Reducing antibiotic prescribing in Australian general practice: time for a national strategy

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In April 2017, the Centre for Research Excellence in Minimising Antibiotic Resistance from Acute Respiratory Infections in primary care hosted a national roundtable meeting. Australian researchers, policy makers and organisations came together to discuss ways of dealing with the antibiotic resistance crisis from a general practice perspective. This narrative review pools the literature used during the discussions and a literature search using PubMed (online Appendix).

The antibiotic resistance crisis will have two substantial consequences. The first one has begun: about 1600 people in Australia die directly from antibiotic resistance annually, extrapolating from overseas data.[1] It will get steadily worse until 2050, when deaths from currently treatable infections will overtake total cancer deaths. The second consequence — yet to arrive — is the risk that antibiotic resistance will pose to now routine high technology medical care. Without reliable antibiotic prophylaxis, procedures such as chemotherapy, bone marrow transplant, much major surgery (eg, joint prostheses) and invasive diagnostic procedures (eg, cardiac catheterisation) will become too dangerous to perform. Many aspects of medical care will retreat into the pre-antibiotic era of the 1930s, the economic consequences of which are catastrophic and have prompted the Chief Medical Officer of the United Kingdom to declare this threat every bit as serious as terrorism.[2] Governments are attempting to provide incentives for the pharmaceutical industry to generate new classes of antibiotics,[2] but action aimed at extending the life of the existing antibiotics by conserving their use is equally important.

This crisis is not directly obvious to GPs working in the community. Yet, GPs contribute to most of the antibiotic tonnage consumed by humans in Australia[3] — exact data are not available in Australia, but in Denmark and Sweden (low community antibiotic-prescribing countries), 90% of antibiotics for human use are prescribed outside hospitals, and 65% are prescribed by GPs.[4,5] Reducing antibiotic usage allows resistance to dissipate,[6] because the unnecessary metabolic load of metabolising resistance genes in the absence of antibiotics puts these organisms at a selective disadvantage. Some areas of primary care are ripe for reducing antibiotics use, especially prescribing for common acute respiratory infections (ARIs), for which a wealth of evidence shows that the benefits of antibiotics are small and that not using them is generally safe. Other countries use less than half the quantity[3] with no increase in serious infections.[5]

Gains cannot be achieved quickly or simply. Countries that have achieved great gains in reducing their prescribing rates have done so using multiple interventions in concert and persisting over many years.[5]

The aim of this narrative review is to describe interventions that, if implemented on a national scale and successfully lowered the volume of antibiotics prescribed in general practice for ARIs, should reduce community-acquired antibiotic resistance.

Summary

- In Australia, the antibiotic resistance crisis may be partly alleviated by reducing antibiotic use in general practice, which has relatively high prescribing rates — antibiotics are mostly prescribed for acute respiratory infections, for which they provide only minor benefits.
- Current surveillance is inadequate for monitoring community antibiotic resistance rates, prescribing rates by indication, and serious complications of acute respiratory infections (which antibiotic use earlier in the infection may have averted), making target setting difficult.
- Categories of interventions that may support general practitioners to reduce prescribing antibiotics are: regulatory (eg, changing the default to "no repeats" in electronic prescribing, changing the packaging of antibiotics to facilitate tailored amounts of antibiotics for the right indication and restricting access to prescribing selected antibiotics to conserve them), externally administered (eg, academic detailing and audit and feedback on total antibiotic use for individual GPs), interventions that GPs can individually implement (eg, delayed prescribing, shared decision making, public declarations in the practice about conserving antibiotics, and self-administered audit), supporting GPs' access to near-patient diagnostic testing, and public awareness campaigns.
- Many unanswered clinical research questions remain, including research into optimal implementation methods.
- Reducing antibiotic use in Australian general practice will require a range of approaches (with various intervention categories), a sustained effort over many years and a commitment of appropriate resources and support.

Reasons for overprescribing

There are several reasons why GPs overprescribe for ARIs.[7] It is difficult — and often impossible — to separate apparently innocuous ARIs from the early stages of very serious ones,[8] such as community-acquired pneumonia, mastoiditis, epiglottitis or even meningitis, and GPs tend to play it safe. GPs value the doctor–patient relationship and may assume that not prescribing antibiotics threatens this relationship.[9] Moreover, time-poor GPs may perceive that it is quicker to finish a consultation for ARI with an antibiotic prescription.[9] There may be also financial concerns, such as not wanting to lose a patient. In addition, clinicians may have misperceptions that may inflate the benefits of medical treatments generally.[10]

Community surveillance and targets

If we are to reduce antibiotic prescribing, a question arises: reduce to what level? However, before setting targets, we need to decide

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which outcomes to monitor through surveillance. There are three potential main sets of data.

