AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

3 Strategies and tools for antimicrobial stewardship

Antimicrobial Stewardship in Australian Health Care

2018

Please note that revised antimicrobial stewardship actions are included in the Preventing and Controlling Infections Standard, which was released in May 2021. This version of the Standard supersedes the 2017 Preventing and Controlling Healthcare-Associated Infection Standard. The AMS Book will be updated to incorporate reference to the 2021 Standard.

Chapter contents

Acronyms and abbreviations

Abbreviation	Definition
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
Commission	Australian Commission on Safety and Quality in Health Care
DTC	drug and therapeutics committee
ICU	intensive care unit
ID	infectious diseases
LHD	Local Health District
LHN	Local Hospital Network
NAPS	National Antimicrobial Prescribing Survey
NSQHS Standards	National Safety and Quality Health Service Standards
PBS	Pharmaceutical Benefits Scheme
PCR	polymerase chain reaction
POCI	point-of-care intervention
TGA	Therapeutic Goods Administration

Key points

- The use of evidence-based guidelines has been shown to be effective in improving prescribing practice.
- Involving clinicians in the development and implementation of guidelines and tailoring implementation strategies to suit the local context can increase guideline uptake.
- Care bundles can be a useful way to package a group of simple evidence-based steps that can help promote evidence-based care.
- A formulary for antimicrobials, with restrictions on use, and an approval system for antimicrobials are effective in changing prescribing practices.
- Timely review of antimicrobial prescriptions, ideally by an antimicrobial stewardship (AMS) team comprising an infectious diseases (ID) physician and clinical pharmacist, is a useful strategy to optimise antimicrobial use.
- Point-of-care interventions, based on reviews or data, can improve patient management and patient outcomes.
- It is important that hospitals have access to ID physicians or AMS pharmacists to provide AMS support when needed. Strategies to include expert advice in AMS programs may include networking and using telehealth.

3.1 Introduction

This chapter discusses four of the essential strategies for an antimicrobial stewardship (AMS) program outlined in Chapter 2: 'Establishing and sustaining an antimicrobial stewardship program':

- Implementing clinical guidelines consistent with *Therapeutic Guidelines: Antibiotic*[1] that take into account local microbiology and antimicrobial susceptibility patterns
- Implementing formulary restriction and approval systems that include restricting broad-spectrum and later-generation antimicrobials to patients in whom their use is clinically justified
- Reviewing antimicrobial prescribing, with intervention and direct feedback to the prescriber
- Implementing point-of-care interventions (POCIs), including directed therapy, intravenous-to-oral switching and dose optimisation.

The chapter provides information about practical methods to bring the principles of AMS to the point of prescribing. These represent a mix of strategies – restrictive, persuasive and enablement – that influence prescribing behaviour[2]:

- Restrictive strategies require prescribers to adhere to a set of rules (for example, as decided by a formulary), and prevent prescribers from gaining access to certain antimicrobial agents unless criteria are met and formal approval is granted. This may occur before the prescription is written or at a decided time after the prescription has been filled as part of the post-prescription review
- Persuasive strategies aim to improve prescriber knowledge, and change attitudes and beliefs about prescribing through review and feedback
- Enablement strategies make it easier for prescribers to gain access to the information they need to prescribe appropriately.

Persuasive strategies are more widely practised and more readily accepted by clinicians, and provide greater opportunity to educate prescribers than restrictive strategies.[3] Several leading guidelines on AMS endorse the use of a mix of restrictive, persuasive and enablement strategies to enable comprehensive stewardship in hospital settings. A Cochrane systematic review in 2013 suggested that restrictive strategies have the greatest immediate effect on prescribing behaviour, whereas persuasive strategies may have a slower but more sustained effect.[4] A later review reported that enablement strategies – such as prospective review, audit and feedback, academic detailing, and electronic clinical decision support – increased the effect of other AMS interventions, including those with restrictive elements.[2]

Table 3.1 summarises these strategies, the guidance to support them and the practical tools that enable their implementation. Each of these is discussed in more detail in subsequent sections of this chapter.

Issues that are especially relevant for certain settings – rural and remote hospitals, private hospitals and aged care – are tagged as R, P and AC, respectively, throughout the text.

Table 3.1: Strategies, rules and tools for antimicrobial stewardship programs

Strategy	Rules	Tools
Implementing clinical guidelines consistent with *Therapeutic Guidelines: Antibiotic* that take into account local microbiology and antimicrobial susceptibility patterns	• Prescribers prescribe according to current evidence-based guidelines • Prescribers are encouraged to follow care bundles	• Easy access to the current versions of guidelines, including *Therapeutic Guidelines: Antibiotic* • Endorsement of evidence-based guidelines by clinical champions • Barriers to guideline uptake analysed and minimised • Leadership support for new guidelines • Awareness raising and communication activities about guidelines and care bundles • Monitoring and evaluation of AMS over time
Implementing formulary restriction and approval systems that include restricting broad-spectrum and later-generation antimicrobials to patients in whom their use is clinically justified	• Prescribers prescribe according to the formulary • Approval is required for all highly restricted antimicrobials before use; an approval system must be used to register the indication for use of all restricted antimicrobials, and further approval sought if use exceeds three days	• Posters and web pages that make the formulary rules explicit to all prescribers • A formalised approval system should be in place (fax, phone or electronic)
Reviewing antimicrobial prescribing, with intervention and direct feedback to the prescriber	• AMS teams are expected to review all patients receiving highly restricted antimicrobials, or courses of restricted antimicrobials for more than three days	• AMS team to provide regular individualised prescription review • Electronic tools may help prompt review and triage patients
Implementing POCIs (including directed therapy, intravenous-to-oral switching and dose optimisation)	• AMS teams, microbiology services initiate/advise on specific interventions to optimise therapy	• AMS team provides advice on de-escalation, empirical to directed therapy, duration, cessation of therapy and management • Some standard POCIs may be able to be implemented as part of pathways or care bundles (e.g. intravenous-to-oral switching)

AMS = antimicrobial stewardship; POCI = point-of-care intervention

3.2 Prescribing guidelines

Appropriate antimicrobial use happens when antimicrobials are prescribed according to evidence-based guidelines, with choice, dose and duration selected to optimise clinical outcomes and minimise adverse consequences.[5] Prescribing guidelines are an essential requirement for AMS programs. They describe evidence-based best practice and provide a standard for prescribing behaviour for other clinical situations that are not explicitly described in the guidelines.

