterial infections in children. See the Resources section of this chapter for a link to the full table of recommendations.

In outpatient and primary care settings, the quantity of antimicrobial therapy prescribed should be limited according to clinical guidance, rather than PBS pack size. Repeat prescriptions should not be prescribed unless clinically indicated. Prescribing software should have the default repeat setting on antimicrobials set to no repeats.[94] Pharmacists should clarify clinical appropriateness before dispensing repeat prescriptions for antimicrobials when significant time has elapsed between the original dispensing and the repeat dispense request.[95] Routine issue of repeat prescriptions for antimicrobials creates a reservoir of antimicrobials that can be accessed by consumers. Survey results indicate many Australian consumers retain antimicrobial repeat prescriptions for future use.[96] Parents require clear instructions about the prescribed duration of therapy to prevent truncated or excessive use. Pharmacists should also advise parents of the potential harms associated with using repeat prescriptions for antimicrobials later without further assessment by a doctor.

14.3.3 Intravenous to oral switch

Where possible, the use of oral antimicrobials is preferred in children. Treatment using the oral route avoids the use of vascular access devices, and associated risk of catheter related-infection. Oral therapy often has less serious adverse effects than parenteral therapy, facilitates early discharge, improves drug administration efficiency and reduces financial burden on the family and healthcare system.[97]

Oral antimicrobials alone may be sufficient where intravenous antimicrobials have traditionally been used. A Cochrane review of antibiotics for acute pyelonephritis in children found no difference in duration of fever, treatment failure or long-term renal damage in children treated with oral antibiotic therapy for 10 to 14 days compared with children treated with three days of intravenous antibiotic therapy followed by 10 days of oral antibiotic therapy.[98] Further, a systematic review of pneumonia in children under five years of age found oral amoxicillin to be as effective as intravenous ampicillin in severe and non-severe pneumonia.[99]

When intravenous antibiotics are necessary, optimising the duration of intravenous and oral antibiotics aims to provide the shortest safe duration of antibiotics to treat infection. A randomised controlled trial on acute haematogenous osteomyelitis in children showed that only three to four days of intravenous antibiotics were necessary, with the remainder of the course by the oral route; this finding has substantially changed practice.[100] The ANZPID-ASAP have developed evidence-based guidance for the duration and timing of intravenous to oral switch for 36 paediatric infectious diseases.[101] See Figure 2 for general principles to guide clinical decisions for intravenous to oral switch of antimicrobials.

Figure 2: General principles guiding intravenous to oral switch of antimicrobials[102]

Clinical condition

- **Clinically stable without signs of severe sepsis (fever alone need not prevent switch)**

Ability to absorb oral antimicrobials

- **Able to tolerate oral medication (not vomiting or nil by mouth)**
- **No impairment to absorption (e.g. mucositis)**
- **Older than 28 days (under 28 days is not an absolute contraindication, but absorption is variable)**

Availability of an appropriate antimicrobial

- **Antimicrobial treats the infecting or expected organism**
- **Antimicrobial is available in appropriate or palatable paediatric formulation**
- **Antimicrobial has sufficient penetration of affected tissues**

Practical issues

- **Adherence to oral antimicrobials**
- **Family agreement to the plan**

Factors that prevent intravenous to oral switch can include: perceived pressure from patient (or parent) expectation regarding treatment; hierarchy of the medical team structure not facilitating opportunities for de-escalation of antibiotics, or the perception that intravenous antibiotics are more potent.[103]

Intravenous to oral switch can be supported by:[104, 105]

- Shared decision making between prescribers and parents or carers about therapy, including intravenous to oral switch
- Education about the benefits and risks associated with differing routes of antimicrobial therapy
- Access to prescribing guidelines for infections that can be treated with oral agents
- Promotion of clinical criteria for considering intravenous to oral switch, with clear inclusion and exclusion criteria that describe when switch is safe and appropriate, for example flow charts
- A multidisciplinary approach, with nursing and pharmacy staff to prompt reviews of intravenous therapy
- Multimodal communication resources to promote intravenous to oral switch, for example lanyard cards, posters and pamphlets

