Antimicrobial Stewardship in General Practice

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Abstract

Background

Antimicrobial resistance (AMR) is a global problem exacerbated by use of antibiotics. In 2017, 41.5% of the Australian population consumed one or more systemic antibiotics; these were mostly prescribed by general practitioners (GPs). Australia's antibiotic consumption is higher than in similar countries, without a clear reason. Unnecessary use has been demonstrated, particularly for upper respiratory tract infections. Antimicrobial stewardship (AMS) aims to promote the appropriate use of antimicrobials, optimise patient's outcomes and reduce unintended consequences of antibiotic use, such as AMR. AMS is yet to be widely implemented in Australian general practice and more information is required to guide the best way forward.

Aim

To develop a framework to guide the implementation of AMS in general practice in Australia.

Methods

Three studies were conducted:

1. Quantitative analysis of a general practice dataset (MAGNET) to determine its utility for monitoring general practice antibiotic prescribing.

2. A scoping review to identify the core components of approaches to AMS in general practice in similar countries.

3. Key stakeholder interviews to determine the validity and feasibility of a proposed framework incorporating the core components identified for future implementation in Australian general practice.

The studies were integrated in a partially mixed, equal status, mixed methods design using a human factors engineering approach with insights from complexity science.

Results

The quantitative analysis showed that general practice data as it currently exists is only partly suitable for the monitoring of antibiotic prescribing. While it provides more information than dispensed prescription data, it lacks enough reason-for-prescription data to fully assess guideline concordance.

The scoping review identified six components necessary for AMS which were subsequently incorporated into a proposed framework: governance; monitoring; education; consultation support; pharmacy and nursing support; and research.

Stakeholders regarded the proposed AMS framework as comprehensive, with the components feasible and valid for Australian general practice. The framework was perceived as providing a structure to drive the objectives of Australia's National AMR Strategy 2020 into action. Governance and meaningful monitoring were perceived to be lacking.

Conclusions and implications

This research has successfully identified a framework of six components to guide AMS into general practice. The lack of a recognised governance structure to drive AMS implementation, and a system to monitor antimicrobial prescribing which includes prescribing guideline concordance and patient outcomes were identified. Other gaps include regular public awareness/education campaigns in a range of languages, formats and media, which may help reduce antibiotic demand. Integrated decision support may assist GPs by providing easy access to recommended prescribing guidelines and approved patient education resources. The role of community pharmacies and practice nurses in AMS has been largely unexplored in Australia, but this research has highlighted potential AMS roles for patient triage, education and delayed prescribing strategies. Research is required to further develop an evidence-base for these interventions. Australia needs to urgently develop a collaborative approach to lead AMS in general practice; an improved or innovative infrastructure for monitoring of antimicrobial prescribing; and evidence-based alternatives to antibiotic prescribing to address the problem of AMR – this work informs that process.

Declaration

This thesis is an original work of my research and contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Print Name: Lesley Hawes Date: 20 July 2020

Thesis including published works declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes two original papers published in peer reviewed journals and two submitted publications. The core theme of the thesis is antimicrobial stewardship in general practice. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the Department of General Practice under the supervision of Professor Danielle Mazza and Professor Kirsty Buising of the National Centre for Antimicrobial Stewardship.

This thesis has not been submitted to an editor.

In the case of Chapters 3, 4 and 5 my contribution to the work involved the following:

Thesis Chapter	**Publication Title**	**Status**	**Nature and % of student contribution**	**Co-author name(s) Nature and % of Co-author's contribution**	**Co-author(s), Monash student Y/N**
3	Use of electronic medical records to describe general practitioner antibiotic prescribing patterns	Published	70% Conducted the background literature review and review of current monitoring datasets, contributed to the study design, conducted all data analyses; conceptualised, drafted and revised the manuscript.	**Lyle Turner** (10%) Ethics approval, collection of the dataset. Contributed to the study design and data analysis, input into final stages of manuscript preparation. **Kirsty Buising** (10%) Contributed to the study design and data analysis, provided critical feedback on manuscript. **Danielle Mazza** (10%) Ethics approval, contributed to the study design and data analysis, provided critical feedback on manuscript.	No
3	Workflow-based data solutions are required to support antimicrobial stewardship in general practice	Published	70% Conducted the background literature review, contributed to the study design, conducted data analyses; conceptualised, drafted and revised the manuscript.	**Lyle Turner** (10%) Ethics approval, collection of the dataset. Contributed to the study design and data analysis, input into final stages of manuscript preparation. **Kirsty Buising** (10%) Contributed to the study design and data analysis, provided critical feedback on manuscript. **Danielle Mazza** (10%) Ethics approval, contributed to the study design and data analysis, provided critical feedback on manuscript.	No

4	Antimicrobial stewardship in general practice: a scoping review of the component parts	Published	70% Conducted the background literature review, contributed to the study design, collected data, conducted data analyses; conceptualised, drafted and revised the manuscript.	**Kirsty Buising** (15%) Contributed to the study design and data analysis, provided critical feedback on manuscript. **Danielle Mazza** (15%) Ethics approval, Contributed to the study design and data analysis, provided critical feedback on manuscript.	No
5	Building a framework for antimicrobial stewardship in general practice: Key stakeholder interviews	Submitted for publication	70% Conducted the background literature review, contributed to the study design, conducted all interviews, conducted data analyses; conceptualised, drafted and revised the manuscript.	**Kirsty Buising** (12.5%) Contributed to the study design and data analysis, provided critical feedback on manuscript. **Danielle Mazza** (12.5%) Ethics approval, contributed to the study design and data analysis, provided critical feedback on manuscript. **Jaclyn Bishop** (5%) Data analysis, critical feedback on manuscript	No

I have not renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Additional publications and presentations

Additional peer reviewed publications

1. Yan J, **Hawes L**, Turner L, Mazza D, Pearce C, Buttery J. Antimicrobial prescribing for children in primary care. J Paediatr Child Health 2019; 55(1):54-8.

2. Saha SK, **Hawes L**, Mazza D. Improving antibiotic prescribing by general practitioners: a protocol for a systematic review of interventions involving pharmacists. BMJ Open 2018; 8: e020583.

3. Saha SK, **Hawes L**, Mazza D. Effectiveness of interventions involving pharmacists on antibiotic prescribing by general practitioners: a systematic review and meta-analysis. J Antimicrob Chemother 2019; 74: 1173-81.

4. Buising K, Rajkhowa A, Mazza D, **Hawes L.** Antimicrobial stewardship in the community: understanding the data. Med Today 2019;20(4):43-5.

Presentations

International peer-reviewed conference presentation

Date	**Conference**	**Presentation details**
3 July 2019	Society for Academic Primary Care, annual conference. Exeter, England	**Lesley Hawes,** Kirsty Buising, Danielle Mazza. Antibiotic stewardship in general practice: a scoping review of the component parts. (Poster with oral presentation)

National peer-reviewed conference presentations

Date	Conference	Presentation details
4 May 2017	Choosing Wisely national meeting, Melbourne.	**Lesley Hawes**, Lyle Turner, Kirsty Buising, Danielle Mazza. *An Examination of Antibiotic Prescribing Patterns in Australian General Practice*. (Poster)
7-9 Aug 2017	Primary Health Care Research & Information Service (PHCRIS) Research conference, Brisbane.	**Lesley Hawes**, Lyle Turner, Kirsty Buising, Danielle Mazza. *An Examination of Antibiotic Prescribing Patterns in Australian General Practice.* (Oral presentation)
		Jennifer Yan, **Lesley Hawes**, Lyle Turner, Danielle Mazza, Jim Buttery. *Antimicrobial prescribing patterns for children in primary care.* (Poster)
2 Aug 2018	Primary Health Care Research & Information Service Research conference, Melbourne	**Lesley Hawes**, Lyle Turner, Kirsty Buising, Danielle Mazza. *Reasons for Antibiotic Prescriptions Needed for Antimicrobial Stewardship in General Practice.* (Poster with 5 min oral presentation)
24 Oct 2019	GP19 annual conference, Adelaide	**Lesley Hawes**, Kirsty Buising, Danielle Mazza. Antimicrobial stewardship components in GP: scoping review. (Oral presentation)

Other presentations and radio interview

Date	Conference	Presentation details
9 Nov 2016	National annual AMR and AMS forum, Melbourne.	**Lesley Hawes**, Lyle Turner, Kirsty Buising, Danielle Mazza. *Antimicrobial Stewardship in General Practice.* (Oral presentation and poster)
25 Sept 2017	Monash SPAHC Research Showcase, Peninsula campus.	**Lesley Hawes**. Analysis of GP Antibiotic Prescriptions – Antimicrobial Stewardship. (Oral presentation)
3 Nov 2017	National annual AMR and AMS Forum, Brisbane.	**Lesley Hawes,** Lyle Turner, Kirsty Buising, Danielle Mazza**.** *Analysis of Antibiotic Prescribing Patterns in General Practice.* (Poster)
6 Dec 2017	National Centre for Antimicrobial Stewardship (NCAS) Journal Club	**Lesley Hawes.** *Antibiotic use in general practice*.
17 Sept 2018	NCAS Journal Club	**Lesley Hawes.** *Reducing antibiotic prescribing in general practice.*
29 Oct 2018	Radio 3CR	Radio interview to promote the 2018 Annual AMR and AMS forum, organised by NCAS.
20 Mar 2019	NCAS Journal Club	**Lesley Hawes** *Antimicrobial stewardship in general practice: Lessons learned in Sweden's Strama program*

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I would like to thank the interviewed stakeholders who volunteered their extensive knowledge and experience in the interviews. You were incredibly generous and demonstrated your commitment to improving antimicrobial stewardship in general practice. Thank you to the library staff at Monash University, whose advice was invaluable for conducting the scoping review (particularly Anne Young).

To my children, thank you for your support. You have both been so encouraging; it has kept me going when things have not gone so well. Sarah, I loved that we could study together in ‘Shut up and Write’ sessions and that somehow, you often ended up cooking and looking after me when we visited each other. Congratulations on obtaining your Master of Applied Learning and Teaching! William, your practical support cooking meals, keeping the house running especially while I have been away at conferences, and cleaning up after the flood and the massive hailstorm damage has been greatly appreciated.

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To my friends, particularly Vicki, Meegan and Robyn, thank you for all your encouragement and practical support.

Abbreviations

ACRRM	Australian College of Rural and Remote Medicine
ACSQHC	Australian Commission on Safety and Quality of Health care
AIHW	Australian Institute of Health and Welfare
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
ARGG	The Antimicrobial Resistance Governance Group
ASTAG	Australian Strategic and Technical Advisory Group on AMR
AURA	Antimicrobial Use and Resistance in Australia report
BEACH survey	Bettering the Evaluation and Care of Health survey
DGP	Department of General Practice
EMR	Electronic medical record
GP	General practitioner
MAGNET	**M**elbourne East Mon**A**sh **G**e**N**eral Practic**E** Da**T**abase (now POLAR)
NCAS	National Centre for Antimicrobial Stewardship
NPS MedicineInsight	National Prescribing Service MedicineInsight program
NPS MedicineWise	National Prescribing Service MedicineWise service
OECD	Organisation for Economic Co-operation and Development
PBS	Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme
PHN(s)	Primary Health Network(s)
POLAR	POpulation Level Analysis and Reporting for general practice
RACGP	Royal Australian College of General Practitioners
RTI	Respiratory tract infection
SEIPS	Systems Engineering Initiative for Patient Safety
RTI	Respiratory tract infection
TGA	Therapeutic Goods Administration
WHO	World Health Organization

Definitions

ACSQHC	A leader and coordinator in the safety and quality of health care.
Antibiotic	A drug that kills or suppresses the growth of bacteria.
Antibiotic resistant/resistance	Bacteria that survive exposure to an antibiotic that would normally kill or slow their growth. Resistance may be transmitted between bacteria.
Antimicrobial agent	A drug that kills or suppresses the growth of microorganisms: antibiotics (kills or suppresses bacteria); antiviral (viruses); antifungal/antimycotic (fungi); antiparasitic (parasites).
Antimicrobial resistant/resistance	Microorganisms (bacteria, viruses, fungi, parasites) that survive exposure to an antimicrobial agent that would normally kill or slow their growth.
Antimicrobial stewardship	The safe and appropriate use of antimicrobials to reduce harm while also curtailing the incidence of antimicrobial resistance.[1]
AURA reports	Public reports on antimicrobial use and AMR in human health.
Consumers Health Forum	The Consumers Health Forum of Australia (CHF) is the national peak body representing the interests of Australian healthcare consumers. CHF works to achieve safe, quality, timely healthcare for all Australians, supported by accessible health information and systems.[2]
General practice	A part of the primary health care system that provides person centred, continuing, comprehensive and coordinated whole person health care to individuals and families in their communities.[3]
General practitioner	A medical specialist who is typically an individual's first point of contact with the health system and usually works in a general practice.
MAGNET	A research database containing anonymised electronic medical records of patients from 50 general practices across Melbourne's inner east. These practices are from one Medicare Local (now Primary Health Network).
Microbiota	The microorganisms living in and on all humans, plants and animals. They include bacteria, fungi, viruses and parasites.
NPS MedicineInsight	MedicineInsight is a national medicine quality improvement program funded by the Australian Department of Health and managed by NPS MedicineWise. It collects de-identified data from a cohort of GP electronic clinical records and provides public reporting to AURA and peer comparison feedback to GPs.
NPS MedicineWise	(Previously the National Prescription Service) is an independent government funded consumer-centred service that promotes quality the use of medicines.
Optimal or appropriate treatment	Optimal or appropriate treatment means treating patients with the right antibiotic to treat their condition, at the right dose, by the right route, at the right time and for the right duration based on accurate assessment and timely review.[4]
Primary health care	The first level of the health care system; addresses community health problems.
Primary Health Networks	Government funded independent organisations to commission and support local health care services.[5]
Private prescription (off-label)	A prescription for a drug other than for which it was registered. This may be a different disease, route of administration, course length, and/or dose. The cost of a private prescription is borne by the patient; there is no PBS subsidy.

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Chapter 1 Background literature

In this chapter, I first present an overview of the linked problems of antimicrobial resistance (AMR) and the use of antimicrobial agents. To control AMR, antimicrobial stewardship (AMS) was developed; AMS is established in hospitals but still in development for Australian general practice. I then provide an overview of Australian general practice including its standards and the difficulties around AMS in general practice. I have limited the literature to countries similar to Australia where antibiotics are predominantly available by prescription only and are of a guaranteed standard. I will not discuss the related area of infection prevention and control, nor the use of disinfectants. This thesis will principally refer to antibiotics (which are active against bacteria) and antibiotic resistance, but the findings are relevant to other antimicrobial agents (including antiviral, antifungal, antihelminthic, and antiparasitic agents).

1.1 Antimicrobial resistance in the Australian community

Since it was first recognised, antimicrobial resistance AMR has been a problem that spans the community, however early discussions of the problem tended to focus solely on the hospital-based impacts. The impact of AMR on pathogens causing common community-based infections is now being more widely appreciated.

Australia has a newly developed monitoring system for AMR - the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System – established in 2014 and reporting in 2016, 2017 and 2019.[6-8] From these reports examples of some of the contemporary problems with AMR in Australia can be described. Three common community-acquired pathogens which cause significant disease that are reported in AURA are: *Neisseria gonorrhoeae (N. gonorrhoeae*), *Staphylococcus aureus (S. aureus)*, and *Streptococcus pneumoniae* (*S. pneumoniae*) illustrate some of the emerging issues.

N. gonorrhoeae, the cause of the sexually transmitted infection gonorrhoea, is increasingly resistant to the antibiotics used to treat it. Azithromycin resistance has increased from 2.6% in 2015 to 9.3% in 2017. Penicillin and ciprofloxacin resistance remain stable at about 30% of isolates.[8] Standard treatment is now with two antibiotics.[9] In 2018 two cases of multi-drug resistant gonorrhoea, resistant to all standard antibiotic therapy, were detected in Australia.[10] If antimicrobial therapies are not effective, infections will be more readily transmitted leading to major increases in case numbers, and subsequent public health impact.

S. aureus causes both minor and serious infections. Some minor infections, such as many skin infections, (e.g. boils) may be managed without antibiotics, but serious infections including bone and joint infections, pneumonia, and septicaemia (infection in the blood) require urgent effective antibiotic treatment to avoid significant patient morbidity and mortality. Resistance to methicillin/flucloxacillin amongst *S. aureus* (MRSA) has emerged as a major problem in Australia,[11 12] and was detected first in hospitals during the 1970s and then in the community.[6 8 13] Infections with MRSA are associated with poorer clinical outcomes than *S. aureus* infections which are susceptible to flucloxacillin.[14 15] The rates of MRSA in Australia are higher in Australia compared with other countries[6] and the incidence varies by state. MRSA is only notifiable in Tasmania (where it is least prevalent), so there is a lack of accurate data on its prevalence in other states. Passive surveillance data shows that community acquired MRSA may be more common in regional and rural areas than in metropolitan areas.[16] Nationally, 19.1% of community *S. aureus* isolates in 2017 were MRSA, but in remote and very remote areas the percentage rose to over 40%.[8] This impacts upon the likelihood of efficacy on first line antibiotic treatments for many common infections, and guidelines do need to vary by region to match local epidemiology.

S. pneumoniae causes a range of infections including pneumonia, acute otitis media (ear infection), acute sinusitis, meningitis and septicaemia. *S. pneumoniae* has increasing rates of resistance to penicillin, and resistance to erythromycin and trimethoprim–sulfamethoxazole is now over 20% and clindamycin at 19.5% of community isolates.[8] This impacts upon the likelihood of first line antibiotic treatments being effective.

Travel is a risk factor for multi-drug resistant infections[17] such as typhoid fever,[18] or common pathogens causing urinary tract infections which may be brought in by visitors or returning residents. Travellers may also acquire drug resistant organisms in their intestines (asymptomatic carriage), especially if they have been to areas with high levels of resistance or if they have been hospitalised.[17 19-21] These organisms are then brought into Australia and may be transmitted e.g. by improperly washed hands after toileting.

The costs of AMR infections to individuals and society are high, and these costs may be measured clinically and economically. Infections caused by AMR pathogens often result in the need to use less effective antibiotics or antibiotics with higher toxicities, leading to prolonged illness and poorer outcomes. Some people die from the delay in adequate treatment or from infection-related complications.[22 23] There is an economic cost to the increased length of sickness and time off work, the prolonged treatment and any hospitalisation. It is estimated that by 2050 AMR associated infections are likely to kill 10 million people a year – which is more than deaths from cancer and diabetes combined - and will cost the global economy up to $US 100 trillion.[24]

1.2 The association between antimicrobial use and resistance

A major factor contributing to AMR is exposure of microbes to antimicrobial agents.[25-30] Unlike other drugs which affect only the individual, antimicrobial agents can exert an effect beyond the individual. Antimicrobial agents may cause genetic changes in microbes to make them resistant to that agent.[27 31] Resistance may be induced by selective pressure e.g. increasing resistance gene expression (such as beta-lactamase), altering the antibiotic's target, or by increasing the efflux of the antibiotic.[30] There is some evidence from animal models that once resistance has evolved, it may be perpetuated by exposure to antibiotics other than the inducing antibiotic.[26] The continued use of antimicrobial agents amplifies the number of AMR microbes present, which may then be transmitted between humans, animals and the environment.[32-39] Microbes may also spread the genes for resistance to other microbes – even between bacteria of different species.[30 40 41] This spread of genes and microbes has led to the global problem with AMR. Some antibiotic resistant genes may persist for years, even without additional antibiotic use.[42] The development of new antibiotics has stagnated, which has compounded the problem of combating bacterial antibiotic resistance.[43-46]

1.2.1 Reducing antibiotic use reduces resistance and is safe for patients

International evidence from hospitals and the community suggests that antibiotic use may safely be reduced, and that reduced use reduces colonisation and infections with AMR organisms. The proportion of patients prescribed antibiotics for self-limiting respiratory tract infections (RTI) in 610 general practices in the UK has decreased over time. For male patients, it has decreased from 53.9% in 2005 to 50.5% in 2014 and in females from 54.5% to 51.5%. Over that time, new episodes of pneumonia increased by 0.4%, but new episodes of meningitis, mastoiditis, and peritonsillar abscess decreased annually by 5.3%, 4.6%, and 1.0%, respectively.[47] In a similar study in Sweden using an administrative database of 2.3 million people (about 23% of the population), data from patients with a diagnosis of acute otitis media, tonsillitis, sinusitis or acute upper respiratory tract infection were examined for complications and antibiotic use. Antibiotic use for respiratory tract infections fell by 22% in volume between 2006-15, with no significant trend in mastoiditis, peritonsillar abscess, invasive group A streptococcal disease, orbital abscess, extradural and subdural abscesses or pansinusitis.[48] In Wessex, England between September 1994 and May 1996, an 11 practice open randomised trial comparing an immediate prescription with a delayed or no prescription for managing sore throat in 714 patients aged 4 years and over who were otherwise healthy, showed no associated increase in early return or complications for those not given the immediate prescriptions. The patient survey showed that patients given the immediate prescription were more likely to believe that antibiotics were effective and were more likely to intend returning for future episodes of sore throat. Patient satisfaction was highest for those given immediate antibiotics but was also closely related to managing patients concerns.[49] Limiting the community prescribing of fluoroquinolones and clindamycin in North East Scotland reduced total *Clostridioides difficile* (*C. difficile*) community infections. There was a threshold effect, past which higher use of these antibiotics was associated with more infections.[50] *C. difficile* is a common cause of antibiotic-associated diarrhoea. Hypervirulent strains have emerged, including in Australia, which have been associated with severe diarrhoea and death.[51]

The impact of reduced antibiotic prescribing on the rate of AMR colonisation and infection is harder to measure. Hospital modelling predicts that a reduction of antibiotic use may reduce AMR organism transmission.[52] The implementation of hospital AMS programs has been associated in time with reduced colonisation rates and, in some cases, reduced infections with AMR bacteria and *C. difficile*.[53-57] Reduced antibiotic prescribing in Sweden's primary care between 1993 and 2005 was associated with steadying the prevalence of penicillin resistant pneumococci and beta-lactamase producing *Haemophilus influenzae*. While not quantified, the authors stated that hospital admissions for pneumonia decreased for all ages and there were "no signs" of an increased frequency of mastoiditis, quinsy, or rheumatic complications of streptococcal infections.[58] In Scotland, in a study of community-associated coliform bacteraemia, reduced prescribing of cephalosporins was followed in 1.5 years by a flattening in the resistance rates of the coliforms while the reversal of the rising rates of fluoroquinolone resistance took 3.5 years. There was no significant effect in the reduction of resistance to amoxicillin-clavulanate over the 3.5 years, but its use remained high.[59] Interestingly, Levy in 1994 proposed a threshold effect, where low use of an antibiotic affects the individual, but increased use of an antibiotic affects the environment. Levy postulated that if total antibiotic use could be kept below a threshold, this would enable use of the antibiotic while managing AMR.[60] There may be a threshold effect, where resistance rates increase after a certain level of antibiotic use, but more research is needed to study this further.[50 57 61]

1.3 The development of antimicrobial stewardship

The term antimicrobial stewardship was promoted widely after recommendations made by the Infectious Diseases Society of America (IDSA) in 2007. IDSA's stated primary goal of AMS was "to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as *C. difficile*), and the emergence of resistance."[62] In Australia, AMS has been defined as "coordinated actions designed to promote and increase the appropriate use of antimicrobials and is a key strategy to conserve the effectiveness of antibiotics;"[63] and "the safe and appropriate use of antimicrobials to reduce harm while also curtailing the incidence of antimicrobial resistance."[1] The World Health Organization

(WHO) defines the appropriate use of antimicrobials as “the cost-effective use of antimicrobials which maximises clinical therapeutic effect while minimising both drug-related toxicity and the development of antimicrobial resistance.”[64]

An early global AMS initiative occurred in 1998, when the World Health Assembly developed a Resolution that urged Member States to encourage the appropriate use of antimicrobials, detect resistant pathogens and to monitor volumes and patterns of antimicrobial use.[64] Also in 1998, in Australia the Joint Expert Advisory Committee on Antibiotic Resistance (JETACAR) was appointed by the (then) Commonwealth Departments of Health and Aged Care, and Agriculture, Fisheries and Forestry.[65] The JETACAR report noted that resistance existed to all known antibiotics in use, that resistance genes were present in hospitals and farms, and that AMR bacteria and their resistance genes were being amplified by antibiotic exposure. It described selection pressure for the development of AMR being higher with long-term antibiotic exposure and with treatment of large numbers of humans or animals, than with short-course treatment of one or a few individuals. Most human use of antibiotics was found to be for the treatment of minor infections, with respiratory tract infections singled out as having mostly unnecessary antibiotic treatment. There was also broader spectrum prescribing than appeared necessary. JETACAR proposed an antibiotic-resistance management program with five key elements for a coordinated multidisciplinary approach to both human and veterinary medicine:

1. Regulatory controls (Recommendations 1-9)
2. Monitoring and surveillance (Recommendations 10 and 11)
3. Infection prevention strategies and hygienic measures (Recommendations 12-14
4. Education (Recommendations 15-17) and
5. Further research (Recommendation 18).

There were several more detailed recommendations made; those that are relevant to this research are provided below (with the number assigned in the JETACAR report):

1. A conservative approach to minimise the use of antibiotics (is recommended).
6. That all antibiotics for use in human and animals be classified as S4 (prescription only).
10. That a comprehensive surveillance system be established incorporating passive and active components measuring incidence and prevalence of antibiotic-resistant bacteria and resistance genes.
11. That a comprehensive monitoring and audit system for antibiotic usage be established that covers all areas of antibiotic use.
15. That prudent use codes of practice for antibiotics be developed and regularly updated by medical and veterinary peak bodies.

16. That regularly updated ‘antibiotic use guidelines’… supported and endorsed by the appropriate professional organisations… are widely disseminated and adopted as a ‘standard of care’.
17. (That) learned and professional societies develop continuing educational programs on the issue of antibiotic resistance, including a focus on the prudent use principles, antibiotic use guidelines and alternatives to antibiotic usage.
19. That an ongoing funded education strategy be developed… to provide appropriately targeted information about infection, the role and benefits of prudent antibiotic use and the risks of overuse to the public, relevant professional bodies and stakeholders.
20. That a recognised expert authority… assume responsibility for… the communication of data on antibiotic usage…
21. The coordination of efforts of professional, regulatory and industry bodies… will require the formation of an overarching, multidisciplinary, credible and independent authority.[65]

A Senate enquiry was established in 2013 to examine the failure to act on the recommendations of the JETACAR report. A progress review in 2013 found that most recommendations had not been actioned. Australia’s approach to AMR was described as fragmented, as “no one agency, or minister was responsible or accountable.” Further, “unlike other countries, Australia had no overall coordinated approach to this major problem, and that the response to this threat was disparate, under resourced and therefore likely to be ineffective.” [66]

> *The JETACAR report was too far ahead of its time. It really did not resonate with people. It had a lot of foresight in identifying what was going to become a problem, but it did not translate into genuine awareness in the community and among policy makers as to the fact that an ounce of prevention was worth a lot of cure.*
>
> Professor Lindsay Grayson [66]

The progress review in 2013 made 10 recommendations which included (with the number assigned in the report):

1. … the Commonwealth establish an independent body or national centre, to develop a strategy, report publicly on resistance data and measures taken to combat antimicrobial resistance and to manage the response to antimicrobial resistance in Australia.
2. …the independent body be resourced to implement a rigorous monitoring and reporting regime of antibiotic use in humans and animals and of multiple drug resistant infections in humans and animals.
5. …the Australian Commission on Safety and Quality in Health Care consider mechanisms to improve coordination and tighten access to antimicrobials in healthcare services, particularly in relation to any new antimicrobials that become available.

6. …the Department of Health and Ageing investigate additional mechanisms to improve antibiotic stewardship in general practice.
10. …the Commonwealth consider measures to support research into strategies to deal with antimicrobial resistance, including research into new antibiotics and consideration of antimicrobial resistance being designated a National Research Priority Area.[66]

More recently, in March 2019, the Australian Government responded to the recommendations in the 2013 Senate inquiry (into the failure to respond to the JETACAR report recommendations). Included in this response, the Department of Health agreed that it should "investigate additional mechanisms to improve antibiotic stewardship (AMS) in general practice."[67] However, to date, no action has occurred.

Alongside this national activity, there has been complementary global activity on AMR and AMS. In 2015 the World Health Assembly adopted a Global Action Plan on AMR with five objectives:[68]

- to improve awareness and understanding of antimicrobial resistance through effective communication, education and training;
- to strengthen the knowledge and evidence base through surveillance and research;
- to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures;
- to optimize the use of antimicrobial medicines in human and animal health;
- to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions.[68]

On 21 September 2016, the United Nations General Assembly held a high-level meeting on antimicrobial resistance,[69] which was only the fourth time the United Nations had discussed a health topic at this level. Global leaders and Heads of State committed to develop national action plans on AMR, based on the 2015 Global Action Plan on AMR.[68]

Australia released its first National AMR Strategy in 2015: *Responding to the threat of antimicrobial resistance: Australia's first National Antimicrobial Resistance Strategy 2015-2019* (the Strategy)[63] and an Implementation Plan in 2016:[70] The Strategy had seven objectives, reproduced here in full:

1. Increase awareness and understanding of antimicrobial resistance, its implications, and actions to combat it through effective communication, education and training.
2. Implement effective antimicrobial stewardship practices across human health and animal care settings to ensure the appropriate and judicious prescribing, dispensing and administering of antimicrobials.
3. Develop nationally coordinated One Health surveillance of antimicrobial resistance and antimicrobial usage.
4. Improve infection prevention and control measures across human health and animal care settings to help prevent infections and the spread of antimicrobial resistance.
5. Agree a national research agenda and promote investment in the discovery and development of new products and approaches to prevent, detect and contain antimicrobial resistance.
6. Strengthen international partnerships and collaboration on regional and global efforts to respond to antimicrobial resistance.
7. Establish and support clear governance arrangements at the local, jurisdictional, national and international levels to ensure leadership, engagement and accountability for actions to combat antimicrobial resistance.[63]

All objectives are applicable to general practice. Australia’s first National AMR Strategy in 2015 noted that AMS outside hospitals was not well established and called for “best-practice, setting-specific approaches to AMS” and “structured AMS programmes” to be developed. (page 14)[63] It refers to the RACGP Standards for General Practice as encouraging AMS but notes that they are not as prescriptive as those for hospitals, that accreditation to the standards is voluntary, and that “additional approaches” are required.[63] Section 2.5 (page 15) has a list of suggested measures including: integrating guidelines into prescribing software, enhancing decision support tools, unit dispensing, and including monitoring, but does not describe how these will be achieved.

Australia's second national strategy, *Australia's National Antimicrobial Resistance Strategy 2020 and beyond*[1] was released in March 2020. It contains a vision and a goal:[1]

> Vision*: A society in which antimicrobials are recognised and managed as a valuable shared resource; and their efficacy is maintained so that the health of humans, animals and the environment is protected now and into the future.*
>
> Goal*: Minimise the development and spread of antimicrobial resistance and ensure the continued availability of effective antimicrobials.*

There are seven key objectives to guide all sectors:

1. Clear governance for antimicrobial resistance initiatives
2. Prevention and control of infection and the spread of resistance
3. Greater engagement in the combat against resistance
4. Appropriate usage and stewardship practices
5. Integrated surveillance and response to resistance and usage
6. A strong collaborative research agenda across all sectors
7. Strengthen global collaboration and partnerships[1]

The 2020 Strategy also recognises that there cannot be a "one size fits all" solution;[1] that responses must reflect the regulatory environment and the "needs and challenges of each sector". It was also expanded from a focus on antibiotics in the 2015 strategy to include all antimicrobials.

Systemic antibiotics in Australia are only available by prescription from a medical provider. A few, like the fluoroquinolone class, are further regulated to conserve their potency as a reserve antimicrobial, requiring an authority to prescribe for specific indications only.[71] However by 1977, staff in Melbourne hospitals recognised there was a problem with AMR infections and the inappropriate use of antibiotics. They agreed that antibiotic prescribing guidelines were required, and that prescribing advice needed to be evidence based, and free of the influences of industry, so they produced and published Antibiotic Guidelines in 1978.[72] These became the Therapeutic Guidelines: Antibiotic which have been regularly updated, informed by a wide selection of clinicians from varied disciplines. The guidelines have been in use for over 40 years and are generally well known and widely accepted by Australian clinicians. The content has been expanded to include other therapeutic areas and the guidelines are now available in an integrated online version.[9] Therapeutic Guidelines Limited is an independent not-for-profit organisation that does not receive government funding, so a subscription fee is charged to access the guidelines.[9]

To guide the development of AMS programs across the health system, in 2011 the ACSQHC published an evidence-based guidebook - Antimicrobial Stewardship in Australian Hospitals. This was followed in 2018 by Antimicrobial Stewardship in Australian Health Care - which provides the essential requirements and strategies for an AMS program in more varied settings. The essential elements for AMS programs were considered to include an AMS team of at least a doctor and a pharmacist, ongoing AMS education, implementation of clinical guidelines consistent with Therapeutic Guidelines: Antibiotic, optimal specimen collections for microbiology testing, and monitoring of antimicrobial use and outcomes. (Page 40)[73]

In Australia, campaigns promoting the responsible use of antibiotics have been run for many years by NPS MedicineWise (previously the National Prescription Service; an independent government funded consumer-centred service that promotes the quality use of medicines). Campaigns targeted the Australian population and health professionals from 2000-04,[74 75] and again from 2009-2015,[76] and were associated with increased awareness and reduced antibiotic use.[74 76] While apparently impactful, the funding for these campaigns has been intermittent.