First, we need to know and monitor the background level of antibiotic resistance in the community — reducing this level being the primary objective. The main sources of resistance in patients being admitted to hospital, once originating from hospitals themselves, now originate as often from the community.[11] The problem is that this community-originated resistance is only currently being monitored passively, by collation of clinically submitted data.[3] This type of resistance represents only a small proportion of potential infections, since most respiratory infections in general practice (eg, sore throat) are treated without testing[12] and are, therefore, likely to be heavily distorted towards more complicated or recalcitrant, and hence resistant, specimens. We propose that resistance levels in the community could be monitored using sentinel general practices to systematically sample infections or even uninfected attending patients. Routine monitoring resistance in aerobes (collected by nasal swabs) should be straightforward — although anaerobes (collected by faecal swabs) would be more difficult.

Second, we need to monitor the rates of total antibiotic prescribing, which is the main behaviour that needs to change, even if the focus is on ARIs. Some data are collected by the Drug Utilisation Sub Committee of the Pharmaceutical Benefits Scheme (PBS), but they do not provide clinical indications for antibiotic use, which must come from GPs themselves. Until now, the Bettering the Evaluation and Care of Health program (with a rolling survey of a national sample of 1000 GPs' clinical activities) gathered data on antibiotic use from GPs, but has just been defunded.[13] An alternative, sampled less representatively, comes from GP registrars in training,[14] and a longitudinal GP data collection for the MedicineInsight program[15] may provide such data in future.

Finally, it is important that we monitor patient safety indicators, such as serious infections not treated with antibiotics when they should have been. Reporting hospital admissions for serious ARIs would achieve this patient safety control, which is done routinely in some countries.[4,5] But in Australia, this monitoring would require setting up from relevant hospital discharge separation data.

The next step is to set targets. Community resistance targets will have to await baseline data; however, overall antibiotic prescribing targets could be set. These targets are likely to be controversial and may be unwelcomed by GPs worrying about safety. They could be set with reference to international best practice (the prescription rate in Australia is about double that of, for example, the Netherlands),[3] but recent data show that, currently, GPs prescribe 6–9 times the rates indicated by guidelines.[16] This prescription rate suggests the enormous scope for safely reducing prescribing by using the set targets without resorting to normative data.

Interventions to support GPs to reduce their antibiotic prescribing

Regulatory interventions

Some interventions could produce rapid results. Many GPs' electronic health records default to repeat prescribing to the maximum allowable under the PBS, which may have unintended consequences, such as sending a message to patients that another course of antibiotics is necessary or routine, or leaving an unused repeat prescription (or even more antibiotics) available for use for another illness somewhere in the community. This issue could be redressed either by mandating GP software defaults to "no repeat" prescriptions of antibiotics (with an option to override when clinically indicated), or by changing the PBS criteria and restrictions.

Another action that the Australian Government could implement quickly is to restrict access to several antibiotics earmarked for special conservation, in order to reserve them. Australia has a success story in the lack of resistance to quinolones, which, because they are used little, remain relatively resistance-free compared with other countries.[17] The mechanism for implementing this restriction is the Authority Prescribing System, in which an extra administrative step requires confirmation of a pre-set diagnostic requirement.

More intractable problems include the dissonance between guideline-suggested durations of antibiotic therapy and the pack size available on the PBS dispensed by pharmacists.[18] For example, for a child with acute otitis media requiring antibiotics, the duration recommended by the Therapeutic Guidelines[19] (ie, 5 days) means that a one-year-old child who weighs 10 kg and is prescribed a 100 mL bottle of 25 mg/5 mL of amoxicillin is left with two surplus doses. In theory, GPs could now prescribe guideline-appropriate quantities (as happens in other countries), but the associated breaking of packs may be resisted by pharmacists.