14.3.4 Antimicrobial dose optimisation

Children exhibit age-related pharmacokinetic and pharmacodynamic variability. For example, the average clearance of linezolid in children aged 2 to 11 years is 2.3 times higher than that of adolescents and adults.[106] There is a lack of pharmacokinetic and pharmacodymanic evidence for many antimicrobials used in children. Many of the current dosing guidelines for antimicrobial treatment in children are extrapolated from adult studies. This can lead to sub-optimal dosing, with associated issues of lower efficacy and increased AMR, or over-dosing and antimicrobial toxicity.[107]

In addition to the dose optimisation strategies discussed in Section 1.2.2. of this chapter, therapeutic drug monitoring (TDM) is an important tool used in paediatric dose optimisation to support personalised dosing of antibiotics in order to increase antimicrobial effectiveness, reduce AMR and minimise toxicity.[108] Understanding the link between antimicrobial exposure (pharmacokinetics) and microbiological response (pharmacodynamics) is important to enable dosing optimisation of the limited number of antibiotics available for paediatric use. Using area under the curve and minimum inhibitory concentration approaches may improve outcomes for some paediatric patients, especially those with life-threatening infections such as sepsis where studies have shown standard dosing rates can be sub-optimal.[109,110] Dosing informed by TDM can also facilitate the continued use of narrower-spectrum antibiotics when treating multidrug-resistant organisms.[111] Therapeutic drug monitoring can be essential when using antimicrobials that are not licensed for use in children. For example, posaconazole is not approved for use in children under 13 years of age; despite this, it is often used off-label in specialist paediatric hospitals. Therapeutic drug monitoring is required to ensure target plasma concentrations of posaconazole are achieved to avoid breakthrough invasive fungal disease.[112]

Therapeutic drug monitoring requires collaboration between paediatricians, pharmacists, pathologists and clinical pharmacologists. Some practical limitations to the use of TDM for dose optimisation in infants and children include: difficulties with venous access and a reluctance to use frequent blood tests to optimise dose or monitor toxicity; the need for large sample volumes compared to circulating blood volumes, particularly in neonates; and lack of access to sufficiently rapid diagnostic testing.[113]

14.3.5 Rapid diagnostics

Recent advances in rapid diagnostics are assisting the earlier identification of pathogens and detection of select antibiotic-resistance genes. Rapid diagnostic tests are associated with reduced time to targeted therapy, reduced mortality, early discharge, and decreased hospital costs.[114] Rapid diagnostics may assist in reducing diagnostic uncertainty. Procalcitonin (PCT) is a diagnostic test used to distinguish bacterial infections from other infectious and inflammatory conditions. There is growing evidence of the value of the infection biomarker PCT to improve diagnosis of bacterial infections, reduce initiation of antibiotic treatment in low risk presentations and guide judicious antibiotic prescribing for children with more severe infections.[115]

14.4 Implementing and leading antimicrobial stewardship in paediatric care

General requirements for implementing and sustaining an AMS program, as described in Chapters 2, 4 and 5 of the AMS Book, are also applicable to the paediatric setting. However, some modification for the paediatric setting is required.

14.4.1 A team approach to AMS

In healthcare settings that provide paediatric care, the AMS team should consist of clinical staff with paediatric-specific knowledge, experience and expertise.

In specialist paediatric hospitals the AMS team may be paediatric specific. In other generalist hospitals that provide care for children, a clinician with paediatric AMS expertise should be involved in the development of the hospital's AMS program and be a member of the AMS team to provide guidance on paediatric-specific issues. In the absence of a specialist paediatrician, advice should be sought from the AMS team from a specialist paediatric hospital. Alternatively, the hospital could enter into a collaborative arrangement with a statewide specialist paediatric network, if available, for advice and support in selecting and developing paediatric AMS strategies.