The involvement of clinicians in the development and implementation of evidence-based practice guidelines can improve antimicrobial prescribing behaviour and thereby influence patient outcomes. The use of practice guidelines has been demonstrated to be effective. For example:

- Implementation of a multidisciplinary practice guideline in a surgical intensive care unit led to a 77% reduction in antimicrobial use, a 30% reduction in overall cost of care, decreased mortality and shorter length of stay[6]
- Implementation of guidelines for managing patients with pneumonia was associated with earlier antimicrobial therapy, which in turn was associated with faster clinical stability, lower inpatient mortality at 48 hours and lower 30-day mortality when care was compliant with recommendations[7]
- The use of guidelines for managing paediatric surgical conditions such as appendicitis was associated with shorter durations of antimicrobial therapy, reduced costs and shorter lengths of hospital stay, without compromising clinical outcomes.[8]

3.2.1 National guidelines

The National Safety and Quality Health Service (NSQHS) Standards require all hospitals and health service organisations to provide ready access to current, evidence-based guidelines for prescribers.[9] In Australia, *Therapeutic Guidelines: Antibiotic*[1] is recognised as the national best-practice guide for antimicrobial prescribing. These guidelines are developed using a rigorous process of consultation with experts from different disciplines, and states and territories. They cover prescribing in the hospital and the community, for adult and paediatric patients, and in urban and rural settings.

3.2.2 Local guidelines

Therapeutic Guidelines: Antibiotic[1] provides treatment recommendations for most infections seen in hospital and community settings. If local prescribing guidelines are necessary, they should reflect the nationally agreed practice described in *Therapeutic Guidelines: Antibiotic*. This also applies to antimicrobial treatment recommendations in clinical guidelines, local care pathways and algorithms. If local guidelines are already in place, they should be reviewed against *Therapeutic Guidelines: Antibiotic*. Where differences are warranted – for example, in response to local antimicrobial resistance (AMR) patterns or an outbreak of a new resistant bacterial strain – an evidence-based rationale should be provided for any variation in practice.

For conditions not covered by *Therapeutic Guidelines: Antibiotic*[1], organisations should refer to the best available evidence to develop guidelines appropriate to the local context. Local guideline development should involve expert guidance from infectious diseases (ID) physicians, microbiologists and pharmacists, and the guidelines should be reviewed and endorsed by the AMS committee.

Existing prescribing guidelines relevant to rural and remote practice, such as the Centre for Remote Health's *CARPA Standard Treatment Manual*[10], can be customised to suit the local conditions and may be useful for nurse-run facilities.

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Health service organisations that do not have on-site access to ID physicians should have antimicrobial prescribing guidelines that are tailored to the local situation, but based on the principles stated above. In the public sector, the Local Hospital Network (LHN) or Local Health District (LHD) should be consulted to ensure that local guidelines are consistent with LHN/LHD policy. The guidelines should describe situations that require discussion with an ID physician or clinical microbiologist, or escalation to larger hospitals, and the relevant referral processes.

R P AC

Local guidelines should be regularly reviewed and updated in consultation with key clinicians to ensure that evidence-based best practice is upheld. An important part of the review process is ensuring that only the latest versions of guidelines are available for use. The frequency of review may be routinely over a two-year cycle, or sooner if there have been major changes in protocols or information about emergent antimicrobial resistance. An update at least once per year has been recommended if changes are in response to local pathogen variations.[11]

3.2.3 Promoting guideline uptake

Effort is required to promote prescribing according to guidelines and to ensure appropriate care – this is the key to translating evidence into practice. The existence of a guideline is usually not enough to achieve change, and adherence varies among the workforce, clinical areas and organisations. The 2015 National Antimicrobial Prescribing Survey (NAPS) found that, overall, 23.3% of antimicrobial prescriptions in hospitals were noncompliant with guidelines.[12] Prescriptions for surgical prophylaxis and bronchitis had the highest rate of noncompliance – 41% of prescriptions for these indications did not comply with guidelines. In the community, data from the NPS MedicineInsight program for 2015 showed that a large proportion of the antimicrobials prescribed were not consistent with the first recommendation in Australian guidelines.[13] Concordance with guidelines varied from 27% for sinusitis to 67% for pneumonia.[13]

Guideline development needs to be accompanied by a carefully planned implementation process that includes a program of audit and feedback. To inform implementation planning and promote uptake, it is essential to understand the existing culture and prescribing practices, the drivers affecting them and any barriers to change (see Section 2.5.1 in Chapter 2: 'Establishing and sustaining an antimicrobial stewardship program'). Each of these needs to be considered as part of a local guideline implementation plan.

Guidelines should be considered and endorsed by clinical champions; absence of support can adversely affect effective implementation. During the development phase, concerns raised should be identified and addressed. In Principal Referral Hospitals, where senior medical clinicians influence trainees' prescribing, it is especially important to engage these senior clinicians in the development or promotion of local guidelines. A study in the Netherlands reported increased compliance with guidelines (from 67% to 86%) when clinicians were widely consulted in the revision of guidelines for antimicrobial therapy; active dissemination was also important.[14]

Importantly, the workflow of the workforce involved also needs to be understood so that opportunities to guide change are identified. The AMS team may need to visit relevant hospital departments and attend unit meetings to discuss the guidelines, to promote awareness and to ensure that they are appropriate for the local context. In general, the aim is to make it easier for the workforce to do the right thing. Advice should be readily available, and prompts should be visible during a prescriber's everyday work (see Tools and resources to support guideline implementation).

Ideally, prescribing guidelines should be implemented within a quality improvement framework. The guidelines serve as the starting point for a quality improvement cycle that leads to ongoing refinement of the guidelines, continual guideline implementation, and ongoing improvement in patient outcomes. The process requires ongoing data collection, analysis and feedback to clinicians to ensure awareness of improvements and ongoing compliance with the guidelines. Evaluating the use of prescribing guidelines can help to identify whether implementation strategies are effective and whether alternative approaches are needed, and enables unintended consequences to be identified and addressed (see Section 6.8.3 in Chapter 6: 'Measuring performance and evaluating antimicrobial stewardship programs').