In 2014, Australia’s Antimicrobial Stewardship Clinical Care Standard was released by the ACSQHC. It contains nine quality statements which aim to describe expectations for high quality and safe care when patients are provided with antimicrobial therapies. The Clinical Care Standard is intended to be relevant in all healthcare contexts including general practice. Optimal treatment is defined as “treating patients with the right antibiotic to treat their condition, the right dose, by the right route, at the right time and for the right duration based on accurate assessment and timely review.” (Page 3) Amongst other things this Clinical Care Standard recommends that all antibiotics are prescribed in accordance with Therapeutic Guidelines, taking into account the patient’s clinical condition and the results of any microbiology tests.[4]

1.4 Antibiotic prescribing in general practice

Worldwide, most antibiotics are supplied in the community setting,[77-81] including in Australia.[7] In 2017, over 41.5% (n=10,215,109) of the Australian population consumed one or more systemic antibiotics.[8] The Defined Daily Dose per 1000 population puts Australia's antibiotic consumption per capita above the OECD average; higher than in similar countries such as Canada, Netherlands, United Kingdom, Sweden and Austria.[8 82] In Australia approximately 75% of these community antibiotics are prescribed by GPs,[83] and there is a predominance of moderate- (66% of use) and broad-spectrum (25%) antibiotics prescribed over narrow-spectrum antibiotics (9%).[83] It is considered that broader-spectrum antibiotic use may contribute more to the development of AMR.[83] Upper respiratory tract infections are among the most frequently managed conditions in Australian general practice[84] and it has been estimated that antibiotics are overprescribed for many of these at rates 4 – 9 times higher than is recommended by Therapeutic Guidelines.[85] A detailed analysis of Australian GP antibiotic prescribing sources is provided in Chapter 3 of this thesis.

Variation in community antibiotic prescribing rates has been reported within[86 87] and between countries,[82 88 89] between clinicians and clinics[88 90] including in Australia,[91] across patient age groups,[92] by GP characteristics, and between diagnoses.[93 94] To understand the reasons behind variation both patient and clinician factors have been examined. A systematic review described seven determinants of antibiotic use in patients: demographic, patient-doctor interactions, treatment characteristics, attitudes, access to treatment, the conditions' characteristics, and knowledge.[95] Patient perceptions are important. Studies have suggested that the public do not fully understand the causes of AMR,[96] its implications,[97] do not believe that they contribute to its development,[98] and may incorrectly perceive themselves to be "low users" of antibiotics – "maybe twice a year".[97] A systematic review of clinicians' knowledge and beliefs around AMR showed that while 98% of clinicians believed AMR was a serious problem globally, 67% did not believe it was a problem in their practice, and had knowledge gaps about the mechanism of AMR development.[99] A survey of Australian GPs found that they were uncertain about the factors that increase AMR;[100] nearly half (46%) believed it is more of a hospital-based problem and 43% were neutral when asked if AMR could last up to 12 months after a single antibiotic use (it may).[100] An international review of 17 qualitative studies examining GP perceptions found that GPs wanted patients to feel satisfied and perceived a pressure for antibiotics, they were worried about diagnostic uncertainty and conditions worsening, and that it was quicker to write a prescription than to educate a patient.[101] An Australian study found that variables significantly associated with higher antibiotic prescribing were male GPs, male patients, patients aged between 1 and 14 years, and patients being new to the practice.[102] There is some evidence that overseas-trained trainee GPs prescribe more antibiotics than do Australian-trained trainee GPs.[103] However, GPs trained overseas see a different patient mix, manage different morbidities and provide different treatments (including more prescribed medications) than do Australian trained GPs.[104] There is also some evidence that female GPs prescribe fewer medications (all medications, not just antimicrobials).[105] In Sweden there was no significant difference in antibiotic prescribing between GPs trained in Sweden and those trained elsewhere – and no group prescribed according to national guidelines. In the UK, the strongest predictor of higher antibiotic prescribing behaviour was practice location in the north of England.[106] In Canada and the US, overseas trained physicians prescribed fewer broad-spectrum antibiotics than did those trained in Canada and the US. Thus, there are a range of patient and GP factors that may influence antibiotic prescribing and these factors may vary between GPs, practices, regions and countries. Until there is complete monitoring of antibiotic prescribing with GP, patient and practice characteristics, definitive conclusions cannot be made.

1.5 General practice in Australia

General practice is part of the community-based primary health care system, also known worldwide as ambulatory care, family medicine, family practice, office-based medicine or outpatients. (This use of "outpatients" is not to be confused with the Australian use of "outpatients" to describe hospital-based specialist clinics.) The Royal Australian College of General Practitioners (RACGP) defines general practice as providing "person centred, continuing, comprehensive and coordinated whole person health care to individuals and families in their communities."[107] Person- or patient-centred health care is "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions."[108] Patient-centred care emphasises the importance of the patient's experiences and preferences in the GP-patient consultation,[109] which may transcend evidence-based medicine.[110] For instance, patients present with comorbidities (47.3% of Australians had one or more chronic conditions in 2017-18; this rose to 80% in people aged 65 and over),[111] and have work, economic and cultural constraints as competing priorities.[112] Patients may present early in a disease, where diagnostic criteria are not clear,[112] or be treated by multiple specialists and receive conflicting advice or burdensome treatment plans. Their GPs are often the practitioners who prioritise and personalise the care to the patient.[113]

General practices in Australia are government funded on an activity basis, but are mostly small private businesses, owned by one or more GPs or by a corporate entity. They may charge the patient a limited range of fees.

1.5.1 Standards for general practice

The RACGP sets the Standards for General Practices[114] by which general practices may be accredited, and the National General Practice Accreditation (NGPA) Scheme[115] assesses practices against these standards. Accreditation is not compulsory, but over 6500 general practices are accredited[116] which is estimated to be 90% of general practices.[117] There is no information about the extent to which these AMS recommendations are followed

The Australian Standards for General Practices 5th edition (the Standards) encourages, but does not mandate, AMS:

> "*Antimicrobial resistance is a significant and growing global health issue that must be addressed in a unified and strategic manner. By including an antimicrobial stewardship program in your service, you can help to maintain the effectiveness of antibiotics. Antimicrobial stewardship can help prevent the emergence of antimicrobial resistance and decrease preventable healthcare-associated infection."* (Criterion QI 2.2, page 101)[114]

The use of Therapeutic Guidelines is also recommended but not mandated: Criterion QI 2.2 Safe and quality use of medicines: "Your practice could use guidelines for the quality use of medicines. Some available resources include:… Therapeutic Guidelines" (page 102), and again under Criterion GP4.1 – Infection prevention and control, including sterilisation: "Practitioners must have access to appropriate guidelines, such as the Therapeutic guidelines: Antibiotic, to promote and support informed prescribing of antibiotics." (page 144) AMS options in the Standards include: conduct an audit on antibiotic prescribing (QI 1.3B); reinforce key messages about appropriate antibiotic use with patients (QI 2.2); implement practice policies or protocols on antibiotics (QI 2.2C); introduce an AMS program e.g. educate patients with shared decision making around antibiotics, display AMS posters, provide leaflets, conduct a clinical audit of prescribing and monitor against the practice's AMS policies (GP 4.1). The Standards have an accompanying Resource Guide.[118] This includes links to Australian-developed patient information resources, a clinical e-audit activity (in April 2020 I found this was closed to new enrolments), the ACSQHC AMS website, the Antimicrobial Stewardship Clinical Care Standard, the UK's RCGP TARGET (Treat Antibiotics Responsibly; Guidance, Education, Tools) antibiotics toolkit and sample resources from the University of Queensland.[118] Sample policies or programs are not provided. There is no description of how an AMS program may be developed by a practice and no separate funding to assist with its introduction.

1.5.2 AMS governance for general practice

Australia's National AMR Strategy 2020 is nationally coordinated, with linkages between the sectors, by the Antimicrobial Resistance Governance Group (ARGG). Membership of ARGG includes the Chief Medical Officer and Chief Veterinary Officer.[1] ARGG is provided with expert advice by the Australian Strategic and Technical Advisory Group (ASTAG)[1] The Royal Australian College of General Practitioners (RACGP) and the Australian College of Rural and Remote Medicine (ACRRM), along with a range of other stakeholders, are members of ASTAG.[119] An Implementation plan has not yet been released to accompany *Australia's National Antimicrobial Resistance Strategy 2020 and beyond*. The Implementation Plan[70] from 2016 provides information on the governance for AMS. Objective 7 states *"Clear lines of responsibility and accountability at the international, national, jurisdictional and local levels are needed to support progress.*" However, the responsibility is not clear for general practice. Section 5.2.2. (page 48) states "*Continue Research Roundtable meetings for AMR to establish and encourage collaboration among researchers and stakeholders involved in AMR in general practice in Australia. This collaborative approach should assist in reducing duplications of efforts and provision of complementary expertise to areas of focus on research."* The lead organisations named for this are "Bond University with Queensland University of Technology, National Centre for Antimicrobial Stewardship, ACSQHC, The Royal Australian College of General Practitioners, Australian Government Department of Health."[70] In the 2016 Implementation Plan, the focus for general practice is to "*identify, test and implement stewardship interventions" (page 8).[70] Priorities include ensuring adequate access to Therapeutic Guidelines; monitoring of antibiotic prescribing with feedback to prescribers; involving Primary Health Networks (PHNs) to support AMS in general practice; optimising clinical software for AMS practices; updating general practice accreditation standards around infection prevention and control (IPC); identifying and addressing the barriers and enablers to standards implementation; strengthen consumer and health professional awareness of IPC*."[70] It does not describe how these will be achieved. Thus, there is advice from ASTAG, activities (mostly unspecified) from the Department of Health, with research developed at roundtable meetings between stakeholders and researchers, but no clear vision of exactly who is to drive AMS in general practice or how it will be achieved. In 2020, the lines of responsibility and accountability for general practice AMS in Australia are still not clear, and the roadmap to achieving progress has not yet been articulated.

The clearest description in the literature of effective governance for AMS in general practice that encompasses a range of activities and support for all health sectors including general practice, is from Sweden. Sweden has reduced its community antibiotic prescribing by the development of The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (Strama).[120] Strama started at local levels in 1994, with microbiology, infectious diseases, pharmacy, general practice and other medical specialties represented.[121] It has a One Health approach and has since expanded to include all health, public, animal and environmental sectors.[122] Strama now has a national steering group with broad representation to coordinate activities[120] via a national action plan.[122] It has multidisciplinary regional groups, usually led by the country medical officer for communicable disease control[120] which form the link between national and local groups. The program is nationally funded.[122] No similar organisations in other countries are identifiable in the research literature. The activities of Sweden's Strama over several decades have been associated with reduced antibiotic prescribing, especially in children, without causing an increase in hospital admissions for serious complications.[120 122]

1.5.3 AMS interventions in general practice

In a systematic review examining the quality of 825 published AMS interventions, with 205 of the studies from the community setting, the commonest community interventions to support AMS were education, audit and feedback, and decision support. Most outcomes focused on process measures, such as proportion of patients treated with antibiotics or revisits for infection, with few community studies reporting clinical or microbial outcomes. Study design quality was low and showed no improvement over time.[123] In a review of eight reviews examining clinician-targeted interventions for acute respiratory infections, Tonkin-Crine et al.[124] found that C-reactive protein point of care testing, shared decision making and procalcitonin-guided management had moderate quality evidence for reduced antibiotic prescribing. The evidence around educational materials and decision support for the clinician was of low quality and they were unable to draw any conclusions of its efficacy in reducing antibiotic prescribing.[124] Reviews of published general practice AMS interventions have produced mixed findings. A Cochrane review found that ambulatory care interventions targeting a change to recommended antibiotics were more successful than interventions targeting a reduction in prescribing,[125] but a review of 58 reports from hospital and community settings found that interventions aimed at reducing overall antibiotic prescribing were more effective than those targeting antibiotic selection.[126] Drekonja et al.'s systematic review of 50 reports found interventions with communication skills training and laboratory testing reduced prescribing, but most did not measure patient outcomes nor changes in AMR.[127] Arnold and Straus's 39-study systematic review of interventions to improve antibiotic prescribing in ambulatory care found that "*No single intervention can be recommended for all behaviours in any setting"*; and that "*local barriers should be removed before implementation".*[125] Multi-faceted campaigns to the public and GPs have been reported to be associated with reduced antibiotic prescribing in high-income countries, but the sustainability of these is unclear.[128]

In a meta-ethnographic review, Germeni et al. found that there were differences in the way that interventions may be experienced by primary care professionals (PCPs). These may range from supportive to unnecessary or a source of distress, and that PCPs assumed different roles during consultations for patients with acute respiratory infections depending on the context of the consultation. Interventions that were context sensitive and accounted for PCPs varying roles and changing priorities were likely to be more acceptable.[129] Cultural determinants have been described as exerting a "ubiquitous influence" on all stages of a patient's disease process, the prescriber's decisions and the patient's adherence to treatment, in ways that are multiple and complex.[130]

1.6 Conclusions

This literature review has provided an overview of the global problem of antibiotic resistance and the imperative to reduce antibiotic prescribing. It has described how Australia has antibiotic resistant organisms in the community and how we are a high-antibiotic-consuming nation when compared to similar OECD countries,[82 131] with about 75% of the community's antibiotics prescribed by GPs.[83] The Australian JETACAR[65] report and subsequent reports[66 67] have specifically called for the introduction of AMS into general practice. Acute respiratory tract infections have been singled out as having mostly unnecessary antibiotic treatment. The use of broader-spectrum antibiotics than may be necessary to treat infections has been observed in Australian general practice.[65] These may be factors contributing to the development of AMR, and may be amendable to change through AMS activity.

However, AMS has still not been widely adopted by Australian general practices, it is not mandated and the governance structure for AMS in the community is not clear. General practices are almost exclusively private businesses with no specific funding for AMS activities. GPs may consider that AMR is not a problem for their practice. There are few Australian AMS specific resources to assist GPs, little evidence to show what interventions may be effective and no obvious AMS action plan. There is unexplained variation in antibiotic prescribing rates between GPs[102] and practices;[91] and interventions to reduce antibiotic prescribing have produced conflicting outcomes, with no single intervention found effective across all general practices.[125] Clearly, there are many hurdles to overcome. This thesis has examined the evidence to develop an actionable comprehensive framework to further guide AMS for general practice.

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Chapter 2 Aim, objectives and methodology

2.1 Aim:

The aim of this PhD is to develop a framework for antimicrobial stewardship in general practice.

2.2 Objectives:

1. Analyse current antimicrobial prescribing data sources and the MAGNET dataset of de-identified clinical records to determine their utility for real-time monitoring of general practice antibiotic prescribing.
2. Identify the component parts necessary for AMS in general practice, to inform a framework which may be used to guide activity in this health care context.
3. Describe the views of expert stakeholders on the potential AMS framework to better understand to what extent the core components are feasible and valid for Australian general practice.
4. Describe the roles and responsibilities of organisations with responsibility for AMS in primary health care, together with evidence-based strategies that may be implemented to direct AMS in Australian general practice.

This thesis' contributions to AMS in general practice are:

1. An appraisal of Australian GP antibiotic prescribing data sources, including the MAGNET clinical record dataset, to determine the extent of their suitability for use in AMS monitoring and to make recommendations for how these can be improved.
2. Identification and analysis of the core components required for AMS in general practice.
3. The development of a framework for guiding AMS in Australian general practice into the future.
4. An evaluation of the feasibility and validity of the framework by key stakeholders.

Studies undertaken

To achieve the aim and objectives of this thesis, three studies were conducted, each addressing different objectives.

- Study 1 was a critical appraisal of the current sources of GP antibiotic prescribing data followed by a quantitative descriptive study of a new dataset (objectives 1 and 2).
- Study 2 was a scoping review to identify the core components required for AMS in general practice (objective 3).
- Study 3 was a qualitative study describing the views of expert stakeholders to better understand to what extent the core components are feasible and valid for Australian general practice. (objective 4).

The three studies were then integrated in a mixed methods design to answer objective 4.

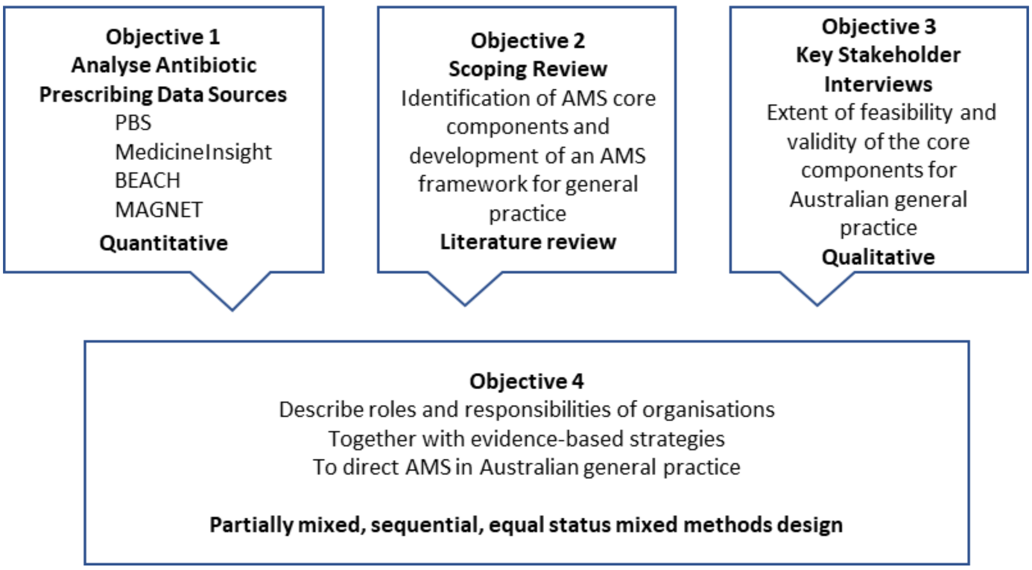
2.3 Methodology

2.3.1 Mixed methods

Mixed methods is a research paradigm positioned between the quantitative and qualitative paradigms by including both in the same research. It has been used to understand context, multi-level perspectives and cultural influences in greater depth than by the use of quantitative or qualitative methodology alone.[132 133] It has been used to improve knowledge and explore factors contributing to healthcare problems, including antibiotic use and AMS.[134-140] Mixed methods' goal has been described as increasing the "breadth and depth of understanding and corroboration."[141] Mixed methods research has been described for five different purposes: 1. triangulation of results from different methods to increase the validity of results; 2. complementarity that uses the results from one method to clarify or enhance the results from another method; 3. development which uses the results of one method to inform the development of another method; 4. initiation to increase the breadth and depth by discovering paradoxes or contradictions between the methods; and 5. expansion to increase the scope of inquiry by using different methods for the different components.[142] Other purposes have been added: instrument development – using qualitative research to develop questionnaires; illustration – using qualitative data to illustrate the quantitative data; and diversity of views – revealing meaning by combining researchers' quantitative data with participant's qualitative data.[143] However, these purposes are not mutually exclusive.[144] Each of the quantitative and qualitative methodologies must follow their respective standards,[133] and the mixed methods design should have a supporting theoretical orientation.[132] There are guides to mixed methodologies[141 142 145-151] but few recent descriptions of best practice.[132] The quantitative and qualitative data may be collected simultaneously or sequentially - where the quantitative data may inform the qualitative or vice versa; [143] or a convergent design combining the two methods during data collection or interpretation of results.[152] Data may be mixed at different stages of research e.g. at the design, data collection, or analysis stages and may have different or equal priority or status.[143] Equal status considers that both perspectives will add insights to most or all the research questions; for example, a qualitative dominant status recognises that a quantitative component will provide benefit to a "constructivist-poststructuralist-critical" qualitative view; and that a postpositivist quantitative dominant research status will benefit by the addition of a qualitative component.[141]

This thesis contains separate quantitative and qualitative studies to achieve the aims of this thesis. The data obtained from each study was analysed separately and then mixed during data interpretation to develop the proposed framework, hence it is a partially mixed methods design (Figure 1). I chose mixed methods to improve my understanding of the context of general practice, and to help validate my findings by expansion – increasing the scope of the research by using different methods for the different components of the proposed framework. It is a convergent design as the quantitative and qualitative data did not inform the collection of each other; they were combined during interpretation. The quantitative and qualitative studies have equal status as each is essential for the development of the framework. It also includes an analysis of the objectives of the National AMR Strategy 2020. Thus, this research is an partially mixed, equal status, mixed methods design.[147] The integration aims to design a potential framework for AMS in Australian general practice which is informed by and provides feedback on current prescribing practices, provides resources to GPs for use in consultations, is monitored for changes in antibiotic prescribing, patient outcomes and ultimately, AMR, and contains feedback loops for further improvements. The theoretical orientation that will inform this mixed methods research is human factors engineering and complexity science.

Figure 1 *This thesis is a partially mixed, sequential, equal status mixed methods research design*



2.4 Theoretical orientation

The theoretical orientation for the development of the AMS framework is based on human factors engineering with additional insights from complexity science. These were chosen as JETACAR and subsequent reviews recommended a strategic multidisciplinary broad approach with accountability.[65-67] I also considered, but rejected, a psychological approach (such as the Behaviour Change Wheel/Theoretical Domains Framework,[153] Theory of Planned Behaviour[154][155] which focuses on changing behaviour. A realist approach explores the theories and causal mechanisms for complex interventions using a context + mechanisms = outcome configuration.[156] This provides an analysis of "what works for whom, in what circumstances, in what respects and how",[157] but doesn't offer enough of a health system wide framework for this research.

2.4.1 Human factors engineering approach

Human factors engineering, also known as ergonomics,

> *"is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data and methods to design in order to optimize human well-being and overall system performance."*[158]

A human factors engineering approach focusses on adaptive human behaviour in a complex sociotechnical system.[159][160] It recognises the complexity of healthcare and uses knowledge about human behaviour to design safer systems,[161] and provides a proactive 'resource envelope' to allow users the flexibility to adapt and cope with unanticipated task demands.[160] Human factors engineering in healthcare arose from attempts to stop multiple small system breakdowns from causing an error which harms a patient;[162][163] and to improve the design of medical equipment.[164][165] It has also helped to change healthcare culture from one of blaming an individual for an error, to one that encourages the reporting of errors so that the system may be analysed and improved.[166][167] By changing the focus from how individuals ought to act, to a predictive model,[160] human factors engineering also works to enhance teamwork, communication and leadership. It includes the interactions between people, the elements and levels of the system and the environment,[168] It can provide a framework to investigate the reasons behind non-compliance or workarounds where policy, procedure or protocols are not followed,[169] for example, the lack of prescribing guideline compliance. Human factors engineering considers the physical and organisational environment along with an individual's cognition.[170] It considers the design of the system, including the physical, cognitive and psychosocial components; the system's implementation including issues of "participation, feedback, training and learning, project management, organizational support and management commitment"[168] and the system's post-implementation operation which includes changes and adaptions, learning and sense making.[168]

However, early human factors engineering models did not capture the complexity of the health system, so the Systems Engineering Initiative for Patient Safety (SEIPS) model of patient safety[171] and SEIPS 2.0[172] systems of human factors engineering were developed.

SEIPS is based on Donabedian's quality of care model.[173 174] Donabedian included, among other factors, the doctor-patient interactions, patient preferences, care obtained in the community, and the processes and outcomes of care in quality of care measures.[173 174] SEIPS attempts to capture and model healthcare's complexity[171 172] by showing how the sociotechnical work system, the care and other processes, and the outcomes are linked. A schematic adaption of the SEIPS 2 model of the healthcare system is provided in Figure 2, with AMS examples provided in Table 1.[171 172 175] The work system contributes to the process of work done by the patient, the health professionals and collaboratively to get an outcome for the patient, the professional and the organisation (Figure 2 and Table 1). It includes feedback loops from the processes and from outcomes back to the work system (Figure 2).[171 176] The work system contains five components - the person, their tasks, the tools and technologies, the organisation, and the physical environment (Figure 2 and Table 1). The person is placed centrally in SEIPS to emphasise that design should support people, not people adapt to systems. The patient may be the recipient of the outcome or the person at the centre undertaking their own health care.[171 176] The tasks are the work actions including their difficulty and sequence;[172] the organisation includes time, space, and resources; the physical environment includes the physical lighting, noise, available space etc.[171] Processes includes the physical, cognitive and social/behavioural care processes associated with professional work, collaborative work and patient work. It also includes the other processes to support care delivery such as information flow, maintenance, and supply chain. These combine to produce patient, professional and organisational outcomes, which may be desirable or undesirable.[172 176] In SEIPS 2.0 the external environment is also included. This includes the "macro-level societal, economic, ecological and policy factors outside an organisation."[172] SEIPS 2.0 also includes engagement, configuration and adaption. Engagement includes all persons into the central 'persons' component of the work system – patients, healthcare professionals and others. This includes the patient's preferences, goals and needs and considers that others apart from healthcare professionals may do some of the work e.g. a family member may manage a patient's health information. Configuration posits that process performance is an emergent property of the whole interacting system and is dynamic and situation specific. Adaption represents the feedback loops which are a consequence of complex sociotechnical systems and may cause intended and unintended adaptions.[172] SEIPS 2.0 also recognises the hierarchical multilevel interactions in the work system and the external environment in which the system operates.[172] The World Health Organization (WHO) recognised the paucity of information on human factors engineering in primary care and issued a technical series which covers patient engagement, the health workforce, care processes and electronic tools. It incorporates the SEIPS model and includes the macro-ergonomic interaction of primary care with other parts of the health system. The series recognises that multifaceted interventions may be required, and that local knowledge and priorities are important when transferring strategies between regions.[170]

Human factors engineering has been used extensively for patient safety and error management and to reduce potential risks but its use for AMS has lagged, especially in general practice. The SEIPS 2.0 model was used by Keller et. al. to analyse a systematic review of published AMS interventions to “identify barriers and facilitators to successful implementation of ambulatory AS [AMS] interventions.”[175] The authors found the model provided some answers and identified many facets that have not been studied in general practice. For example, the authors found that prescribing guidelines were not always used, as they were not always trusted, may be too long or too difficult to find. The role of the non-prescribing members of the team, such as clinic staff, had not been well studied, nor had the physical environment. They recommended that the entire work system should be addressed in future interventions. The external environment of regulation and culture was recommended for further research.[175]

Human factors engineering offers a method for examining technical systems, ensuring that GPs and patients are at the heart of the system, but it does not supply sufficient insight into the organisational and external environments and the context of general practice for the introduction of AMS. Holden acknowledges that SEIPS 2.0 may need further components,[172] and Keller has identified the external environment as a focus for research.[175] Carayon has called for the inclusion of other organisational theories besides the traditional sociotechnical system to improve the organisational and inter-organisational levels.[168]

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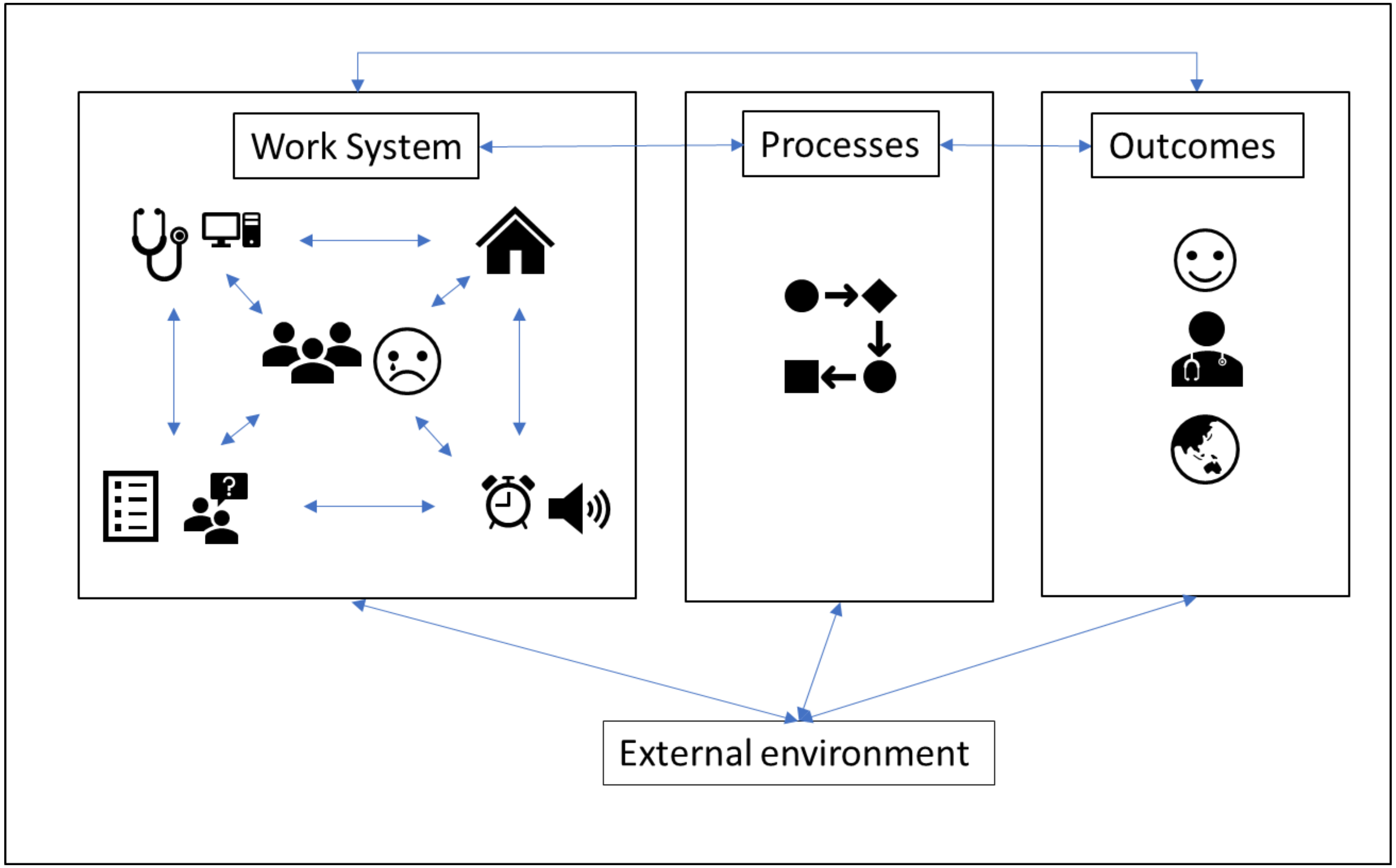
***Figure 2* Schematic adaption of the SEIPS 2.0 human factors engineering health care model**



The blue lines indicate workflow and feedback loops. See also Table 1 below.

Table 1 Examples of SEIPS 2.0 components relating to antimicrobial prescribing

System	Components	Examples
Work	Persons	Patient, health professionals, family, carers.
	Tasks	Writing a (delayed) prescription; providing education to a patient.
	Tools and technologies	Integrated clinical decision support.
	Organisation	Time for education in consultation, team support for AMS.
	Physical environment	Lighting, noise, access to resources.
Processes	Physical, cognitive, social/behavioural	Professional, patient and collaborative work. E.g. Antibiotic prescription or alternative management plan decided with patient.
Outcomes	Patient, Professional, Societal	Patient recovers without antibiotics, health professional satisfaction, AMR is reduced.
External environment	Macro-level societal, economic, ecological and policy factors	External monitoring of prescribing; community support for patient self-management of self-limiting infections; fewer antibiotics in environment.