The NSW Agency for Clinical Innovation's Paediatric Network is an example of a collaborative arrangement. The Paediatric Network links local paediatric units within NSW to support quality care close to home for paediatric patients. The Network supports local paediatric units with activities and resources such as shared

clinical guidance documents and education and training opportunities.[116]

Other core members of the AMS team include infectious diseases physicians, clinical pharmacists, infectious diseases nurses, clinical nurse consultants, educators and clinical microbiologists with paediatric expertise. Team members could be included on AMS team rounds in paediatric wards, work with members of the AMS team to develop local paediatric AMS resources, provide paediatric-specific AMS education, and participate in audit and feedback activities. Paediatric specialist nurses and paediatric nurse practitioners can support programs, act as AMS champions (especially where there is no on-site paediatrician), and liaise with specialist paediatricians from established networks.

A survey of 14 tertiary paediatric hospitals located in Australia and New Zealand, identified only half of the surveyed hospitals had a dedicated AMS team or AMS team with a paediatric representative. Staff have identified a lack of dedicated staff with paediatric expertise, particularly in the areas of infectious diseases medicine and pharmacy as an important barrier to paediatric AMS implementation.[117]

The AMS team in general practice has different characteristics, and needs, to that of hospitals. Team members may include GPs, practice nurses, practice managers, as well as pharmacists and pathology providers. The AMS team is required to develop an AMS program that maintains the effectiveness of antimicrobials and decrease preventable infection associated with healthcare.[118] The team should consist of clinical staff with paediatric-specific knowledge and expertise and the program should address the effective use of antimicrobials in patients of all ages including neonates, infants, and children. Further information about implementing and leading antimicrobial stewardship in general practice is provided in Chapter 13 of the AMS Book.

14.4.2 Plans and strategies for AMS programs

All health service organisations are required to implement an AMS program to meet the requirements of the National Safety and Quality Health Service (NSQHS) Standards.[119] Health service organisations that provide paediatric care should ensure that the organisation's AMS program also addresses the unique requirements of children.

Prescribing guidance

Paediatric-specific prescribing guidelines (either national or locally developed) should be available to prescribers to guide empirical therapy, including duration of therapy and intravenous to oral switching in children. Health service organisations are required to provide prescribers access to appropriate guidelines for antimicrobial prescribing, this includes access to the national antibiotic guidelines, Therapeutic Guidelines: Antibiotic.[120] National paediatric-specific prescribing guidelines have also been developed by the ANZPID-ASAP.[121] Where national guidance is not available, guidelines may need to be sourced from a local tertiary paediatric service or locally developed. Local evidence-based guidelines should be developed in collaboration with experts and draw from quality evidence (where available). The guideline development process should also include input from a multidisciplinary team with paediatric expertise.

Health service organisations should develop an antimicrobial policy (see Chapter 2 of the AMS Book) that includes recommendations that are specific to paediatrics, such as:

- The need to document the patient's weight on prescriptions and medication charts, and regularly review this throughout the duration of care. The National Inpatient Medication Chart Paediatric promotes safe prescribing of medicines in hospitalised children (see resources).
- Guidance on conditions for which paediatric-specific advice should be sought, and when to seek the advice of paediatric infectious diseases experts.
- How to access paediatric infectious diseases or microbiology advice in the absence of on-site services.

As uptake of electronic healthcare records and electronic medication management increases over time, further opportunities will arise to embed prescribing guidance and principles of antimicrobial policy within prescribing, dispensing and medicines administration functions. See Chapter 4 of the AMS Book for further detail on information technology to support antimicrobial stewardship.