3.2.4 Tools and resources to support guideline implementation

Resources such as posters, checklists, clinical pathways, visual prompts and aids, that are available at the point of care and specific to the local context, can promote guideline uptake. Posters can raise awareness of AMR, and influence attitudes of both prescribers and their patients towards careful antimicrobial prescribing.[15] Other tools – such as laminated cards, booklets and phone apps – may simplify guidelines and make recommendations easily available for prescribers.[16] Links to such tools are provided in Resources.

Checklists, algorithms and clinical pathways have been used by clinicians in hospital and community settings to help to standardise care and promote optimal prescribing.[17] They help promote guideline-concordant practice in everyday care. They can be especially useful in a busy environment (such as those with a high volume of elective procedures that follow fairly predictable clinical courses), because the pathway can prompt decisions in a stepwise, structured fashion. For example, in one hospital, a clinical pathway to manage perforated appendicitis in paediatric patients helped to standardise antimicrobial prescribing, resulting in decreased use of postoperative antimicrobials without an increase in adverse outcomes.[18] Similarly, clinical pathways for the management of pneumonia have been used to promote appropriate empirical antimicrobial choices and investigations, prompt routine daily

consideration of de-escalation and intravenous-to-oral switching, and ensure the appropriate duration of antimicrobials.[19]

Public Health England's Start Smart – Then Focus toolkit for antimicrobial treatment and surgical prophylaxis is one algorithm that can be used as a reminder of the principles of good antimicrobial prescribing.[20] Visual prompts on medication charts, such as brightly coloured stickers, have been used with some success in settings such as intensive care units (ICUs), where multiple carers can be involved in clinical decision-making over a few days.[21] They help to make intentions explicit, especially by clearly documenting the indication for starting the antimicrobial, and the intended duration or a planned review date to prompt consideration of cessation when microbiological results are available. They can be especially useful in communicating antimicrobial plans on discharge of patients from the ICU to the ward.

Electronic tools can also promote guideline-concordant prescribing by incorporating alerts, sidebars with icons to enable ready access to information, or more structured decision support algorithms (see Chapter 4: 'Information technology to support antimicrobial stewardship'). Smartphone apps can also be used to access guidelines and prescribing information.

3.2.5 Education and feedback

Guideline implementation and adherence can be facilitated through education (see Chapter 5: 'Antimicrobial stewardship education for clinicians'). Making prescribers aware of local and national guidelines and resources is important in all healthcare settings.[22] Education about the available resources and antimicrobial prescribing should be an ongoing part of continuing education and professional development for all clinicians. Guidelines can form the basis for educating prescribers and other clinicians on accepted practice for antimicrobial prescribing in the organisation. This includes the importance of documenting in the patient's healthcare record the indication for the prescribing decision and, where the prescriber varies from guideline-concordant practice, the rationale for the decision.

General education can be coupled with feedback and local information. Topics addressed should include local antimicrobial prescribing patterns, local AMR patterns for common pathogens, local patterns of infection and, where possible, patient outcomes. Workforce rotations are common in many settings, so effort should be made to repeat communication regularly. Review, feedback and reflection are critical components of any efforts to improve practice (see Post-prescription reviews).

3.2.6 Antimicrobial stewardship care bundles

Care bundles are increasingly used in healthcare quality improvement as a structured way of improving the processes of care and patient outcomes. A bundle may comprise a set of three to five evidence-based practices that, when performed collectively and reliably, have been proven to improve patient outcomes.[23]

Cooke et al.proposed the use of care bundles to improve appropriate antimicrobial prescribing in acute care and surgical prophylaxis (Box 3.1).[24,25] The bundles were broken down into individual measurable practices, and compliance with each element was monitored and used as a target for improving practice.[25] This approach requires routine documentation of the reason for starting the antimicrobial, along with a stop date or review date (see Quality Statement 6 of the Antimicrobial Stewardship Clinical Care Standard[26]).

The two care bundles (treatment and surgical prophylaxis) can be implemented separately or in combination, and AMS teams can adapt the focus of the proposed bundles to their local context. These bundles may be of particular value for smaller services where AMS resources are accessed remotely. Clinical teams could take ownership of the bundle and incorporate it into the existing quality improvement framework.

3.3 Formularies and approval systems

In its simplest form, a formulary is a list of medicines, including antimicrobial agents, that has been approved by an authority (within an organisation or network, or nationally) for use. Formulary systems establish rules governing medicine use.

3.3.1 National formulary

The Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefits Scheme (PBS) form the regulatory system that produces the formulary of

Box 3.1: Antimicrobial care bundles

Treatment bundle

At initiation of treatment, the prescriber:

- Provides a clinical rationale for antimicrobial initiation
- Sends the appropriate specimens to a diagnostic microbiology laboratory (according to local policy)
- Selects the antimicrobial according to local policy and having considered the patient risk group (including drug allergy profile)
- Considers removal of any foreign body, drainage of pus or other surgical intervention, as appropriate.

During continuation of treatment, there is:

- Daily consideration of de-escalation, intravenous-to-oral switching or stopping antimicrobials (based on the clinical picture and laboratory results)
- Monitoring of antimicrobial levels, as required by local policy.

Surgical prophylaxis bundle

- Select antimicrobials that match local guidelines (having considered patient allergies)
- Time the first dose to be within 60 minutes pre-incision
- Stop antimicrobial administration within 24 hours of the preoperative dose or the first dose after post-prescription review.

medicines for Australia. This is done by requiring medicines to be registered before they are allowed onto the market (TGA) and determining which medicines will be subsidised (PBS).