2.4.2 Complexity science

In this thesis the phrase 'complexity science', will be used to include the terms 'complex adaptive systems', 'complex systems' and 'complexity theory'. There is no single definition of nor agreed approach about how to use complexity science.[177] A broad definition is supplied by Plsek and Greenhalgh: "A complex adaptive system is a collection of individual agents with freedom to act in ways that are not always totally predictable, and whose actions are interconnected so that one agent's actions changes the context for other agents."[178] Braithwaite describes healthcare as a complex adaptive system, in that it's "performance and behaviour changes over time and cannot be completely understood by simply knowing about the individual components."[179] In studying general practice training, McKay et al. regarded general practice as a complex sociotechnical system.[180] Holland states that complex adaptive systems "involve many components that adapt or learn as they interact".[181] Cilliers states complexity theory is "a characteristic of a system". Complex behaviour arises because of the interaction between the components of a system and lists 12 characteristics of complex systems: 1. They are open, 2. not at equilibrium, 3. have many components and 4. their output is a function of their inputs with some being non-linear. 5. The state of the system is determined by the value of the inputs and outputs. 6. Interactions are defined by dynamic input-output relationships, 7. components interact with many other components, 8. there are feedback routes, 9. behaviour results from the interaction between components (emergence), 10. a temporal, spatial and functional asymmetrical structure develops and is maintained by internal dynamic processes even if components are exchanged or renewed, 11. behaviour adapts over different timescales and has memory, 12. more than one description of a complex system is possible.[182]

Chu et. al. describes the importance of contextuality, which occurs when components have multiple roles and functions across different systems and may cause unforeseen effects on interventions. Thus, a model cannot explain the full complexity of an open system and interventions may produce unpredictable effects and suggests focussing on the contextual properties of the system rather than details of mechanisms.[183] People are part of wider dynamic social, political and cultural systems.[184] Their internal 'instincts, constructs and mental models' are not fixed and may not be explicit. Patients will have priorities, choices and a context - which may not be compatible with evidence-based medicine.[178]

Other aspects of complex systems are important. Attractors, also known as facilitators, have been described: An attractor is "the structure or behaviour of a complex system that make it consistently pull, usually toward some stable state… a tension that draws things together."[185] Attractors have also been described as the motivators and values of individuals, who seek feedback to support movement towards the attractors.[186] Complexity science offers strategies for driving successful change using these attractors. Miller et. al. offer three strategies: i). joining or enhancing the existing attractors; ii) transforming an attractor; ii) learning to increase awareness of attractors. “Joining” works by providing tools so that an approach can be individualised. “Transforming” may be via “hammering, wedging, and shocking”. For example, where income generation is an attractor, financial incentives being used is a form of “hammering”. “Wedging” is providing external feedback to facilitate small positive changes but is recognised as a risky strategy as a small change may exhibit a marked effect due to non-linearity. “Shocking” occurs when major change is introduced e.g. a practice buyout or new regulations. “Learning” is similar to wedging, but occurs within the practice, by making agents aware of their own internal models.[186] Miller et. al. found that there is an invalid assumption that an intervention will directly lead to the desired improvement especially when there is a delay between an action and a consequence.[186] Braithwaite acknowledged that there are a huge number of variables interacting unpredictably in healthcare and that behaviour and culture may be entrenched;[179] referring to a “memory” of feedback loops constraining change.[185]

Reed et al. produced a framework for evidence translation: Successful Healthcare Improvement From Translating Evidence in complex systems (SHIFTEvidence), which provides three strategic principles, each with four rules.

1. “Act scientifically and pragmatically”, has rules of understanding the problems and opportunities; iteratively developing solutions by identification and testing; assessing whether improvement has occurred, capturing and sharing the learning; and investing in continual improvement.
2. “Embrace complexity” has rules of: understand the processes and practices of care, understand the types and sources of variation, identify systemic issues, and seek political, strategic and financial alignment.
3. “Engage and empower” has rules of: engaging those responsible for and affected by change; facilitate dialogue, foster a culture of willingness to learn and freedom to act, provide resources, training and support.[187]

This framework reflects that the initial conditions may not be the same in each setting, that there must be a commitment to improvement as the system adapts, and that multiple interventions may be required.[187] Change must take account of how care is delivered “at the coalface” as standardised templates of change often fail, and we must acknowledge that of all the complex work clinicians do, they do most of it correctly. Healthcare should be a learning system with “strong feedback loops” to build a momentum for change.[179] Despite the unpredictability of complex systems, there are patterns. Networks, groups and teams are relatively enduring, with entrenched social structures and cultural settings.[185] Braithwaite argues that a system should be examined on different levels - individual, network and a community or organisational scale, for example, a large scale is public health, fine scale is the tasks of patient care.[185] Components are important, but so too are the relationships between the components where people learn from each other and the context so adjusting their behaviour; these changes cannot always be predicted,[184] and are locally specific.[188] Hawe et. al. stated that interventions be allowed to adapt to context and needs and incorporate behaviour change science or relevant change theory. The components may be fixed, but their form may vary in different settings.[189] Using complexity science, education is moving from a predefined content-oriented manner of enhancing knowledge, skills and attitudes, to a process-oriented self-directed learning driven by needs. [190]

Both human factors engineering and complexity science are useful models to help understand the challenge of AMS in general practice. It is proposed that the development of a framework to guide AMS implementation in general practice can be informed by an awareness of these theoretical models.

2.5 Ethics approval

The quantitative research in Study 1 was granted ethics approval by The Monash University Human Research Ethics Committee (number CF12/1057 – 2012000504).

The qualitative interviews in Study 2 was granted ethics approval by the Monash University Human Research Ethics Committee, project number 20721. Participants provided written informed consent for the interviews and the recording.

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Chapter 3 Australian antimicrobial prescribing data sources

This chapter fulfils objective 1 of this thesis: "Analyse current antimicrobial prescribing data sources and a new dataset to determine to what extent they can be used for real-time auditing of general practice antibiotic prescribing." The introduction details the current data sources for general practitioner antimicrobial prescribing, examines the data they provide, and discusses their limitations. A new data source was explored in this research to examine its suitability for data monitoring. Two papers were published from this research and the research was presented at three national conferences.

3.1 Antimicrobial prescribing data sources

To date there have been three main data sources for community antimicrobial use available in Australia: The Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme (PBS),[83] the Bettering the Evaluation and Care of Health (BEACH) program,[84] and the MedicineInsight program run by NPS MedicineWise.[191] There is also an ongoing study of registrars clinical encounters during training which has collected data on antibiotic prescribing. All have limitations.

3.1.1 The PBS

Medicines in Australia are regulated by the Therapeutic Goods Administration (TGA) to ensure that there is evidence that they are safe and effective for use. Then most medicines in Australia will be submitted for, and gain approval, for subsidy through the PBS to ensure people can afford the medicines they need. The Pharmaceutical Benefits Advisory Committee (an independent expert committee) recommends which medicines should be listed for subsidy and their indications for use.[192] If a doctor prescribes a medicine that is either not listed, or is being used for a different purpose than is indicated, this becomes a "private prescription" for which there is no subsidy and the patient pays the full price of the medicine.[193] In 2011, it was estimated that private prescriptions accounted for 7% of all antibiotic prescriptions dispensed. From 2012, private prescriptions have not been included in the PBS database, so there is no accurate data on the number of private prescriptions currently dispensed.[8 194] The 2019 AURA report estimates that more than 90% of community dispensed antibiotic prescriptions are captured by the PBS but notes that "this estimate has not been updated for some years."[8]

Prior to 1 April 2012, prescriptions were not included in the PBS dataset if the medicine cost less than the subsidy; full inclusion occurred from 1 July 2012.[83] Also, prescriptions supplied by most Aboriginal and Torres Strait Islander health services (which may include GP providers) are not counted in the PBS.[8 195] Thus, the PBS does not supply a complete dataset of all antimicrobial prescriptions dispensed in the community. Antibiotic prescriptions written by GPs contribute to 75% of the PBS data; 21% are written by other medical prescribers (e.g. other community-based specialists), 3% are written by dentists and <1% each for optometrists, midwives and nurse practitioners.[83] Most GPs work in a community-based general practice, but there are an unknown number of GPs employed by hospitals and other organisations.[196] PBS data also includes prescriptions provided to hospital out-patients, discharged patients (up to one month's supply) and day admitted patients in five states and one territory.[194] (New South Wales and the Australian Capital Territory are not included.)[193] In 2013, hospital pharmacies supplied two percent of the antibiotic prescriptions or 2.16% of antibiotic use by Defined Daily Dose (DDD)/1000 population/day.[83] Discharged patients and hospital outpatients have the option to take their hospital-written prescriptions to their community pharmacy. Distinguishing community GP-prescribed antimicrobials from the total prescriptions dispensed is not possible from the current published PBS data sources.

PBS data includes the medicine name, form prescribed (e.g. capsule, tablet), administration route, the quantity dispensed, whether it is a repeat or original supply and a date. The date may be the date on the prescription, the date of supply, or the date of pharmacy claim processing by the Department of Health.[193 197] Demographic information about the patient to whom it is prescribed is limited, mainly to whether the patient was a general or concessional patient and the State of the dispensing pharmacy. The clinical indication is not included on the prescription. The Department of Veterans' Affairs RPBS contains the health claims and medical records of Australian defence force veterans and their eligible dependants.[193 198] However, these may not be representative of the whole population.

In summary, the PBS is an incomplete data set of dispensed prescriptions and it is difficult to identify those written by community-based GPs. Private prescriptions written by GPs are not included; the dates do not allow for accurate monitoring of seasonal prescribing trends, and there is no information about the indication for the prescription or the demographics of the patient.

3.1.2 The BEACH program

The Bettering the Evaluation and Care of Health (BEACH) program started in April 1998 and was a continuous national paper-based survey of 1000 randomly selected GPs a year. (This is 3.5% of the 28,359 registered GPs in 2020)[199] Each GP collected extensive information on 100 consecutive consenting patients. BEACH collected GP, practice and patient demographics, presenting problems, patient management and details of prescriptions. It was a very rich cross-sectional data source, but funding ceased in 2016 after 18 continuous years of data collection. The collected data is still available to researchers,[84 200] and its analysis has greatly contributed to our understanding of GP prescribing practices as it included useful qualitative information that was not available in the PBS – most importantly the indication for the prescription (that is the clinical problem that the medication was being used for) and prescribing guideline modifying factors.[85 91 102 201]

3.1.3 MedicineInsight

MedicineInsight is a national medicine quality improvement program funded by the Australian Department of Health and managed by NPS MedicineWise.[191] Established in 2011, it collects longitudinal, deidentified data directly from voluntarily participating GPs' electronic medical records.[202] Its purpose is to review all medications; antimicrobial agents are but one part of its scope. Aggregated data is provided for reports, including the Australian reports on Antimicrobial Use and Resistance in Human Health (AURA reports).[203] Feedback is also provided to participating GPs on their own prescribing, with comparisons to participating peers.[191] The program had 671 practices participating in 2018, which is 8.3% of the total number of practices.[204] The supplementary data for the 2019 AURA report states that in 2015, 535 general practices with 3,196,155 patients across all states and territories contributed data; for 2016 the figures were 543 general practices, 3,649,131 patients; and in 2017, 545 general practices and 4,090,261 patients.[8] There is no information available about how representative these practices are of the whole cohort apart from "remote areas of Australia are under-represented in participating MedicineInsight practices."[8] The data set excludes "patients who infrequently attend a general practitioner clinic."[6] "Infrequently" was not defined. Patients were not linked across practices.[202] (In Australia, patients may attend any general practice.) MedicineInsight reported in 2016-17 that 14.5% of all drug prescriptions were private but gave no separate figure for antibiotics. There is no linkage with dispensing data, so there is no information on whether the patient had the prescription dispensed, or when.[202]

It should be noted that MedicineInsight and BEACH data refer to systemic antibiotics, the PBS data in AURA includes all dispensed antibiotics. The publicly available data are not directly comparable.

3.1.4 The ReCEnT study

The Registrar Clinical Encounters in Training (ReCEnT) study is a longitudinal cohort study of Australian General Practice (GP) trainees. Registrars record the details of 60 consecutive patient encounters every six months over the 18-24 months of the training program. The data collected includes registrar and patient demographics, details of the consultation, reasons for encounter and problems managed. Registrars also record educational factors related to the encounter. ReCEnT started with three training providers in NSW, Victoria, and Tasmania, then from 2010-2015 five regional training providers in NSW, QLD, SA, TAS and VIC and from 2016, in three of the nine training providers in Australia.[205 206] ReCEnT has reported that antibiotics are provided at higher rates for URTI, acute bronchitis/bronchiolitis,[207] acute sore throat,[208] acute otitis media and acute sinusitis.[103] However, it is limited by not including all registrars in all states, nor all their patients. Also, registrar prescribing may not reflect the prescribing of registered GPs.

3.2 What does the existing data tell us about GP antibiotic prescribing and community antibiotic use?

In 2017, 41.5% (n = 10,215,109) of the Australian population had at least one systemic antibiotic dispensed under the PBS.[8] This consumption of antibiotics is higher, as measured by Defined Daily Doses (DDD) per 1000 inhabitants per day, than in many comparable European countries,[6 7 209] and is higher than the OECD average.[82 131]

PBS community antimicrobial dispensing data, as reported in the 2019 AURA report which includes systemic and topical prescriptions, shows a peak in 2015 with a total of 29,264,932 antimicrobials dispensed, then a decline in 2016 (27,324,648) and 2017 to 26,553,451 antimicrobials dispensed (Table 3.10).[8] [Note, the text and the table heading refer to the volume of antibiotic prescriptions dispensed, but the column headings refer to antimicrobials.] Also, during 2016 chloramphenicol eye drops (a topical antibiotic) were re-scheduled to non-prescription,[8] thus were not counted in the PBS data set after 2015. In 2015, for the non-J01 antimicrobial subset of the data, the number of antimicrobials dispensed was 2,451,345; this was followed in 2016 by a marked drop to 397,715 (16.2% of the 2015 figure), but there was an increase to 629,127 in 2017. This chloramphenicol eye-drop re-scheduling may have masked what appears to be a small increase in the number of systemic (J01) antimicrobial agents dispensed from 26,813,587 in 2015 to 26,926,933 in 2016. There was, however, a decline in 2017 to 25,924,324 systemic antimicrobial agents dispensed.[8] There are no figures on how many chloramphenicol eye drops are now sold over the counter in pharmacies.[8]

The three most commonly dispensed antibiotics under the PBS in 2017 were cefalexin, amoxicillin and amoxicillin-clavulanic acid, which accounted for more than 50% of all antibiotics dispensed.[8] In PBS data collected between January 1994 and March 2014, repeat prescriptions were ordered on the majority of cefalexin (53%), amoxycillin-clavulanic acid (68%) and roxithromycin (71%) prescriptions,[83] despite repeat prescriptions not being required to complete a course of treatment for most common infections if the recommendations from Therapeutic guidelines were being followed.[7] (GP prescribing software may default to issue a repeat on a prescription as a default.) While the majority of repeat prescriptions were not dispensed (only 19-20% of repeats were dispensed for the above three antibiotics), some repeats were dispensed weeks to months after the date the prescription was written. For instance, for amoxicillin, 51% of supplied repeats were dispensed within 10 days of the original being dispensed, but 19% were dispensed more than 60 days after the original supply. The figures for cefalexin are 57% and 15% respectively, and 67% and 12% for amoxycillin-clavulanic acid. It is unlikely that patients are treating the same infection after these long delays between the original and the repeat being dispensed.[83] In 2015, of the 10,701,804 people (44.7% of the population) who had at least one antimicrobial dispensed, 18.5% had only one antimicrobial dispensed, but 3.2% had seven or more antimicrobial prescriptions dispensed, including repeats.[7] It is uncertain why cefalexin is the most commonly prescribed antibiotic. The reasons may include paediatric formulations, pharmaceutical marketing to GPs about its broad applicability (which is likely to be an important consideration when a diagnosis is uncertain), it is subsidised on the PBS, the barriers to the use of Therapeutic Guidelines which recommends narrower-spectrum antibiotics, and habit – it has been in use since about 1970 and is presumably perceived as safe and effective. A survey is needed to understand the reasons.

Using MedicineInsight data from 2017, the AURA report tells us that for urinary tract infections, 44.9% of females aged >18 years received the TG recommended first-line trimethoprim and that the second-line cefalexin was used for 21.4% of urinary tract infections.[8] Ciprofloxacin is also used to treat urinary tract infections, with urinary tract infections the third most common indication (12.8%) for its prescribing. This is of concern as the prescribing of fluoroquinolones is regulated as “authority required” however, GPs may write a private prescription where no PBS rebate is paid. For tonsillitis 94% of MedicineInsight patients aged >1 year received an antibiotic, whereas the recommend rate is between 19-40%. Of these, 50.7% received the recommended penicillin V.[8]

MedicineInsight data, as reported in the 2019 AURA report, shows declining rates of prescribed systemic antibiotics from 31.7% of patients in 2015 to 29.3% in 2016 to 26.0% in 2017.[8] Private prescriptions are included in MedicineInsight data and in 2017, 52.5% of ciprofloxacin prescriptions, 47.5% of azithromycin, and 13.9% of doxycycline prescriptions were ordered as private prescriptions, which is an increase in proportion from 2015. Six systemic antibiotics showed increases in the number of prescriptions written during the 2010-2017 winter months. These were amoxicillin, amoxicillin–clavulanic acid, doxycycline, roxithromycin, ciprofloxacin and azithromycin. However, not all community issued azithromycin prescriptions are included in this data set, as it is also used to treat chlamydia and gonorrhoea which may be treated at sexual health clinics. Sexual health clinics have a different data reporting system. By contrast cefalexin showed slight summer peaks. As we do not have access to the reason for the prescription it remains a matter of speculation as to why cefalexin prescribing increases in summer. There was poor recording of the reason-for-prescription in an extractable field, with only 33.4% of antibiotic prescriptions having an explicit recorded reason-for-prescription. Another 36.5% of antibiotic prescriptions could be associated with a reason-for-encounter or -diagnosis on the same day as the prescription, but 30% could not be associated with any indications in extractable fields. Where the reason-for-prescription was ascertained, many prescriptions were not consistent with recommendations for first-line treatment. A large percentage of patients were prescribed antibiotics for conditions in which there is no evidence of benefit. This included influenza (52.2% of patients with this condition received antibiotics) and acute bronchitis (92.4% of patients).[8] There were differences in prescribing between age groups. Children aged 0–4 years were most commonly prescribed amoxicillin, and people aged 90–94 years were most commonly prescribed cefalexin or ciprofloxacin. People aged over 64 had the highest prescribing rates per 100 patients. Prescribing rates were higher among people living in the most disadvantaged Socio-Economic Indexes for Areas (26.3 per 100 patients) than in the least disadvantaged areas (25.5 per 100 patients).[8]

BEACH data shows us that the prescribing rate of systemic antibiotics declined from 9.4 per 100 problems managed in 2006–07 to 8.3 in 2015–16, but due to the increase in encounter rate this means that about 3.8 million more antibiotic prescriptions were written in 2015–16 than in 2006–07.[84] The three most frequently prescribed antibiotics per 100 problems were amoxycillin, cefalexin, and amoxycillin-clavulanate. Amoxicillin prescribing declined from 2.2 prescriptions per 100 problems in 2006-07 to 1.8 in 2015-16, cefalexin prescribing remained stable at 1.6 prescriptions per 100 problems and amoxycillin-clavulanate increased slightly from 1.1 in 2006-07 to 1.3 prescriptions per 100 problems in 2015-16. Roxithromycin prescribing declined from 0.9 to 0.5 per 100 problems over the same time frame.[84] In the five years between April 2010 to March 2015, using BEACH data, an estimated 5.97 million respiratory tract infections (RTIs) per year were managed in Australian general practice with at least one antibiotic, equivalent to an estimated 230 cases per full time equivalent GP/year. Yet antibiotics are not recommended by Therapeutic Guidelines for many acute RTIs such as acute bronchitis/bronchiolitis (for which the current prescribing rate is 85%) or influenza (11%). For acute rhinosinusitis, most infections resolve without antibiotics and the expected prescribing rate has been estimated by one group of researchers to be 8% or less, but the current prescribing rate is 41%. One study has suggested that had GPs adhered to the acute respiratory tract prescribing guidelines, they would have prescribed antibiotics at 11-23% of the current prescribing rate.[85] On average, between April 2010 and March 2015, 57% of patients with acute RTIs were prescribed an antibiotic, which is much higher than the Australian Therapeutic Guidelines recommends.[85]

3.3 Conclusions about the current antimicrobial prescribing datasets

We do not have ready access to current GP-specific data which contains the reasons for the prescriptions. Without the reason-for-prescription, clinical information and patient demographic details we cannot gauge if prescriptions are appropriate, target interventions to specific areas nor accurately monitor changes in response to AMS programs. Patient outcomes are also required to monitor for any under-prescribing. Under-prescribing is where a patient deteriorates as they were not treated with the appropriate antibiotic at the right time or dose. No data sources can currently provide this information.[85]

3.4 The MAGNET dataset

The Melbourne East Monash General Practice Database (MAGNET) contained the deidentified electronic medical records from 50 general practices and over one million patients across what was the Inner East Melbourne Medicare Local (now part of the Eastern Melbourne Primary Health Network), a primary care organisation in Melbourne's eastern suburbs. MAGNET was designed to improve upon and replace existing general practice audit systems.[210] This quality improvement is a practice-level activity, not a research activity, to inform clinical care. It can identify and link patients who attend different participating practices, and collects data from specified fields, including prescription details, the reason-for-prescription and patients' demographic information.[210] [MAGNET has been further developed and is now the POpulation Level Analysis and Reporting (POLAR) tool used by the Primary Health Networks (PHN) for quality management.[211]] To find an alternative data source which contains the antibiotic prescription details with the reason-for-prescription and patient demographic data, I conducted an analysis of the antibiotic prescriptions in the MAGNET dataset between January 2010 and December 2014. The cleaning of the dataset is reported in Appendix 1.

Two papers were published from this research. Paper 1 describes the antibiotic prescriptions and was published in the Australian Journal of General Practice;[212] paper 2 examines the extent to which the dataset contains the reasons for the antibiotic prescriptions in an extractable field. It was published as a short report in BMJ Open Quality.[213]

Work from these studies was also presented as a poster at the Choosing Wisely national meeting, Melbourne, 4 May 2017; as an oral paper at the Primary Health Care Research & Information Service (PHCRIS) Research conference, Brisbane 7-9 Aug 2017; and a poster with 5 min oral presentation at the Primary Health Care Research & Information Service (PHCRIS) Research conference, Melbourne, 2 Aug 2018.

Use of electronic medical records to describe general practitioner antibiotic prescribing patterns

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Background and objectives
The computerised medical records of general practice patients can inform our understanding of antibiotic prescribing and assist in antimicrobial stewardship (AMS). The aim of this study was to describe Australian general practitioner (GP) antibiotic prescribing patterns using data extracted from electronic medical records (EMR).

Method
A descriptive analysis of patient records from 44 general practices, between 2010 and 2014, in the eastern region of metropolitan Melbourne was undertaken.

Results
Of the 615,362 antibiotic prescriptions, cefalexin, amoxicillin–clavulanic acid, roxithromycin, doxycycline and clarithromycin were the most frequently prescribed antibiotics. Except for cefalexin, prescribing rates of the antibiotics increased in winter. Of 472,197 patients consulting a GP in one of these practices, 34.8% received an antibiotic at some point over the five years. There was a higher rate of prescribing per consultation in patients aged <20 years.

Discussion
This study shows that it is possible to examine EMR for antibiotic prescriptions, and that a descriptive analysis can identify AMS targets.

IN 2014, 46% of Australians received at least one antibiotic prescription.[1] This prescribing rate is higher per capita than in many comparable countries, including England, Canada, Sweden and the Netherlands.[1] The volume prescribed is higher than the Organisation for Economic Co-operation and Development average.[2] The difference is considerable, with consumption in Australia apparently twice that of Canada and three times that of Sweden.[1] There are no obvious reasons why antibiotic use should be higher in the Australian community setting; therefore, it is likely that some antibiotic use may be unnecessary.

Antibiotic use exposes patients to the risk of adverse effects and the development of resistance. This may include drug side effects and the development of antibiotic resistance among bacteria in that individual and in the population more broadly.[3] Antimicrobial stewardship (AMS) aims to guide the use of antimicrobial drugs to optimise patient outcomes while minimising any adverse effects. Most human antimicrobial use is from antibiotics prescribed in primary care; therefore, general practitioners (GPs) have a critical role in AMS.[4]

To address AMS, we need accurate data on antibiotic prescribing by Australian GPs, but this is not available from current data sources. Three main sources of data are the Pharmaceutical Benefits Scheme (PBS)/Repatriation Pharmaceutical Benefits Scheme, the MedicineInsight program and the Bettering the Evaluation and Care of Health (BEACH) survey, but each has significant limitations. PBS data are administrative data with no clinical information. Up to 25% of PBS prescriptions are from non-GP providers, and private prescriptions (outside the PBS restrictions) are not included.[5] The MedicineInsight program,[6] managed by NPS MedicineWise, aggregates data from GP electronic medical records (EMR) for reports as required.[1] While Australia-wide, it is a voluntary program with antibiotic prescriptions only one part of its remit. BEACH was a paper-based survey of 100 consecutive patient presentations from a representative sample of 1000 GPs per year. It collected data including problems managed and medications prescribed, but was discontinued in 2016. While the extensive data are still available, the survey cannot be used for ongoing monitoring.[7]

A range of clinical software is used in Australian general practices. As a result of limited interoperability, this has limited the secondary analysis of EMR.[8] There is a need to develop a sustainable, ongoing way to accurately monitor GP prescribing and to meaningfully interpret the data available.

The aim of this research was to extract routinely collected data from general practice EMR and to use this to describe antibiotic prescribing patterns.

Method

We retrospectively analysed routinely collected GP data from the EMR of patients from 50 general practices across Melbourne's inner eastern suburbs using POLAR (Population Level Analysis and Reporting for general practice formerly known as MAGNET).[9]

Patient-level data were extracted for consultations and antibiotic prescriptions between 1 January 2010 and 31 December 2014. Unique linkage keys linked consultation data with antibiotic prescriptions and could track patients across practices. Consultation data included dates of consultations and the age of the patient. Antibiotics were identified and coded according to the Anatomical Therapeutic Chemical Classification.[10] Only the original prescription was included; repeats on the same prescription were not examined as the majority of repeat antibiotic prescriptions were not dispensed.[5] Systemic and topical antibiotic prescriptions were included in the analysis, except for topical chloramphenicol, which is available without prescription in Australia. During this pilot research, some links between the consultation data and the antibiotic data were inadvertently broken. Where the antibiotic prescription did not link directly to a consultation, the previous or subsequent consultation in that year was used to determine the patient's age at time of consultation. If there was no other consultation in that year by the patient, or no age was available, the age was recorded as missing. Ages were examined in four broad ranges: under 1, 1–19, 20–49 and ≥50.

Descriptive analysis of the data was undertaken using Stata 13.1 (StataCorp). We examined the numbers of each antibiotic prescribed and the number of consultations. Antibiotic prescribing was assessed across the days of the week, months and years and by the age of the patient.

The Monash University Human Research Ethics Committee granted ethics approval for this research(number CF12/1057 – 2012000504).

Results

Antibiotic prescribing data were complete for 44 of the 50 practices, with 615,362 antibiotic prescriptions provided to 166,772 patients over the five years. Ten antibiotics accounted for 518,016 (84.2%) of the antibiotic prescriptions (Table 1). Cefalexin (146,155, 23.8%), was the most frequently prescribed antibiotic. The number of cefalexin prescriptions remained constant over the five-year period (Figure 1). Trimethoprim and metronidazole, the sixth and tenth most commonly prescribed antibiotics respectively (Table 1), also remained constant over time (Figure 2). By contrast, the remaining seven most commonly prescribed antibiotics – amoxicillin–clavulanic acid, roxithromycin, doxycycline, clarithromycin (Figure 1), cefaclor, erythromycin, and phenoxymethylpenicillin (not shown) – had prescribing peaks in winter. Amoxicillin–clavulanic acid (93,380, 15.2%) was more commonly prescribed than amoxicillin (7390, 1.2%) and other forms of penicillin (Table 1). Phenoxymethylpenicillin (22,090, 3.6%) was the only narrow-spectrum beta-lactam antibiotic in the ten most frequently prescribed antibiotics (Table 1). The number of prescriptions and winter peaks for roxithromycin (Figure 1), cefaclor and erythromycin declined over time, but they were still being prescribed in large numbers in 2014. The most commonly prescribed quinolone was norfloxacin, with 9843 prescriptions over five years (1.6% of total; Table 1). Macrolides (roxithromycin, clarithromycin and erythromycin) comprised 129,132 (21%) prescriptions (Table 1).

Consultation data were complete for 39 of the above 44 practices, with 6,227,104 recorded consultations in the five-year period involving 472,197 patients. A total of 164,522 (34.8%) of the patients received 597,302 antibiotic prescriptions.

The antibiotic prescribing rate per consultation varied with age, which was available for 590,105 (98.8%) of the prescriptions. Patients aged 1–19 years had fewer consultations but received antibiotics at a higher rate per consultation than infants aged <1 and adults aged >19 years. The rate of antibiotic prescribing per consultation per year fell between 2010 and 2014 in age groups ≤49 years, with the largest declines occurring in age group 1–19 years. Age group ≥50 years showed little variation in the antibiotic prescribing rate per consultation over time. Cefalexin was the most prescribed antibiotic across all age groups.

Examination of the reason-for-prescription field (which did not include the progress notes) revealed that for

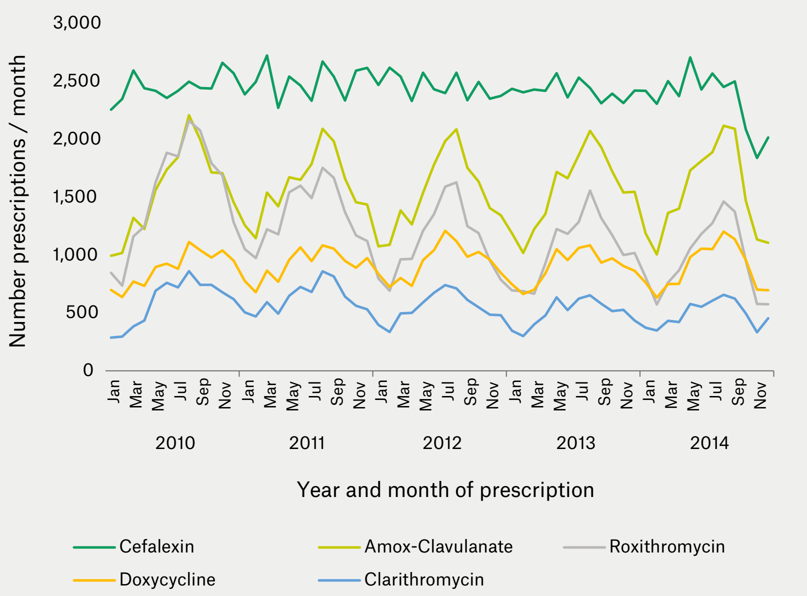

Figure 1. The five most frequently prescribed antibiotics by year and month of prescription (44 practices)

Note: Summer is December to February and winter is June to August.

494,085 (82.7%) of the prescriptions, no reason was available.

Discussion

This research shows the utility of data extracted from general practice EMRs and that a descriptive analysis, using this cohort as the example, can provide information to direct AMS activities.

Not only is the Australian prescribing rate high in comparison to European countries,[1,2] with most antibiotics prescribed by GPs,[11] but there is a preference for broad-spectrum antibiotic agents in this cohort. In 2013, on the basis of PBS data, amoxicillin, cefalexin and amoxicillin-clavulanic acid were the most dispensed antibiotics Australia-wide.[5] However, amoxicillin accounted for only 1.2% of the total antibiotic use in this cohort. Explanations for this cannot be obtained from the available data. Why this cohort of practices showed such low rates of penicillin, amoxicillin and flucloxacillin prescribing and high rates of cefalexin and amoxicillin-clavulanic acid prescribing needs further investigation to understand the clinical and non-clinical drivers. Macrolides were commonly prescribed. This local preference for broad-spectrum antibiotics contrasts with self-reported intentions of Australian GPs, with 70% reporting in 2013 that they would always/often prescribe narrow-spectrum antibiotics.[12] It is possible that GPs may not perceive cephalosporins, amoxicillin-clavulanic acid and macrolides to be broad-spectrum agents. In 2012 in Europe, narrow-spectrum penicillins were the most frequently used group of antibiotics in the community.[13,14] Infections encountered in community practice in Europe would be expected to be similar to those in Australia, and therefore it would be expected to be safe to use these for many common conditions (informed by any local differences in pathogen resistance patterns). Promotion of narrow-spectrum penicillins could be a local AMS target. The prescription of quinolones is restricted in Australia, and no quinolone was represented in the ten most frequently prescribed antibiotics.

The lack of seasonality in prescribing of cefalexin, trimethoprim and metronidazole probably reflects use in year-round infections such as skin, urinary tract, genital and intestinal infections. Of note, the *Therapeutic Guidelines* recommended flucloxacillin as the first-line antibiotic for skin and soft tissue infection;[15] however, it was not among the most commonly prescribed antibiotics in these practices.

The winter prescribing peaks suggest prescribing for respiratory tract infections, which has been described in Australian[16] and international studies.[17,18] During 2010, *Therapeutic Guidelines* ceased recommending the use of cefaclor and roxithromycin for pneumonia, but in 2014 they were still being prescribed with a winter peak frequency. It suggests that this cohort of prescribers had either incomplete awareness of the changed guideline or used different guidelines. *Therapeutic Guidelines* did not recommend amoxicillin–clavulanic acid for community respiratory tract infections,[15] but the winter peaks in prescribing suggest that it was being prescribed for this reason. A study of which guidelines these GPs use and how guideline changes are notified to them seems indicated.