Adherence to evidence-based treatment

Facilitating or encouraging adherence to evidence-based treatment is a core component of paediatric AMS programs. The two main strategies used are audit of antibiotic use with feedback (persuasive strategy) and antimicrobial pre-authorisation prior to use (restrictive strategy).[122]

In the first strategy prescriptions provided for antimicrobials are reviewed in the context of the patient's medical record, compared with prescribing guidelines and feedback is provided to the prescriber or clinical unit. Whilst this strategy is largely used in general practice and other non-admitted settings, persuasive AMS strategies

have also been demonstrated to be effective in the hospital setting.

'Handshake Stewardship' created and implemented in a United States children's hospital involves shared review of all prescribed antimicrobials by a pharmacist and a physician, and in-person feedback to prescribers at daily rounds to support appropriate use of antimicrobials. This method has demonstrated a reduction in overall antimicrobial use, reductions in broad spectrum antimicrobial use in the first year of implementation,[123] and a sustained reduction in antimicrobial use over five years.[124] The approach also demonstrated high rates of acceptance amongst medical staff.[125]

The second strategy is an antimicrobial restriction system that involves the review and approval of antimicrobial prescriptions prior to commencing treatment. These systems are often used in hospitals. Electronic decision support and restricted prescribing systems are effective in reducing total and broad-spectrum antimicrobial use and reducing antimicrobial costs.[126,127,128]

There is also some evidence of reduced healthcare-associated infection rates associated with the implementation of electronic AMS support systems.[129,130] The context of the facility providing care to the paediatric population is an important consideration as to what is feasible and effective.

A Cochrane review found that restrictive strategies have a more immediate effect and persuasive strategies have a more sustainable effect, such that six months after implementation persuasive and restrictive strategies are equally effective in reducing inappropriate prescribing of antimicrobials.[131] A possible explanation for the reduced effect of restrictive practices over time is the development of workarounds to avoid access restrictions.

A study of after-hours access to antimicrobials in an Australian paediatric hospital with an electronic antimicrobial restriction system identified over two-thirds of the antimicrobials accessed after-hours were not AMS adherent, and half of the restricted antimicrobials accessed were not approved. The most common restricted antimicrobials accessed after hours were ceftriaxone, azithromycin, and clindamycin [132]

Interventions to improve adherence to evidence-based treatment guidelines consist of both persuasive strategies that facilitate appropriate treatment selection (including treatment without antimicrobial use) and restrictive measures that limit the opportunity to select inappropriate antimicrobial treatment. A combination of both these options are more effective than persuasive or restrictive strategies use alone.[133]

14.4.3 Targeted approaches

AMS programs in the hospital setting have largely targeted specific antimicrobials using pre-prescription approval processes or post-prescription audit and feedback. As AMS programs evolve, and with increasing focus on AMS in primary care, there has been a growing interest in targeting specific infective diseases.[134]

Specific strategies should be developed for targeted approaches to AMS that are more likely to be effective in children. Priority areas for targeting could be those where high rates of inappropriate prescribing in children have been identified (such as surgical prophylaxis in the hospital setting and otitis media in primary care).

Antimicrobial stewardship programs may also include targeting of sub-populations in which a small percentage of children receive a disproportionally high percentage of antimicrobials. Examples may include children with a diagnosis of cystic fibrosis, neonates, children with malignancy and children presenting to emergency departments. An Australian AMS program that targets paediatric patients receiving outpatient parenteral antimicrobial therapy as part of a hospital-in-the-home program, has achieved: high rates of appropriate antimicrobial prescribing; reductions in inappropriately long durations of antimicrobial therapy; and reductions in the median number of days patients received broad-spectrum antimicrobial treatment, whilst retaining low rates of infection and antimicrobial-associated complications.[135]

When developing a targeted strategy, it is important to consider what type of measures to use, for example process, outcome or balancing measures. It is important to choose measures that are relevant and achievable. Measuring AMS performance is discussed further in section 14.5.