The PBS provides the mechanism whereby access to subsidised antimicrobials can be restricted to approved indications. This acts as a financial disincentive to use those antimicrobials outside the approved indications. A phone-based approval system with documentation of the indication is used, and audits can be conducted to check compliance. Phone-based authorisation and documentation of the indication are also required for antimicrobials that are prescribed beyond the standard durations (for example, for several weeks), which helps to minimise prescriptions for extended durations of therapy. This system has been thought to be responsible for the relatively low consumption of ciprofloxacin in Australia and consequently the low incidence of fluoroquinolone resistance among community-acquired bacterial pathogens in Australia compared with other countries.[27]

3.3.2 State and territory formularies

Several states in Australia, including Queensland, South Australia, Tasmania and Western Australia, have developed statewide antimicrobial formularies. This promotes consistency of prescribing in hospitals, and means that clinicians have clear, common expectations about the availability of broad-spectrum antimicrobials.

3.3.3 Hospital formularies

A formulary that includes a list of restricted antimicrobials is an essential component of a hospital AMS program. The antimicrobial formulary should be appropriate to the needs of the hospital and should consider the range of antimicrobials required, the clinical orientation of the hospital and local AMR. It should be updated periodically, and compliance should be audited.

Responsibility for creating and maintaining a formulary usually lies with a hospital's drug and therapeutics committee (DTC). The DTC evaluates the evidence regarding the efficacy, safety and cost of new agents before deciding whether to endorse their use in the hospital and list them on the formulary. The DTC may have an antimicrobial subcommittee or may use the AMS team to evaluate requests for new antimicrobial agents or new indications for use, and to make recommendations for formulary listing.

It is important that antimicrobial formulary decisions are informed by local microbiological data. For example, if resistance to one antimicrobial class has been emerging locally, the DTC may respond

by directing prescribing towards alternative agents or making alternatives available. This may require a change in criteria for approval to use the alternative agents. It is therefore important for microbiologists and ID physicians to provide continuous expert advice to DTCs (through membership of the committee or liaison with the AMS team). Hospitals participating in national passive AMR surveillance, NAPS and the National Antimicrobial Utilisation Surveillance Program will have access to data to inform this decision-making.

In many circumstances, medicines on the formulary have conditions attached to their approval – for example, use may be approved only for a particular unit, for patients with a particular condition, or when other options are contraindicated because of intolerance or demonstrated failure. In the case of antimicrobials, certain medicines may be restricted for use only with approval by nominated expert prescribers, such as ID physicians or microbiologists. When the use of an agent is confined to particular situations, this may guide the way in which stock is made available in the hospital. For example, the hospital might store only selected antimicrobials in theatre and may withdraw antimicrobials from the operating suites if their use is not approved for surgical prophylaxis. Highly restricted antimicrobials might be removed from ward imprest cupboards so that pharmacists are involved in their dispensing, to improve oversight and ensure that their use meets formulary conditions.

It has been well demonstrated that restrictive formularies can direct prescribing patterns in hospitals. Many studies have described changes in formulary restrictions that led to changes in prescribing patterns and, in some cases, changes in local rates of antimicrobial-resistant pathogens.[28-39] However, studies involving multiple centres over longer periods are needed.

Although a restricted antimicrobial list is often used in public hospitals, restrictive formularies have not been common in the private sector.[40] However, the NSQHS Standards include the requirement for AMS programs to have a restrictive formulary and approval system. Therefore, private hospitals and small public hospitals staffed by visiting medical officers will need to consider how best to establish prescribing restrictions, given their resources and prescribing workflow. This may be achieved by using an off-site expert who can provide approval by telephone or an electronic decision support system.

Rural and remote hospitals may be able to access formularies developed at the LHN/LHD level, or at the state or territory level. Restricting access to some antimicrobials[40] may be the most efficient and direct method of monitoring and limiting antimicrobial use in hospitals with limited resources (see the NSW Clinical Excellence Commission's *Antimicrobial Restrictions in Small to Medium-Sized Hospitals fact sheet*). Interested local physicians or pharmacists with access to an ID physician or clinical microbiologist can be used as stewards of the approval system. Smaller hospitals without on-site physicians or pharmacists may use other models.

3.3.4 Antimicrobial approval systems

Approval to use an antimicrobial that the DTC has labelled 'restricted' may occur before the medicine is prescribed (pre-prescription), at a certain time after therapy has started (post-prescription) or at both these times. A 2017 Cochrane review of AMS strategies[2] noted that several studies suggest that antimicrobial approval systems can reduce the volume of broad-spectrum antimicrobials prescribed, thereby reducing medicine expenditure.[41-44] A reduction in adverse drug reactions for patients has also been described.[45] Effects on patient outcomes are less well described, although reduced lengths of hospital stay have been reported after an antimicrobial approval system was deployed and after improvements were made in the appropriateness of empirical antimicrobial therapy.

Many hospitals use a graded approach to classify restrictions, sometimes known as a traffic-light approach, which categorises antimicrobials as unrestricted (green), restricted (orange) or highly restricted (red) (Table 3.2).

Internationally, the World Health Organization Essential Medicines Group is taking action regarding antimicrobial restrictions.[46] The AWARE listing divides antimicrobials into three groups:

- ACCESS – those that should be accessible in all countries to treat common infections
- WATCH – medicines that should be conserved for situations in which use is clearly justifiable, and not freely available to all
- RESTRICT – last-line agents that should be reserved for use only when narrower-spectrum agents will not be effective, and generally only used with some degree of expert supervision.

Pre-prescription approval processes should clearly document the prescriber, the patient, the medicine and the indication for use. This allows a nominated expert or the AMS team to triage such patients for post-prescription review at 48–72 hours.

