Evidence-based strategies for better antibiotic prescribing



CPD

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Background

Antibiotic resistance is a key global health threat, and antibiotic overuse is a significant contributing factor. Antibiotic stewardship is a vital issue for general practice.

Objective

The aim of this article is to discuss evidence-based strategies for general practitioners (GPs) and general practices to contribute to antibiotic stewardship and, thus, reduce the overall burden of antibiotic prescribing in the community.

Discussion

For individual GPs, and for practices, there is good evidence for the effectiveness of several strategies. As well as having a firm grasp of the clinical evidence in the area, important strategies for GPs include: eliciting and exploring patient understanding and expectations, and incorporating these in communication and management; offering delayed prescribing; using appropriate non-antibiotic symptomatic management; and, when prescribing antibiotics, doing so only for genuine clinical indications, with the appropriate antibiotic, at the appropriate dose, for the shortest appropriate duration. Practices can adopt a practice culture and practicewide prescribing policies that promote antibiotic stewardship.

ANTIBIOTIC RESISTANCE is one of the key emerging threats to global health, with its importance to Australia underlined by publication of the Australian Commission on Safety and Quality in Health Care's AURA 2021 report.¹ Antibiotic overuse is the key driver of antibiotic resistance, and antibiotic stewardship is an important tool used to prevent this. Antibiotic stewardship applies to all healthcare settings (and to over-the-counter antibiotic sale and veterinary and agricultural settings). It is particularly important in general practice – the health sector where most antibiotics are prescribed.²

While antibiotic stewardship is relevant to all infections, the majority of antibiotic prescribing in general practice, including non-evidence based prescribing, is for respiratory tract infections. Non-pneumonia acute respiratory infections (ARIs) have two key features that make them an important target for antibiotic stewardship interventions: they are very common (upper respiratory tract infections and acute bronchitis are managed in 5.5% and 2.0%, respectively, of all general practice consultations),³ and there is evidence from multiple randomised controlled trials (RCTs) that antibiotics are of minimal or no benefit.

For common ARIs in Australia, antibiotics are prescribed at rates 4–9 times higher than is recommended.⁴ While there are other common conditions with a high prevalence of non-evidence based antibiotic prescribing, in this article ARIs will serve as the exemplar for antibiotic stewardship in general practice. Reference is also made to urinary tract infections (UTIs), skin and soft tissue infections and conjunctivitis.

Science and art

The science involved in the management of common ARIs with which patients present to general practice is generally straightforward. There is high-quality evidence that antibiotics are not indicated for the great majority of presentations of ARIs.5-10 For the two most common presentations, the 'common cold' and acute bronchitis, antibiotics are not indicated at all.11 The art of medicine relating to ARIs is often not as straightforward as the science. Management takes place within a biopsychosocial context with multiple barriers to recommended practice and to optimal antibiotic stewardship.

Patient perceptions and expectations, practitioner clinical uncertainty and practice culture may all be barriers to antibiotic stewardship.¹²

There is, however, much evidence that can inform a framework to approach the art of practice in antibiotic stewardship in ARIs at both the individual clinician and practice levels.

What can be done at the individual level?

Patient perceptions and expectations

Patient perceptions and expectations may not be congruent with current evidence for the use of antibiotics in ARIs, and patients' expectations may not always be accurately assessed or understood by GPs.

Patients presenting with ARIs are usually expecting information or reassurance, and information/reassurance is more strongly associated with patient satisfaction than an antibiotic prescription.¹³ There is good evidence for several information and reassurance strategies (including decision aids and patient leaflets) for engagement of patients in coming to agreement about an appropriate management plan for ARIs that does not include antibiotic prescribing. This is outlined in an article by Del Mar et al in this issue of *Australian Journal of General Practice (AJGP)*.¹⁴

A further consideration is that patient understanding (and expectations for antibiotics) may not be aided by GPs' characterisation of an episode of ARI as 'viral' rather than 'bacterial' - and this may, in any case, be a false dichotomy, both microbiologically and aetiologically.15 The RCTs of antibiotics and ARIs that inform practice enrolled patients on the basis of clinical presentation, not on the causative organism(s). Hence, GPs should frame ARIs syndromically (using shared understanding of ARI syndrome 'labels'16) rather than aetiologically. This is how the evidence is framed (as common cold, acute bronchitis, acute sore throat, acute sinusitis, acute otitis media, etc⁵⁻¹⁰) and how patients present. Even for conjunctivitis, where management recommendations are often framed on the basis of viral versus bacterial,11 aetiological differentiation may be difficult,17 and recommendations for topical antibiotic treatment are for patients with 'marked symptoms'.11

Practitioner clinical uncertainty

GPs' clinical uncertainty can drive antibiotic prescription if they adopt a 'default' of antibiotic prescription in response to concern or worry about whether a diagnosis is correct or whether there is potential for significant disease progression. The context is that GPs often see early presentations of illness and undifferentiated presentations.