Externally administered interventions

Audit and feedback. Providing feedback to clinicians about their prescribing rates compared with the normative data of their peers can influence behaviour.[20] Feedback based on PBS data is currently used by NPS MedicineWise as an intervention within a variety of national educational programs, including for antibiotic prescribing, but has not been trialled against controls. A variation of the method was trialled in the UK for high-prescribing GPs, who were sent a letter from the Chief Medical Officer, which resulted in a reduction in prescribing rates[21] (Box 1). A similar mailing was sent by the Australian Commonwealth Officer recently.[34]

Academic detailing. Academic detailing comprises educational visits involving face-to-face education of prescribers by trained health care professionals. These visits can occur one to one or with small groups, and sometimes incorporate individual or practice level clinical and prescribing data. NPS MedicineWise has implemented national educational programs that include antibiotic prescribing.

Activities that GPs can individually implement

Delayed prescribing. In situations where the GP feels it is safe not to use antibiotics, but perceives that the patient (or parent) is anxious or feeling unsupported, a delayed prescription is an option. In this case, the GP writes an antibiotic prescription, but advises the patient not to have it dispensed unless some expected improvement does not take place or there is deterioration (described to the patient in detail). Evidence from a Cochrane review of randomised trials shows that this technique is effective at reducing antibiotic prescribing[22] (Box 1).

Shared decision making. Australia lags behind the rest of the world in implementing this combination of communication skills and evidence-based practice.[25,26,35] It is especially appropriate in decision making about antibiotic use for ARIs, where the benefits and harms are nearly balanced and, therefore, patient preferences become prominent.[25] Trials of shared decision making for antibiotic use in ARIs show that this approach is effective at reducing antibiotic use[24] (Box 1). However, existing interventions are difficult for GPs to adopt, as few would afford the time and costs of learning how. Brief patient decision aids are a tool to support

1 Interventions to support the reduction of antibiotic prescribing in Australian general practice

Intervention	Details	Effect size estimates	Comment
Regulatory interventions			
Repeats for antibiotics	Make the default "no repeat" prescriptions	Untested, therefore unknown, but likely to be small	Regulatory options are likely to produce a small but important reduction in prescribing
Conserving some antibiotics by restricting access	Make some antibiotics (eg, fluoroquinolones) more difficult to prescribe by using PBS restrictions (specific indications), or restricting some to authority to prescribe. However, introducing restrictions on a target antibiotic may result in increased use of unrestricted ones	Rates of fluoroquinolone use and resistance are low in Australia compared with equivalent countries (from ecological rates of use and resistance)[17]	This access restriction can only affect expensive antibiotics (or GPs could simply prescribe privately to avoid authority to prescribe requirements)
Changing the packaging	Matching the dose (number of tablets or capsules) to guidelines for common indications	Untested, therefore unknown, but likely to be small	Pharmacists may resist pack breaking
Audit and feedback	Antibiotic prescribing data are currently collected by PBS and fed back to GPs individually and confidentially, compared with norms of other peers	There is evidence of generic effectiveness of a small increase (4–5%) in clinician use of desired activity (more if the baseline performance is low and the audit and feedback is repeated),[20] but has been trialled only among other interventions for antibiotic reduction Currently used in several strategies in national educational programs	
Personal letter to GPs from an authoritative figure	Letter from a senior government medical doctor (eg, the Commonwealth Medical Officer) to high prescribers	3% decrease (95% CI, 2–4%) if sent to 20% top-prescribing practices.[21] Whether repeating several times usefully increases the response is unknown	Implemented in Australia in 2017
Activities that GPs can individually implement			
Delayed prescribing	An adversarial relationship with the patient is avoided by offering prescriptions to patients who are inappropriately insistent on an antibiotic, but suggesting it should not be dispensed unless symptoms worsen or fail to improve after a specified time	62% (95% CI, 34–75%) reduction in antibiotic prescribing (in a systematic review)[22]	Uptake very low in trials, but higher (13%) in UK observational studies[23]
Shared decision making	A combination of communication and evidence-based practice skills, in which the clinician explicitly evaluates the concerns, fears and expectations of the patient before detailing the benefits and harms of each management option (ie, antibiotics or none), and arriving at a shared decision that incorporates patient values and preferences[25,26]	18% reduction in antibiotic prescribing (in a systematic review)[24] A trial is underway in Australia using a brief intervention (provision of patient decision aids)[27]	Existing interventions trialled are expensive to implement. Less lengthy interventions are needed to facilitate uptake by Australian GPs
"Nudge" techniques	Public declaration displayed in the practice of commitment to conserving antibiotics, together with supplemental information to patients	20% reduction in inappropriate antibiotic prescribing, but from only a single RCT.[28] This needs replicating in other settings	GPs have to overcome only a few barriers to implement these techniques quickly
Voluntary audit and feedback activities	Self-audit tools for the collection, feedback and reflection on management of respiratory tract infections[29] MedicineInsight general practice reports on antibiotic prescribing in comparison with various indicators[15]	Unknown, and as yet untested in trials for antibiotic prescribing[20]	
Supporting GPs' access to near-patient diagnostic testing			
CRP	A means of identifying patients at risk of serious bacterial infection	A systematic review of observational and cluster randomised trials suggests a reduction in prescribing of ~ 19%[30] Training is quite quick: < 1 hour[31]	All near-patient testing may add costs to the consultation, which would be difficult to ask either patients or their GPs to pay for
Procalcitonin		A Cochrane review included two trials in primary care (~ 1000 patients), which achieved a 40% reduction in prescribing[30,31]	
Streptococcal tests	Serological test kits can detect whether group A β-haemolytic streptococcus is causing a sore throat	A systematic review found the evidence contradictory[32]	
Public awareness campaigns			
Community education	Campaigns communicated through multiple media channels to raise awareness of the dangers of antibiotic resistance, that not using antibiotics dissipates resistance and that antibiotics are not needed for common colds and influenza NPS MedicineWise already invests many resources in campaigns each winter	As an example, the French campaign *Les antibiotiques c'est pas automatiques* (ie, antibiotics are not automatic), together with other intervention effects (ie, academic detailing and supporting near-patient testing), reduced antibiotic prescribing by > 25%, but the costs were high: €500 million	Costs can be very high to achieve broad reach and impact[33]