Table 3.2: Categories of antimicrobial restrictions

Antimicrobial category	Details and examples
Unrestricted	• Can be prescribed without an approval • Examples include benzylpenicillin and doxycycline
Restricted or 'protected'	• Require an approval within a nominated time of the medicine being prescribed (e.g. within 24 hours) • Individual prescription review is required for prolonged use (beyond 48–72 hours) • Examples include broad-spectrum antimicrobials with potential to promote resistance – such as ceftriaxone, vancomycin, ciprofloxacin and meropenem – and those that are common targets for antimicrobial stewardship programs
Highly restricted	• Require discussion with a nominated expert to obtain approval before the medicine can be initiated, to ensure that use is appropriate and to enable ongoing patient follow-up • Often, a full, formal, specialist clinical consultation for these patients is also recommended • Examples include antimicrobials viewed as last-line agents and reserved for highly resistant pathogens, or medicines with high potential toxicity or high cost, such as echinocandins, colistin and linezolid

A requirement for post-prescription review and approval for prolonged antimicrobial use can help to encourage de-escalation or cessation of these medicines wherever possible. In some sites, a 'no approval, no drug' policy that forces the prescriber to seek approval before the medicine is dispensed may be used. In other centres, the hospital policy may allow the medicine to be dispensed for 24 hours, during which approval should be obtained or dispensing will stop. Some sites with electronic approval programs also use an alert system in which dispensing continues, but an electronic alert is raised to the AMS team to request review of the non-approved prescription.

Approvals may be administered by several mechanisms, including paper-based order forms[37], fax- or telephone-based[41] systems, or electronic systems.[47-49] The choice of system largely depends on the resources available to the site and processes for auditing or following up approvals. Telephone-based approval systems may be onerous because of workflow interruptions, the systems needed to support appropriate record keeping, and communication with the clinical workforce to reduce variation in advice between approvers. However, even the antimicrobial approval systems that are personnel intensive have been shown to be cost-effective in hospitals.[50]

Many hospitals in Australia have successfully introduced electronic antimicrobial approval systems to streamline the workflow for AMS programs (see Section 4.2.2 in Chapter 4: 'Information technology to support antimicrobial stewardship'). The advantages of electronic systems are that they can be accessed 24 hours a day and provide consistent information regarding approved indications for antimicrobial use. The institution may nominate certain standard indications and durations for which approval may be obtained via the computer, and then require individual approval for more complex indications or prolonged durations. This process focuses the AMS team's attention on the complex cases and does not burden the team with routine indications. However, it ensures that the prescriber is still aware of hospital policy and prescribing guidelines at the time of prescribing. Electronic approval systems also support audit and feedback processes.[51]

In the published literature, the use of electronic approval systems for individual antimicrobial agents and larger numbers of antimicrobials is generally reported as resulting in reduced consumption of the restricted agents.[48]

3.4 Post-prescription reviews

Regular ward rounds for post-prescription antimicrobial review, often called AMS ward rounds, have been adopted at many Australian hospitals. They can provide insight into many aspects of antimicrobial prescribing that may not be recognised through more passive mechanisms of audit. Importantly, regular AMS rounds provide teaching opportunities for the junior and senior workforce, and can help to increase awareness of AMS within health service organisations.[2]

Post-prescription review has been associated with a reduction in the volume of prescribing of several key classes of antimicrobial agents at some hospitals, and significant cost savings.[52,53] These reviews provide a valuable opportunity to change the original prescription by using information that was not available at the time the antimicrobials were prescribed (such as from radiological and microbiological tests).[54]

A key strength of programs that use individual prescription review is that they can assess the individual patient's clinical situation. Clinical guidelines cannot encompass all situations, and many important patient-specific factors require consideration, such as long-term care goals for the patient.

The options of de-escalation, streamlining, switching from intravenous to oral delivery or ceasing antimicrobial therapy may not show an immediate improvement in patient outcomes compared with continuation of broad-spectrum therapy. However, it is important to show that there are no new harms or adverse events when optimising antimicrobial therapy, in addition to showing any cost savings that may be realised. If available, evidence showing patient safety outcomes (such as reduced length of stay) should be included as part of the feedback and education process when rationalising antimicrobial therapy.

3.4.1 Who should perform reviews in hospitals?

Post-prescription review of antimicrobials in hospitals may be undertaken by a single clinician – for example, an ID physician or a clinical pharmacist – or by a multidisciplinary team with two or more members representing specialties such as infectious diseases, pharmacy, infection control and microbiology.

Both the individual approach and the team approach have been found to improve antimicrobial prescribing. However, international peak bodies recommend a team approach because it is more likely to have a positive effect.[20,55] AMS teams play a key role in this process and are supported by the Australian Commission on Safety and Quality in Health Care (the Commission). The composition of the expert team will depend on the availability of local resources. Increasingly, nurses, midwives, infection control practitioners, pharmacists, and doctors who are not necessarily ID physicians but who have additional training in AMS are able to participate very effectively in these teams (see Chapter 2: 'Establishing and sustaining an antimicrobial stewardship program').

In Australia, clinical pharmacists are generally available in larger hospitals to review medication charts, identify prescribing errors and identify antimicrobial prescribing that requires review. They can also refer cases to the nominated AMS clinician or team as needed. Establishing systems that support referral to the AMS team by other members of the clinical workforce will enable workforce members to feel that concerns about antimicrobials will be promptly addressed (see Chapter 11: 'Role of the pharmacist and pharmacy services in antimicrobial stewardship').

Some hospitals do not employ ID physicians directly, and other approaches are used to ensure that visiting medical officers and other contracted workforce members receive the guidance they need. Some hospitals use clinician networks for referrals and consultations – for example, surgeons may involve one of a small group of general physicians to assist in perioperative care of their patients. It may be useful to involve these groups of physicians in AMS initiatives such as post-prescription review. (See also Chapter 4: 'Information technology to support antimicrobial stewardship' and Chapter 8: 'Role of the infectious diseases service in antimicrobial stewardship'.)

In organisations with no on-site ID physicians or pharmacists, nurses, midwives, infection control practitioners or other doctors with appropriate training can assist with post-prescription review by identifying high-risk patients, or patients from a predetermined list of key indications or antimicrobials (see Chapter 12: 'Role of nurses, midwives and infection control practitioners in antimicrobial stewardship'). Action regarding these patients might include:

- Scanning copies of charts and forwarding them to an off-site pharmacy department for review

- Having regular teleconferences with off-site pharmacists, ID physicians or clinical microbiologists to review patients' prescriptions and discuss cases
- Using telehealth to include off-site experts in ward rounds of high-risk or high-use areas.