14.4.4 Education

Educational programs that include the unique needs of children are important for the successful implementation of AMS in the paediatric setting. Education of healthcare providers on appropriate antibiotic prescribing has been shown to enhance other AMS interventions.[136]

Education of staff (medical, pharmacy, nursing, pathology) on orientation and repeatedly as part of ongoing professional development is required. Where possible, inter-professional learning opportunities should be provided. Key education program components include:

- Common paediatric infections
- Local resistance patterns
- Different microbiology of infections between children and adults

- Developmental and physiological aspects relating to prescribing antimicrobials in paediatric patients
- The pharmacokinetics and pharmacodynamics of antimicrobials in neonates and children
- Therapeutic drug monitoring in paediatric patients
- Duration of therapy
- Principles of intravenous-to-oral switch
- Managing diagnostic uncertainty
- Discontinuing therapy.[137,138]

Passive educational techniques such as didactic presentations are modestly effective for increasing health professional knowledge. Interactive or dynamic techniques such as case-based learning, interactive small group sessions, e-learning, retrospective audit with feedback and academic detailing are more effective in influencing prescribing behaviour.[139] A lack of education was identified as the most common perceived barrier to successful paediatric AMS in hospitals in Australasia and in other high-income countries.[140,141]

Education interventions aimed at parents and carers can assist in addressing misperceptions about antibiotic use in childhood infections, and reduce parental expectation of antimicrobial treatment for children. Most parents want to be more involved in shared decision making about antimicrobial treatment.[142] Whilst education materials such posters, brochures and informational videos can be effective, evidence indicates communication between prescribers and parents or carers is the most effective education intervention. In addition, interventions that target both prescribers and parents or carers are more effective than those that only target prescribers or parents/carers alone.[143]

Parents and carers also require education on the correct administration of antimicrobials to their children. Children as young as four years can be taught to swallow tablets, and parents and families should be assisted in teaching the child how to do this. A number of organisations have produced resources to support education of parents, families and staff in administering oral medicines to children (see resources).

14.5 Measuring AMS performance

One of the key differences between AMS programs for children and AMS programs for adults is outcome measurement. Approaches to measuring the performance of AMS programs are discussed in Chapter 5 of the AMS Book. The targeted use of audit and feedback is an important component of an AMS strategy.

14.5.1 Rate of antimicrobial use

The standard measurement of rate of antimicrobial use in adults is defined daily dose (DDD) per 1,000 occupied bed days. Because dosing for children is largely based on body weight or body surface area, the DDD measurement of antimicrobial consumption is not appropriate. Modification of the DDD method to include standardised weight bands for different paediatric age groups has been proposed as a strategy to enable comparison between adults and children benchmarking between hospitals.[144,

Most Australian paediatric hospitals monitor use by unit of use (for example, number of vials) or cost or both.[145] These approaches do not provide an accurate measure of consumption, but they do have some utility in monitoring trends. This difference in measurement approach also precludes comparison of paediatric and adult rates of antimicrobial use. Variation in measures can also prevent benchmarking between hospitals providing paediatric care.

In North America the most commonly used measure for adults and children is days of therapy (DOT).[146,147] Days of therapy is measured as days of therapy over a total number of days such as per 1,000 patient days. To improve the usefulness of DOT, a length of therapy (LOT) measure can also be used. The DOT/LOT ratio provides a measure of the mean number of antibiotics received per person per day.[148] Use of DOT in Australia is limited, as data collation is laborious. Increased uptake of electronic medicines management systems in Australian paediatric hospitals in the future should facilitate the collection of data required to monitor paediatric antimicrobial usage using DOT.[149]

14.5.2 Appropriateness of use

A limitation of antimicrobial usage metrics is that they cannot account for the appropriateness of antimicrobial use. The overuse of broad-spectrum antimicrobials could result in a reduced usage rate compared with the appropriate use of a multidrug narrow-spectrum targeted therapy. Monitoring patterns of antimicrobial prescribing is important in order to understand current practice, evaluate

AMS program performance and identify priority areas for improvement.