The 2014 PBS figure of 46% of the Australian population being dispensed at least one antimicrobial agent per year[1] is higher than the 34.8% of patients in this cohort.[19] This may be due to PBS including dispensing data from other providers (such as community-based specialists, emergency department and private hospital inpatients).[5] MedicineInsight data (a larger Australia-wide general practice

Table 1. Antibiotics by frequency of prescription 2010–14 (44 practices, n = 615,362)

Antibiotic	Frequency	Percentage
Cefalexin	146,155	23.8
Amoxicillin-Clavulanic acid	93,380	15.2
Roxithromycin	72,089	11.7
Doxycycline	54,389	8.8
Clarithromycin	33,215	5.4
Trimethoprim	27,679	4.5
Cefaclor	24,354	4.0
Erythromycin	23,828	3.9
Phenoxymethylpenicillin	22,090	3.6
Metronidazole	20,837	3.4
Mupirocin	18,899	3.0
Framycetin	14,062	2.3
Flucloxacillin	12,719	2.1
Norfloxacin	9,843	1.6
Amoxicillin	7,390	1.2
Tinidazole	6,691	1.1
Minocycline	6,163	1
Trimethoprim/sulfamethoxazole	5,589	0.9
Other antibiotics	15,990	2.6

electronic medical record extraction program) showed that 30% of patients were prescribed systematic antimicrobials in 2014.[1] This is comparable to our data, which included topical antibiotics.

The reason for the decline in prescribing rate between 2010 and 2014 in age groups <20 years is unknown. It may relate to a decline in general practice presentations for upper respiratory tract infections, throat complaints and ear pain/earache between 2006–07 and 2015–16[7] or the fall in cefaclor and roxithromycin prescriptions seen in this study. Community campaigns during this period were discouraging antibiotics for common colds, which may have influenced behaviour. This would require a more detailed investigation.

This research examined routinely collected data from the EMR of general practice patients. In Australia, patients may attend any general practice; an advantage of POLAR is that it could track patients across practices within the POLAR catchment. A major limitation is that the data extracted are entirely dependent on the clinical software package and what GPs chose to document and where.[20] The reason-for-prescription field in some software packages was free text and in all packages was optional, resulting in a low completion rate. We were unable to determine the reasons for the antibiotic prescriptions and note that antibiotics may be prescribed for common conditions such as acne rosacea or acne vulgaris and for prophylaxis (eg malaria). This limitation requires information technology and standardisation solutions beyond the scope of this research. However, despite this serious limitation, we have shown how data available in general practice EMR might be used for AMS. Of the 50 practices in the dataset, six did not have a complete medication dataset, and a further five practices had incomplete consultation data. This may be due to software changes/updates between entry and extraction,[8,21] and requires further investigation. This dataset represents the doctors and patients in a defined urban area, so may not be typical of other regions. However, this may facilitate targeting of AMS initiatives to specific practices or defined localities.

Comorbidities were not examined in this study but would be a valuable addition to future studies. The data presented here are antibiotic prescriptions written by GPs. There is no linkage with dispensed data, so it is not known how many of these prescriptions may have been delayed prescriptions provided to a patient with instructions of only filling the prescription if the patient's condition deteriorated, or if a patient chose not to fill the prescription.

Implications for general practice

This study shows that Australian general practice EMR data can be extracted, and that a descriptive analysis of antibiotic prescriptions can identify targets for intervention in AMS programs and monitor change over time. For example, in this cohort, we revealed high use of broad-spectrum antibiotics and winter prescribing peaks. The continued prescribing of cefaclor and roxithromycin in winter peaks suggests incomplete awareness of changes in *Therapeutic Guidelines* for treatment of respiratory infections, or the use of alternative guidelines. Information for AMS would be significantly enhanced if reasons for prescription were documented in the EMR in a standardised field. GPs should be encouraged to complete the reason-for-prescription field. Software changes are required to improve data capture at the GP-software interface. GPs and Primary Health Networks should be encouraged to conduct AMS audits of antibiotic prescriptions from EMR.

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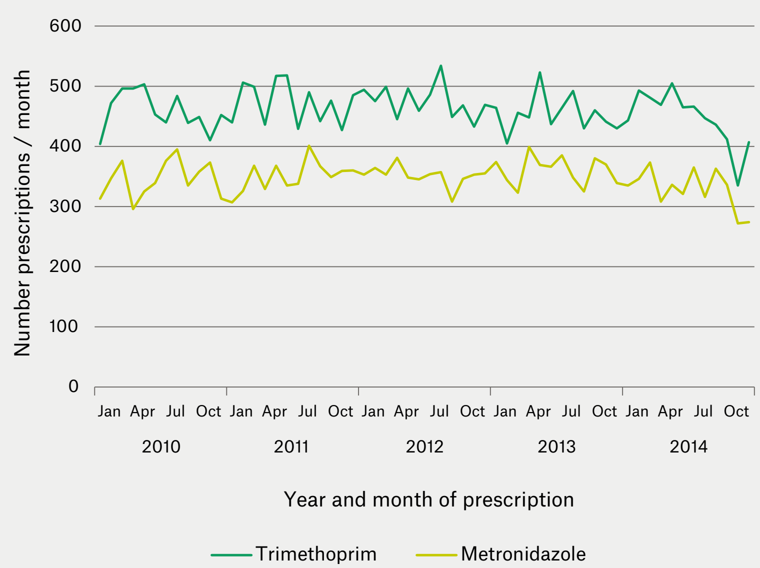

Figure 2. Trimethoprim and metronidazole prescriptions by year and month of prescription (6th and 10th most frequently prescribed)

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Workflow-based data solutions are required to support antimicrobial stewardship in general practice

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INTRODUCTION

Overuse of antibiotics contributes to the growing problem of antibiotic resistance in pathogens, which is impacting not only on health systems but the global economy.[1 2] To manage the problem, we must ensure adequate treatment and prevention of infection, while looking for opportunities to minimise the harm from unnecessary use of antibiotics.[3] To optimise antibiotic prescribing, we must know which antibiotics are being prescribed, to whom they are prescribed and the clinical indications for those prescriptions. These data can then be analysed for opportunities to effect and monitor change in antimicrobial stewardship (AMS) programmes. Most of the antibiotics consumed by humans are prescribed in the community,[4–8] so the general practice setting is important for AMS. Community antibiotic data often come from dispensed prescriptions (sales),[5] but dispensed prescriptions may include prescriptions from other community settings and providers (eg, residential facilities, hospital outpatients)[7 9] or may not include all general practice prescriptions (eg, private prescriptions).[10] This obscures the specific contribution by general practitioners in general practice. The reasons for prescriptions are not available in most dispensed prescriptions. Surveys are also used,[11–13] which collect the reason(s) for prescription, but these are resource intensive. A range of commercially available clinical software is used in general practice but they have limited interoperability, so the secondary analysis of electronic medical records (EMRs) and the targeting and monitoring of AMS initiatives has been difficult.

The aim of this study is to investigate the extent to which prescribing data available from Australian general practice EMRs can be used to identify possible targets for AMS by comparing antibiotic prescribing with antibiotic prescribing guidelines.

METHODS

Data were extracted from the deidentified patient records of consultations conducted between 1 January 2010 and 31 December 2014 from 50 general practices in Melbourne's eastern suburbs using POpulation Level Analysis and Reporting (POLAR) for general practice (formerly known as MAGNET).[14] Importantly, data were extracted from nominated fields in the EMR but not from free-text progress notes. Further details are provided with the analysis of the prescribed antibiotics.[15]

RESULTS

Data related to antibiotic prescriptions were available from 39 of the 50 practices. The other 11 practices did not have data for all 5 years. Over the 5 years, 597 302 antibiotic prescriptions were provided to 164 552 patients. Thirteen (33.3%) of the 39 practices (231 388 (38.7%) of the prescriptions) had no reason-for-prescription (reason) data recorded in the nominated field of the EMR. None of the other 26 practices had a reason documented for all antibiotic prescriptions, and there were 5748 different versions of reasons used for the antibiotic prescriptions. Many entries were free text, with some being uninterpretable (eg, single letters), or containing typographical errors. The number of antibiotic prescriptions with an interpretable reason was 103 217 (17.3%). Some reasons provided for an antibiotic prescription were attributed to an underlying condition, for example, asthma, or a symptom/sign, for example, fever, rather than a diagnosis.

DISCUSSION

We found recording of an interpretable reason for prescription of an antibiotic to be low in the EMRs currently in use in this cohort of Australian general practices. The separate field available for recording this information does not appear to be useful to general practitioners (GPs). This problem has also been reported in the 2019 Antimicrobial Use and Resistance in Australia (AURA) report. Since 2015, only 33.4% of prescribed systemic antibiotics had a reason for prescription recorded (p 85).[16] The AURA report gathers data from the largest, but non-randomised, voluntary sample of Australia-wide general practice EMR data (MedicineInsight).[17] The lack of reason-for-prescription has also been reported from general practices in England, where 31%,[18] and 33.2%[19] of systemic antibiotic prescriptions could not be linked to a reason for prescription. In Denmark, 32% of systemic antibiotic prescriptions had no clinical indication and, of those with a clinical indication, 26% were 'infection'.[20] Among a 19 million person cohort of privately insured patients in the USA, where reason for prescription is inferred from the diagnosis code, 28.5% of oral antibiotic prescriptions had no diagnosis code.[21] In the Netherlands, where prescribers are now required to write the indication on the prescription for 39 medicines (including some antimicrobial agents), there was poor recording of diagnosis codes and the authors called for improvements to Dutch prescribing software to allow easy linkage with the indication.[22]

A limitation is the small sample size, but a range of commercially available clinical software was used in these 39 practices. This study highlighted that some software uses standardised coding, others use free-text entries, and in some software or practices, this field may either be absent or is able to be turned off.

Poor and missing diagnostic coding in antibiotic prescribing and a lack of EMR standardisation are jeopardising the ability to conduct effective AMS in general practices. To enable meaningful analysis and feedback, the reason for prescription should be recorded in a standardised field suitable for data extraction. Clinical software packages should be designed to better facilitate consistent documentation of the reason for prescription and to fit within the workflow of a GP consultation. Information technology solutions[23–25] are urgently required to improve the EMR to support antimicrobial stewardship initiatives in the general practice setting. Until these are in place, it will be difficult to accurately target AMS programmes to general practice and to monitor progress over time.

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Contributors LH undertook the research and wrote the manuscript. LT, KB and DM assisted with interpretation of the analysis and contributed to the manuscript. All authors approve the manuscript and its submission.

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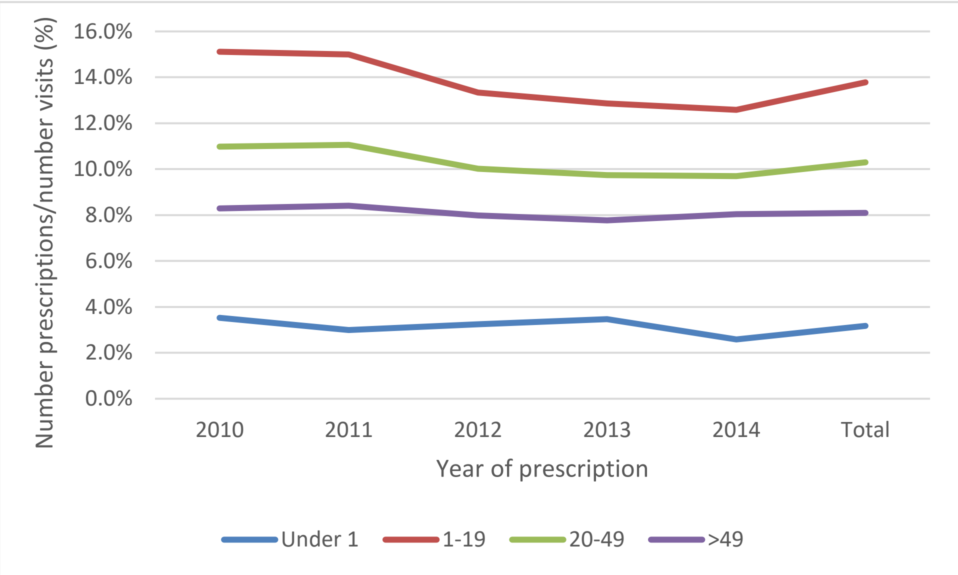
3.4.1 Age group analysis

An age group analysis was performed on the MAGNET dataset.

Results

The antibiotic prescribing rate per consultation varied with age. Age was available for 590,105 (98.8%) of the prescriptions. Patients aged 1-19 years made fewer consultations but received antibiotics at a higher rate per consultation than infants aged <1 and adults aged >19 years (figure 3). The rate of prescribing fell between 2010 and 2014 in age groups <50 years, with the largest declines occurring in age groups 1-19 years. Age groups >49 years showed little variation in the prescribing rate over time (figure 4). Cefalexin was the most prescribed antibiotic across all age groups. Women comprised 3,768,867 (60.5%) of the consultations; trimethoprim and metronidazole were more commonly prescribed amongst women than men.

Figure 3 Number of antibiotic prescriptions by number of visits (%) by age and year of prescription



Discussion

Prescribing rates varied with age and time. The high rates of antibiotic prescribing for children and adolescents demonstrated in this research suggests that this cohort may be useful to target in AMS interventions. The reason for the decline in prescribing rate in age groups <20 years is unknown. It may relate to a decline in general practice presentations for upper respiratory tract infections, throat complaints and ear pain/earache between 2006–07 and 2015–16.[84] The decline may also relate to the fall in cefaclor and roxithromycin prescriptions. These were often used for the above indications in children, and it suggests that they are not being replaced by other antibiotics. This should be investigated, with trends examined over subsequent years.

3.5 Conclusions about the monitoring of antibiotic prescriptions

The contribution of this research to my thesis has determined that current datasets are not adequate for complete monitoring of antibiotic prescribing. Monitoring and surveillance are key components of AMS. As illustrated in the literature review (Chapter 1) numerous recommendations have been made for robust meaningful monitoring and surveillance of antibiotic use. Recommendation 11 from the JETACAR report in 1999 was “that a comprehensive monitoring and audit system for antibiotic usage be established that covers all areas of antibiotic use.”[65] The first National AMR Strategy’s objective 2 was to implement AMS “to ensure the appropriate and judicious prescribing, dispensing and administering of antimicrobials.” Objective 3 is for surveillance of antimicrobial usage.[63] In the second National AMR Strategy 2020, objective 5 is for “integrated surveillance and response to resistance and usage, with a priority area for action“ Action 5.4 is to use evidence-based surveillance and monitoring data to inform actions and responses to contain antimicrobial resistance.”[1] Until we have complete antimicrobial prescribing data which can be assessed for guideline concordance, we cannot monitor if antibiotic prescribing is truly “judicious”. Use of electronic clinical software records, as used in the MAGNET/POLAR and MedicineInsight datasets, are the only current data sources that provide any reason-for-prescription data and both offer longitudinal patient data. POLAR is now used in several PHNs, in combination with other software extraction methods, for the Practice Incentive Payment Quality Improvement (PIP QI) process measures. However, this PIP QI dataset is not used for any clinical monitoring. MedicineInsight is a voluntary system managed by NPS MedicineWise for the monitoring of all prescribing. It provides antibiotic prescribing data to the Antimicrobial Use and Resistance in Australia (AURA) surveillance reports,[6-8] but represents less than 10% of all general practices.[204]

3.6 Recommendations

- A system which captures data from all general practices, provides reason-for-prescription, co-morbidities, demographic data and patient outcomes is required for complete monitoring of antimicrobial prescribing.

- Improved linkages between GP and hospital datasets are required for researchers to monitor patient outcomes. This will require government cooperation as hospitals are managed by the states, and GPs by the Commonwealth. GPs will also need to agree to the access of their records and have patient permission for this. Another possibility is to use anonymised My Health record data as this will contain patient treatments and outcomes.

- The reason-for-prescription field does not seem to either fit within GP workflow or to be useful for GPs and the use of free text hinders analysis. Clinical software developers should be encouraged to use standardised coding for the reason-for-prescription field and to make its use fit within GP workflow. Interventions to promote the use of the reason-for-prescription field may encourage some use in its current format, particularly if the existing data could be analysed and fed back to GPs with actionable AMS recommendations. However, without standard coding, it will require extensive cleaning and coding to be usable.

- Interim measures include analysis and feedback with peer comparisons of the rate of amoxicillin-clavulanate prescribing and the ratio of narrow spectrum (e.g. phenoxymethylpenicillin, amoxicillin and flucloxacillin) to broad-spectrum prescribing (e.g. amoxicillin-clavulanate and cefalexin).

Given the difficulties identified in monitoring antimicrobial prescribing, a more comprehensive framework for AMS in needed.

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Chapter 4 Developing a framework for antimicrobial stewardship in general practice

The literature review in Chapter 1 described the imperative for antimicrobial stewardship (AMS) in general practice. However, there was little description of what can be offered and how this is to be achieved. This chapter focusses on identifying the key components required for AMS in general practice by conducting a scoping review of international approaches to AMS in general practice. This manuscript was submitted to the journal *Antibiotics* for the special issue on *AMS in primary care* and is presented on the journal's template.

Outcomes arising from this research were presented at the Society of Academic Primary Care (SAPC) conference in Exeter, UK 3-5 July 2019 and at the RACGP GP19 conference, Adelaide, 23-25 Oct 2019.

antibiotics

MDPI

Review

Antimicrobial Stewardship in General Practice: A Scoping Review of the Component Parts

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Abstract: There is no published health-system-wide framework to guide antimicrobial stewardship (AMS) in general practice. The aim of this scoping review was to identify the component parts necessary to inform a framework to guide AMS in general practice. Six databases and nine websites were searched. The sixteen papers included were those that reported on AMS in general practice in a country where antibiotics were available by prescription from a registered provider. Six multidimensional components were identified: 1. Governance, including a national action plan with accountability, prescriber accreditation, and practice level policies. 2. Education of general practitioners (GPs) and the public about AMS and antimicrobial resistance (AMR). 3. Consultation support, including decision support with patient information resources and prescribing guidelines. 4. Pharmacist and nurse involvement. 5. Monitoring of antibiotic prescribing and AMR with feedback to GPs. 6. Research into gaps in AMS and AMR evidence with translation into practice. This framework for AMS in general practice identifies health-system-wide components to support GPs to improve the quality of antibiotic prescribing. It may assist in the development and evaluation of AMS interventions in general practice. It also provides a guide to components for inclusion in reports on AMS interventions.

Keywords: general practice; ambulatory care; general practitioner; family physician; antimicrobial stewardship; antibiotics; antibiotic prescriptions; health policy; framework

1. Introduction

Antimicrobial stewardship (AMS) may be defined as "a coherent set of actions which promote using antimicrobials responsibly" [1]. An AMS program is "an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness" [2]. The primary aim for AMS programs is to improve the safety and quality of patient care. It is important to optimize treatment while minimizing potential harms related to antimicrobial use for both the individual and the population. AMS typically applies to all antimicrobial agents, but this paper will also refer to antibiotics, as they are the most commonly prescribed antimicrobial agents in general practice (family medicine, ambulatory care).

AMS programs are now common in hospitals, but most of the antibiotics consumed by the population are from prescriptions written by general practitioners (GPs) in general practice (also known as ambulatory care) [3–6], where AMS remains embryonic. Studies of antibiotic use in the community strongly suggest high rates of inappropriate prescribing, particularly unnecessary use for self-limiting illnesses [7–10]. It is estimated that the escalation of antimicrobial resistance (AMR) will lead to 10 million deaths a year by 2030 [11], thus the need for action on AMS in the community is urgent. However, we do not fully understand what external or local practice factors may be important, nor do we understand the contributions from policy makers and non-prescribing practice team members. The reasons for antibiotic prescriptions are multi-factorial and may include the patient expectation that antibiotics will help manage a viral or self-limiting infection, a lack of alternative treatments, and a mismatch between pack size and prescribing guidelines and GP prescribing and communication habits [12]. Patient populations and health systems differ, thus a variety of approaches at different levels may be required. AMS interventions have been heterogenous, demonstrating little superiority of any intervention or combination of interventions [13–16]. There is little evidence for the sustainability, acceptability or scalability of interventions [15–19]. Regulatory and cultural environments are not well described [20]. The reasons why interventions do not work are under researched [21].

Identifying the component parts of a framework for AMS in general practice, along with a description of the roles and responsibilities of key stakeholders, is an essential step towards developing an AMS model that can be effectively implemented. Such a framework can also highlight gaps and priorities for AMS in general practice. A preliminary literature search did not find any published existing health system frameworks specific to AMS in general practice. A scoping literature review was therefore chosen, as this can describe the quantity of research in an area, identify gaps that can be addressed through ongoing research and map the key concepts that underpin a research area [22–24].

1.1. Aim of This Scoping Review

The aim of this scoping review was to identify the health-system-wide component parts of AMS in general practice to inform a framework which may be used to guide activity in this health care context.

1.2. Scoping Review Question

What are the core components of general practice AMS frameworks or model frameworks that have been described in the existing published literature?

A secondary question was asked: Which stakeholders have responsibility for governance of general practice AMS?

2. Results

The database searches returned 1261 non-duplicate citations, and after title and abstract screening, 81 papers were screened by full text. Five papers were selected from the database searches [25–29]; four papers were identified by searching the references of included papers [30–33]; one paper from a personal library [20]; and six papers from the website searches [2,34–38]; resulting in 16 papers that were included in the final review (Figure 1).

Seven papers described single-country AMS frameworks: two were from England [25,30], two from Sweden [31,32], two from Australia [26,34] and one from the United States of America (USA) [33]. One paper was a description of general practice AMS in France, which was presented along with an 'inventory of AMS programs' from 15 other European countries, the USA, and Canada [29]. One paper detailed the European Union (EU) guidelines for AMS [36] (the EU in 2018 had 28 member states). Two were within the United Kingdom [2,37], the other five papers were not geographically limited [20,27,28,35,38] (Supplementary File 1).

Ten papers described a health-system-wide approach to AMS which included general practice along with other health sectors such as hospital and aged care services [2,25,30–32,34–38]. When a component was not clearly identified as applicable to only one part of the health system (e.g., hospital or aged care only) it was assumed that the component was applicable to general practice. The other six papers focused on general practice-specific AMS frameworks [20,26–29,33], of which two were further limited to the management of respiratory tract infections (RTI) [26,27]. These were included as RTIs account for a large proportion of antibiotic prescribing in general practice [39,40], and one was "envisaged as a prototype that can be adapted to other infections in the long term" [27] (Supplementary File 1).

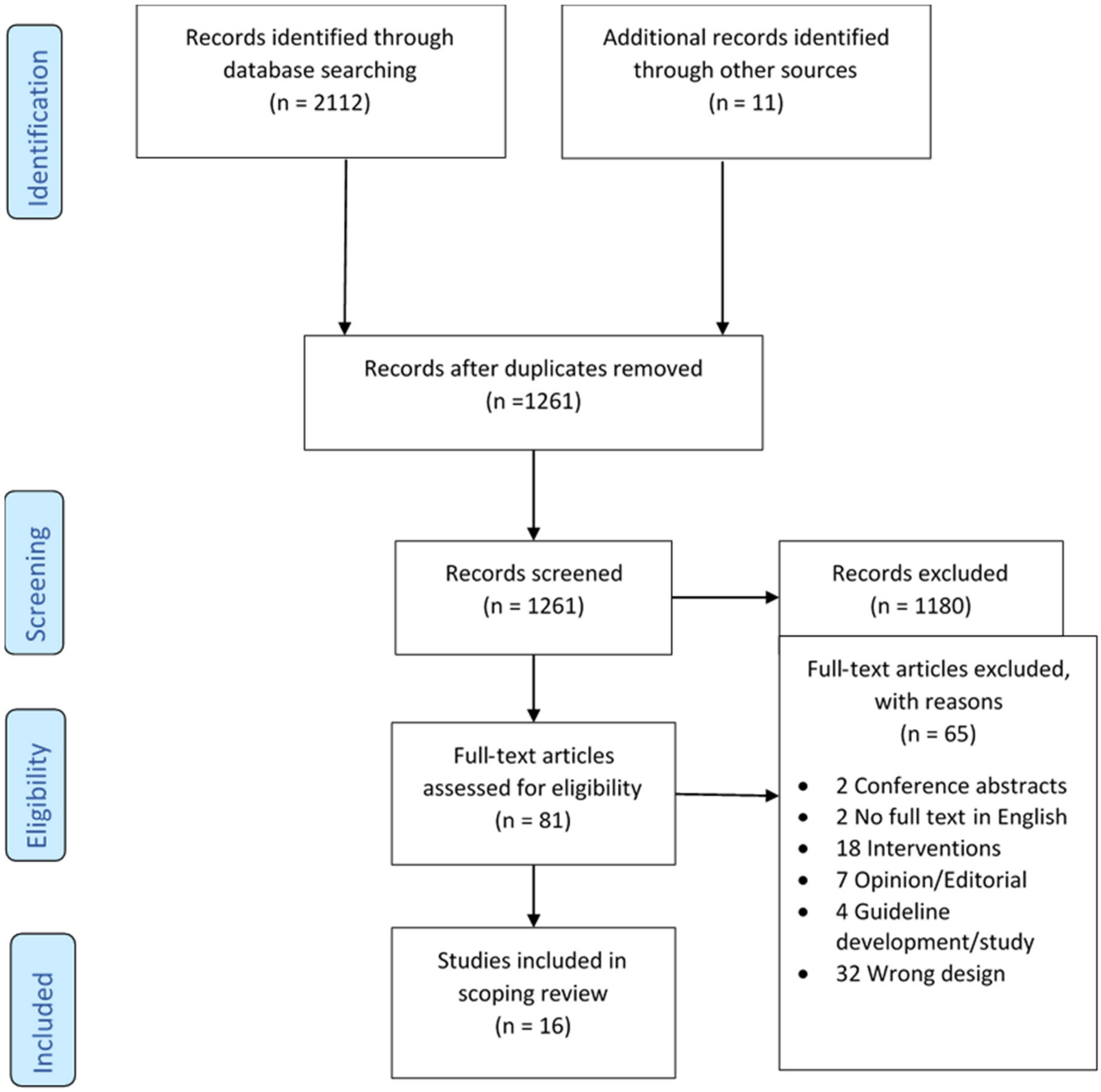

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) flow diagram.

One paper was published in 2001 [28]; the other 15 papers were published between 2012 and 2018 [2,20,25–27,29–38] (Supplementary File 1).

Funding sources were not stated in nine papers [25,28,29,31,32,34,36–38], five papers received non-commercial support [2,20,26,30,33], and two papers received funding from commercial entities [27,35] (Supplementary File 1).

2.1. The Identified Components

Using the focus of the scoping review question "What are the core components of general practice AMS frameworks or model frameworks?", the components were categorized under six broad headings of: governance, education, consultation support, pharmacy and nurse based approaches, monitoring, and research (Table 1). Each has subcomponents. The secondary question of "which stakeholders have responsibility for governance of general practice AMS?" is addressed under governance.

Table 1. AMS in general practice: Chart of identified component parts.

Component/Author, Date	**Ashiru-Oredope, 2012 [30]**	**Ashiru-Oredope, 2013 [25]**	**ACSQHC, 2018 [34]**	**BSAC, 2018 [35]**	**Del Mar, 2017 [26]**	**Essack, 2013 [27]**	**European Commission, 2017 [36]**	**Keller, 2018 [20]**	**McNulty, 2001 [28]**	**Molstad, 2008 [31]**	**Molstad, 2017 [32]**	**NICE, 2015 [2]**	**Sanchez, 2016 [33]**	**UK Faculty [37]**	**Wang, 2015 [29]**	**WHO, 2015 [38]**
2.1.1. Governance																
National action plan, policy or strategy	x		x	x		x	x			x	x				x	x
AMR included on national risk register																x
Regulations around AMS and antibiotic prescribing	x	x	x	x	x	x	x					x			x	x
Accreditation of prescribers				x												x
Funding for AMR/AMS			x	x			x				x					x
Planning for release of new antibiotics				x								x		x		x
Practice level AMS policy/program/activities	x		x	x			x					x	x			
2.1.2. Monitoring and Feedback																
Monitoring of antibiotic prescriptions	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Monitoring of antimicrobial resistance		x	x	x	x	x	x		x	x	x	x	x	x		x
Feedback to prescribers and reporting		x	x	x	x		x	x	x	x	x	x	x		x	
2.1.3. Education																
Community and patient education about AMR and AMS	x		x	x	x	x	x	x	x	x	x		x	x	x	x
GP continuing education in AMS and AMR	x		x	x	x	x	x	x	x		x	x	x		x	x
GP education on communication skills, patient-centred approaches and shared decision making	x		x	x	x	x	x	x				x	x			
GP education on non-antibiotic management of self-limiting infection			x	x	x	x	x		x			x	x	x		
GP education on delayed prescribing/watchful waiting			x	x	x	x	x	x				x	x	x	x	
General practice team member education			x	x				x	x		x		x			
Independent education (restrict pharma marketing)			x	x		x	x		x							x

Table 1. *Cont.*

Component/Author, Date	Ashiru-Oredope, 2012 [30]	Ashiru-Oredope, 2013 [25]	ACSQHC, 2018 [34]	BSAC, 2018 [35]	Del Mar, 2017 [26]	Essack, 2013 [27]	European Commission, 2017 [36]	Keller, 2018 [20]	McNulty, 2001 [28]	Molstad, 2008 [31]	Molstad, 2017 [32]	NICE, 2015 [2]	Sanchez, 2016 [33]	UK Faculty [37]	Wang, 2015 [29]	WHO, 2015 [38]
2.1.4. Consultation Support																
Prescribing guidelines			x	x		x	x	x	x	x	x	x	x		x	x
Point of care tests			x	x	x		x	x	x	x	x	x			x	x
Microbiology testing and reporting			x	x		x	x		x		x	x			x	x
Allergy testing			x				x									
Electronic decision support for prescribers			x	x			x	x	x			x	x		x	
Expert advice			x	x		x	x						x		x	
Decision support for use with patients			x	x	x		x	x	x		x	x	x		x	
2.1.5. Pharmacy and Nursing Approaches																
Unit dispensing					x		x					x			x	
Supply of and timely access to antibiotics	x		x				x				x	NA				x
Pharmacy review and advice			x	x		x	x						x		x	
Appropriate disposal of left-over antibiotics			x				x					NA				
Nurse triage, patient assessment and education			x	x			x	x			x		x			
2.1.6. Research																
Research into AMR/AMS gaps, translation into practice			x	x	x		x	x	x		x	x	x			x
Research into context, culture of general practice and behaviour change strategies		x	x	x		x	x	x			x					

Abbreviations: AMR Antimicrobial resistance; AMS antimicrobial stewardship; GP general practitioner; NA: Not applicable/excluded in this paper.

2.1.1. Governance

Governance, including descriptions of strategies, policies, action plans, regulations and responsibility to support AMS in general practice, was reported in several frameworks (Table 1, with examples in Supplementary File 2).

The need for a national action plan or strategy or policies for antimicrobial resistance (AMR) was described in nine papers [27,29–32,34–36,38]. Descriptions of responsibility were often generic, such as "Overall accountability for antimicrobial management lies at the highest level of each health service organisation, and with the clinicians responsible for delivering services efficiently and effectively" [34]. The clearest description of specific responsibility was in Sweden's AMR program (Strama) "Strama is composed of a national steering group and regional Strama groups in every Swedish county . . . " [31]. England and Australia have called for commissioning groups [37] or primary care networks to assist [34], and England's Antimicrobial Stewardship subgroup of the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection has a remit which includes the development of AMS tools [30], which may indicate emerging structures.

The World Health Organization (WHO) suggested the inclusion of AMR on the national risk register as "an effective mechanism for cross government commitment" [38]. Ten papers described regulations around antibiotic prescribing as being critical components of community-based AMS activity [2,25–27,29,30,34–36,38]. Two papers specifically described the accreditation or appraisal of health professionals' competency to prescribe antibiotics [35,38]. Explicit policies and plans to govern the use of new antibiotics when released were described in four papers, with a focus on curtailing misuse and restricting use to indications of need [2,35,37,38]. The need for practice-level AMS policies was discussed in six papers, although specific examples were limited [2,30,33–36]. Five papers reported on the need for funding to support AMS activities in general practice, but few details were described about who was responsible for providing this funding or what specifically was funded [32,34–36,38].

2.1.2. Monitoring and Feedback

Monitoring (audit, surveillance or tracking), including monitoring of antibiotic prescribing and local patterns of AMR amongst pathogens, was universally included in the frameworks. More specifically, monitoring of antibiotic prescriptions was included in all 16 papers [2,20,25–38], while monitoring of AMR in pathogens was described in 13 papers [2,25–28,31–38]. Feedback to prescribers was described in 12 papers [2,20,25,26,28,29,31–36], but specific examples were limited. Various linkages were described to potentially enhance the utility of this monitoring, including links between prescribing data and antimicrobial resistance, as well as prescribing data links to clinical data including patient demographics, patient management and outcomes data, incidence of infections, and comparisons with prescribing guidelines (Table 1, examples in Supplementary File 2).

2.1.3. Education

The educational activities identified in this scoping review included education of the public and/or patients, as well as continuing education and professional development for the prescribers in general practice (Table 1, examples in Supplementary File 2).