CI = confidence interval. CRP = C-reactive protein. GP = general practitioner. PBS = Pharmaceutical Benefits Scheme. RCT = randomised controlled trial. UK = United Kingdom. ◆

shared decision making conversations and summarise and clearly communicate the evidence of benefits and harms of using and not using antibiotics. These decision aids may be effective and easy to implement[36] and are currently being trialled in Australia.[27]

"Nudge" techniques. These techniques are small behaviour changes that may deliver greater gains. In one randomised trial, GPs declared their commitment to antibiotic conservation in a signed poster with a picture of the GP displayed in the practice. Together with additional information available to provide to patients, this technique reduced antibiotic use[28] (Box 1).

Voluntary audit and feedback activities. NPS MedicineWise has free electronic audit tools available to GPs to collect feedback and reflect on their management of ten consecutive patients with respiratory tract infections. More rigorously, GPs in practices participating in the MedicineInsight program, in which data are routinely extracted and de-identified from electronic patient records, have access to more detailed reports about their prescribing in comparison to their peers.[15] This access to data reduces any confounding of changing diagnostic thresholds that bedevil documenting the management of ARIs.[37]

Symptom management. Practical advice on managing symptoms may be offered as an alternative to prescribing antibiotics, which may also manage the patient's expectation of a prescription (ie, "filling the therapeutic vacuum").[38]

Supporting GPs' access to near-patient diagnostic testing

One of the concerns GPs face is diagnostic uncertainty. Although almost all ARIs are safe to manage with expectant observation, every GP knows that in the next patient presenting with an ARI, the condition may be the precursor to or the early stages of a more sinister illness, such as meningococcal meningitis, community-acquired pneumonia, peritonsillar abscess, mastoiditis and even the non-suppurative complications of acute rheumatic fever, or acute glomerulonephritis. Clinical decisions can be supported by near-patient testing and diverse methods, such as streptococcal tests, C-reactive protein and procalcitonin, have been trialled with mixed success[30,31] (Box 1). Some countries (eg, Denmark) have invested in this technology wholesale. However, the acceptability to clinicians and patients has been poorly studied in Australia, and it is uncertain whether there would be political support for an increase in the cost of GP consultations — which may about double with near-patient testing — when antibiotics remain inexpensive.

Public awareness campaigns

Community education is essential in supporting the shift of GPs' attention to reduced antibiotic prescribing. One concern is that GPs feel pressure to prescribe because of their perception that many patients expect antibiotics more often than is indicated, believing that antibiotics reduce symptom duration more than they actually do.[39] GPs place a high value on rapport with their patients — for clinical, as well as financial reasons, in open-access and fee-for-service primary care. This perception may often be wrong — a good reason for employing shared decision making — but, nonetheless, some patients certainly expect antibiotics more often than is realistic. NPS MedicineWise has conducted several consumer campaigns to change these community expectations, using simple advertising and innovative social media campaigns (http://i2p.com.au/nps-media-releases-antibiotic-resistance). A social marketing approach has been used, including strategies that leverage collectivism, use a social norms approach, nudge theory, gamification, celebrity endorsement and cocreation. Consumer campaigns have been implemented mainly during winter, and include the use of traditional media, social media, television (including in GP waiting rooms), magazines, newspapers, outdoor advertising and short film competitions. A sustained, concerted, effort on public awareness is needed to effect change.[33,40]