Point prevalence surveys can also be used to measure the appropriateness of paediatric antimicrobial prescribing. Many of the measures discussed in Chapter 5 also apply to paediatric settings or can be adapted for paediatric use. For example, proportion of patients with documented indication, duration of therapy, surgical prophylaxis beyond 24 hours, allergy mismatch, compliance with guidelines, and appropriateness of use. More specific paediatric measures could include documentation of weight with regular review in very young patients, and specifying the dose calculation on the prescription. Issues of poor or incomplete documentation can be a limitation to assessing appropriateness from a point prevalence survey in paediatric populations. For example, it will not be possible to determine appropriateness of dose if an accurate weight has not been obtained or documented.

Audit teams in general hospitals should include a paediatrician when assessing appropriateness of prescribing in children.

Other measures to determine appropriateness of antimicrobial use in children may include: time to optimal therapy for patients with an invasive infection; percent of peripherally inserted central catheters potentially avoided; and time to conversion from intravenous to oral administration of antibiotics, where intravenous to oral switch is indicated. These measures are also helpful in identifying areas to target AMS efforts.[150]

14.5.3 Outcome measures

When measuring AMS performance in paediatric care it is important to choose outcome measures that are relevant and achievable in children. AMS outcome measures that are often used or recommended in adult settings are not necessarily suitable for use in paediatrics. For example, it is common to measure rates of *Clostridioides (Clostridium) difficile* infection (CDI) in the adult setting. However, this is a poor marker in paediatric settings because of the high carriage rate of this organism in children under two years of age.[151]

Changes in the prevalence of resistant organisms has been described as a better measure, although baseline rates of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci and extended-spectrum beta-lactamase-producing organisms are often low in children. Lack of change may not reflect lack of improvement in prescribing; other factors, such as community prevalence of resistance can influence outcomes. There may be more value in communicating changes in other outcomes measures such as length of stay or readmission rates. For example, a reduced duration of therapy for patients with community-acquired pneumonia (five days) does not increase hospital readmissions.[152]

Antimicrobial stewardship in paediatric sepsis

Sepsis results from a dysregulated host response to infection leading to organ dysfunction. Major improvements in patient outcomes can be achieved by institutional pathways that improve the timely recognition and treatment of sepsis in adults and children. However, there is concern regarding the potential adverse impact of sepsis pathways on appropriate antimicrobial use.

In 2017, the Queensland Statewide Sepsis Collaborative incorporated expertise from AMS pharmacists and infectious disease specialists when designing and implementing a new statewide sepsis pathway.[153] The evaluation of the Collaborative includes AMS at the core of a range of balancing measures. Given a limited evidence base upon which to evaluate the impact of the pathway on AMS, a range of internationally recognised AMS interventions (such as antimicrobial review, and intravenous to oral switch) and metrics (of appropriateness and consumption) were adapted for use in children evaluated on the sepsis pathway.

These interventions are now being incorporated into a digital sepsis pathway, which will incorporate AMS metrics into performance dashboards for clinician feedback and benchmarking.