Thirteen papers described the need for public education campaigns to raise awareness of AMR and/or unnecessary use of antibiotics as a core component of an AMS framework [20,26–36,38].

Thirteen papers discussed the importance of providing ongoing education to GPs about AMS and AMR [2,20,26–30,32–36,38]. Six papers described the importance of GPs providing education to patients about appropriate use of antibiotics during a consultation [20,27,33,34,36,37] and nine papers discussed GPs teaching patients to manage self-limiting infections without antibiotics [2,26–28,33–37]. Nine papers discussed training GPs to enhance their communication skills; this included training to use patient-centred approaches and shared decision making [2,20,26,27,30,33–36]. Ten papers described training GPs to use strategies such as delayed prescribing (providing prescriptions to commence only if symptoms worsen and informing patients on how to recognize this) and/or watchful waiting (informing patients about symptoms of concern that should prompt a rapid return for review) [2,20,26,27,29,33–37].

Six papers described education about AMS and AMR for other general practice team members, including practice nurses and community pharmacists [20,28,32–35].

The promotion and marketing of antibiotics by pharmaceutical companies was recognized as a driver for antibiotic prescribing, and the need for independent education was addressed in six papers [27,28,34–36,38].

2.1.4. Consultation Support

Several frameworks discussed providing access to tools and resources that a GP might utilize at the point of care to help inform prescribing decisions. These included: prescribing guidelines; point of care tests and/or laboratory-based investigations including microbiology tests; allergy testing; electronic decision support for prescribers; access to expert advice (such as a clinical microbiologist or infectious diseases specialist phone advice); resources to support shared decision making with patients (Table 1, examples in Supplementary File 2).

The promotion and use of antibiotic prescribing guidelines was described in 12 papers [2,20,27–29,31–36,38].

Point of care or rapid diagnostic (office-based) tests (e.g., C-reactive protein; influenza antigens, group A streptococcal antigen) were discussed in 11 papers [2,20,26,28,29,31,32,34–36,38]. The discussion included both advantages and possible disadvantages to their use [35].

Nine papers addressed the importance of access to suitable microbiology testing and reporting [2,27–29,32,34–36,38]. This included having access to reliable tests when needed, taking samples correctly, and appropriate review of results. The role of laboratory reporting in guiding the use of antibiotics was also acknowledged, e.g., selective reporting of antimicrobial susceptibilities to direct users to narrow spectrum agents in line with treatment guidelines.

Two papers mentioned access to beta-lactam allergy testing which may help clarify suitable treatment options for the future [34,36].

Electronic decision support for GPs, namely organised patient health and prescribing information to aid decisions, was mentioned in eight papers [2,20,28,29,33–36].

Access to expert advice was described in six papers [27,29,33–36]. Two different types of expert advice were mentioned. The first was individual patient specific management advice in which GPs could discuss clinical concerns directly with an expert (e.g., a clinical microbiologist, pharmacist) [33–36], the second was expert advice for the practice-level AMS program [27,35]. This involved discussion of general strategies for patient management rather than being individual-patient-focused.

Decision support tools for use with patients, including shared decision-making tools (e.g., infographics to guide discussions about options—which might include the natural history of the infection, the likely value of antibiotics, and potential side effects of medications) and patient-focused information about infections and antibiotics (e.g., printed materials), were described in ten papers [2,20,26,28,29,32–36]. Two of the ten papers also mentioned the importance of patient-focused information being available in other languages [29,32].

2.1.5. Pharmacy and Nursing Approaches

These were mainly pharmacy-based, with some recognition of a role for practice-based nurses (Table 1, examples in Supplementary File 2). Pharmacy supply of, and access to, antibiotics was addressed in five papers [30,32,34,36,38]. Pharmacy interventions such as unit-dispensing of medication (dispensing only the prescribed quantity) were mentioned in four papers [2,26,29,36]. Pharmacy review of prescriptions and advice to consumers and health professionals was described in six papers [27,29,33–36]. Two papers described the disposal of left-over antibiotics as being important [34,36].

A role for practice- or community-based nurses in AMS was described in six papers [20,32–36] (Table 1, with examples in Supplementary File 2). Three papers suggested that nurses could perform a pre-visit triage [20,32,33], two of which were nurse phone call hot lines [32,33], while the third paper described the use of a nurse for pre-visit patient assessment, triage and patient education [20].

2.1.6. Research

The need for targeted, prioritized research into AMR and AMS in the community was addressed in ten papers [2,20,26,28,32–36,38], with specific needs mentioned for implementation research and evaluation of the translation of evidence to practice. Research that recognises the context and culture of general practice and the use of behaviour change science was described in seven papers [2,20,25,27,34–36]. Two of these stated that there is no 'one size fits all' approach to AMS programs [34,35], and a third noted that "Few studies focused on the organization component of the work system model or the structures and roles that organize a clinic" [20] (Table 1, examples in Supplementary File).

3. Discussion

Our scoping review of the literature on frameworks for AMS in general practice found the core components to be: 1. Governance. 2. Monitoring of antibiotic prescribing and AMR with feedback to GPs. 3. Education of the public and health professionals about AMR and AMS. 4. Consultation support. 5. Pharmacy- and nursing-based approaches. 6. Research.

The lack of clear descriptions about who was responsible for implementing and coordinating these activities was striking. National-level responsibility for the monitoring of antibiotic resistance and prescribing was described, but there was no clear description of any governing body responsible for all aspects of this framework, with the exception perhaps of Strama in Sweden [31,32]. England and Australia have called for commissioning groups or primary care networks to assist [34,37], and England's Antimicrobial Stewardship subgroup of the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection has a remit which includes the development of AMS tools [30], which may indicate emerging structures. There was no clear description of GPs' perceptions about governance or clinical autonomy.

Monitoring of antimicrobial resistance and prescribing was almost universal but, apart from Sweden's Strama program [31,32], it was not clear who should provide the analysis and regular feedback to GPs, where the data should be published or what GPs' perceptions were of the monitoring process or feedback. Where GPs were to analyse their own prescribing, it was not stated how patients should be selected, which leaves open the possibility of selection bias, and there were few descriptions of what GPs should be monitoring.

While there were calls for health professional education on AMS, apart from noting that pharmaceutical companies should not be responsible for this, no mandatory education programs were described, nor was it clear who should be responsible for the development, delivery and evaluation of education programs, or to what extent AMS education should be provided to general practice support staff. Similarly, GPs were called upon to educate patients about management and treatment of their infections (including non-antibiotic management and treatment), with patient information leaflets and posters of the main aids offered. It was not clear who should develop these, what should be included, or how to check that they met basic literacy standards or that different language versions were checked for cultural appropriateness. Public awareness campaigns about AMR and AMS occurred but were not well described. It was recognised that expert advice regarding general practice antibiotic prescribing decisions may be useful but is difficult to arrange during a consultation. The only description of an established expert advice program for general practitioners was telephone advice in France [29].

Pharmacist- and nurse-based approaches were poorly described. Their roles in AMS and that of the general practice team needs further research. To ensure consistent messages are provided to patients, AMS programs may benefit by including all general practice staff and community providers.

In research, customising interventions for the context and culture of the health service were recognised as critical to the success of AMS programs. Factors such as practice size and time for appointments [41], patient age, GP–patient relationship, being located in a rural area and socio-economic status affect antibiotic prescribing rates [42–44]. Local barriers and enablers may partly explain variation in AMS outcomes. For example, a GP with a high workload and few resources may find it easier to prescribe a requested antibiotic than to attempt to educate the patient about why they do not need an antibiotic for that condition. Social science and behaviour change principles would also appear to be important in the development of future AMS interventions [2,20,25,27,34–36].

There are several potential limitations to this review. The search strategy may have missed studies which were not indexed under the search terms. Only a limited search was made for grey literature and all papers were restricted to the English language, with eight papers (50%) from Europe. The selected papers may not have included a full description of their AMS frameworks—one paper explicitly excluded public awareness of AMR and disposal of waste medicines [2], but others may not have stated their exclusions. One reviewer conducted the screening and extraction, which may have introduced selection bias. All three authors provided input into the development of the framework. Scoping reviews do not rate the quality of the evidence [45], and the included papers reported few challenges with implementing frameworks, such as resistance from GPs. Thus, implications for policy cannot be graded [45]. This scoping review may have limited applicability for other primary care community prescribers, e.g., dentists, nurse practitioners or pharmacists, and in countries that were not represented in the papers assessed, including countries where antibiotics are available without prescription. Identification of resources to support the identified components, such as educational resources, was beyond the scope of this research.

Interestingly, this review demonstrated that none of the selected papers had articulated the framework in this way. This may be because the evidence for AMS in general practice is still emerging. Although the core elements of the framework appear to have face validity, the method did not enable the authors to examine possible inter-dependencies between components, or examine whether components should be introduced in any order. Missing components or unexplored interdependencies may partly explain why AMS interventions have succeed in some contexts but not in others [17,46]. Possible synergy between the diverse components [26] may explain why multi-faceted interventions were more likely to be successful in reducing antibiotic prescribing [17,47], e.g., it is possible that GPs and/or communities require access to a range of resources. Further research amongst relevant stakeholders is required to determine the validity of these components and to determine the framework's utility for the development, evaluation and reporting of AMS interventions in general practice.

4. Materials and Methods

The scoping review was conducted according to the Joanna Briggs Institute's standardised method [45]. Selection criteria were developed a priori then iteratively refined to capture papers that answered the scoping review question.

4.1. Selection Criteria

To be included, the paper had to describe an AMS framework that was applicable to GPs working in a community-based general practice, in a country with a developed health care system where systemic antibiotics are primarily available by prescription from a registered provider (e.g., OECD country). All eligible publications were included even if there were multiple publications about the same framework, but with varied analysis (e.g., improvements to or sustainability of the framework). Publications which included, e.g., hospitals and aged care were included if they described a health-system-wide approach to AMS which included general practice.

The search strategy excluded AMS activities that targeted only:

- Hospitals, including their emergency departments and outpatient (specialist) clinics, residential care including nursing or aged care homes; veterinary clinics;

- Other community prescribers (e.g., nurse practitioners, dentists, other medical specialists, veterinarians);
- Patients or community members; animals; the environment;
- Settings where antibiotics were frequently available without a prescription.

Reports about antibiotic usage or AMR; clinical guidelines on infections and their treatment; the development, use of and/or promotion of antibiotic prescribing guidelines; the development of new antibiotics or vaccines; infection prevention, the relationship between antibiotic use and resistance; the economic burden of resistance were also excluded. Reports about interventions were excluded if they did not also describe the health system context in which they were carried out.

The search was limited to English language documents, and no time limits were imposed.

4.2. Search Strategy

The Ovid Medline database was searched to identify relevant keywords and index terms. The identified keywords and index terms were then used to search the Embase, Ovid Medline, Scopus, CINHAL, PsychINFO and Cochrane databases from inception to September 2018. Pre-determined search terms included the headings (with synonyms) for antibiotics AND antibiotic prescriptions AND general practitioners AND general practice AND stewardship AND framework (the search strategy is provided in Supplementary File 3). The reference lists of included studies and personal libraries were also reviewed.

A limited English-language grey literature search examined the websites of the Australian Commission on Safety and Quality in Health Care, Royal Australian College of General Practitioners, the European Centre for Disease Prevention and Control (ECDC), England's National Health Service, the National Institute for Health and Care Excellence, the Royal College of General Practitioners, the British Society for Antimicrobial Chemotherapy, USA's Centers for Disease Control and Prevention (CDC), and the World Health Organization (Supplementary File 3); searching for 'antibiotic' or 'antimicrobial stewardship', or 'general practice' or 'family medicine' and included papers if they met the inclusion and exclusion criteria.

4.3. Data Collection, Charting and Identification of AMS Components

Database citations were downloaded to Covidence [48] and duplicates removed. Titles and abstracts were reviewed for inclusion, followed by full text screening. This was done by one author (LH) with a second reviewer (DM) available for discussion where required. The full texts of the selected references were uploaded into NVivo 12 Plus [49] for coding by one author (LH). Each text was read through, then analysed thematically using line-by-line inductive coding [50]. All three authors then developed and refined the coding into themes. This involved inductive analysis using repetition of themes across the papers [50,51] and deductive/a priori analysis based on experience in hospital AMS programs (KB) and general practice quality improvement programs (DM and LH). Component parts were mapped onto a table developed for this review with input from all three authors.

5. Conclusions

This manuscript reviews the existing literature on general practice AMS frameworks and describes, for the first time, a comprehensive multifaceted framework with the potential to focus attention on neglected areas in AMS in general practice. The articulation of the six core components into an actionable framework should help guide future activity to strengthen AMS in general practice. It not only provides a framework to guide AMS activity, it also provides a guide to the components that may be considered and reported in future publications about AMS interventions. Gaps in the AMS framework are highlighted, including that identification of responsibility for the components was lacking, as were the perceptions of GPs.

Supplementary Materials: The following are available online at http://www.mdpi.com/2079-6382/9/8/498/s1, File S1: The characteristics of the included papers. File S2: Examples of the components. File S3: The search strategy.

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Supplementary file 1 Characteristics of the included papers

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Ashiru-Oredope, 2012[1]	England	Department of Health's Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection.	This paper describes the development of new antimicrobial stewardship programmes for primary care and hospitals by the Department of Health's Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection: Antimicrobial Stewardship in Primary Care Initiative.	Narrative description of government initiative	Not stated	Description of components being implemented	RCGP supported	MIHR, CIPM, CPSSQ/NIHR, BSAC, British Infection Association

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Ashiru-Oredope, 2013[2]	England	English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR).	Public Health England has developed a new national programme, the English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). The programme will bring together the elements of antimicrobial utilization and resistance surveillance in both primary and secondary care settings, alongside the development of quality measures and methods to monitor unintended outcomes of antimicrobial stewardship and both public and professional behaviour interventions. This article reports on the background to the programme development, the current oversight group membership and the public reporting structure.	Narrative description of government initiative	Not stated	Description of components being implemented	RCGP represented	Not stated

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
ACSQHC, 2018[3]	Australia	Australian Commission on Safety and Quality in Health Care	This publication is designed to provide clinicians and managers working in all healthcare sectors with the evidence, expert guidance and tools they need to initiate and sustain AMS activities in a diverse range of practice settings – hospitals (public and private, metropolitan and rural), primary care and aged care homes	Chapters 1–7 provide strategies for implementing and sustaining AMS. Chapters 8–12 examine the roles of the different clinicians in AMS.	Clinicians and managers working in all healthcare sectors.	Recommended framework	Advice and review	Not stated
BSAC, 2018[4]	Global workbook for AMS across health system	British Society for Antimicrobial Chemotherapy [BSAC]	E-book on Global Antimicrobial Stewardship that is relevant to health care professions working in preventing and managing infection across the healthcare communities and health care facilities	Interactive e-book on global AMS, building on a massive open on-line stewardship course.	It aims to support health care professionals, or teams, or policy makers interested in learning about bringing the principles of stewardship to the bed side.	Theoretical model with real-world case studies	Not stated	Alere now Abbott, Accelerate Diagnostics, MSD, Pfizer Inc
Del Mar, 2017[5]	Australia	Bond Uni, Uni Qld, TG, NPS	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.	Narrative review of literature and discussion at national roundtable meeting in 2017.	Australian researchers, policy makers and organisations came together to discuss ways of dealing with the antibiotic resistance crisis from a general practice perspective.	Theoretical model	Lead author. GPs attendees at the national roundtable.	NHMRC for CRE-MAR

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Essack, 2013[6]	Global	In collaboration with the Global Respiratory Infection Partnership: Attila Altiner (Germany), John Bell (Australia), Martin Duerden (UK), Sabiha Essack (South Africa), Roman Kozlov (Russia), John Oxford (UK), Antonio Carlos Pignatari (Brazil), Aurelio Sessa (Italy), Alike van der Velden (The Netherlands).	The global respiratory infection partnership has formulated a pentagonal (five P) framework for the non-antibiotic management of upper respiratory tract infections (URTIs) – one of the most common conditions in primary care for which antibiotics are prescribed.	Framework developed by GRIP and reviewed by healthcare professionals in 18 countries.	The global framework is strengthened through a collaborative approach by multiple primary healthcare provider specialties and is applicable across countries and continents. It is envisaged as a prototype that can be adapted to other infections in the long term	Theoretical model	Collaboration with primary healthcare provider specialties	Reckitt Benckiser Group PLC Editorial assistance during the development and revision of this manuscript was provided by Mash Health Limited and supported by Reckitt Benckiser Group PLC. The authors provided substantial contributions to the development and revision of the manuscript and approved the final version of the manuscript.

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
European Commission, 2017[7]	Europe	European Centre for Disease Prevention and Control	These guidelines aim to reduce inappropriate use and promote prudent use of antimicrobials. The guidelines are complementary to infection prevention and control guidelines which may exist at national level. These guidelines are intended to be used to inform and assist activities to promote the prudent use of antimicrobials in humans.	These Guidelines on prudent use of antimicrobials in human health are based on a technical report prepared by the European Centre for Disease Prevention and Control (ECDC) with input from EU Member States experts and stakeholders, which should be referred to for details of the methodology used in creating the guidelines as well as for additional references	They target all actors who are responsible for, or play a role in, antimicrobial use and whose contribution is necessary to ensure that antimicrobials are used appropriately.	Recommended model	Not stated	Not stated

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Keller, 2018[8]	Global Systematic literature review	USA: Johns Hopkins University School of Medicine; Agency for Healthcare Research and Quality; University of Pennsylvania Perelman School of Medicine; North western University Feinberg School of Medicine	Our aim in using this approach was to identify how aspects of the clinic work system could affect AS intervention successes. [Set within "a wider external environment"]	Systematic literature review. 42 quantitative and 17 qualitative articles met the eligibility criteria, with 1 study considered both quantitative and qualitative. We evaluated identified sources and recorded study design and aspects of the studies that could be interpreted in the context of the SEIPS 2.0 model. We also described how measures and outcomes of the studies could be interpreted in the context of the SEIPS 2.0 work system. The SEIPS 2.0 work system includes 5 components within a wider external environment: (1) person(s), (2) tools and technologies, (3) organization, (4) tasks, and (5) physical environment.	Not stated	Theoretical model developed using a human engineering framework to incorporate the entire work system	Not stated	Agency for Healthcare Research and Quality. SCK received funding from the National Center for Advancing Translational Sciences/Johns Hopkins Institute for Clinical and Translational research.

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
McNulty, 2001[9]	Global	UK: Gloucester Royal Hospital	Improving appropriate use of antimicrobials in primary care will require a multi-faceted approach including not only education of primary care health professionals, but also a wider evidence base underlying management of infections, prescribing advice and support, monitoring of antibiotic prescribing and resistance and increasing public awareness.	Narrative literature review	Not stated	Theoretical model	Not stated	Not stated
Molstad, 2008[10]	Sweden	Strama (Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance)	The aim of this review is to describe the Strama programme and summarise the results of the first 10 years.	Description of Sweden's Strama (AMS) program across primary care, hospital care, nursing homes, and day-care centres.	Not stated	Report of Strama after 10 years of implementation	Represented in regional Strama groups	Not stated
Molstad, 2017[11]	Sweden	Strama	This paper outlines the stepwise development of the strategic programme against antibiotic resistance in Sweden over a period of 20 years.	We describe the structure, key functions and interventions of the initiative across different working areas in human medicine.	The work described here and the lessons learnt could inform countries implementing their own national action plans against antibiotic resistance.	Report of Strama after 20 years of implementation	Represented in local multi-professional groups	Not stated

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
NICE, 2015[12]	England, Wales	National Institute for Health and Care Excellence	The purpose of this guideline is to provide good practice recommendations on systems and processes for the effective use of antimicrobials.	Scoping search, systematic literature review, meta-analysis, call for evidence, discussed by multi-disciplinary group, reviewed clinical and cost-effectiveness, recommendations made. 4-week public consultation.	This guideline may be of interest to adults, young people and children (including neonates) using antimicrobials or those caring for these groups. This includes people and organisations involved with the prescribing and management of antimicrobials in health and social care settings.	Recommended model	Yes	NICE commissioned the NICE Medicines and Prescribing Centre to produce this guideline.

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Sanchez, 2016[13]	USA	Centers for Disease Control and Prevention	The Core Elements of Outpatient Antibiotic Stewardship provides a framework for antibiotic stewardship for outpatient clinicians and facilities that routinely provide antibiotic treatment.	CDC's Core Elements of Outpatient Antibiotic Stewardship were developed through a combination of consolidating evidence-based antibiotic stewardship practices and building on or adapting known best practices for antibiotic stewardship across other clinical settings, such as the core elements outlined for hospitals and nursing homes. A narrative review of evidence on outpatient antibiotic stewardship interventions, policies, and practices through May 2016 was conducted…Subject-matter experts were asked for specific feedback on the feasibility, acceptability, recommended supplementary materials, and potential for the core elements to promote effective and meaningful improvements in outpatient antibiotic prescribing.	The intended audiences for this guidance include clinicians (e.g., physicians, dentists, nurse practitioners, and physician assistants) and clinic leaders in primary care, medical and surgical specialties, emergency departments, retail health and urgent care settings, and dentistry, as well as community pharmacists, other health care professionals, hospital clinics, outpatient facilities, and health care systems involved in outpatient care	Recommended model	Subject matter experts were identified with expertise in pediatrics, internal medicine, family medicine, emergency medicine, infectious diseases, and pharmacy.	CDC did not accept commercial support for this continuing education activity.

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
UK Faculty of Public Health.[14]	UK	UK Faculty of Public Health, Royal College of Physicians, Royal Pharmaceutical Society, Royal College of Nursing, Royal College of General Practitioners.	Our recommendations for action focus on those areas where there is the potential for immediate action.	Not described	The professional bodies supporting this joint statement consider that action must be taken collegiately by the professions, commissioners, service providers, quality assurance bodies and regulators across the UK to reduce the threat of AMR. Leadership and action must be taken at local, regional, national and international level in support of the AMR strategy, and to tackle this issue in a concerted manner.	Recommended model	Yes	Not stated

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
Wang, 2015[15]	France and 17 countries of Europe and North America.	France: CHU de Nancy–Hôpitaux de Brabois; université de Lorraine.	We had for aim to identify measures implemented in France and abroad for antibiotic stewardship in general practice.	A literature review was conducted from January 2000 to July 2014. Emails were sent to every infectious diseases department, to all regional health authorities (ARS), to the health insurance offices (CPAM) with the highest and lowest antibiotic use, and to the ministry of health to make an inventory of all antibiotic stewardship programs. The ministry of health, the board of general practitioners, infectious diseases specialists, pharmacists, and the medical and pharmacy schools of the nation's capital were contacted in 17 countries of Europe and North America.	Our results could be useful to guide policy for antibiotic stewardship in France.	Case study model	Not stated	Not stated

First author, year of publication	Country(s) for application	Lead organisations	Aim or purpose of framework	Methodology of paper	Intended audience	Stage of framework	GP input into or support for framework	Funding sources
WHO, 2015[16]	Global	World Health Organization	This global action plan provides the framework for national action plans to combat antimicrobial resistance. The overall goal of the action plan is to ensure, for as long as possible, continuity of the ability to treat and prevent infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them.	The Secretariat used the recommendations of the Strategic and Technical Advisory Group on antimicrobial resistance, existing national and regional action plans, WHO's guidance and action plans on related subjects, as well as other available evidence and analysis… the Strategic and Technical Advisory Group considered input from more than 30 additional participants, including representatives of intergovernmental organizations, civil society, public health and regulatory agencies, industry associations, professional organizations and patient groups…Member States, stakeholders and the Secretariat convened additional high-level technical, political and interagency discussions to contribute to the action plan.	The framework presented below tabulates the actions that the Member States, Secretariat and international and national partners need to take in order to attain the goal and meet the objectives of the global plan.	Recommended model. It is expected that countries will develop their own national action plans on antimicrobial resistance in line with the global plan.	Not stated	Not stated

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Supplementary file 2 Examples of components and sub-components

Component	Examples
2.1.1. Governance	
National action plan, policy or strategy; identification of responsibility	[In 1999 the Department of Health] Set out an action plan for the NHS, aimed at reducing the emergence and spread of antimicrobial resistance and its impact on the treatment of infection. Includes strategies to monitor and optimize antimicrobial prescribing by implementing antibiotic guidelines, supporting professional development on appropriate prescribing, reducing inappropriate prescribing and using clinical governance arrangements to support improved prescribing… [1]. Policy measures to advance appropriate, rational antibiotic use need to be country-specific and tailored to local circumstances including, but not limited to, the prevailing burden of disease, taking into account underlying comorbidities, such as HIV and AIDS, and existing resistance rates [2]. At the national level, operational action plans to combat antimicrobial resistance are needed to support strategic frameworks. All Member States are urged to have in place, within two years of the endorsement of the action plan by the Health Assembly, national action plans on antimicrobial resistance that are aligned with the global action plan and with standards and guidelines established by intergovernmental bodies... These national action plans are needed to provide the basis for an assessment of the resource needs, and should take into account national and regional priorities [3]. **Secondary question: Which stakeholders have responsibility for governance of general practice AMS?** Establish clear governance arrangements. The Australian Government Department of Health and Department of Agriculture and Water Resources are responsible for the National Antimicrobial Resistance Strategy…Overall accountability for antimicrobial management lies at the highest level of each health service organisation, and with the clinicians responsible for delivering services efficiently and effectively… [4]. Policymakers are called upon to create an environment where the use of antibiotics is not the norm, by introducing disincentives to antibiotic use and surveillance programs, along with guidance that encourages and promotes self-management with symptomatic medications as the treatment in the first instance [2]. Strama is composed of a national steering group and regional Strama groups in every Swedish county [5]. Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context…Ensure that roles, responsibilities and accountabilities are clearly defined within an antimicrobial stewardship programme [6]. The professional bodies supporting this joint statement consider that action must be taken collegiately by the professions, commissioners, service providers, quality assurance bodies and regulators across the UK to reduce the threat of AMR. Leadership and action must be taken at local, regional, national and international level in support of the AMR strategy, and to tackle this issue in a concerted manner [7].
AMR included on national risk register	Recognize antimicrobial resistance as a priority need for action across all government ministries through inclusion in national risk registers or other effective mechanisms for cross government commitment [3].
Regulations around AMS & antibiotic prescribing	National, regional and local governments… responsibilities include legislation, regulation and auditing compliance with legal, policy and professional standards. [8]. Provide leadership to strengthen medicines regulatory systems at national and regional levels, so that appropriate practices for optimizing use of antimicrobial medicines are supported by appropriate and enforceable regulation, and that promotional practices can be adequately regulated [3].
Accreditation of prescribers	In the United Kingdom (UK) it is recommended that defined antimicrobial prescribing and stewardship competencies are incorporated into appraisals for prescribers. [9]. Professional organizations and societies should establish antimicrobial resistance as a core component of education, training, examination, professional registration or certification, and professional development…distribution, prescription, and dispensing of antimicrobials is carried out by accredited health or veterinary professionals under statutory body supervision…[3].
Funding for AMR/AMS activities	Sustainable funding is required to allocate time for clinical experts to work closely with prescribers. A mandate and financial support from the government is needed [10]. Member States should consider assessing investment needs for implementation of their national action plans on antimicrobial resistance, and should develop plans to secure and apply the required financing [3].

Planning for release of new antibiotics	Consider using multiple approaches to support the introduction of a new antimicrobial, including: electronic alerts to notify prescribers about the antimicrobial; prescribing guidance about when and where to use the antimicrobial in practice; issuing new or updated formulary guidelines and antimicrobial prescribing guidelines; peer advocacy and advice from other prescribers; providing education or informal teaching on ward rounds; shared risk management strategies for antimicrobials that are potentially useful but may be associated with patient safety incidents [6].
Practice level AMS policy and program	The stewardship programme is established with clear lines of accountability and there is a structure within the organisation/setting that can allow the implementation of a stewardship programme to take place, support the scheme, monitor its performance and hold it to account for performance and outcome measures… [9]. Outpatient clinicians and clinic leaders can implement policies and interventions to promote appropriate antibiotic prescribing practices. A stepwise approach with achievable goals can facilitate policy and practice changes and help clinicians and staff members from feeling overwhelmed. [11].
2.1.2. Monitoring and feedback	
Monitoring of antibiotic prescriptions	Understanding local, regional and national variation in antimicrobial prescribing is essential for assessing the impact of interventions to change prescribing behaviour. Prescribing data need to be linked to antimicrobial resistance data and patient outcomes to ensure that both positive and negative potential outcomes are evaluated [12]. Consider using the following antimicrobial stewardship interventions: review of prescribing by antimicrobial stewardship teams to explore the reasons for increasing, very high or very low volumes of antimicrobial prescribing, or use of antimicrobials not recommended in local (where available) or national guidelines…Consider developing local systems and processes for peer review of prescribing. Encourage an open and transparent culture that allows health professionals to question antimicrobial prescribing practices of colleagues when these are not in line with local (where available) or national guidelines and no reason is documented [6]. When setting up tracking and reporting systems, decisions need to be made about the level at which to track and report (i.e., at the individual clinician level or at the facility level), which outcomes to track and report, and how to obtain the data for tracking and reporting. … Analysis can occur at the individual clinician level or at the facility level (i.e., aggregate of all clinician antibiotic prescriptions). The preferred approach, when possible, is to track antibiotic prescribing at the individual clinician level…Systems also can track the percentage of visits for which an individual clinician prescribes antibiotics (e.g., number of all antibiotics prescribed for all diagnoses by a clinician divided by the total number of visits for all diagnoses for that clinician). [11]. **Secondary question: Which stakeholders have responsibility for monitoring of antibiotic prescribing in the general practice setting?** Strama groups in every Swedish county (panel). The national Strama group includes a broad representation of professional organisations and relevant authorities. The main objectives of the national group are to coordinate activities for the containment of antibiotic resistance at the national level. Activities include the analysis of trends in antibiotic resistance and consumption [5]. MedQual …is a network dedicated to monitoring antibiotic use and antibiotic resistance [13].
Monitoring of antimicrobial resistance	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 [14]. Particularly important gaps in knowledge that need to be filled include the following: Information on: the incidence, prevalence, range across pathogens and geographical patterns related to antimicrobial resistance is needed to be made accessible in a timely manner in order to guide the treatment of patients; to inform local, national and regional actions; and to monitor the effectiveness of interventions…[3]. **Secondary question: Which stakeholders have responsibility for developing and implementing monitoring of general practice antibiotic resistance?** The [clinical microbiology service] should provide annual analyses of cumulative AMR to groups with responsibility for local antimicrobial therapy guidelines to inform recommendations for local empirical therapy and formulary management [4]. Develop a national surveillance system for antimicrobial resistance that: includes a national reference centre with the ability systematically to collect and analyse data – including those on a core set of organisms and antimicrobial medicines from both health care facilities and the community – in order to inform national policies and decision-making; includes at least one reference laboratory capable of susceptibility testing to fulfil the core data requirements, using standardized tests for identification of resistant microorganisms and operating to agreed quality standards [3].

Feedback to prescribers and reporting	The how and why of measurement in antimicrobial stewardship is important but more important is that once you have gone to the effort to collect and analyse the data that you use it, that you share it with front-line clinicians to enable them to reflect on their practice and change their prescribing behaviour to improve patient outcomes and minimise resistance and other harm. It is important to share data in as near real time as possible…Comparison with peers and identification of prescribers who are outliers are useful techniques to change behaviour… [9]. Consider developing systems and processes for providing regular updates (at least every year) to individual prescribers and prescribing leads on: local and national antimicrobial resistance rates and trends; individual prescribing benchmarked against local and national antimicrobial prescribing rates and trends; patient safety incidents related to antimicrobial use, including hospital admissions for potentially avoidable life-threatening infections, infections with C. difficile or adverse drug reactions such as anaphylaxis [6].
2.1.3. Education	
Community & patient education about AMR and AMS	Consumers should be provided with information about the risks and benefits of the most effective and appropriate treatment options for them. This includes information about specific antimicrobials (if appropriate) and the risks associated with AMR. When discussing the use of antimicrobials and AMR with consumers, it is important that the messages are clear, simple and consistent. Information may need to be provided in different formats and styles, tailored to the needs and preferences of the consumer [4]. Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training. Steps need to be taken immediately in order to raise awareness of antimicrobial resistance and promote behavioural change, through public communication programmes that target different audiences in human health, animal health and agricultural practice as well as consumers. Inclusion of the use of antimicrobial agents and resistance in school curricula will promote better understanding and awareness from an early age [3]. **Secondary question: Which stakeholders have responsibility for implementing community and patient education about AMR and AMS?** All staff members in outpatient facilities, including administrative staff members, medical assistants, nurses, allied health professionals, and medical directors, can improve antibiotic prescribing by using consistent messages when communicating with patients about the indications for antibiotics [11]. Other stakeholders – including civil society organizations, trade and industry bodies, employee organizations, foundations with an interest in science education, and the media – should help to promote public awareness and understanding of infection prevention and use of antimicrobial medicines across all sectors [3].
GP continuing education in AMS & AMR	For clinicians, AMS education should start during undergraduate training and continue throughout their careers. Local education programs should include local AMS recommendations. Programs that are multifaceted and include one or more active educational activities are more likely to be successful in changing clinicians' behaviour [4]. Support multiprofessional local groups in the implementation of infection treatment recommendations, e.g. by producing locally adapted materials and local educational meetings and events [10]. **Secondary question: Which stakeholders have responsibility for implementing GP continuing education?** Professional colleges and associations can take a proactive role in supporting AMS – for example, by updating their members about changes to guidelines and providing continuing education or discussion forums. … A multidisciplinary group that includes ID physicians, clinical microbiologists, clinical pharmacists, nurses, midwives and infection control practitioners, or the AMS team, should be responsible for planning, developing and delivering a local education program. This will help to ensure that the approach to education is suitable for the intended audience and relevant to the local practice context [4].
GP education on communication skills, patient-centred approaches & shared decision making	Communications skills training can be used to promote strategies to address patient concerns regarding prognosis, benefits, and harms of antibiotic treatment; management of self-limiting conditions; and clinician concerns regarding managing patient expectations for antibiotics during a clinical visit [11].