Unanswered questions

In addition to the interventions described, more research is necessary to answer a myriad of unanswered questions (Box 2). Many of the interventions listed need testing in Australia's fee-for-service environment. In particular, we need to understand the passage of antibiotic resistance from patients treated in the community to where this resistance does the most harm: in hospital

2 Unanswered questions to further inform strategies in Australian general practice to reduce antibiotic resistance

Sets of unanswered questions	How unanswered questions may inform strategies to reduce antibiotic resistance
What is the relationship between antibiotic use and the development of antibiotic resistance? How does this change with different antibiotics used?	A central assumption in the imperative to reduce prescribing is that use causes resistance. This has shown to be true for some antibiotics and some infections.[6] However, use does not always induce resistance (eg, penicillin for the group A streptococcus of sore throats)[6]
What are the effects of antibiotics against common uncomplicated skin infections (eg, cellulitis) and urinary tract infections (eg, in pre-menopausal women)	In contrast to the evidence for acute respiratory infections, which is substantial, there are few trials of antibiotics against placebo for skin and soft tissue infections, or urinary tract infections[41,42] These two indications are also common reasons for antibiotic use in primary care, and being able to quantify the benefits and harms would enable better decision making
Are interventions that are effective in trials conducted in international settings (Box 1) as effective in Australia?	In Australia, there are some specific health service characteristics (eg, fee-for-service funding of primary care, a disconnection in funding for primary care and hospital services, and lack of patient registration to general practices) that may affect the effectiveness of approaches trialled in other countries
What are the effective symptom management alternatives to antibiotics?	There is a long list of such potentially effective treatments, ranging from simple analgesics and systemic steroids to complementary and alternative medicines. The evidence is sparse on evaluating and quantifying their effects[43,44]
What approaches should be taken to deal with overprescribing of antibiotics in residential aged care facilities?	Studies have uncovered a very serious problem in some residential aged care facilities, with, for example, 40% of antibiotics being used without evidence of infection. There are specific challenges in caring for patients in these settings, with increased difficulties in making diagnoses, multiple carers and pathology services. The problems appear to be very different from mainstream general practice, with several workforce, logistical and cultural factors[45]

care.[2] What alternatives can be suggested to fill the "therapeutic vacuum" left by not offering antibiotics?

So far, the focus has properly been on ARIs because these are the conditions for which most antibiotics are prescribed. But another reason is that, historically, ARIs have the most evidence — in the form of randomised placebo controlled trials — about the benefits and harms of antibiotic use. For the two other major groups of indications for antibiotics in general practice (ie, skin and soft tissue infections and urinary tract infections), there are very few placebo controlled trials. There is some evidence that uncomplicated urinary tract infections in pre-menopausal women may be treated almost as effectively with non-steroidal anti-inflammatory drugs.[41,42] But in the main, GPs currently need to resort to pathophysiological and microbiological information to estimate the effect that antibiotics will have — an approach that led to overprescribing for ARIs in the past, until systematically reviewed placebo randomised trials showed that antibiotics have small benefits.

Conclusions

Extrapolating from the initiatives in other countries to decrease antibiotic usage and their impact on resistance, it is highly likely that reducing antibiotic use in Australian general practice will decrease antibiotic resistance. Therefore, it seems prudent to start practising antibiotic conservation now to proceed in parallel with any future new antibiotic class development.

There are two notable characteristics about the interventions described in this review. The first one is the diversity of potential interventions. We cannot be sure how their effects interact, but their different modes of action suggest that they are likely to be additive and possibly synergistic. Second, the effects accumulate slowly over the years. Data from Sweden, which has had a concerted drive against antibiotics in general practice to become one of the lowest antibiotic prescribers in the world, show that the gains are incremental, a steady few percentage reduction over many years.[5,46] The Medical Research Future Fund has prioritised an initial $5.9 million to support antimicrobial resistance research,[47] although what proportion of this fund will focus on reducing antibiotic use in the community remains to be seen. Strategies in Australia will require appropriate resources and implementation support for employing multiple modalities and a commitment for a sustained effort.

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