Resources

- Australasian Neonatal Medicines Formulary: https://www.anmfonline.org/
- Australia and New Zealand Paediatric Infectious Diseases Group - Australasian Stewardship of Antimicrobials in Paediatrics - antimicrobial stewardship resources including antibiotic duration and IV-oral switch: https://www.asid.net.au/groups/antimicrobial-stewardship
- Australian Government. Australia's National Antimicrobial Resistance Strategy - 2020 and beyond
- https://www.amr.gov.au/resources/australias-national-antimicrobial-resistance-strategy-2020-and-beyond
- Children's Healthcare Australasia: https://children.wcha.asn.au/
- Children's Health Queensland Hospital and Health Service: https://www.childrens.health.qld.gov.au/
- Children's Health Queensland Hospital and Health Service - Antimicrobial Treatment: Early Intravenous to Oral Switch - Paediatric Guideline: https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/ams/DUG-Early-Intra.pdf
- Clinical Excellence Commission - parent and carer information about antibiotics and IV-to-oral switch: http://www.cec.health.nsw.gov.au/keep-patients-safe/medication-safety-and-quality/antimicrobial-stewardship/information-for-patients
- Clinical Excellence Commission - supporting intravenous to oral switch: cec.health.nsw.gov.au/__data/assets/pdf_file/0004/383089/Using-a-QI-approach-to-support-timely-oral-antibiotic-switch-Evette-Buono.pdf
- Don't Forget the Bubbles - paediatric information for clinicians: https://dontforgetthebubbles.com/the-dftb-team/
- IDStewardship - educational resources to teach children about antimicrobial stewardship: https://www.idstewardship.com/antimicrobial-stewardship-kids-tools-teach-children-hygiene-microbes-science/
- Kaiser Permanente. Neonatal early-onset sepsis calculator: https://neonatalsepsiscalculator.kaiserpermanente.org/
- Monash Children's Hospital: https://monashchildrenshospital.org/
- NPS antibiotic resistance resources: https://www.nps.org.au/professionals/reducing-antibiotic-resistance
- NPS MedicineWise Fact Sheet - What every parent should know about coughs, colds, earaches and sore throats: https://www.nps.org.au/consumers/what-every-parent-should-know-about-coughs-colds-earaches-and-sore-throats
- National Inpatient Medication Chart Paediatric - promotes safe prescribing in hospitalised children: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-inpatient-medication-chart-nimc-paediatric
- NSW Health - Guidelines for Networking Paediatric Services: https://www.health.nsw.gov.au/kidsfamilies/paediatric/Publications/guidelines-paediatric-networking.pdf
- Pediatric Infectious Diseases Society (American Academy of Pediatrics) – Pediatric Antibiotic Stewardship Program Toolkit: https://www.pids.org/asp-toolkit.html
- Paediatric Improvement Collaborative Clinical Practice Guidelines: https://www.rch.org.au/clinicalguide/
- Pediatric Infectious Diseases Society: https://www.pids.org/
- Perth Children's Hospital: https://pch.health.wa.gov.au/
- Perth Children's Hospital - Children's Antimicrobial Management Program (ChAMP): https://pch.health.wa.gov.au/For-health-professionals/Childrens-Antimicrobial-Management-Program
- Preventing and Controlling Healthcare-Associated Infection Standard: https://www.safetyandquality.gov.au/standards/nsqhs-standards/preventing-and-controlling-healthcare-associated-infection-standard

- RACGP Standards for General Practices. 5th Edition: https://www.racgp.org.au/running-a-practice/practice-standards/standards-5th-edition
- SA Health – Paediatric Clinical Practice Guidelines: https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+programs+and+practice+guidelines/children+and+youth/paediatric+clinical+practice+guidelines
- SA Health – Neonatal Medication Guidelines: https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+programs+and+practice+guidelines/womens+and+babies+health/neonatal+medication+guidelines/neonatal+medication+guidelines
- Sharing Antimicrobial Reports for Pediatric Stewardship (SHARPS) http://pediatrics.wustl.edu/sharps
- Telethon Kids Institute: https://www.telethonkids.org.au/
- Telethon Kids Institute - Infectious Diseases Research: https://infectiousdiseases.telethonkids.org.au/about-the-wesfarmers-centre/
- Therapeutic Guidelines - Antibiotic: www.tg.org.au
- The Royal Children's Hospital Melbourne - teaching children how to swallow tablets and capsules: https://www.rch.org.au/pharmacy/medicinesinformation/Teaching_children_how_to_swallow_tablets_and_capsules/
- The Sydney Children's Hospitals Network: https://www.schn.health.nsw.gov.au/#

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