It is important for practitioners to understand that antibiotic prescription is not the 'safe default'. In acute otitis media, for example, the number needed to benefit for antibiotics appears to be greater than the number needed to harm.9 In other words, antibiotics are not a zero-risk intervention. In fact, they not only carry the risk of adverse effects to the individual during a course, but of future antibiotic resistant infections within that individual.¹⁸ There is also emerging evidence that antibiotic use in infancy and early childhood increases the risk of obesity in adulthood because of a complex interaction with the host microbiome.19,20

'Missing' a serious infection is a very real concern for GPs. A common concern is misdiagnosing pneumonia as acute bronchitis. But chest X-rays (CXRs) are generally accessible for GPs' patients with a fast turnaround of results (a diagnosis of pneumonia requires a CXR11). Also, any pneumonia-bronchitis diagnostic uncertainty will involve mild rather than severe or moderately severe pneumonia. Delayed antibiotic treatment of clinically unsuspected mild community-acquired pneumonia is unlikely to have an adverse outcome. In a large European primary care RCT of patients with acute lower respiratory tract infection, after excluding patients suspected clinically of having pneumonia, immediate prescription of antibiotics provided little benefit and caused slight harms.21

An aspect of clinical uncertainty is that produced by the false dichotomy of viral or bacterial aetiology. As above, addressing the syndromic presentation rather than aetiological diagnosis^{5-10,22} will lessen uncertainty as a driver of antibiotic prescribing in ARIs and infective conjunctivitis.

Delayed prescribing

A practicable strategy for reducing overall antibiotic prescribing in general practice is delayed prescribing, which 'may offer an acceptable compromise between immediate and no antibiotic prescription'.²³ Delayed prescribing involves offering a prescription, but with advice to only fill the prescription if symptoms do not resolve within a certain timeframe,²⁴ typically 48-72 hours. Both no-prescribing and delayed-prescribing strategies reduce inappropriate antibiotic consumption for ARIs when compared with immediate prescribing, with no difference in patient satisfaction between delayed and immediate prescribing.24 Both delayedprescribing and no-prescribing strategies appear to be safe,²⁵ and delayed prescribing has similar symptom control to immediate prescribing.26 Delayed prescribing may have benefits in educating and empowering patients, as well as building trust and the doctor-patient relationship.27 Delayed prescribing must be delivered within the context of 'safety netting'28 communicating uncertainty and providing information on which to base appropriate and timely patient-initiated re-assessment which should be employed whether or not antibiotics are prescribed.

Delayed prescribing has particular use for general practice registrars in dealing with clinical uncertainty and with practice cultures not conducive to judicious antibiotic prescribing,²⁷ and Australian registrars use delayed prescribing frequently.²⁹

Offer practicable and efficacious alternatives to antibiotics for symptomatic treatment

Declining to prescribe antibiotics without providing alternative symptomatic management is not adequate patient management. In fact, many patients may be seeking symptomatic treatment (eg pain relief for sore throat) and have a perception that antibiotics will best achieve this.³⁰ As well as engaging with the patient regarding the lack of efficacy of antibiotics, symptomatic therapies should be offered; paracetamol,³¹ ibuprofen,³¹ honey³² or topical nasal preparations¹¹ may be suitable for common ARI presentations. Provision of appropriate sickness certification is also part of symptomatic management.

Treat when appropriate (with the appropriate antibiotic and regimen)

Just as a default position of antibiotic prescribing is non-evidence based, a default position of no antibiotic prescribing is inappropriate in some defined circumstances. Treatment of UTIs, pneumonia and carefully selected presentations of, for example, sore throat, otitis media, impetigo and conjunctivitis is appropriate. In these scenarios, it is important to prescribe the most narrowspectrum appropriate antibiotic, at the appropriate duration (eg short-course' UTI treatment regimens³³). Use of topical rather than systemic antibiotics, when appropriate, also contributes to antibiotic stewardship (eg for impetigo³⁴).