GP education about non-antibiotic management of self-limiting infection	If antimicrobial treatment is not considered necessary, give the patient advice about the expected natural history of the illness, the limited or absent benefit of antimicrobial treatment, and the potential unwanted side effects of antimicrobials such as diarrhoea and rash, recommendations for symptom management, as well as advice about actions in case of worsening clinical condition (safety netting) [8]. If immediate antimicrobial prescribing is not the most appropriate option, discuss with the patient and/or their family members or carers (as appropriate) other options such as self-care with over-the-counter preparations, back-up (delayed) prescribing, other non-pharmacological interventions, for example, draining the site of infection [6].
GP education about delayed prescribing or watchful waiting	Senior leaders, including medical directors, Clinical Commissioning Group (CCG) chairs and directors of public health, need to support and empower prescribers, and other health and public health professionals who advise on prescribing decisions, to make the decision not to prescribe where other appropriate strategies exist such as 'watchful waiting' or delayed prescribing [7].
General practice team member education	Communicate with all clinic staff members to set patient expectations. Patient visits for acute illnesses might or might not result in an antibiotic prescription. All staff members in outpatient facilities, including administrative staff members, medical assistants, nurses, allied health professionals, and medical directors, can improve antibiotic prescribing by using consistent messages when communicating with patients about the indications for antibiotics. Education for clinicians and clinic staff members can reinforce appropriate antibiotic prescribing and improve the quality of care [11].
Independent education (restrict pharma marketing)	Drug advertising and academic detailing by pharmaceutical companies influences physicians prescribing behaviours. Further regulation of the material supplied to clinicians by the pharmaceutical industry may be needed if overuse of broad-spectrum antimicrobials is to be reduced. [15]. In some cases, industry spending on promoting products is greater than governmental investment in promoting rational use of antimicrobial medicines or providing objective information…Professional bodies and associations, including industry associations, health insurance providers and other payers, should develop a code of conduct for appropriate training in, education about, and marketing, purchasing, reimbursement and use of antimicrobial agents. This code should include commitment to comply with national and international regulations and standards, and to eliminate dependence on the pharmaceutical industry for information and education on medicines and, in some cases, income [3].
2.1.4. Consultation support	
Prescribing guidelines	Evidence-based prescribing guidelines for antimicrobials are a fundamental component of AMS programs because they guide appropriate antimicrobial use. They can also be used to educate prescribers and students 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 [4]. Organizational structures could pose barriers to [AMS]. Clinic visits were often too brief to discuss guidelines with patients…External guidelines were not always used because they were sometimes difficult to locate, too long, or not seen as relevant…external guidelines needed to be accessible to clinicians and trusted by clinicians [16]. …national treatment guidelines must include: diagnostic criteria for each condition; an analysis of the antibiotic risks and benefits both for the patient and for society; and recommendations for when to reevaluate a patient's treatment. Second, to ease the implementation of national guidelines in primary health care, they need to be transformed into simple treatment algorithms, e.g. clear advice to health professionals on when and when not to prescribe an antibiotic…easily accessible summaries of guidelines for common infections have been well received and used [10]. **Secondary question: Which stakeholders have responsibility for implementing prescribing guidelines?** In 2010 the UK Health Protection Agency developed and updated antibiotic guidance for GPs, which was locally adaptable by primary care trusts and distributed to practices [1]. Require explicit written justification in the medical record for nonrecommended antibiotic prescribing. This technique has reduced inappropriate prescribing by holding clinicians accountable in the medical record for their decisions [11].

Point of care tests	In POC testing interventions, participants found that it was unclear which staff members to train in POC testing, as various organizational roles performed the test in different clinics [16]. A disadvantage of near patient testing is that it may increase patients' expectations and increase re-consultation by medicalising self limiting illnesses such as sore throat [15]. Decisions to prescribe antibiotics are rarely based on definitive diagnoses. Effective, rapid, low-cost diagnostic tools are needed for guiding optimal use of antibiotics in human and animal medicine, and such tools should be easily integrated into clinical, pharmacy and veterinary practices [3].
Microbiology testing and reporting	Microbiology testing is a key component of antimicrobial stewardship (AMS). The clinical microbiology service (CMS) performs the combined role of patient-specific diagnostic testing to guide direct patient care, and system-wide diagnostic stewardship, surveillance of resistant organisms and outbreak investigation. a positive microbiology diagnostic test is used to confirm a provisional clinical diagnosis, and the antimicrobial susceptibility results guide targeted antimicrobial management. Optimal specimen collection and transport are critical elements of the testing process. [4]. Restrictive reporting of the results of antimicrobial susceptibility testing is one stewardship activity that varies from laboratory to laboratory and, perhaps, may be underused… [9]. Considering that most bacterial infections are also self-limiting (5), antibiotic prescription on the basis of a positive result in an otherwise healthy individual should be carefully considered [2].
Allergy testing	Promote allergy testing for patients with a history of allergic reaction to beta-lactams, as a measure to promote use of first-line antimicrobials in non-allergic patients [8].
Electronic decision support for prescribers	eCDSSs [Electronic clinical decision support systems] can organise and present appropriate information to the user in a way that supports them to make clinical decisions with increased accuracy and reduced error… may include online access to documents such as formulary restrictions, local antimicrobial prescribing guidelines and Therapeutic Guidelines: Antibiotic [4]. Advanced decision support systems use complex logic, mathematical modelling or case-based probabilities to provide patient-specific recommendations. They can provide decision support by helping identify potential infections, pathogens and treatment options based on inputs about patient symptoms… CDSSs are simply assistive tools and cannot replace expert decision-making. They may support the prescriber or the AMS program, or both [9].
Expert advice	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…Telehealth can support improved access to clinical services, specialist advice, diagnostic information and education, over distance, as part of formalised service networks [4]. Strategies to encourage appropriate prescribing in primary care include the development of evidence-based policies, in collaboration with local experts, who provide practical guidance on how to rule out serious infections and how to handle patient demand for an antibiotic, complemented by information on various symptomatic treatment options [2]. Clinical microbiologists should be available to clinicians for counselling on diagnostics of infectious diseases, including correct sampling and interpretation of test results, difficult-to-treat pathogens and complicated infections. Pharmacists in community and hospital settings have expertise in medicines and are the gatekeepers to the use of antimicrobials. As such, pharmacists can act as an important source of advice and information for patients and prescribers on the safe, rational and effective use of antimicrobials [8]. Telephone advice lines are provided in a few regions of France. These are provided by hospitals or health networks and may be staffed by an infectious disease specialist or a trained GP [13].
Decision support for use with patients	Providing easy-to-understand information to consumers about the expected duration of symptoms, and how to identify signs and symptoms of more serious illness, may help to manage their expectations about antimicrobials. Consumers should be provided with information about the risks and benefits of the most effective and appropriate treatment options for them... When discussing the use of antimicrobials and AMR with consumers, it is important that the messages are clear, simple and consistent. Information may need to be provided in different formats and styles, tailored to the needs and preferences of the consumer [4]. Patient information leaflets on common infections are produced in six languages to target a large proportion of the immigrant population [10].
2.1.5. Pharmacy and nursing approaches	
Unit dispensing	Explore per unit dispensing of antimicrobials taking into consideration all relevant guidelines and regulations [8].

Supply of and timely access to antibiotics	Ensure the adequate supply of, and timely access to, antimicrobials…Certain interventions, such as removing broad-spectrum antimicrobials from clinical areas to limit their inappropriate use, may delay antimicrobial delivery if appropriate pathways for antimicrobial supply do not accompany the restrictions [4]. Ensure access to the antimicrobials recommended in clinical guidance, by conducting a review of national market availability, implementing measures to support sustained market availability for both innovative and generic products and tackling shortages. At the same time, limit the use of last-resort antimicrobials to safeguard their effectiveness, by establishing restrictive measures for use… [8].
Pharmacy review & advice	In addition to clinically reviewing and dispensing antimicrobial prescriptions, community pharmacists can educate patients and carers about using antimicrobials appropriately…Pharmacists should consider whether there is still a clinical need to fill all prescriptions presented – for example, original and repeat prescriptions that are presented for dispensing several months after they were written (when it would be expected that the original infection would have resolved), or prescriptions for long-term use (for example, for several months). Such prescriptions should only be dispensed if the pharmacist is satisfied that the use is appropriate. If not, there should be discussion with the prescriber. Community pharmacy is an important site of community education and activities for AMS in primary care because of the ease and frequency of the public's access to community pharmacists compared with other clinicians…At the system level, the pharmacist's role may include planning and implementing AMS programs and other initiatives that encourage appropriate antimicrobial use [4]. It is important that any advice on medications and formulations is tailored to the patient's specific symptoms and preferences. In addition, pharmacy staff need to be able to identify red-flag symptoms and other risk factors for a serious infection and refer patients to physicians where necessary… [2].
Appropriate disposal of left-over antibiotics	It should be routine practice that consumers who have been dispensed antimicrobials, or their carers, are…Advised not to keep any unused antimicrobials, but to return them to a pharmacy for disposal [4].
Nurse triage, patient assessment & education	…professional associations and experts, internationally and in Australia, highlight that nurses, midwives and infection control practitioners (ICPs) play key roles in preventing and controlling AMR. They can help to safeguard the effectiveness of antimicrobials through infection prevention and control, education, and involvement in AMS activities. [4]. Materials are created for nurses providing education about common infections to parents of newborns at child health-centres and for schoolchildren… [10]. Use call centers, nurse hotlines, or pharmacist consultations as triage systems to prevent unnecessary visits [11].
2.1.6. Research	
Research into AMR/AMS gaps, translation into practice	Agree a national research agenda and promote investment in innovative approaches to containing antimicrobial resistance…Priority areas for action are to: Identify current gaps, and agree to national research and development priorities… More research is needed to understand any unintended consequences of the use of restrictive interventions [4]. Few studies focused on the organization component of the work system model or the structures and roles that organize a clinic… [16]. There is a paucity of studies on the potential harm of withholding or overuse of antibiotics and how to identify which patients may benefit, and by how much [15]. …implementation research is needed to determine which outpatient stewardship interventions work best in different outpatient settings, effective strategies to implement interventions, and sustainable approaches to outpatient stewardship [11].
Research into context, culture of general practice and behaviour change strategies	In general, prescribing has been shown to be influenced by several factors, including the cultural beliefs of the patient and the prescriber, patient demand, socio-economic factors and clinical autonomy. [12]. Understanding the organisational context, culture and workplace norms, including local prescribing rules and behaviours, is critical to successfully establishing an AMS program. A 'one size fits all' approach is not appropriate and does not sufficiently recognise that each setting has unique elements to be considered, such as enablers and barriers for appropriate antimicrobial prescribing and use… Education strategies that incorporate behaviour change principles such as audit and feedback, along with more active strategies including academic detailing, consensus-building sessions and educational workshops, are more effective in changing behaviour than the passive dissemination of information alone [4].

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Supplementary file 3 Search strategy

The websites searched

- Australian Commission on Safety and Quality in Health Care (ACSQHC) www.safetyandquality.gov.au
- British Society for Antimicrobial Chemotherapy www.bsac.org.uk
- Centres for Disease Control and prevention www.cdc.gov
- European Centre for Disease Prevention and Control https://ecdc.europa.eu/en/home
- National Health Service www.nhs.uk
- National Institute for Health and Care Excellence www.nice.org.uk
- Royal Australian College of General Practitioners www.racgp.org.au
- Royal College of General Practitioners www.rcgp.org.uk
- World Health Organization www.who.int

Embase via Ovid; 1974 to 21 Sept 2018

1. Index term: exp antibiotic agent/
2. Text terms: (Antibacterial? OR Anti-bacterial? OR Antibiotic? OR Anti-biotic? OR Antimicrobial? OR Anti-microbial?).mp
3. **1 OR 2 [Antibiotics**]
4. Index: exp Prescription/
5. Text: (prescrib* OR prescrip* OR antibiotic therapy OR antibiotic treatment OR antibiotic prescription$).mp
6. **4 OR 5 [Antibiotic prescriptions]**
7. Index term: exp general practitioner/
8. Text terms (general practitioner$ OR family medicine practitioner$ OR family medicine physician$ OR family physician$).mp
9. **7 OR 8 [GPs]**
10. Index term: exp primary medical care/ OR exp primary health care/ OR exp ambulatory care/ OR exp outpatient care/ OR exp general practice/
11. Text terms: (primary care OR primary health care OR primary healthcare OR outpatient? OR office visit* OR ambulatory care facilities OR community health cent* OR ambulatory care OR general practice OR family practice).mp
12. **10 OR 11 [General practice]**
13. Index: exp inappropriate prescribing/ OR exp practice guideline/
14. Text: (stewardship OR inappropriate prescribing OR antibiotic overuse OR formulary restriction OR restrictive strateg* OR restrictive polic* OR optimi#ation OR authori#ation OR guideline).mp
15. **13 OR 14 [Stewardship**]
16. **3 AND 6 AND 9 AND 12 AND 15 [Antibiotic prescribing by GPs in general practice with AMS]**
17. Index term: Exp Health care policy/ OR exp accreditation /OR exp Health care quality/
18. Text: (framework OR approach OR model OR system OR policy OR strategy).mp
19. **17 OR 18 [Policy + Framework]**
20. **16 AND 19 [GPs+ AMS + gen practice +framework]**

Ovid MEDLINE(R) 1946 to 21 Sept 2018

1. exp Anti-Bacterial Agents/ OR (Antibacterial? OR Anti-bacterial? OR Antibiotic? OR Anti-biotic? OR Antimicrobial? OR Anti-microbial?).mp
2. exp Prescriptions/ OR (prescrib* OR prescrip* OR antibiotic therapy OR antibiotic treatment OR antibiotic prescription$).mp
3. exp general practitioners/ OR exp physicians, family/ OR exp physicians, primary care/ OR (general practitioner$ OR family medicine practitioner$ OR family medicine physician$ OR family physician$ OR physician$).mp
4. exp general practice/ OR exp family practice/ OR (primary care OR primary health care OR primary healthcare OR outpatients OR office visit* OR ambulatory care facilities OR community health cent* OR ambulatory care OR general practice OR family practice).mp
5. exp Antimicrobial Stewardship/ OR exp inappropriate prescribing/ OR exp Guideline Adherence/ OR (stewardship OR inappropriate prescribing OR antibiotic overuse OR formulary restriction OR restrictive strateg* OR restrictive polic* OR optimi#ation OR authori#ation OR guideline OR program* OR standard$).mp
6. exp Health Policy/ OR exp accreditation/ OR exp Quality of Health Care/ OR (framework OR approach OR model OR systems OR policy OR strategy).mp

1 AND 2 AND 3 AND 4 AND 5 AND 6

PsycINFO; 1806 to Sept week 3, 2018

exp Antibiotics/

(Antibacterial? OR Anti-bacterial? OR Antibiotic? OR Anti-biotic? OR Antimicrobial? OR Anti-microbial?).mp

1 OR 2 [Antibiotics]

exp "PRESCRIBING (DRUGS)"/

(prescrib* OR prescrip* OR antibiotic therapy OR antibiotic treatment OR antibiotic prescription$).mp

4 OR 5 [Antibiotic prescriptions/prescribing]

exp general practitioners/ OR exp family physicians/

(general practitioner$ OR family medicine practitioner$ OR family medicine physician$ OR family physician$).mp

7 OR 8 [GPs]

exp primary health care/ OR exp outpatients / OR exp outpatient treatment / OR family medicine/

(primary care OR primary health care OR primary healthcare OR outpatient? OR office visit* OR ambulatory care facilities OR community health cent* OR ambulatory care OR general practice OR family practice).mp

10 OR 11 [General practice]

exp treatment guidelines/ OR exp Evidence based practice/

(stewardship OR inappropriate prescribing OR antibiotic overuse OR formulary restriction OR restrictive strateg* OR restrictive polic* OR optimi#ation OR authori#ation OR guideline? OR evidence based practice OR program*).mp

13 OR 14 [Stewardship]

3 AND 6 AND 9 AND 12 AND 15 [Antibiotic prescribing by GPs in general practice with AMS] (18 results only)

exp quality control/ or exp "quality of care"/ or exp "quality of services"/

(framework OR approach OR model OR system OR policy OR strategy)

17 OR 18

16 AND 19

EBSCOhost CINAHL Plus; 1997 - 20 May 2018
(MH "Antibiotics+") OR (Antibacterial* OR Anti-bacterial* OR Antibiotic* OR Anti-biotic* OR Antimicrobial* OR Anti-microbial*)
AND
(MH "Prescriptions, Drug") OR (MH "Drugs, Prescription") OR (prescrib* OR prescrip* OR “antibiotic therapy” OR “antibiotic treatment” OR “antibiotic prescription*”)
AND
(MH “Physicians, Family”) OR (“general practitioner*” OR “family medic* practitioner*” OR “family medic* physician*” OR “family physician*”)
AND
(MH “Primary Health Care”) OR (MH “Outpatients”) OR (MH “Ambulatory Care Facilities”) OR (MH “Outpatient Service”) OR (MH “Family Practice”) OR (MH “Ambulatory Care”) OR (MH "Community Health Centers+") OR (“primary care” OR “primary health care” OR “primary healthcare” OR outpatient* OR “office visit*” OR “ambulatory care facilities” OR **“**community health cent*” OR “ambulatory care” OR “general practice” OR “family practice”)
AND
(MH “Inappropriate Prescribing”) OR (MH “Guideline Adherence”) OR (MH “Prescribing Patterns”) OR (stewardship OR “inappropriate prescribing” OR “antibiotic overuse” OR “formulary restriction” OR “restrictive strateg*” OR “restrictive polic*” OR optimi#ation OR authori#ation OR guideline OR program*)
AND
(MH "Quality of Health Care+") OR (MH "Accreditation") OR (framework OR approach OR model OR system* OR policy OR strategy)

Scopus; Searched on 11/10/18.
Antibacterial* OR Anti-bacterial* OR Antibiotic* OR Anti-biotic* OR Antimicrobial* OR Anti-microbial*
AND
prescrib* OR prescrip* OR “antibiotic therapy” OR “antibiotic treatment” OR “antibiotic prescription*”
AND
“general practitioner*” OR “family medicine practitioner*” OR “family medicine physician*” OR “family physician*”
AND
“primary care” OR “primary health care” OR “primary healthcare” OR outpatients OR “office visit*” OR “ambulatory care facilit*” OR **“**community health cent*” OR “ambulatory care” OR “general practice*” OR “family practice*”
AND
stewardship OR “inappropriate prescribing” OR “antibiotic overuse” OR “formulary restriction” OR “restrictive strateg*” OR “restrictive polic*” OR optimi#ation OR authori#ation OR guideline OR program* OR standard$
AND
Framework* OR approach OR model OR system* OR policy OR strategy

Cochrane Database

1. MeSH descriptor: [Anti-Bacterial Agents] explode all trees
2. (Antibacterial? OR Anti-bacterial? OR Antibiotic? OR Anti-biotic? OR Antimicrobial? OR Anti-microbial?):ti,ab,kw
3. #1 or #2
4. MeSH descriptor: [Prescriptions] explode all trees
5. (prescrib* OR prescrip* OR antibiotic therapy OR antibiotic treatment OR antibiotic prescription$):ti,ab,kw
6. #4 OR #5
7. MeSH descriptor: [General Practitioners] explode all trees
8. MeSH descriptor: [Physicians, Family] explode all trees
9. MeSH descriptor: [Physicians, Primary Care] explode all trees
10. (general practitioner$ OR family medicine practitioner$ OR family medicine physician$ OR family physician$):ti,ab,kw
11. #7 OR #8 OR #9 OR 10
12. MeSH descriptor: [General Practice] explode all trees
13. MeSH descriptor: [Primary Health Care] explode all trees
14. MeSH descriptor: [Family Practice] explode all trees
15. (primary care OR primary health care OR primary healthcare OR outpatient? OR office visit* OR ambulatory care facilities OR community health cent* OR ambulatory care OR general practice OR family practice):ti,ab,kw
16. #12 OR #13 OR #14 OR #15
17. MeSH descriptor: [Antimicrobial Stewardship] explode all trees
18. MeSH descriptor: [Inappropriate Prescribing] explode all trees
19. (stewardship OR inappropriate prescribing OR antibiotic overuse OR formulary restriction OR restrictive strateg* OR restrictive polic* OR optimization OR authorization OR guideline OR optimisation OR authorisation):ti,ab,kw
20. #17 OR #18 OR #19
21. #3 AND #6 AND #11 AND #16 AND #20
22. MeSH descriptor: [Health Policy] explode all trees
23. MeSH descriptor: [Quality of Health Care] explode all trees
24. (framework OR approach OR model OR system OR policy OR strategy). ti,ab,kw
25. #22 OR #23 OR #24
26. #21 AND #25

4.1 Conclusions

This scoping review analysed the international literature on AMS frameworks in general practice and proposed an AMS framework comprising six components. Before it can be considered for Australian general practice, its validity and feasibility should be assessed. My approach was to obtain the views of key stakeholder through the conduct of interviews.

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Chapter 5 Building a framework for antimicrobial stewardship in general practice: Key stakeholder interviews

In the previous chapter, six key components of AMS in general practice were identified from a scoping review of international general practice AMS frameworks. The next step was to conduct interviews to determine the feasibility and validity of these components for the Australian general practice context and identify responsibilities. This chapter explores the components from the perspectives of the key stakeholders. The list of the sub-components for antimicrobial stewardship in general practice that was supplied to the stakeholders is provided here:

1. Governance
    a. National action plan
    b. Antimicrobial resistance included on national risk register
    c. Multi-level and/or multi-disciplinary response
    d. Regulations around antimicrobial stewardship & antibiotic prescribing
    e. Accreditation of prescribers
    f. Funding for antimicrobial resistance and stewardship activities
    g. Planning for release of new antibiotics
    h. Practice level antimicrobial stewardship policy/program/activities
    i. Handover of antibiotic information

2. Education
    a. Community & patient education
    b. GP continuing education in antimicrobial stewardship
    c. GP education on communication skills, patient-centred approaches & shared decision making
    d. GP education on non-antibiotic management of self-limiting infection
    e. GP education on delayed prescribing
    f. General practice team member education
    g. Independent education (restrict pharma marketing)

3. Consultation support
    a. Prescribing guidelines
    b. Point of care tests
    c. Microbiology testing and reporting
    d. Allergy testing
    e. Electronic decision support for prescribers
    f. Expert advice
    g. Decision support for use with patients

4. Allied health support for antimicrobial stewardship
    a. Unit dispensing
    b. Supply and timely access to antibiotics
    c. Pharmacy review & advice
    d. Appropriate disposal of leftover antibiotics
    e. Nurse triage, patient assessment & education

5. Data monitoring
    a. Monitoring of antibiotic prescriptions
    b. Monitoring of antimicrobial resistance
    c. Feedback to prescribers and reporting

6. Research
    a. Research into AMR/AMS gaps, translation into practice

This study was approved by the Monash University Human Research Ethics Committee, project number 20721. The participant information sheet, consent form and interview guide are supplied in Appendix 2.

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Type of the Paper: Research

Building a framework for antimicrobial stewardship in general practice: Key stakeholder interviews

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Abstract: There is little guidance about developing systems for antimicrobial stewardship (AMS) for general practice. A literature review identified six key components: governance, monitoring of antibiotic prescribing and resistance with feedback to prescribers, consultation support, education of the public and general practitioners, pharmacist and nurse involvement, and research, which were incorporated into a potential framework for the general practice context. Objectives: to determine the feasibility and validity of the proposed AMS framework. A secondary objective was to identify likely bodies responsible for implementation in Australia. We undertook interviews with 12 key stakeholders from government, research, and professional groups. Data were analysed with a thematic approach. The framework was considered valid and feasible. No clear organisation was identified to lead AMS implementation in general practice. The current volume-based antibiotic prescription monitoring system was considered insufficient. AMS education for the public, further development of GP education, and improved consultation support were strongly recommended. The role of community-based pharmacists and nurses is largely unexplored, but their involvement was recommended. A clear leader to drive AMS in general practice is essential for an action framework to gain traction. Monitoring and feedback of antibiotic prescribing require urgent development to include monitoring of prescribing appropriateness and patient outcomes.

Keywords: Antimicrobial stewardship; General practice; Family practice; Antibiotic; Health Policy; Quality of health care; Antibiotics; Public health; Pharmacist; Nurse.

1. Introduction

The consumption of antibiotics in the Australian community is high in comparison with similar countries [1], with most antibiotics prescribed by general practitioners [1]. There is a high rate of prescribing of moderate- (66% of use) and broad-spectrum antibiotics (25%) [2], and inappropriate use is still common for conditions such as upper respiratory tract infections [1]. For these conditions antibiotics are prescribed at rates 4-9 times that recommended by the Australian national antibiotic prescribing guidelines Therapeutic Guidelines Antibiotic [3]. Australia's National Antimicrobial Resistance Strategy calls for the introduction of antimicrobial stewardship (AMS) to address inappropriate antibiotic prescribing [4]. However, there is little guidance for how to implement AMS across Australian general practice.

Through a review of international health system approaches to AMS in general practice [5-20], a potential framework to guide AMS in general practice was formulated. This framework contains six key components: governance, monitoring of antimicrobial resistance and prescribing with feedback to GPs, education for general practitioners (GPs) and the public, consultation support, the involvement of community-based pharmacists and nurses, and research [21].

The aim of this study was to interview key stakeholders to determine the likely feasibility and validity of the proposed AMS framework and a secondary aim was to identify any existing organisations who may take on responsibility for implementation in Australia.

2. Results

Of the 24 invited stakeholders, 13 accepted. Two declined, another was on extended leave and eight did not respond to two emails. One respondent accepted but could not be interviewed in the timeframe. The 12 interviewed stakeholders' background, relevant expertise and location are outlined in Table 1. The COREQ checklist is available in Supplementary file 1.

Table 1 The professional background, antimicrobial stewardship involvement and location of the 12 interviewed stakeholders.

Professional background (not necessarily current employment)	**Number**
General practitioner	6
Pharmacist	5
Medical Microbiologist	1
TOTAL	**12**
AMS Involvement (Stakeholders may have multiple roles)	
Clinical Quality Improvement/AMS committee/professional organisation representative	9
Researcher in general practice AMS	4
Health Department	2
Primary Health Network	2
Microbiology Laboratory	1
Location	
New South Wales and/or Australian Capital Territory	4
Victoria	4
Queensland	3
Tasmania	1

TOTAL	**12**

Overall, stakeholders reported that the proposed AMS framework for general practice and its components were feasible and valid; and that it provided a link between the objectives of Australia's National AMR Strategy and an action. However, most stakeholders highlighted that it would require leadership and prioritisation for implementation to have the desired impact. Importantly the stakeholders had difficulty nominating the best organisation to oversee this implementation. (Representative quotes are supplied, additional quotes are available in Supplementary file 2.)

It seems very comprehensive to me… able to be implemented… I think we need to have an agreed upon governance structure and agreed upon priorities… I don't think there is one clear person or group who is responsible for the whole caboodle of this. (Participant (P) 6)

Asked how they would define success, stakeholders nominated short- and long-term goals. Short-term goals were increased adherence to prescribing guidelines and improved patient outcomes with no increase in harm. Stakeholders also commented that increased professional support provided by such a framework may lead to improved professional satisfaction for GPs. The long-term goals that they stated were a decrease, or at least, no increase in antimicrobial resistance (AMR).

Governance was reported by the stakeholders to be important to set strategic priorities and harmonize approaches. The importance of aligning work in primary care with work in other sectors was highlighted. A national action plan for AMS in general practice was regarded as a Commonwealth responsibility, with the Office of Health Protection (within the Department of Health) suggested to lead stakeholder engagement.

I think within the implementation plan the Office of Health Protection has an important role… I mean they have the remit of the strategy. In terms of the organisations that will have a responsibility some of them are probably clear, and some of them just need coordination. The important part of that is to work in a collaborative way, coordinated way… We shouldn't be… isolating sectors such as hospital, aged care… primary care. (P5)

There were calls to make practice accreditation mandatory and to include AMS activities such as antibiotic monitoring or education in this. Suggestions were made for financial incentives to encourage AMS activity in general practice.

Stakeholders also generally supported greater regulatory controls on prescriptions, the removal of automatic repeats and promotion of unit dispensing (dispensed quantities match antibiotic guideline recommendations, not pack sizes).

People you can educate as much as you like, but until you actually restrict the antibiotics people aren't going to stop using them... (P6)

Monitoring and feedback on antibiotic prescribing was perceived as effective for changing behaviour, but the current process was viewed as problematic. Unresolved practical considerations included that complete data sets are not available, the possible defensiveness of GPs about their data being reviewed, questions about who would analyse and provide feedback to GPs and whether collection should be mandatory or incentivised. The government was regarded as responsible for obtaining complete datasets. Stakeholders saw potential for the Practice Incentives Program - Quality Improvement Incentive [22] (GP data collected by the Primary Health Networks (PHNs) for process measures) to include antibiotic monitoring. Stakeholders said that feedback should include peer comparisons, and ideally link in with education and consultation support. The potential use of positive variance was described, that is, investigating the strategies used by those who prescribe fewer antibiotics than their peers.

Government needs to incentivize, to capture [antibiotic prescribing] *information. You know organisations like the PHNs are really well suited to that.* (P11)

In terms of investigating what works, one thing that we do poorly is to look for positive variance. (P7)

Community education in the form of ongoing tailored public health campaigns was considered important and viewed as a government responsibility. There were suggestions that health literacy education for antibiotic awareness should start at school.

We do need the consumer to come on board to… not have that expectation [for antibiotics], *which then does make the consultation very difficult*. (P8)

GP education endorsed by the Royal Australian College of General Practitioners (RACGP) or supplied by PHNs or medical specialists was well regarded and trusted. NPS MedicineWise (independent organisation supporting quality use of medicines) was acknowledged as an existing channel for GP education, but it was questioned as to whether what was currently provided was at the depth necessary to have the largest impact. There were concerns that pharmaceutical marketing may undermine AMS messages.

What type of education do GPs trust? And often that'll be one that comes from kind of RACGP-branded things, or PHNs, and sometimes specialist. (P4)

Stakeholders wanted improved clinical software that integrated prescribing guidelines, patient information resources and alerts. There was a suggestion that some GPs are using product information rather than guidelines to inform decision making because unlike guidelines, product information is integrated into the clinical software. Government funded health services (e.g. NPS MedicineWise, PHNs) were suggested as potential developers of patient information resources with PHN Health Pathways as another potential host to make the resources widely available. Keeping the resources current was identified as a challenge.

I think electronic decision support can work well if it's in real time…. the first line choices of antibiotics are… if you couple that with patient information that will be… made available to the patient, that's helpful. (P7)

Rapid and point-of-care-tests elicited mixed comments. Some thought these could be useful if subsidised. Others thought they should only be available if it would change the decision to prescribe an antibiotic. Selective reporting of antibiotic susceptibilities was suggested as a priority along with standardised information for GPs about the use of microbiology testing, particularly around specimen collection and interpretation of results. It was suggested that the Royal College of Pathologists of Australasia (RCPA) should oversee this. Expert advice sought from hospital specialists was often based on relationships developed during training. There were calls for a central advice line, or lines of communication to enable consistent messages or access to the local hospital specialist's guidance.

Not all labs do selective reporting of antibiotics; it should be implemented… we need one official form rather than lots of different ones – they are not as strong as one consistent message. (P12)

Respondents suggested that adding the reason-for-prescription (subject to privacy requirements) and providing an exact duration of antibiotic therapy to the prescription would help community pharmacists be more engaged in AMS. It was perceived that to successfully implement delayed prescriptions (where the patient is told when and under what conditions antibiotics should be dispensed) better communication between GPs and community pharmacists is needed Pharmacists employed by the general practice was identified as an opportunity for practice level AMS support.

[pharmacists] *have to put a sticker on the box of antibiotics that says finish the course… we should change the stickers to 'take as long as prescribed'…* (P8)

Stakeholders thought that nurses may have a role in AMS e.g. patient triage and education in the community and in the practice, but there was a perceived lack of funding.