R P In rural, remote and private hospitals, effective networked models of service delivery, involving off-site ID experts to discuss more complex cases with the local pharmacists, can be established with formalised protocols and with the support of telehealth. Several studies have shown that targeted AMS interventions can be effective in hospitals with few ID resources. Yam et al. describe an AMS program at a rural hospital without an ID physician and pharmacist.[56] There, six antimicrobials with high potential for misuse were targeted for interventions that included prospective review with streamlining of therapy, discontinuation, antimicrobial change and dose optimisation. The streamlining rate doubled from 44% to more than 90%, and antimicrobial purchase costs per 1,000 patient days decreased by 51% over a two-year period.[56] Prescription review efforts in facilities with limited resources should target areas in which AMS interventions will achieve the most significant return. This could include conditions that account for the majority of the antimicrobial prescriptions and those with the most inappropriate antimicrobial prescriptions. Audits such as NAPS can help to identify these conditions, as well as the units, services and prescribers responsible for significant proportions of inappropriate antimicrobial use in the facility.

R Telehealth provides opportunities for the on-site workforce to be supported in a number of settings, including rural and remote hospitals, and also for post-prescription review in small hospitals with no on-site pharmacist (see Case study 3.1 and Chapter 4: 'Information technology to support antimicrobial stewardship').

Case study 3.1: Post-prescription review in small rural facilities using telehealth

A pharmacist-led antimicrobial stewardship telehealth model has been established in far north Queensland to help smaller rural facilities with no on-site pharmacist to meet the National Safety and Quality Health Service Preventing and Controlling Healthcare-Associated Infection Standard.

A regional hospital, which is part of a Local Hospital Network (LHN), initiated a telehealth case conference service to review all inpatients receiving antimicrobial agents in two small rural hospitals with no on-site pharmacist or infectious diseases (ID) physician. A multidisciplinary team, comprising senior medical and nursing personnel, was formed at each site, and weekly case review conferences were established. Patient clinical information was supplied to the pharmacist before the case conference, and service-wide data systems were used for relevant pathology. Pharmacist recommendations were made according to the LHN's antimicrobial stewardship formulary, and included recommendations to contact the ID physician at the regional hospital for the use of restricted antimicrobials or when further advice was required.

Over 24 months, in a total of 112 case conferences, 260 patient cases were reviewed and 212 pharmacist recommendations were made. Recommendations included choice of antimicrobial, dose (including adjustment for decreased renal function), allergy advice, length of treatment and advice for ID consultation as per the LHN formulary.

3.4.2 Which patients should be reviewed?

A review of a patient's antimicrobial therapy may be triggered by a referral from another clinician, the prescription of a particular antimicrobial, a laboratory result, or a clinical condition such as meningitis or sepsis. In many hospitals, electronic tools are being used to identify patients for clinical review by the AMS team, and to prospectively collect data on the types of patients being seen, the advice given and the interventions required so that these data may be audited and considered (see Chapter 4: 'Information technology to support antimicrobial stewardship' and Chapter 6: 'Measuring performance and evaluating antimicrobial stewardship programs').

Routine AMS ward rounds should be done in clinical areas with high antimicrobial use – for example, ICUs, transplant wards and haematology units. This can ensure that the AMS team's expertise and advice are readily available to prescribers. Generally, a consultant or senior fellow from the treating unit attends the AMS ward round to discuss issues directly. The AMS team should also review the use of highly restricted antimicrobials across the whole hospital and episodes of prolonged use of other restricted antimicrobials (this often requires at least twice-weekly ward rounds to capture cases in a timely way).

The frequency of AMS ward rounds depends on the size and resources of the hospital, and the casemix of patients. Generally, an AMS team should aim to do AMS ward rounds at least twice per week in areas of greatest need (for example, the ICU).

3.4.3 What should be included in the feedback?

The review should start by stating the documented indication for antimicrobial use, and then move to discuss any relevant clinical factors or investigation results to date that might influence the antimicrobial prescription. It may be useful to compare the prescription with prescribing guidelines and comment on the appropriateness of the prescription, if possible.

One or more of the following might be used in an assessment of appropriateness:

- The decision to prescribe an antimicrobial
- Choice of antimicrobial
- Whether use was in accordance with local or national prescribing guidelines
- Route of administration (intravenous or oral)
- Appropriateness for treatment for the suspected or confirmed pathogen
- Dosage and frequency
- Clarification of allergy status
- Duration of therapy to date.

The post-prescription review should ensure that the prescription aligns with the Antimicrobial Stewardship Clinical Care Standard.[26] A range of point-of-care stewardship interventions can be used to provide direct and timely feedback to the prescriber at the time of prescription review or laboratory diagnosis (see Point-of-care interventions). This feedback may include recommendations for streamlining or de-escalating therapy, which can help treating teams to plan ahead.

3.4.4 How should feedback be provided?

Feedback, when required, can be communicated in person (such as during a round in the ICU) or discussed during a phone call with the treating team. This feedback should always be included in the patient's healthcare record. If the advice is not urgent and simply provides confirmation that antimicrobial use is appropriate or assistance for planning ahead, it can be communicated solely via the healthcare record. The written documentation should follow an appropriate structure – for example:

> **AMS ward round**
>
> **Review: day 2 of ceftriaxone**
>
> *Admitted with community-acquired pneumonia, chest X-ray changes left base, positive pneumococcal antigen in urine. No allergies.*
>
> *Clinically improved, eating, afebrile, white cell count normalised, oxygen saturations now normal on room air. Sputum and blood cultures no growth.*
>
> *The patient does not have severe pneumonia and thus does not likely need ceftriaxone. Suggest switch to oral amoxicillin 1 g tds with a plan for a further 5 days, as 7 days total antibiotic is usually adequate for mild–moderate pneumonia.*
>
> *Name, date, signature*

Note that the above example follows the recommendations for medical communications known as ISBAR (introduction, situation, background, assessment and recommendation;

see Resources). This approach can be applied to both written and verbal forms of communication.[57]

Given that most AMS teams do not directly take a history or examine the patient, care should be taken with the scope of advice given. It is important to understand that the treating clinician ultimately makes the decision about whether to accept the recommendation of the AMS team and change the prescription. The notes by the AMS team should document its rationale for advice. If the clinical situation is complex, it is recommended that the treating team be called or an ID physician be consulted. This is especially important if it has not been possible to discern the rationale for the current antimicrobial choice or regimen.