Use evidence-based clinical practice guidelines

ARIs are very common in general practice; therefore, broad awareness of evidence (especially of Cochrane reviews) for common ARIs is important for practising clinicians. Authoritative guidelines appropriate to general practice and the Australian context are available (eg eTG Complete,¹¹ which has a convenient 'Antibiotic prescribing in primary care: Therapeutic Guidelines summary table 2019') and should be used – with due consideration of the applicability of the guideline to the individual patient at that particular time.

What can be done at the practice level?

A practice culture of liberal prescription of antibiotics sets patients' expectations and may create dissonance for practitioners attempting to prescribe according to evidence-based guidelines.¹² There are valid concerns about the effects on the practitioner-patient relationship of denying requests for antibiotics. This is particularly problematic for early-career GPs, part-time GPs and, especially, registrars.¹²

Systems-level interventions are effective in improving hospital inpatient antibiotic prescribing.³⁵ Having consistent within-practice approaches to antibiotic prescribing, including practice protocols for common conditions, would also be a reasonable approach in general practice. Given the evidence for patient engagement and patient-clinician communication in general practice antibiotic stewardship improving prescribing practice within research protocols,³⁶ practice protocols could go beyond simple guidelines on antibiotic prescription (yes/no) and contain information on how to engage with patients and on non-antibiotic symptomatic treatments.

Some evidence for the role of interactive meetings in reducing antibiotic prescribing in general practice³⁷ (perhaps with a didactic as well as an interactive element³⁸) suggests that practice clinical meetings targeting rational antibiotic prescribing and implementation of antibiotic stewardship may assist in creating the desired practice culture.

Appropriate posters (specific to the target respiratory illnesses and tailored to the demographics of the practice, including appropriate non-English versions) in the practice waiting room may contribute to patient engagement with the practice antibiotic stewardship culture.³⁹

There is evidence for the role of local opinion leaders in influencing clinicians' evidence-based practice.40 This approach could extend to senior GPs in group practices, especially large practices and teaching practices. Training supervisors and other senior GPs can help set the practice culture regarding evidencebased antibiotic prescribing.12,41 An important perspective is that antibiotic prescribing is a clinical behaviour, and appropriate role-modelling is an important element in behaviour change.42 A further consideration of senior GPs' and registrar supervisors' roles is in practice audit and feedback. There is some evidence for audit and feedback in improving professional practice, especially if the source of feedback is a supervisor or colleague.43

Beyond the individual GP and the individual practice

Elsewhere in this issue of *AJGP*, Glasziou et al discuss external-to-practice influences.⁴⁴

A further source of influence is in local GP opinion leaders (from universities, Primary Health Networks, local GP associations etc) taking responsibility for actively promoting antibiotic stewardship, as this may have significant effects on GPs' practice.⁴⁰

Conclusions

At face value, diagnosis and management of ARIs will be among the most straightforward decisions in a GP's day. However, these decisions may be set in complex or difficult biopsychosocial contexts. There is a body of evidence that can help GPs through these scenarios. Reflecting complex biopsychosocial contexts, translating this evidence to clinical behaviour, at individual clinician and at practice-wide levels, will take time and deliberate practice.

Key points

- It is important not to adopt a default position of antibiotic treatment in the management of ARIs.
- Delayed prescribing is an alternative to immediate prescribing.
- It may be beneficial to adopt practicewide evidence-based approaches to prescribing for ARIs.
- GPs can provide appropriate symptomatic non-antibiotic management, using the best available evidence.
- It will be beneficial to adopt practicewide evidence-based approaches to prescribing for ARIs.

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References

 Australian Commission on Safety and Quality in Health Care. AURA 2021: Fourth Australian report on antimicrobial use and resistance in human health. Sydney, NSW: ACSQHC, 2021.