I think [nurse triage is] fantastic in an ideal world, but we don't have the funding. (P8)

Stakeholders agreed that research into general practice AMS with translation of the evidence into practice was required. Research areas suggested included understanding the potentially negative effects of antibiotics on the gut microbiome, and better understanding of the use of delayed antibiotic prescription "*whether an illness that's been present for more days is more likely to respond to antibiotics*" (P7). Stakeholders also suggested more research to understand low prescribing GPs:

Those who seem to manage to preserve this resource [antibiotics] *really well and apparently not with any problems in terms of the health of their patients. Yeah. How does it work for them? What helps them, what supports them? What can we put in place to enable others to not prescribe?* (P9)

3. Discussion

Stakeholders agreed that the proposed framework was valid and feasible, and provided a suitable action framework for the introduction of AMS into Australian general practice. Central coordination was identified as a priority, but the lack of clarity around who would provide this leadership was surprising particularly given the seniority of the participating stakeholders. The Office of Health Protection (OHP) was suggested to lead and coordinate the introduction of AMS into Australian general practice. Whether the OHP has the capacity for this was not investigated.

Monitoring of and feedback on antibiotic prescribing will enable targeting and evaluation of AMS interventions. Several issues were highlighted including GP trust in a transparent external audit process [23] and a need to obtain complete datasets (including the reason-for-prescription in a standardised format). Inclusion of information on any adverse patient outcomes e.g. hospitalisations would require linkage of datasets [23]. There was a view that monitoring and feedback needs urgent development beyond the current volume-based feedback so that it better meets clinical need. No current monitoring system was identified that could provide the information required.

Regulatory changes were supported. Manufacturer's pack sizes rarely match the recommended duration for common conditions [24], and when antibiotics were supplied by the pack, patients were thought to be likely to save leftovers for future use [25]. Restrictions on repeat prescriptions for five of the most commonly prescribed antibiotics in Australia were introduced on 1 April 2020 [26], illustrating that regulatory changes are achievable.

Electronic decision support was strongly supported and should be further examined in Australia. It has been used to guide prescribing in hospitals, and has been effective at reducing antibiotic prescribing when combined with other AMS interventions [27]. Work is required to develop and pilot suitable electronic decision support to ensure that the tools meet prescriber needs in Australian primary care, are usable, fit in with workflow [28] and have the desired impact.

Stakeholders were unanimous that community education is required to support general practice AMS. Evidence suggests that campaigns may work best when developed in partnership with consumer organisations, are coordinated with health professionals, and promoted at local and national levels [29]. Community awareness of a common colds campaign reflected changes in the frequency of the campaign [30], suggesting that community education should be ongoing. School based programs, such as Europe's eBug [31] and Canada's Do Bugs need Drugs? [32] have introduced AMS to children. Alongside community education, the provision of written patient information was widely supported by Stakeholders and has been associated with reduced antibiotic prescribing in common infections [33]. However, the issues of updating the information, which languages and cultural information are required and the most appropriate place to host these have not yet been well addressed in the literature.

Ongoing work on selective reporting of antibiotic susceptibilities by microbiology services, which has been shown to be effective in influencing prescribing behaviour, [34] should be pursued as a priority in Australia [35].

Increased access to expert advice has been utilized internationally as a method to influence antibiotic prescribing choices. Telephone advice has been provided to GPs in France for patient management [19] and in Sweden, experts provide advice on interpretation of audit results [15]. While stakeholders supported the provision of centralised expert advice, there was no clarity on who should provide it beyond the suggestion that local hospital specialists might participate.

Internationally, pharmacists have participated effectively in activities to help reduce antibiotic prescribing and increase prescribing guideline concordance [36], but Australian community pharmacists may require additional support for this expanded role [37]. Non-dispensing pharmacists in general practice may be suitable for an AMS role. The role in AMS of practice nurses and that of nurses in the community (e.g. phone triage lines) and their need for formal AMS education remains largely unexplored.

There are limitations to this research: the recruited practice nurse stakeholder was unavailable for interview in the timeframe, so there may be additional insights to be gained regarding the involvement of practice-based nurses. There were only 12 interviews conducted and Stakeholder identification was partly reliant on the authors' networks. Areas covered in less detail were the roles for specific organisations in implementation. The RCPA and the Office of Health Protection were specifically named by one stakeholder for each. However other stakeholders referred more generally to the 'professional colleges' and 'Department of Health' respectively. Components in which only three stakeholders commented were: planning for new antibiotics, the role of allergy testing, handover of patient information, unit prescribing, and knowledge about other AMS models. Components discussed by four stakeholders included: pharmaceutical company marketing, nurse involvement, monitoring of AMR. All other components were discussed with at least five stakeholders.

The views of the expert Stakeholders may not reflect those of the wider GP community. Experts are likely to be early adopters or innovators in a field [38], whereas the wider community will include those who fear the consequences of not having antibiotics and those who may not perceive that AMR affects them.

4. Materials and Methods

Study design and participants

A qualitative approach was used. Australian-based senior expert stakeholders in AMS in general practice were identified through the authors' AMS networks (8), relevant organisations' websites (3), and via contact with government and professional organisations (2). Stakeholders were provided with a study information sheet and purposively invited to participate in a telephone interview. Gift cards to the value of $150 were offered as compensation for their time.

Data collection and qualitative analysis

Consented participants received an outline of the proposed AMS framework prior to the interview (Appendix A).

In-depth telephone interviews using a semi-structured interview guide (Appendix B) were conducted and recorded between September-December 2019. Stakeholders were purposively invited until key components had been discussed with at least one stakeholder. Feasibility and validity were assessed by asking participants the extent to which components and subcomponents were being done or if plausible, what needed to be done to make them implementable; their priorities and if they could identify any gaps. Data collection was completed before analysis commenced. Interview recordings were transcribed and returned to stakeholders with a 10-14-day window for amendments. Transcripts underwent thematic analysis using deductive coding targeting comments about the proposed framework and its components; and by open coding for other comments [39]. Two transcripts were independently coded by two authors and an agreed coding framework developed. Three more interviews were dual coded using the agreed framework and adjustments made. Seven transcripts were coded by one author. NVivo 12 qualitative data analysis software (QSR International Pty Ltd) was used to manage the transcripts and coding.

Ethics approval was granted by the Monash University Human Research Ethics Committee, number 20721.

5. Conclusions

The Stakeholders regarded this AMS framework as feasible and valid for Australian general practice. The individual sub-components were viewed as providing a link between the objectives of Australia's National AMR Strategy and an action. However, Stakeholders considered that the framework required an implementation process with priorities and an integrated approach. The identification of a clear leader to drive AMS in general practice is essential for AMS to gain traction. Monitoring and feedback of antibiotic prescribing require urgent development beyond the current volume-based system and should include monitoring of appropriateness of the prescriptions and patient outcomes. AMS education for the public, further development of GP education, and improved consultation support were strongly recommended. The role of community-based pharmacists and nurses is largely unexplored but their involvement, particularly for patient education, was recommended.

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Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Supplementary file S1 The COREQ checklist, S2 Representative quotes for AMS components.

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Appendix A Component list used during the interviews

The detailed list of the sub-components for antimicrobial stewardship in general practice. This list was sent to each Stakeholder before interview and referred to during the interview.

1. Governance
    a. National action plan
    b. Antimicrobial resistance included on national risk register
    c. Multi-level and/or multi-disciplinary response
    d. Regulations around antimicrobial stewardship & antibiotic prescribing
    e. Accreditation of prescribers
    f. Funding for antimicrobial resistance and stewardship activities
    g. Planning for release of new antibiotics
    h. Practice level antimicrobial stewardship policy/program/activities
    i. Handover of antibiotic information
2. Education
    a. Community & patient education
    b. GP continuing education in antimicrobial stewardship
    c. GP education on communication skills, patient-centred approaches & shared decision making
    d. GP education on non-antibiotic management of self-limiting infection
    e. GP education on delayed prescribing
    f. General practice team member education
    g. Independent education (restrict pharma marketing)
3. Consultation support
    a. Prescribing guidelines
    b. Point of care tests
    c. Microbiology testing and reporting
    d. Allergy testing
    e. Electronic decision support for prescribers
    f. Expert advice
    g. Decision support for use with patients
4. Allied health support for antimicrobial stewardship
    a. Unit dispensing
    b. Supply and timely access to antibiotics
    c. Pharmacy review & advice
    d. Appropriate disposal of leftover antibiotics
    e. Nurse triage, patient assessment & education
5. Data monitoring
    a. Monitoring of antibiotic prescriptions

b. Monitoring of antimicrobial resistance
c. Feedback to prescribers and reporting

6. Research
   a. Research into AMR/AMS gaps, translation into practice

Appendix B The semi-structured interview guide

1. What can you tell me about your interest or experience in antimicrobial stewardship?
2. What do you think is required to improve antibiotic prescribing in general practice?

Now I will take 2-3 mins to explain the model framework and then I will ask you for your comments on it.

3. What is your overall impression of this framework?
4. How well does each component reflect what you understand about AMS?
5. Is it plausible?
6. Does anything not ring true?
7. Do you know of any other models?
   a. How do they differ from this model?
8. To what extent are each of these components currently being done?
9. To what extent do you think the other components are implementable?
   a. What needs to be done to make it happen?
10. Who is, or should be, responsible for each of these components?
11. What do you think may happen if all this came to be?
12. Are there any gaps in this framework?
13. What would you prioritise?
14. How do we measure success? (Interviews 6-12 only)
15. Is there anything missing that we haven't discussed?

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Supplementary Data

Supplementary file 1: COREQ Checklist

	Item	Response	Section reported in
1	Interviewer	LH conducted the interviews	Methods
2	Credentials	LH: BSc(Hons), MPH, PhD candidate JB: BPharm(Hons), MPH, PhD candidate KB: MBBS MD MPH FRACP DM: MD, MBBS, FRACGP, DRANZCOG, Grad Dip Women's Health, GAICD[1]	
3	Occupation	LH: Microbiologist/PhD fellow JB: Pharmacist/PhD fellow KB: Infectious diseases physician/Researcher DM: General Practitioner/Researcher	
4	Gender	Not relevant to this study	Not Applicable
5	Experience and training	LH and JB have undertaken training in qualitative research and have previous experience with qualitative research. KB and DM have conducted, supervised and published qualitative research.	Available on request
6	Relationship established	LH/KB/DM identified potential stakeholders. LH conducted recruitment by formal invitations	Methods
7	Participant knowledge of the interviewer	Some stakeholders had previous professional contact with one or more of the research team.	Methods
8	Interviewer characteristics	The invitation to participate explained the purpose of the study, and who and what was involved.	Methods
9	Methodological orientation and theory	Qualitative research	Methods
10	Sampling	Purposive sampling through professional networks.	Methods
11	Method of approach	One email containing explanatory letter and consent form; non-responders were sent one repeat email. Written consent was obtained for the interview.	Methods
12	Sample size	13 participants	Results
13	Non-participation	One participant could not be interviewed in the timeframe (on leave).	Results
14	Setting of data collection	Telephone interviews	Methods
15	Presence of non-participants	The interviewer was alone in a private office. Interviewees chose their own setting.	Not applicable
16	Description of sample	Background profession, State, and experience in AMS	Results
17	Interview guide	A semi-structured interview guide was pilot tested on 3 volunteer GPs, adjusted and one extra question was added after interview 6.	Methods and Appendices A and B
18	Repeat interviews	No repeat interviews were conducted	Not applicable
19	Audio/visual recording	One participant did not consent to recording. Permission was obtained to make notes during the interview. They were transcribed	Methods and Results

		immediately after the interview. All other interviews were recorded.	
20	Field notes	Field notes were made during and after the interviews	Available on request
21	Duration	Interviews lasted between 39 and 68 minutes	Results
22	Data saturation	All components were discussed; those in less detail were specifically named bodies, and the risk register.	Discussion
23	Transcripts returned	Transcripts were returned to all participants	Methods
24	Number of data coders	2 coders: LH and JB	Methods
25	Description of the coding tree	Coding was in two parts: Deductive codes derived from the proposed framework. Open coding for other themes - adding inductive codes to the coding tree.	Methods
26	Derivation of themes	Thematic analysis; deductive and open coding	Methods
27	Software	NVivo 12	Methods
28	Participant checking	All transcripts were returned to participants with a 10-14-day window for amendments or withdrawal.	Methods
29	Quotations presented	Yes	Results and S2.
30	Data and findings consistent	Yes	Results and Discussion
31	Clarity of major themes	Yes	Results and Discussion
32	Clarity of minor themes	Yes	Results and Discussion

Supplementary file 2 Additional quotations

Perceptions of the model framework
It sounds comprehensive… there wasn't anything that stood out to me as a significant gap or a gap… I guess the part of the model and I'm sure you're considering it's how you actually support GPs in implementing a lot of these things that you're sort of outlining. (P5)
I think it sets a very nice summary of all the angles and approaches that have been tested and trialled…I think it's a really nice model. Well done. (P9)
I think it's a useful way of kind of divvying up the different elements that need to happen. (P3)
Governance: National Strategy and Action/Implementation Plan
Leader, input: National Action Plan is generally led by the Commonwealth [Department of Health] but requires that input from all of the other stakeholders including jurisdictions and GPs and everyone else. (P3)
AMS across sectors: Many GPs also service aged care facilities as well… In the more rural remote areas, the GPs there work both in the hospital setting, the community and the aged care setting... GPs in those areas [are] happy to do antimicrobial stewardship, but... don't want to have a different model for every place that we're working in; we want to be saying the same message in the same strategy in the same model. (P10)
Unclear responsibility: So we've got the National Action Plan [National AMR Strategy] which I suppose is the agreed upon priorities for the country… But also knowing that there's no way that one agency can fix this…. Everybody's problem and nobody's responsibility. I don't think there is one clear person or group who is responsible for the whole caboodle of this. (P6)
Implementation: We need some kind of a national action plan. But you know a lot of these action plans are mostly pieces of paper if it doesn't trickle down to something on the ground and so I think that that is an important part. But you need the middle layer, the regional health services and PHNs in the sense of primary care. They all need to be on board and have a panel report and then all the way down to the practice level where GPs operate… But each action, each policy needs to have you know a number of elements that show how it is being implemented, and how it is being monitored, if that implementation is happening or not. So, you need a full circle process... we're first of all on the same page, everyone knows about this, everyone knows their responsibilities, that there is a clear action plan on how we can make this all happen, and that we are then accountable for how that happens at each of those. (P9)
RACGP role: I think [RACGP] have a role in looking at what other policies are recommended by external people including Department of Health and seeing how it would play out in the different environments that GPs work in. From a rural remote Aboriginal or Torres Strait Islander Health, tropical health, urban health. So it's a…set of eyes on policy decisions. (P7)
Professional College involvement in messages: it's got to be global and then come down through… your different organizations that you belong to (P1)
Tailoring of messages: It's not about controlling GPs, it's about better outcomes for your patients and better outcomes for our antibiotics in the longer term. (P2)
Governance: Regulations
PBS: How the PBS matches recommendations. Whether you can actually access the correct antibiotic for the correct length of time according to recommendations under the PBS. (P3)
Repeats: We need to stop putting repeats on things like prescriptions, I mean that's a no brainer. That's just going to happen. (P6)
Off label prescribing: looking at tightening up the regulation around… prescribing things off label. I think is a big problem and you know potentially should just not be allowed. (P6)
Expiry on antibiotic prescriptions: we have a 12-month expiry on prescriptions and that would be a big legislative change to change antibiotics from that 12-month expiry. So I think if we could have some sort of clause in the antibiotic prescribing say if this prescription has not been presented within two weeks you know do not fill. (P1)
Authority to prescribe antibiotics: but what missing piece was you know the regulations; the governance and I think they're very… powerful drivers. For instance, if we look at our quinolone prescribing in Australia are very very good, and so not prescribing lots of quinolones in primary care, so our resistance patterns are very very good. And why is that? Well because you need authority to prescribe a quinolone. And that's a barrier. Oh, it's the regulation. Having those barriers work (P9)
Governance: National risk register
[AMR has] become a Tier 1 priority on… the Australian Health Minister's Advisory Committee… I believe. (P6)
Governance: Accreditation of prescribers and/or general practice
Prescriber accreditation for evidence-based practice: I think the years of doctors being completely autonomous and just doing whatever the hell they like are gone… There needs to be a degree of responsibility for undertaking evidence-based practice. And perhaps even consequences for not doing so… Stuff like do maybe… a stewardship module in RACGP or ACRRM CPD programs and do you make it mandatory? You know if you want to prescribe X, Y, Z antibiotics you have to have done this module. (P6)

Prescriber accreditation for monitoring or education: If you're a GP prescriber of antibiotics you probably do need to be you know compulsorily reviewing or auditing or at least attending some sort of updates about antibiotic prescribing every three years… I would really like to say that is a compulsory part of CPD. (P2)
Mandatory practice accreditation: Accreditation definitely needs to play a role. I know they have got a voluntary accreditation process, but it should be mandatory (P10)
Governance: Funding
Cost of not funding AMS: I actually think that health economists need to look at the consequences of not funding antimicrobial stewardship - so that the potential that an elective surgery and immunosuppression become too dangerous to contemplate. And the cost of untreatable infections and managing those people in isolation. (P7)
Public funds: There's a decent economic argument to a lot of the actions that they passed on climate change. But [AMS] is never going to be an exercise which makes money. So there's always going to have to be a degree of public funds involved in it. Because antibiotics are the epitome of the market failure aren't they?... But I suppose primarily government and the regulating bodies have got the overarching responsibility and when the s**t hits the fan in a big way it will become their problem. (P6)
MBS funding I was thinking at a very high level that MBS funding changes so that funding isn't necessarily just tied to the time of the consultation because obviously you know what the main issue is the fact that it's faster to write out a prescription then go through that communication process explaining why the person doesn't need antibiotics. (P4)
Funding for AMS activities: I think we need to be realistic, that I suspect it's unlikely that anybody is going to turn around and say we've set aside five hundred million dollars to fix AMR in this country. I think we need to have an agreed upon governance structure and a grand agreed upon priorities and then a bunch of things that are ready to go if and when smaller chunks of funding become available. (P6)
Incentives: I guess how practices implement… you can somehow sort of incentivize a level of minimum Implementation or standardization or mandate some of that. (P5)
Governance: Planning for release of new antibiotics
if you're a GP prescriber of antibiotics you probably do need to be … compulsorily … auditing or at least attending some sort of updates about antibiotic prescribing every three years … where they can give stuff about appropriate choice of antibiotics and give information on perhaps the new antibiotics when they are appropriate or not appropriate so. I would really like to say that is a compulsory part of CPD. (P2)
Governance: Practice level antimicrobial stewardship policy/program/activities
Practice level policy development: At a practice level the antimicrobial stewardship policy I think that's underdeveloped. (P4)
Implementation support: How you actually support GPs in implementing a lot of these things that you're sort of outlining… to make it easy for them to do that and part of that I think is like how do you bring people within a practice together to agree on how they're going to do things. (P5)
Whole of practice approach: I'm just wondering if those discussions [monitoring and feedback of prescribing] you know really should be held at the practice level NOT at the GP in the practice… because antimicrobial stewardship is part of the whole practice and should be owned by everyone in the practice. So you know this could be a nice model of looking at how we provide quality care by focusing on the team and all the different members of the team rather than only the prescribing ones…. (P9)
Governance: Handover of antibiotic information
Handover between health facilities: Handover antibiotic information, kind of belongs with the hospitals in terms of that handover thing, but it's clearly a much bigger issue than just antibiotic information, so it will get caught up in bigger, bigger communication things around that. And if just done as a antimicrobial stewardship thing probably isn't going to be terribly effective cos it's got to capture the bigger handover issue. (P3)
Education: Community and patient
GPs and patients together: Alongside any attempt to shift the dial with GPs, you need to shift the dial with patients as well, so that patients aren't wanting antibiotic and GPs not wanting to prescribe them, and then you see a drop off because they can both be on the same side. (P7)
Responsibility for and evaluation of campaigns: Having an idea of what the community understands about resistance and infections and antibiotics and prescribing and then you know monitoring that as education campaigns and that kind of things go up… the only ones that I'm aware of are the ones that have been done by NPS MedicineWise… And there's a website, a federal website… that's one of the sticking points, is it a state responsibility or a federal responsibility and I think there's been a lot of hand balling and somebody just needs to pluck up and say we'll do it… health promotion groups who lead these kinds of campaigns you know so in my head it's a public health campaign and I feel like some of the money that's traditionally gone to non-

communicable diseases could potentially go to some of this kind of thing. So yeah anybody really, as long as it's evidence based and the appropriate stakeholders being consulted to make sure there's no unforeseen adverse outcomes. (P6)
Relevant message: reaching consumers at a time that's relevant to them through mediums that they use requires multiple channels to be used, multiple you know sort of messaging, messaging appropriate to that consumer. And so it needs quite significant funding… and sustained over a period of time and working with communities at community level is important. So You know what's relevant to students as they going through exams versus what's relevant to a retiree… you just can't have the same messages. (P5)
Responsibility for messages: I think the National Prescribing Service; I think we should almost have you know the government messages as well like… government ads regarding obesity over the years. I don't think this is any different. Now we have government messages about don't go to the emergency department. You know I don't see why we're not having government messages… I don't think that's a difficult campaign for the government do. And I think they really need to probably step up and do it... I think it's important that community organizations like the Consumers Health Forum [are involved]. (P8)
Timing of messages: [Antibiotic Awareness Week] ties in with the Northern Hemisphere. And I think we should move that to April… and talking about getting your vaccination for flu. It's a virus. Often it does not need to be treated by antibiotics… I just think there's got to be more education around March-April. So whether it ties in with the vaccination campaign and talks about antibiotic resistance and you know prevention is better than cure and that sort of thing... I think it should be twice a year and regularly twice a year. (P1)
Ongoing campaigns: we do campaigns but they're not ongoing. And so you might sort of educate one group of consumers but then the next group of young parents comes along and they maybe aren't so informed and so I think it just needs to be continuous never ending campaign of awareness for consumers. (P8)
In schools: Some of the aids that are available can still be quite confusing for patients with poor health literacy. And that's where actually that goes back to education, that perhaps more needs to be done in schools and even kinders [kindergarten, pre-school] regarding antibiotic use. (P4)
Personalised messages: I think the conversation needs to change to a personal pros and cons. So how long will you and your family be exposed to resistant organisms as a consequence of this antibiotic? What are the pros and cons for your patients as an individual, on having antibiotics? What's the natural course of the disease they've got without? What are the effective safety netting erm discussions to have? And we know from some really good research that the GPs have a belief that antibiotics are much more effective than they actually are. Patients have the belief that's even more far from the truth. And so attacking the beliefs and skills probably makes more difference than tackling the pure knowledge. (P7)
Consistent messages: I think you know the government has a responsibility for it… But I think it all should be coming from the same sort of platform that everyone should have the same message. But maybe with organizations in their actual affiliation should be delivering them… like the ASTAG AMR… Well whether it's… the NPS that starts it. And they're given you know resources to be able to do that. And then they can deliver it down to doctors, pharmacists, nurses, and community. (P1)
GP continuing education
Good for our patients: I guess it's really a matter of getting the right people to do [education] number one; but secondly not being seen as if it's something that is being done as an imposition on GPs. It's something that's being done because it's really good for our patients and good for the future of our prescribing tools, antibiotics. (P2)
Assumed patient knowledge: I wonder if people who've been doing it for longer and you know much more experienced perhaps forget that patients don't necessarily know these basics [about non-antibiotic management of self-limiting infections]. We assume, sometimes I suspect we assume, knowledge that is not necessarily there. (P6)
Communication re self-limiting infections: Working out the best way to deliver that management, non-antibiotic management, of the self-limiting infection is probably a really key thing that I reckon that we could work on - that communication, the best way to communicate that message… I guess shared decision making… also making more awareness of the increasing number of bugs that… can be self-limiting. (P2)
Easy and customised: I guess you've got to look at making it as easy as possible for [GPs] to participate… I think there's a need for some national coordinated effort to see national objectives being met but there's also a need for being up to provide educational opportunities which may be more variable to different needs, different level, different regions. (P5)
Integrated with resources: I think it works best if it is an integrated approach. So to me there's no point in providing more education if decision aids aren't available or if unit dispensing doesn't change. (P4)
Education vs behaviour change: the standard approach to any wicked medical problem is to is to say let's educate GPs more. It doesn't have a long shelf life once you've educated GPs because you need to ask the question why is the prescribing happening? And then tackle the why's... But I'm not sure there's a massive lack of knowledge, but there might be a belief system that needs to change. (P7)
Education around beliefs: As part of your education you would explore those backgrounds and beliefs… that they have developed throughout their training and how that aligns with what we're trying to achieve here. So I think it starts with that conversation in making those underlying beliefs and attitudes visible. And once you have named them and brought them out in the open that's when you can start addressing them. If they stay implicit and under the surface whatever you do is going to be cosmetic. (P9)

Depth and impact: NPS does education… But are they doing it in the depth that needs to be done… and impact as well you know, do some of these give bigger bang for the buck than others? (P11)
Microbiology: GPs need education with how to use tests, which to do, which are urgent and communication with the lab. There is not much literature on what GPs need or what supports they need. Some tools are more powerful – GPs should be told. (P12)
AMS education for practice team members and allied health
Providers and nurses: In terms of who should do it… I think you know profession-led is the way … I think in terms of everyone being on the same page… When the flu season comes around every year the Public Health Unit will put on the education for the nurses and GPs because you know it's part of the vaccination program. (P8)
Joint education: Many PHNs have an education program that includes both pharmacists and GPs.… what's been quite successful is… where you have a joint education… workshop so making it more interactive… and getting the pharmacists involved in a whole practice approach to how the patients are going to be managed within the GP practice, because obviously you want the same message going out and the GP saying one thing, you want the pharmacist to support it and vice versa. (P10)
Whole of practice education: General practice team member education I think is lacking there. I doubt that many receptionists would have received training about antimicrobial resistance. So I suppose that could go back to linking antimicrobial stewardship to accreditation, as accreditation activities include the whole practice. (P4)
Nurse-patient communication: if [nurses] see something that they think needs antibiotics, not saying that but saying I'll just get the doctor to have a [look]. (P8)
Independent education (restrict pharmaceutical company marketing)
Yeah we're pretty good at not advertising direct patients. There are subtle ways it goes on still. You know GP offices are littered with trade names of antibiotics in general. (P7)
The ads that are in GP magazines. … I do think that sometimes they put inappropriate [advertisements] like Fosfomycin was really being pushed as a UTI treatment and it's not really appropriate to apply… making it clear if they recommending stuff that's not in the antibiotic guidelines for the type thing then that would be really useful to have it as a footnote on that. … this antibiotic is not on the PBS is publicized, but they don't say this antibiotic is not recommended first line by antibiotic guidelines. (P2)
Consultation support: Electronic decision support for prescribers
Automated recommendations: We've just got to get the right tools and the right prompts in place you know so a doctor makes a diagnosis, why doesn't Therapeutic guidelines pop up with the right clinical resources around prescribing for example, the right duration. (P11)
Reason-for-prescription: I think the issue is that medical records served serve two purposes for the GP. One's an aide memoir for the next consult. You know, a little summary of what's happened, and the other's a sort of medical legal record in case something goes horribly wrong. And given that that's the function of them why would anyone put time and effort into completing fields that aren't part of that, those two requirements? (P7)
Software improvements: software companies generally only change from feedback from GPs. So they need to come as a groundswell of… of GPs using the software to… do their education and go that and think oh well we'd like to have reporting on how we're doing, but we… notice that we don't put reasons-for-prescription in because of these reasons and then they write to the software prescribers to get that changed. (P3)
Consultation support: Prescribing guidelines
I still think a lot of GPs may use the product information [PI] for their information on prescribing because it's integrating with your GP software... And as you may know that the evidence that's informed what's in the PI is often way out date particularly if you look at penicillin and stuff like that, they've obviously been registered under the TGA for potentially decades and the information the PI is usually related to that the initial registrations so often the indications that are wildly out of date or been superseded and certainly the dosing when it comes to children but even often even in adults has being superseded by increased evidence... So I do think that's somewhere where getting something like Therapeutic Guidelines or some similar evidence based up to date evidence based software integrated into the GP prescribing software would be a key thing that we could do so that you know based on the GP that choosing the best antibiotics and using the right dose and using the right duration because PI doesn't actually have much of that duration that type thing. (a GP)
Behaviour change: TG has also put out you know a good summary of antibiotics prescribing. The National Prescribing Service also has that small resource, so I think the resources are there. I think it's just more… getting clinicians to use it. (P8)
Consultation support: Decision support for use with patients

Shared decision making: I think shared decision making does [patient education] okay. … it's not easy to do, but I think that's the gold standard approach. And if the patient decides after you've gone through a careful shared decision that for them in their situation that day, they're prepared to take the downsides of antibiotics because of the small chance of a benefit from them, then all well and good, you let them have the antibiotics. You're not creating a platform of conflict there but next time the situation might be different, and there may not be the wedding to go to at the weekend or the sort of discussions that happen, and hopefully the patient will and GP will repeat the same conversation and conclude not to use them or to or to delay the use of them. So it's a chipping away continuous process of changing hearts and minds which can be done without conflict. (P7)
Well-resourced shared decision making. I think the decision support for practitioners and for patients is probably a key thing that we need to improve more because I think there's still that message that sometimes the quickest way to end the consultation is just give them antibiotics. Whereas now you can do that shared decision making. If it's been well thought through and they're well-resourced you can do it just as quickly potentially as giving the script for antibiotics. (P2)
Evidence-based symptom management tools at hand: Having a symptomatic management sort of prescription as an alternative to receiving antibiotic prescriptions, [a] patient action plan for managing their upper respiratory tract infection... I guess having the right information at hand as well to convey to the consumer at the time as well about why antibiotics are likely to be more harmful than good. (P5)
GP-Patient technology: A doctor has an app and the patient has an app and you just click a few things and then it goes straight to the patient's phone and they have… reminders for medications and… reminders for appointments… results… offer [to] send them videos and electronic information. (P6)
Use the resources we have: I think you've got to remember … the consultation is not particularly long. So you don't want to be making it something that takes your consultation 25 minutes… I just think we've got some really good resources out there. So, we're probably a bit lazy using them…. the NPS things are approved. They've been tested with consumers. They're a trusted brand. (P8)
Potential developers of patient information: The combination of people that are writing specific guidelines should be writing patient information packages to go with those guidelines. So I think when the College of GPs writes a guideline like the Red Book [*Guidelines for preventive activities in general practice*] it should have patient facing components that GPs can use as part of their toolkit and as part of the implementation strategy. So then I think a deal done with the Therapeutic Guidelines people for example would lead into particular patient facing pieces so that patients can check from a responsible source what the same information that the GP should be referring to. And I think big organisations that are doing this quite well like Health Direct could be employed to do more of it. The Victorian Better Health Channel and so on. So I think there are a number of organisations that that might be suitably unbiased and used to producing patient resources and testing those. The National Health Service have a number used in the UK for example. The National Prescribing Service is actually funded to do this sort of work so they could be producing patient information leaflets. Anything like that should be tested in you know rapid easy comparative trials rather than just brought out because it seemed like a good idea at the time. (P7)
Where should patient information sheets be hosted? Everywhere was the answer to that. So that… people access for them health information and optimized for Google searching and linked to the decision support. And I think if antimicrobial stewardship was seen as an important thing to promote, then even community pharmacists; although I think you need to be very careful that they're not doing that for commercial reasons to sell probiotics and complementary alternative medicines with little approval value. (P7)
Hosting information in PHN Health Pathways: Health Pathways is a New Zealand product which is then localized for use in Australia... it's really that one stop shop that has clinical guidance, it has access to consumer resources, and it has access to referral pathways, so really the GP can access everything through that but at this stage it's not really up to scratch for antibiotic use. (P4)
Who should keep patient information updated? Need a central clearing house… of accepted and reliable ones that are up to date. And organizations need to have a expiry date on them. But I don't like the idea of creating policy off the top of my head. I think it's best created by groups of people thinking about all the pros and cons. (P7)
Culturally and linguistically appropriate patient information: I think one of the problems with the health information on leaflets and things like that is that it is one size fits all. And if you really want to get through to people, one size fits all is not the approach. And especially if you're dealing with people from diverse cultural and linguistic backgrounds. So just translating something from English into their language… is not enough. Even in the Australian population one size doesn't fit all. We need all kinds of different approaches. (P9)
Consultation support: Delayed prescribing and watch-and-wait strategies
Need for watch and wait: GPs need education about the use of watch-and-wait. (P12)
Better evidence needed for delayed prescribing: What are the pros and cons for your patients as an individual, on having antibiotics? What's the natural course of the disease they've got without? What are the effective safety netting discussions to have?... So the message that it [a delayed prescription] might send if it's not communicated really well is you've not being sick enough for long enough to earn your right for an antibiotic. Please be sick for three more days and then come and have an antibiotic… I think delayed prescribing would only really work if the scripts are dated and date stamped with a limit on them rather than being open ended for up to a year. (P7)