Different methods of feedback after post-prescription review were compared by Cosgrove et al. in a large United States hospital.[58] The study looked at feedback provided by a telephone call, a note in the healthcare record or a text message sent to the clinician's pager. The text messages and notes left in the healthcare record included detailed information on the recommended change, including the dose of the new agent and a rationale for the change. There was no statistical difference in the uptake of recommendations between the groups, and the authors suggested that clinicians may be willing to implement changes regardless of how feedback is provided. In Australia, documentation in the healthcare record has usually been the more accepted method of communication, often accompanied by a phone call if any clarification is needed.

AMS teams should keep records of their interventions to help them identify existing or emerging prescribing issues. This may also help to inform future communication or education campaigns. The team may create summaries of information and feed them back to the units involved to trigger opportunities for discussion.

3.4.5 Prescription review at transitions of care

Specific prescription review should occur at transitions of care (when patients are admitted to or discharged from a facility, or transferred within the facility), and especially for end-of-life care decisions in all healthcare settings. The appropriateness of ongoing prophylactic antimicrobials, in particular, should be questioned. Frequently, such prescriptions can be safely ceased; however, this often requires an intervention to ask why the medicine is being given and whether it is necessary. At the end of life, when comfort is paramount, it is important to determine whether antimicrobials are appropriate and whether they may be causing increased discomfort, such as anorexia, nausea or diarrhoea. It is essential to ensure that the risks and benefits of prescribing antimicrobials are reassessed in the context of the patient's current general health status (see Chapter 10: 'Role of prescribers in antimicrobial stewardship').

3.4.6 Post-prescription reviews in the community setting

Post-prescription review is an endorsed practice in the Antimicrobial Stewardship Clinical Care Standard. In some community medical practices, the general practitioner may schedule a clinical review of a patient who has been prescribed empirical antimicrobial therapy after a given time (for example, at 48 hours), to monitor their clinical progress and review any investigation results; this may be done by telephone. This provides an opportunity to optimise antimicrobial therapy and set a planned cessation date for the antimicrobial in the light of additional clinical information. Clinical review of patients who are not prescribed antimicrobials is also useful to reassure both the patient and the clinician, and to ensure that any deterioration is identified and acted on promptly.

In aged care homes, local policies should require clinical review of residents by a clinician if the resident was prescribed antimicrobials over the phone after hours. Ideally, this should be done within 24 hours of the prescription. This is especially important for locum services or other situations in which the covering doctor may not be familiar with the patient. This type of review can promote appropriate prescribing and set in place processes to cease antimicrobials after defined time periods.

Individual prescription review may also be prompted by a particular laboratory investigation result. Many laboratories will initiate contact with prescribers to discuss antimicrobial therapy when an unusual or potentially serious isolate or test result is identified.

Clinicians may also want to discuss antimicrobial prescriptions with nominated experts based on clinical concerns. Pathways for prescribers in community settings to access such specialist advice should be clearly identified. This may occur through links with ID or pharmacy services at local hospitals, or with clinical microbiologists at laboratory service providers.

3.5 Point-of-care interventions

POCIs are one of the most effective aspects of AMS in hospitals. They can improve patient management and patient outcomes, and provide excellent opportunities to educate the clinical workforce on optimal prescribing. Recommendations from post-prescription review (see Post-prescription reviews) are likely to include one or more POCIs.

Examples of POCIs include advice or actions on:

- Directed therapy based on microscopy and other rapid tests
- Directed therapy based on culture and susceptibility test results
- Dose optimisation
- Limiting toxicity
- Duration of therapy
- Route of administration (intravenous-to-oral switching)
- Escalation to formal expert clinical review.

Which interventions are selected, how they are delivered and by whom will be determined by local resources and the expertise available. POCIs can be delivered by a clinical pharmacist, by an AMS team or during an ID consultation.

3.5.1 Directing therapy based on results from microscopy and other rapid tests

For a small number of conditions, the choice of empirical therapy can be improved using microbiology test results that are available minutes or hours after specimen collection, such as:

- Fast specimen processing of cerebrospinal fluid, which might include the use of on-call workforce members to conduct cell counts, Gram stains and antigen tests for suspected meningitis
- Microscopy for vaginitis, which readily distinguishes between candidiasis, trichomoniasis and bacterial vaginosis
- Polymerase chain reaction (PCR) testing, which can allow earlier diagnoses of conditions such as influenza, or may be used to help differentiate methicillin-susceptible from methicillin-resistant *Staphylococcus aureus* in blood cultures
- Mass spectrometry, which may enable earlier identification of bacterial species from critical sites such as blood cultures
- Rapid procalcitonin tests, which can lead to earlier cessation of antimicrobials in patients whose procalcitonin levels remain low
- Point-of-care tests for C-reactive protein, which may be used to help decide about antimicrobial treatment in respiratory tract infections, primarily in the community setting.[59]

3.5.2 Directing therapy based on culture and susceptibility test results

Bacterial culture results, including identification and susceptibility test results, are usually available 48–72 hours after specimen collection. Results of these tests should be used to improve antimicrobial choices and optimise therapy by streamlining or de-escalating therapy.[55,60-62] Encouraging the treating team to modify therapy (if necessary) can reduce antimicrobial exposure and costs. Typical interventions in this category are:

- Changing the antimicrobial agent (for example, changing from a broad-spectrum agent to one with a narrower spectrum that targets the infecting organism)
- Ceasing additional antimicrobials that will not improve outcomes (for example, stopping dual anaerobic antibacterial therapy)
- Ceasing antimicrobial therapy altogether if the diagnosis is a non-bacterial infection (for example, positive viral PCR) or non-infective condition (for example, cardiac failure rather than pneumonia).

3.5.3 Optimising dosing

When reviewing medication orders and dispensing prescriptions, pharmacists play an important role in identifying variation from recommended dosing schedules and recommending optimal dosing regimens. The pharmacokinetic and pharmacodynamic features of the antimicrobial need to be taken into account in this process.