- Goossens H, Ferech M, Vander Stichele R, Elseviers M; ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: A cross-national database study. Lancet 2005;365(9459):579–87. doi: 10.1016/ S0140-6736(05)17907-0.
- Britt H, Miller GC, Henderson J, et al. General practice activity in Australia 2015–16. General practice series no. 40. Sydney, NSW: Sydney University Press, 2016.
- McCullough AR, Pollack AJ, Plejdrup Hansen M, et al. Antibiotics for acute respiratory infections in general practice: Comparison of prescribing rates with guideline recommendations. Med J Aust 2017;207(2):65–69. doi: 10.5694/mja16.01042.
- Del Mar CB, Glasziou PP, Spinks AB. Antibiotics for sore throat. Cochrane Database Syst Rev 2006;(4):CD000023. doi: 10.1002/14651858. CD000023.pub3.
- Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. Cochrane Database Syst Rev 2013;2013(6):CD000247. doi: 10.1002/14651858.CD000247.pub3.
- Lemiengre MB, van Driel ML, Merenstein D, Young J, De Sutter AI. Antibiotics for clinically diagnosed acute rhinosinusitis in adults. Cochrane Database Syst Rev 2012;10:CD006089. doi: 10.1002/14651858.CD006089.pub4.
- Smith SM, Fahey T, Smucny J, Becker LA. Antibiotics for acute bronchitis. Cochrane Database Syst Rev 2017;6(6):CD000245. doi: 10.1002/14651858.CD000245.pub4.
- Venekamp RP, Sanders SL, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev 2015;2015(6):CD000219. doi: 10.1002/14651858.CD000219.pub4.
- Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database Syst Rev 2013;2013(11):CD000023. doi: 10.1002/14651858. CD000023.pub4.
- Expert Group for Antibiotic. Antibiotic. In: eTG Complete [Internet]. West Melbourne, Vic: Therapeutic Guidelines Limited, 2019.
- Dallas A, van Driel M, van de Mortel T, Magin P. Antibiotic prescribing for the future: Exploring the attitudes of trainees in general practice. Br J Gen Pract 2014;64(626):e561-67. doi: 10.3399/ bjgp14X681373.
- Welschen I, Kuyvenhoven M, Hoes A, Verheij T. Antibiotics for acute respiratory tract symptoms: Patients' expectations, GPs' management and patient satisfaction. Fam Pract 2004;21(3):234–47. doi: 10.1093/fampra/cmh303.
- Del Mar C, Hoffmann T, Bakhit M. How can general practitioners reduce antibiotic prescribing in collaboration with their patients? Aust J Gen Pract 2022;51(1–2):25–30.
- Davis JS, Magin PJ, van Driel ML. The false dichotomy of viral versus bacterial aetiology in upper respiratory tract infections. Med J Aust 2019;211(3):108–09.e1. doi: 10.5694/mja2.50250.
- Stocks N, Fahey T. Labelling of acute respiratory illness: Evidence of between-practitioner variation in the UK. Fam Pract 2002;19(4):375–77. doi: 10.1093/fampra/19.4.375.
- Schneider J, Scheibling C, Segall D, Sambursky R, Ohsfeldt R, Lovejoy L. Epidemiology and economic burden of conjunctivitis: A managed care perspective. J Manag Care Med 2014;17:78–83.
- Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. BMJ 2010;340:c2096. doi: 10.1136/bmj.c2096.