Antimicrobial dosing schedules can be optimised by:

- Checking and adjusting doses to suit patient size and renal function
- Looking for drug–drug interactions (for example, between linezolid and some antidepressants)
- Adjusting the dosing interval, where appropriate – for example, considering extended infusions, or continuous infusion of short half-life β-lactams such as piperacillin–tazobactam, cefepime or meropenem[63,64]

- Monitoring antimicrobial levels in an individual patient, and adjusting dosing to maximise efficacy and minimise toxicity (therapeutic drug monitoring – for example, with aminoglycosides, vancomycin and azole antifungals)
- Guiding antimicrobial selection towards the most appropriate agents (for example, agents with higher cerebrospinal fluid penetration, if required).

3.5.4 Limiting toxicity

Specific advice may be provided to reduce the harm from antimicrobial use. This may include:

- Limiting gentamicin use to less than 48 hours
- Ceasing other drugs that might interact with the antimicrobial agent
- Monitoring renal or hepatic function
- Identifying potential side effects early.

3.5.6 Changing the duration of therapy

Incorrect duration of antimicrobial therapy is a frequent problem in hospital prescribing; surgical prophylaxis that is administered beyond one dose or one day is a common example. In the 2015 NAPS, the proportion of surgical prophylaxis prescriptions extending for more than 24 hours was 27.4% – best practice is less than 5%.[12] Hospitals should have policies for the prophylactic use of antimicrobials that state that a single dose is the preferred option.[20,65] The Commission is working with the Royal Australasian College of Surgeons to develop resources to promote improved surgical prophylaxis.

Almost all infections have standard treatment durations. However, the duration of therapy may need to be tailored to individual responses to treatment. It is important to promote and sustain a prescribing culture that includes daily review and setting a maximum duration of treatment unless there is a clear indication in the healthcare record that therapy should be continued. Planned review dates may also prompt treating teams; review and/or stop dates should be clearly documented in the patient's healthcare record and on their medication chart.[20,26]

3.5.7 Switching from intravenous to oral delivery

Oral therapy is often in the best interests of the patient because continued hospitalisation can be associated with the risk of acquiring a new multidrug-resistant infection (by direct transmission) or a preventable adverse event such as an infection from the intravenous line. Oral therapy allows patients to be discharged to their home environment once they are clinically stable.

Encouraging a switch to oral therapy once the patient has shown significant clinical response to treatment is a well-studied strategy with proven value.[53] Benefits of intravenous-to-oral switching include[55]:

- Lower treatment costs
- Reduced morbidity from intravenous lines
- Reduced length of stay
- Higher patient satisfaction.[66]

Certain antimicrobials – for example, fluoroquinolones, linezolid, fluconazole and voriconazole[63] – have near-complete bioavailability. Patients receiving these therapies are often excellent candidates for early intravenous-to-oral switching.

Defined criteria that allow the AMS team to expedite the change to oral therapy can be established. *Therapeutic Guidelines: Antibiotic*[1] provides guidance on when oral therapy should be used in preference to parenteral therapy. Several states and territories have also developed specific guidance (see Resources).

In the United Kingdom, the National Institute for Health and Care Excellence AMS guidelines recommend that intravenous antimicrobials be reviewed at 48–72 hours to determine whether the antimicrobial needs to be continued and, if appropriate, the patient switched to oral therapy.[67] Public Health England's Start Smart – Then Focus toolkit also promotes daily consideration of opportunities to streamline therapy, including intravenous-to-oral switching.[20]

3.5.8 Escalating to formal expert clinical review

Post-prescription review services often identify patients who have complex problems and are likely to benefit from early clinical review by ID physicians. In Australian tertiary hospitals, escalation to review by ID physicians has been observed to account for 5–10% of reviews; it is noted that this pattern may be very different in other hospitals in Australia and overseas.[68] It is likely that many of these patients would eventually have been referred, but the post-prescription AMS review often facilitates earlier identification. In some cases, critically important clinical problems that were previously overlooked by the treating team have been identified by AMS teams. For some infections, an ID consultation has been demonstrated to reduce mortality through diagnostic precision and the optimisation of antimicrobial management.[69-71] Patients with serious antimicrobial allergies may also be referred to immunologists for specialised advice (see Section 8.3.1 in Chapter 8: 'Role of the infectious diseases service in antimicrobial stewardship').

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It is important that all hospitals have access to advice from ID physicians or specialised pharmacists, to provide support when needed. Options for accessing expert advice when it is not available on site may include:

- Using LHN/LHD clinical networks or other formalised clinical networks
- Using clinical microbiology networks from laboratories that provide diagnostic services
- Using an AMS pharmacist or physician in an LHN/LHD regional or hospital group role
- Using telehealth networks to support formalised networks with specialists (see Section 4.4 in Chapter 4: 'Information technology to support antimicrobial stewardship').
- Contracting ID and clinical microbiology services.

Resources

Prescribing guidelines

- *Therapeutic Guidelines: Antibiotic*
- Public Health England: Antimicrobial Stewardship: Start Smart – Then Focus
- NSW Clinical Excellence Commission: Sample *Antimicrobial Stewardship Policy: for a Local Health District or Network*
- Centre for Remote Health: *CARPA Standard Treatment Manual*

Restricted antimicrobials policies

- NSW Clinical Excellence Commission: *Antimicrobial Restrictions in Small to Medium-Sized Hospitals: Fact sheet*

Post-prescription review

- National Institute for Health and Care Excellence (UK): AMS guidelines
- Hunter New England Area Health Service: ISBAR tools

Point-of-care interventions – intravenous-to-oral switching

- SA Health, South Australian expert Advisory Group on Antimicrobial Resistance: *IV to Oral Switch Guideline for Adults Patients: can antibiotics S.T.O.P.*
- ANZPID–ASAP Group: *Guidelines for Antibiotic Duration and IV–Oral Switch in Children*
- Children's Health Queensland: Intravenous (IV) to oral antimicrobial switch
- Sydney Children's Hospitals Network: *Intravenous to Oral Antimicrobial Switch: Practice guideline*
- Sydney Children's Hospitals Network: *Making the Switch: Changing from intravenous to oral antibiotics* [Information for parents]

Other

- Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis 2016;62:1197–202.

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