- Vallianou N, Dalamaga M, Stratigou T, Karampela I, Tsigalou C. Do antibiotics cause obesity through long-term alterations in the gut microbiome? A review of current evidence. Curr Obes Rep 2021;10(3):244–62. doi: 10.1007/s13679-021-00438-w.
- Wan S, Guo M, Zhang T, et al. Impact of exposure to antibiotics during pregnancy and infancy on childhood obesity: A systematic review and metaanalysis. Obesity 2020;28:793–802. doi: 10.1002/ oby.22747.
- Little P, Stuart B, Moore M, et al; GRACE consortium. Amoxicillin for acute lowerrespiratory-tract infection in primary care when pneumonia is not suspected: A 12-country, randomised, placebo-controlled trial. Lancet Infect Dis 2013;13(2):123–29. doi: 10.1016/S1473-3099(12)70300-6.
- Cherry MD, Tapley A, Quain D, et al. Antibiotic prescribing patterns of general practice registrars for infective conjunctivitis: A cross-sectional analysis. J Prim Health Care 2021;13(1):5–14. doi: 10.1071/HC20040.
- McCullough AR, Glasziou PP. Delayed antibiotic prescribing strategies – Time to implement? JAMA Intern Med 2016;176(1):29–30. doi: 10.1001/ jamainternmed.2015.7095.
- Spurling GK, Del Mar CB, Dooley L, Foxlee R, Farley R. Delayed antibiotic prescriptions for respiratory infections. Cochrane Database Syst Rev 2017;9(9):CD004417. doi: 10.1002/14651858. CD004417.pub5.
- Little P, Stuart B, Smith S, et al. Antibiotic prescription strategies and adverse outcome for uncomplicated lower respiratory tract infections: Prospective cough complication cohort (3C) study. BMJ 2017;357:j2148. doi: 10.1136/bmj.j2148.
- Stuart B, Hounkpatin H, Becque T, et al. Delayed antibiotic prescribing for respiratory tract infections: Protocol of an individual patient data meta-analysis. BMJ Open 2019;9(1):e026925. doi: 10.1136/bmjopen-2018-026925.
- Dallas A, Davey A, Mulquiney K, et al. Delayed prescribing of antibiotics for acute respiratory infections by GP registrars: A qualitative study. Fam Pract 2020;37(3):406–11. doi: 10.1093/ fampra/cmz079.
- Jones D, Dunn L, Watt I, Macleod U. Safety netting for primary care: Evidence from a literature review. Br J Gen Pract 2019;69(678):e70–79. doi: 10.3399/ bjgp18X700193.
- Davey A, Tapley A, Mulquiney KJ, et al. Immediate and delayed antibiotic prescribing strategies used by Australian early-career GPs: A cross-sectional analysis. Br J Gen Pract 2021;71(713):e895-e903. doi: 10.3399/BJGP.2021.0026.
- van Driel ML, De Sutter A, Deveugele M, et al. Are sore throat patients who hope for antibiotics actually asking for pain relief? Ann Fam Med 2006;4(6):494–99. doi: 10.1370/afm.609.
- Allan GM, Arroll B. Prevention and treatment of the common cold: Making sense of the evidence. CMAJ 2014;186(3):190–99. doi: 10.1503/ cmaj.121442.
- 32. The Royal Australian College of General Practitioners. Handbook of non-drug interventions (HANDI): Honey and cough in children with URTI. East Melbourne, Vic: RACGP, 2014.
- Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. Cochrane Database Syst Rev 2008;(3):CD001535. doi: 10.1002/14651858.CD001535.pub2.
- 34. Koning S, van der Sande R, Verhagen AP, et al. Interventions for impetigo. Cochrane

Database Syst Rev 2012;1(1):CD003261. doi: 10.1002/14651858.CD003261.pub3.

- Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2017;2(2):CD003543. doi: 10.1002/14651858. CD003543.pub4.
- Little P, Stuart B, Francis N, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: A multinational, cluster, randomised, factorial, controlled trial. Lancet 2013;382(9899):1175–82. doi: 10.1016/S0140-6736(13)60994-0.
- Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev 2005;2005(4):CD003539. doi: 10.1002/14651858. CD003539.pub2.
- Forsetlund L, Bjørndal A, Rashidian A, et al. Continuing education meetings and workshops: Effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2009;2009(2):CD003030. doi: 10.1002/14651858. CD003030.pub2.
- Avent ML, Hansen MP, Gilks C, et al. General Practitioner Antimicrobial Stewardship Programme Study (GAPS): Protocol for a cluster randomised controlled trial. BMC Fam Pract 2016;17:48. doi: 10.1186/s12875-016-0446-7.
- Flodgren G, O'Brien MA, Parmelli E, Grimshaw JM. Local opinion leaders: Effects on professional practice and healthcare outcomes. Cochrane Database Syst Rev 2019;6(6):CD000125. doi: 10.1002/14651858.CD000125.pub5.
- Deckx L, Anthierens S, Magin PJ, et al. Focus on early-career GPs: Qualitative evaluation of a multi-faceted educational intervention to improve antibiotic prescribing. Fam Pract 2018;35(1):99–104. doi: 10.1093/fampra/cmx074.
- Michie S, van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implement Sci 2011;6:42. doi: 10.1186/1748-5908-6-42.
- Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: Effects on professional practice and healthcare outcomes. Cochrane Database Syst Rev 2012;(6):CD000259. doi: 10.1002/14651858. CD000259.pub3.
- Glasziou P, Dartnell J, Biezen R, Morgan M, Manski-Nankervis JA. Antibiotic stewardship: A review of successful, evidence-based primary care strategies. Aust J Gen Pract 2022;51(1-2):15–20.

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