Pharmacist involvement: Delayed antibiotic prescribing, so if that's going to be successfully implemented, it needs to have that communication process so the pharmacist is aware when they get that prescription it's not to be filled immediately and it should be a bit of counselling around it. But how are they… to be informed about that and what sort of communication strategies can the practice set up with the pharmacy? (P10)
Consultation support: Pathology testing and reporting including rapid tests
Indication for tests: Just because you've got a test available if without the test you would never have gone near antibiotics. You wouldn't want to have that decision altered by the test and also you may find that many of the bacterial infections are just as self-limiting as viral (P7)
Need for support: studies that showed that just putting [point of care tests] in the practices doesn't actually work without a whole lot of guidance and support around them. So yeah, I feel like there's a lot of people who think that those kinds of technological answers are the be all and end all to this; and I would thoroughly disagree. (P6)
Availability and cost of rapid tests: For a GP, rapid tests are not as rapid as if the patient has presented to ED… They are too expensive to do in general practice. (P12)
Rapid tests with watch-and-wait: If the GP feels it is OK to wait before prescribing antibiotics and watchful waiting is done, the GP can then review rapid tests to guide future treatment. (P12)
Rapid diagnosis and communication of results: I certainly don't think that rapid diagnosis is the be all and end all. But… a swab that said you have got human metapneumovirus or you have got respiratory syncytial virus or whatever… here… is the diagnosis, you have got this... therefore, antibiotics are not going to help you. So, I think rapid cheap diagnostics would help a lot. And I think mechanisms to communicate those diagnostic results that don't necessarily involve a patient tracking back to the GP having another appointment… you know in particularly in areas where GP don't bulk bill return visits. Those are all barriers. (P6)
Responsibility: Microbiology testing and reporting often means a combination of the different colleges communicating with each other is often how that improves (P3)
Resource developer: The [Royal] College [of Pathologists of Australasia could] do… e.g. a document for laboratories to provide to patients, comments to guide prescribing, diagnostic stewardship – when not to send specimens to the lab (P12)
Consultation support: Allergy testing
No large impact on AMR: I think it's important and I think there needs to be structures in place for it to happen, but it's one of those one patient at a time things and from my public health mind I don't feel like that will have a big an impact as you know hundreds and thousands of people (P6)
Consultation support: Expert advice
Dependent on relationships: Expert advice for me is very dependent on relationships that I built when I was in the hospital system. So if you've got a good network of experts you can call on but you know from an infection perspective it's… reliant on the goodness of… them giving you their time... (P6)
Patient referral, advice line: I've had patients that I've referred to infectious diseases who are waiting months. Now that's a sticking point… whether or not the government would be interested in having access lines for antibiotic resistance… if someone could ring them up … and get advice probably wouldn't be a bad thing. (P8)
Standard information for GPs: [Private pathology] had one doctor rostered on who answered calls all day. Registrars in [hospital] lab do answer GP calls, but… need something to guide GPs to direct them when they call. We need one official form rather than lots of different ones – they are not as strong as one consistent message. (P12)
Pharmacists: Dispensing antibiotics
Information & data: [pharmacists] don't know why patients are taking the antibiotics... if people should actually be recording... very distinct instructions on the script, then you're going to be able to capture that data in your data mining and then it will also go on to better use of antibiotics at the pharmacy. (P8)
Unit dispensing: Unit dispensing sits under a couple of different things some… sort of legislative basis and some that have a basis in the pharmacy agreement… However, the other way is there's always that back way, of if doctors write on their script three tablets. Then only three tablets get dispensed so that's where there's potentially a regulatory response or there's a cultural response of how people change their prescribing… But that's one of the ones where there's actually two ways of reaching the same endpoint. (P3)
Unit dispensing: breaking packs: I guess the issue is that they then got to suppose another patient will come in and get free and if another patient doesn't come in and get free then they've got to put it in the bin. (P8)
Pack sizes: We don't have a factory to make that size [pack] (P8)

Pharmacist check with GP: a script that says… take for five days one BD [twice a day] and then the GP has actually written the script for 20 keflex because that's how the script pack is. So for the pharmacist to then say look you're going to get a spare 10 please don't take them. That's a conversation to be had at the pharmacy level or say look you've got a spare 10, do you want me to ring your GP and see if he only wants 10 for size. You know that is so important and that doesn't happen. (P8)
Pharmacist: Appropriate disposal of leftover antibiotics
Unaware: I don't think a lot of people are aware that you can return unused antibiotics to a pharmacy. That's obviously something that you could do quite simply and… it doesn't require any changing of legislation or a lot of money to do something like that. (P4)
Incentive: trying to create a public will to return your leftover antibiotics from both veterinary practice and from human medicine. Even getting some money back on the dispensing fee might be a very modest and cheap way to reduce the number of antibiotics sitting around in people's nursing homes in in people's homes. (P7)
Pharmacy review & advice to patients
Triage: [Pharmacists] triage people… we are accessible most days of the week if not all days of the week. And it's easy to just pop into a pharmacy. And we do have a lot of training in our university course for it. (P1)
Safety measure: I think they [pharmacists] can do more around medication management and qualities of medicines… there's issues around having somewhere practical to have sensitive discussions... for things like urinary tract infections, around STI infections… pharmacists have good knowledge about medicines, but their… skills at diagnosis - they're not doctors… The fact that you have … a GP prescribing and then a pharmacist dispensing provides that extra safety measure, that you do have an extra person checking the appropriateness as well. (P4)
Not asking patients for information: [GPs and infectious disease physicians don't] want the pharmacists asking the patients [about their prescriptions] and then making their own judgements because they don't have that whole information… they don't know about other comorbidities… which is not their fault, because that's not their role… It shouldn't be [the patient's] job to try and remember why it was prescribed… If [GPs] put that reason on [the prescription] as you put… duration… it would help with the pharmacy dispensing for pharmacists to do the counselling. (P8)
Pharmacists working with GPs
Funding for pharmacists in general practice: There is a new workforce incentive… payment that's coming in in January [2020] which will allow pharmacists to [be employed by a general practice]. But it's coming from the same bucket of money as payments for nurses, so it's not really anticipated there's going to be a big uptake at this stage. The nurse role is more developed in general practice and additionally the nurses are revenue raising whereas the pharmacists generally aren't. (P4)
Pharmacists in general practice: Pharmacists working in general practice. They'd have a role both educating patients but also the GPs and other practice staff; but also the potential is for them to be involved in auditing and quality improvement activities around antimicrobial prescribing. (P4)
Relationship: it also that relational building between doctors and pharmacists, cos where there's no relationship it's very difficult for pharmacists to ring up a GP and say I think you made the wrong decision. Whereas if they've got a good relationship already there, then that might happen or if they've got a relationship with the practice they might have a regular route for feedback, saying look I've noticed that a lot more fluroquinolones coming through recently, what's been going on here guys? Why have you changed your practice? But in big cities… often, it can be difficult. So I think that is that is a cultural change at doctors being willing to hear from pharmacists but also pharmacists having the time and willingness to bring it up. (P3)
Tension: … you might get a pharmacist calling … and questioning [a GP's] prescription, who at the same time is peddling completely non-evidence-based supplements and all sorts of rubbish to… patients and charging them an arm and a leg to do so. (P6)
Supply and timely access to antibiotics
Antibiotic out of stock: There's also been in this past 18 months some antibiotics not being available so [pharmacist] ringing the doctor getting an alternative because the usual ones are out of stock. (P1)
Nurse triage
Community based nurse: I mean they're not going to the nurse [in the pharmacy] to get antibiotics but I suppose it's more perhaps for that reassurance that they don't need to go to emergency, and they don't need antibiotics. (P4)
Monitoring of Antibiotic Prescriptions

Changes behaviour: You look at the literature, now audit and feedback is a really good methodology for changing behaviour. (P11)
Complete datasets: One of the areas where I think actually government has a role in terms of getting complete datasets. Really I can't see it happening without at least a degree of regulation. (P6)
Private prescriptions: The bit about [monitoring] prescriptions can happen, either the practice level, or at the PBS level but that doesn't capture then private prescription… I don't think the PBS prescribing at the individual level is terribly useful at all. (P3)
Use MedicineInsight: I think the MedicineInsight program is a good one, there's still some issues to iron out … but …. that also has to do with the way software packages are set up and how we enter data into our medical records. But, it has taken a number of years to get to where they are now. And I don't think we need to invest in others to do exactly the same. I think we need to look at you know is this tool useful enough or developed enough to roll out on a much larger scale. (P9)
Against NPS MedicineInsight: No I don't [think NPS should do the monitoring]. I think that they're one of many. (P7)
Reason-for-prescription: some of the software really isn't designed to make it easy to fill [reason for prescription] in either. … sometimes … you've got to think up an obscure name for that particular condition for it to accept it. Things like that don't encourage reporting of reason for prescription. (P3)
Software improvements: once [the reason-for-prescription] gets written into the software then the extraction tools start to become more useful and then you have the ability to be able to do the feedback and reporting. (P3)
Funding: So, I think that [monitoring is] one of those things which needs a big chunk of investment so that we can get it off the ground effectively. (P6)
Patient consent: how much consent do we need to get from patients? (P2)
GPs defensive: I think GPs are… very protective of their data from a patient's point of view because there has been times when patient information has been misused… So I think there has to be done fairly sensitively… there is no suggestion it could be misused but… GPs... get a bit defensive and feel like they've been shamed… if we can separate it somewhat from government or you know regulation people then… GPs will get less defensive about it…. But logically I guess it's going to be only certain people, isn't it… So, it's probably going to have to involve government in some ways (P2)
Low volume prescribers: if you're looking at high prescribers you can look at low prescribers as well you know (P9)
PIP QI incentive: Maybe [monitoring] needs to become part of the QI PIP so that there's a carrot to do it. (P8)
SafeScript model: The SafeScript model that's being implemented for opiates and other drugs of addiction is something that could be considered as a component in general practice. It's probably a little bit more hardcore but a modified version of it could be a way of both collecting data and restricting prescriptions. (P6)
AMR
Laboratory monitoring of AMR, use of PCR: Monitoring of resistance tends to be best done capturing it through the labs… that gets analysed at the state level… and at AURA which is at the Commission [ACSQHC]… I think that some of the [gaps are] the real time monitoring. Yeah and there's definitely a gap in general practice resistance that goes to private pathology labs… There's a few gaps that are developing due to the use of PCR rather than culture and resistance testing. (P3)
Complete datasets: There needs to be an overarching Government responsibility from a regulatory perspective… to get complete datasets... There's lots of passive surveillance systems that get a pretty good view of things but not a complete view of things. You know the organisms for which we really have absolute datasets for are the things that are notifiable… And from one health perspective we need to be able to integrate and it's becoming more and more important that we can integrate surveillance of isolates and resistance across human and animal and food and environmental and effluent and all of those… different sources… the prevalence of resistance is a is a key one that we need that we want to know about. (P6)
Data feedback to GPs
Patient outcomes: PBS… MedicineInsight… doesn't give us follow up data.. You can tell doctors… your colleague has prescribed less than you, then they'll say yeah, but are the… patient outcomes just as good or better or worse than mine? And we can't provide that answer. (P9)
Relevant comparisons: we need to be mindful that people working in [e.g. Aboriginal Health] that if we compare their antibiotic prescribing to their colleagues in you know urban environments that's not the right thing to do…. I really think that comparison to peers works really effectively. And also just showing people you know where they can improve upon, and also I suppose where PHNs can target. Without the data it's hard to tell who you need to work with. (P9)
Link with education & support: [Data extraction] will need to be combined with a cultural change - another one - which links back into the education and the consultation support about adding reason for prescriptions in… (P3)
Feedback on positive variance: But there's nothing that tells us if we are you know being a good custodian… if we're doing the right thing we don't know... I think that that is important. (P9)

Self-monitoring: I think every doctor should be looking at their own data on a regular basis, reflecting and learning from that... I would make antibiotics a mandatory part. You know everyone has their audit on may be on a yearly or maybe on a triennial basis, audit their prescribing for antibiotics and… use that as a way to improve the quality of the care they provide. (P9)
Responsibility: I think more regular feedback and yeah, I think PHNs are well placed to do that with the... [PIP QI] that practices are reporting to PHNs; and they will be getting quarterly reports comparing them against similar practices. (P4)
Embedded pharmacist feedback: From a quality of prescribing point of view, at the entity level of the general practice it should be a pharmacist embedded within that environment whose responsibility to do [feedback]. (P11)
Research
Hospital admissions: Unintended consequences such as hospital admissions for things that could have been prevented with antibiotics. (P3)
Patient knowledge: I wonder if people who've been doing it for longer and you know much more experienced, perhaps forget that patients don't necessarily know these basics… I suspect we assume knowledge that is not necessarily there. (P6)
Gut microbiome; Self-limiting infections: the biome of the gut… could be useful to direct and encourage people to prescribe less antibiotics but also understanding potentially the negative effects of antibiotics… I think the other research thing is… about the self-limiting nature of [disease]. (P2)
Research translation & Patient information resources: There's a keen interest obviously to translate research to something that can be picked up… we need to work on [patient information sheets] continuously in terms of research context and then… how do we implement them nationally when they reach that level of value and evidence behind them? (P5)
Biggest impact: It is complicated, what will have the biggest impact? I'm not sure, research is needed… Some areas are more powerful than others – whatever the research focus says is the most important and some, e.g. disposal of antibiotics, will have less of an impact. (P12)
Real time monitoring and Effect on AMR: we need a much better way of understanding for which patients and why things are being prescribed and that's why an in-depth NPS MedicineWise type system that works in real time and is less clunky, would be useful to assist primary care. The magic question is can we reduce the development, spread of antibiotic resistance through a reduction in antibiotic prescribing? And then there's a question of whether we should be rotating antibiotics globally and say right these antibiotics are going to be put away and not used until resistance has dropped. And then we'll take them out and put some others away in a cupboard. But you'd have to understand the rate of extinction of antimicrobial resistance. (P7)
Pilots: I think there does need to be more of the small-scale piloting things so that we can ensure that what is planned is working before it is rolled out more broadly. (P4)
Evaluation: research to see whether or not campaigns have an impact... (P8)
Measures of success
AMR rates: There's three levels of outcomes. The least ambitious one would be that we… slow down the development of resistance and the spread of resistance and that the accelerating decreases. The second tier is somewhat more ambitious, is that we stop the development of resistance and it just stays where it is now. And the third level is that we that we reverse it. All of which depend on having actually decent amounts of surveillance information data so that we've got an actual idea of where we sit at the moment. So probably the first the first thing is that we would see an increase because if we collect the data properly we will have a better idea of what the levels of resistance are. But once we've got an accurate picture in the ideal world, we would reverse resistance. In a more realistic world if we could… slow the acceleration that'd be nice. If we can help it and keep it at current levels that'd be better. (P6)
Decreased AMR and prescribing; patient outcomes: Are we prescribing less, how are we going with our resistance? We'd have to of course also look at your overall outcomes in patients. (P9)
Decreased AMR; Appropriate antibiotics: Well I would hope that antimicrobial resistance would slow, and antibiotics would be used more appropriately but that would be the first stage. But if you saw antimicrobials would be prescribed and used more appropriately and hopefully that would slow the decline of resistance. (P4)
Empowered GPs decrease prescribing: GPs would be empowered to decrease antibiotic prescribing and that should reduce antimicrobial resistance. (P12)
Professional satisfaction: If you want to make people accountable, responsible, then your outcome should also be looking at levels at the level of the prescribers, and their satisfaction is maybe not the right word, but their support and their confidence, and in how it has impacted their relationship with their patients. So maybe that's the one thing that we haven't really looked at, we have those big data stuff which is very important but success is also depends on how the people who enable it or enact it how they feel about. (P9)
Hospitalisations: I think the way Strama has done it is really nice, the way they also looked at some collateral damage. And the UK have done it to a certain extent. It's probably easier because they have a more centralized approach so it's easier to see who gets admitted to hospitals or who comes back to GP practices if they haven't received an antibiotic for their condition. I'm not too sure how we could track that in Australia. (P10)
Patient outcomes: I think there'd be plenty of really good positive things for the patient really. You know like consultation support stuff I think would make a really big difference… (P2)

Multiple measures: If one of your aims was changing knowledge, you test knowledge. If you want a changed attitude, you look for changed attitudes. If you want to test add[ing] skills to prescribers and dispensers, you look for those skills. If you want to look at your surveillance system, you look how effective the surveillance system is. And if you want to look at unintended consequences, you look at hospital admissions and deaths from infection and you look at cases of overwhelming infection and see whether it was a missed opportunity to prescribe antibiotics at an earlier stage. I think if you want to look for the final common pathway… you can look at the patterns of resistance and see if you can actually demonstrate some improvements in resistance patterns through efforts and whether you can track those to where the processes are happening most. (P7)

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Chapter 6 Discussion, implications and future directions

> *"I really don't think GPs get how bad this* [AMR] *problem is… I don't think health professionals get it... I don't think the community gets it. I don't think the animal industry gets it… We're a little bit oblivious and I don't think we realize just what a calamity is lying ahead of us."* (P8)

The achievements of this thesis have been to:

1. Review the monitoring of antibiotic prescribing in general practice to describe the extent to which current data sources and a new dataset have the capacity to fully monitor antimicrobial prescribing in general practice.
2. Identify the components required to progress AMS in general practice and to develop these into a framework that has not previously been described in the literature.
3. Interview key stakeholders to determine to what extent the framework and its components are valid and feasible for Australian general practice.
4. Map the framework's components to Australia's National AMR Strategy 2020, to connect the objectives of the Strategy with actions.
5. Add to the knowledge of the human factors engineering approach to AMS.

This chapter proposes a framework to comprehensively and rigorously progress AMS in Australian general practice. The framework is outlined in Table 2; it does not appear to have been previously articulated in this way. The framework will now be analysed along with the existing published literature, the newly acquired Stakeholder's views, and informed by human factors engineering and complexity science theory. A fifth paper is planned to add to the knowledge of the human factors engineering approach to AMS.

Table 2 The proposed AMS framework for general practice, listing components and sub-components

Component	Sub-components
1. Governance	• National action plan with accountability • Antimicrobial resistance included on national risk register • Funding for antimicrobial resistance and stewardship activities • Regulations around antibiotic prescribing • Accreditation of prescribers • Standards for antimicrobial stewardship at practice and prescriber levels • Practice level AMS policy/program/activities
2. Data monitoring with feedback	• Monitoring of antimicrobial prescriptions - volume and appropriateness/ guideline concordance • Monitoring of antimicrobial resistance • Feedback to prescribers with local and national comparisons
3. Education	• Community & patient education – multimedia, coordinated, languages • GP continuing education in AMS • GP education on communication skills, patient-centred approaches & shared decision making (including delayed prescribing) • GP education on non-antibiotic management of self-limiting infection • General practice team member education, e.g. practice nurses • Community pharmacist AMS education • Other community care provider AMS education e.g. maternal nurse, wound care nurse, nurse hot line • Independent education (restrict pharma marketing)
4. Consultation support	• Access to prescribing guidelines • Point of care tests to assist with diagnosis • Access to microbiology testing and reporting and selective reporting of antibiotic susceptibilities • Electronic decision support for prescribers • Access to expert advice (clinical microbiologist, infectious diseases physician) • Patient directed resources e.g. information on management and red flags • Access to antibiotic allergy testing and/or guidance
5. Pharmacy and nursing approaches	• Unit dispensing of antimicrobials (to match guidelines and minimize excess doses) • Supply and timely access to antimicrobials (ensure guideline concordant antimicrobials available) • Pharmacy review & advice (when to prompt GP review, advice on medication use, advice re delayed prescriptions) • Appropriate disposal of leftover antimicrobials • Nurse triage, patient assessment e.g. when to refer for antimicrobials • Practice nurses providing patient education – e.g. at healthy child or aged persons review
6. Research	• Research into AMR/AMS gaps in knowledge • Research into efficacy of general practice-based interventions • Translation into practice – health service research

6.1 Governance

As illustrated in Chapter 1's Background literature, Australian general practices are predominantly small private businesses; they do not have the capacity or funding to individually develop resources to implement AMS. There is no apparent requirement for the PHNs, the Australian Commission on Safety and Quality in Health Care (ACSQHC) or other bodies to assist with the development of AMS in general practice.

The framework proposes that AMS needs an action plan which explicitly sets out who has responsibility to drive AMS in general practice. This aligns with Australia's second AMR strategy, objective 1 of "Clear Governance for Antimicrobial Resistance Initiatives", and provides the detail for priority action item 1.2 "Develop, implement and/or maintain sector-specific action plans."[1] However, as stated in Chapter 1's background literature, it is not clear in either the Strategy[1] or the Implementation plan (from the first strategy)[70] which specific organisation has the authority to drive AMS in general practice. Despite the seniority and wide experience of the interviewed stakeholders, they also were not clear about who should lead AMS in general practice. The Commonwealth Department of Health's Office of Health Protection was nominated as the lead organisation, with professional colleges providing input and tailoring messages to their members. The willingness and capacity of the colleges to take on this role was not explored. In addition, there may be concern that increased requirements for individual GPs or practices (e.g. for AMS accreditation or recertification) may not be popular amongst members. The role of colleges may include ensuring that appropriate education is available both in prevocational and continuing education. They may also liaise to ensure that changes initiated by the Department of Health are acceptable to members. Whether the Department of Health has the expertise and capacity to develop and implement interventions into general practice was also not explored. It was surprising that stakeholders could not clarify a role for the ACSQHC. There was acknowledgement that the ACSQHC had produced the handbook "Antimicrobial stewardship in Australian health care,"[73] and that it coordinates the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, but no other roles were suggested for the ACSQHC. It was perhaps perceived that the Commission was focused on hospital care more than general practice. Interestingly the stakeholders did not identify the PHNs as having a role despite their obvious focus on general practice. Stakeholders did not identify state-based groups which have been active in hospital AMS, such as the Clinical Excellence Commission in NSW, or Safer Care Victoria. This may be because general practice is typically funded at the Commonwealth level and not by states and territories. It indicates that messaging between sectors is unlikely to be coordinated. An additional barrier in Australia is that GPs work across healthcare settings, including aged care, rural hospitals and Aboriginal and Torres Strait Islander peoples' health services. General practices are administered by the Commonwealth Government, whereas hospitals are administered by the

State and Territory Governments. Coordination between Governments will help to ensure AMS activities are coordinated between hospital and primary care sectors. The state- and territory-based organisations that employ GPs will need to buy-in to GP focussed AMS initiatives. Complexity science informs us that designated leadership (someone formally in charge) blended with distributed leadership (professionals and partner organisations) is likely to enhance the development and implementation of coordinated interventions in general practice; while the inclusion of key stakeholders will help to ensure activities are tailored to suit the diversity of general practice settings.

This lack of identified accountability is not new; it was first noted in the JETACAR report of 1999[65] and the progress review in 2013.[66] In 2015 Australia's first AMR Strategy was introduced,[63] but neither it nor the second AMR strategy introduced in March 2020 have identified an accountable, coordinated approach to AMS in general practice. The interviewed Stakeholders were also concerned that the many GPs who work across the different health sectors will not want to have to comply with multiple sets of standards. Thus, integration of AMS across health sectors to provide consistent messaging and activities was viewed as important. This ties in with the National AMR strategy 2020 which states that "sectors should work collaboratively wherever possible, sharing information and resources, to reduce the risk of duplication of effort." Stakeholders indicated that leadership would also help to ensure that AMS activities were not omitted or duplicated. The lack of clarity about who is responsible for the implementation and coordination of an overall framework for AMS in general practice was also noticed in the literature. The European Centre for Disease Prevention and Control has nominated "national, regional and local governments as having ultimate responsibility for developing, implementing, and supporting the policies and infrastructure necessary to ensure the prudent use of antimicrobials".[214] As described in Chapter 1, one of the clearest English-language descriptions of a specific AMS organisation is of the Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (Strama) that leads and coordinates AMS across all healthcare settings.[120 122 215] Strama has a national steering group in Sweden's Public Health Agency and is formally funded at national and local levels. Local multi-professional groups link the national and local levels of Strama and adapt national AMS initiatives to local conditions. The USA Centers for Disease Control and Prevention also has a centralized role in AMS across all healthcare sectors. Similarly, the European Centre for Disease Prevention and Control performs these functions in Europe. Both have considerable specialized in-house expertise to develop and provide educational resources about emerging issues in AMS, and to collect, analyse and report data. Australia does not have an equivalent entity.

The governance component from the scoping review included several subcomponents (Table 2) which are further described below.

6.1.1 Governance: AMR included on the national risk register

The inclusion of AMR on the national risk register was described by the WHO in the Global Action Plan on AMR to recognise it as a 'priority need for action' and to enable 'cross-government commitment.'[68] It was also endorsed and publicised by Dame Sally Davies, previous Chief Medical Officer of England.[216] Stakeholders interviewed for this thesis referred to AMR as a "tier 1 priority" at the Australian Health Minister's Advisory Committee level which indicates recognition that it is a priority health concern at all levels, and is important to gain traction for further action.

6.1.2 Governance: Funding

Funding for AMS activities was repeatedly reported in the literature as being critical,[68 73 122 217 218] but apart from Sweden's Strama,[120 122] it was unclear who was responsible for providing and allocating funding for the implementation of AMS in general practice, or how much is required. Strama in 2017 was reportedly funded by the Government of Sweden at 2 million euros nationally and between 3-5 million Euros at local levels;[122] (approximately $AUD 8-11 million) per year. Stakeholders agreed with the need for government funding for AMS activities and expressed the view that health economists should assess the cost of not funding AMS. The Review on Antimicrobial Resistance, chaired by economist Lord Jim O'Neill, estimated that globally by 2050, AMR will cost 10 million lives every year, and reduce Gross Domestic Product (GDP) by 2-3.5%, costing $US 100 trillion.[24] There is no separate estimation for Australia. To provide a very rough estimate, the World Bank recorded Australia's GDP as $US 1.434 trillion in 2018;[219] 2% of this is $US 28 billion (approximately $AUD 42 billion). By comparison, Australia's total health budget for 2019-20 is $AUD 81.8 billion.[220] Thus, the economic impact of AMR in Australia is likely to be significant. Stakeholders suggested financial incentives would encourage practices to participate in AMS activities. This could be in the form of a PIP QI e.g. for participation in programs that monitor antimicrobial prescriptions or educational programs.

An incentive may help to raise the priority of an intervention.[221] It may also improve documentation - a financial incentive to improve immunisation rates improved documentation in some practices rather than the immunisation rate.[222] Given poor documentation, especially around reason-for-prescription, improved documentation could also be a valid reason for an incentive.

Economic factors are allocated to the external environment in the SEIPS 2.0 framework,[172] but are not otherwise described. Complexity science suggests that resources are established for the whole system, not to individual parts, as a pooled budget may encourage generative relationships and enhance patient care across boundaries,[223] and that cooperation with other disciplines, including economics and politics may be useful.[168] This suggests that national level funding rather than poorly coordinated activities at the jurisdictional level would be important.

6.1.3 Governance: Regulations

It is clear from the literature that specific regulatory changes can impact general practice antimicrobial use.[224] This includes increased restrictions on some antibiotics,[225] enforced availability by prescription only,[68 226] removal of authorisation for repeats, and requirements for unit dispensing (dispensing the exact amount required, rather than by pack).[227] These have been very effective in hospital AMS programs.[228] Stakeholders suggested regulatory changes including enabling unit dispensing, removing automatic repeats from antibiotic prescriptions, reducing the 12-month expiry on antibiotic prescriptions and increasing controls on private (off-label) prescriptions. In April 2020, the Australian PBS reduced the repeat authorisation for amoxicillin, amoxicillin-clavulanate, cefalexin and roxithromycin prescriptions.[229] Sometimes changes can be met with hostility,[228] so regulatory and other changes should be analysed carefully before introduction for the likely effect on GPs, patients and the health system to avoid any unintended harm.[230] For example, in 1996, a recommendation letter was sent by the then Health Insurance Commission (provider of subsidised medications) to the top 2000 prescribers of amoxicillin-clavulanic acid. It stated that amoxicillin-clavulanic acid should only be used where resistance to amoxicillin is suspected or proven, there may be hepatic complications of amoxicillin-clavulanic acid treatment and that there would be a follow up audit to assess compliance. There were no recommendations about alternatives to amoxicillin-clavulanic acid or resources provided. The message was also widely disseminated in the medical and pharmaceutic marketing literature. There was a significant decrease in the number of prescriptions of amoxicillin-clavulanic acid, but no overall decrease in total antibiotic prescribing. However, a study of 34,242 patients from four general practices across three states found that there was a shift away from best-practice antibiotic prescribing with increases in the number of prescriptions of cephalosporins and macrolides. The number of adverse outcomes, radiology and pathology investigations increased as did the number of hospitalisations and patient referrals.[230] Complexity science offers explanations of interconnected actions; that if the relationship is non-linear, the outcome may be unexpected.[183 186] It is not noted if GPs were involved in the design this intervention,[230] but Reed et al.'s SHIFTEvidence use of complexity science's principle "Engage and empower" would suggest that those who are affected by the change should be engaged in the intervention and those affected be provided with resources, training and support.[187 231 232] The 1996 intervention did not provide GPs with resources, training or support to change their prescribing from amoxicillin-clavulanate. As new antibiotics become available, it is important that their place in therapy is carefully assessed.[68 217 233 234] Stakeholders spoke of keeping new antibiotics in reserve and regulations may be used to implement this. It would appear important however to be clear about what circumstances might warrant their use and provide mechanisms for access.

6.1.4 Governance: Accreditation and a practice level AMS policy and program

The scoping review suggested that accreditation of individual prescribers was necessary, but the interviewed Stakeholders perceived that accreditation of general practices to AMS standards was more relevant to the Australian context. It is estimated that 90% of general practices are currently accredited,[117] but as illustrated in Chapter 1, the practice standards 5th edition[114] used for accreditation do not provide compulsory AMS standards or a structure for assessing AMS implementation. According to the literature, a practice level AMS policy is part of AMS implementation[73 217 218 224 233 235] but few details were provided about what should be included in the policy. Stakeholders agreed that the practice level AMS policy area is underdeveloped in Australia. They also commented that an AMS program should be at the practice level, not the individual GP level, as patients may be seen by different GPs in a practice; thus it is important that the whole practice acts on AMS for consistency. Apart from practice standards, there are Clinical Care Standards in AMS[4] which are applicable to general practice and listed as a resource in the RACGP Standards' resource guide.[118] The Stakeholders did not mention any mechanism to promote these at an individual or practice level but they may provide a framework to describe quality and safety of antimicrobial prescribing. Without some compulsion or incentive, there is little to encourage practices to do anything additional to support AMS. It is recommended that standards for general practices require the implementation of AMS and that they offer resources for this. A sample AMS policy and program developed from relevant standards and guidelines are provided in Appendices 3 and 4 respectively. These could be offered in the Resource Guide[118] that accompanies the Standards for General Practice and used in an accreditation audit against the Standards.[114]

6.1.5 Governance and the human factors engineering framework

Most of the governance components described above fit into the external environment of the SEIPS 2.0 framework of "macro-level societal, economic, ecological and policy factors outside an organisation."[172] The practice level policy and AMS program fit into the work system - organisation component and, surprisingly, have not previously been included, although time for clinic meetings and agreement on prescribing practices were mentioned and are relevant.[175] It is recommended that the following factors are specified in the external environment: that AMR in general practice is formally recognised as a priority health concern at all levels of the health system; funding is provided at a national level to promote coordination of activities at the jurisdictional level; regulations enable unit dispensing, repeats on antibiotic prescriptions are provided only when indicated e.g. according to prescribing guidelines or authority/expert advice, and consideration is given to reducing the expiry dates on antibiotic prescriptions and increasing controls on private (off-label) prescriptions. The organisation component of the work system is recommended to specify a practice level AMS policy and program/action plan. By putting the GP at the centre of the work system, it may be recognised that the extent of coordination of AMS standards and interventions between the additional sectors in which GPs work (such as rural hospitals and aged care) may affect a GP's ability and willingness to participate in AMS programs.

6.2 Monitoring of antimicrobial prescribing

Monitoring of antimicrobial prescribing is required in objective 5 of Australia's National AMR Strategy 2020 "Integrated surveillance and response to resistance and usage".[1] Specifically, action item 5.1 is to "Create a sustainably funded national One Health surveillance system that integrates human, animal, food and environmental usage and resistance data" and action item 5.4 is to "Use evidence-based surveillance and monitoring data to inform actions and responses to contain antimicrobial resistance".[1] Monitoring was a key component of the international AMS frameworks examined in Study 2 and was regarded as important by the key Stakeholders in Study 3's interviews. The JETACAR report of 1999[65] and the progress review in 2013 also highlighted that a "rigorous monitoring and reporting regime of antibiotic use" is required.[66] Baseline antimicrobial prescribing data enables the targeting of AMS initiatives to health professionals and the community and the effect of the initiatives to be measured. Monitoring also requires a measure of the appropriateness of each prescription i.e. the details of the reason-for-prescription along with any guideline modifiers such as co-morbidities, allergies, other therapies, the patient's age and for some patients, additional modifiers such as social circumstances. The illness' outcome is also important, for example whether an infection became more serious after an antibiotic was not provided, or an antibiotic-associated adverse outcome such as *C. difficile* diarrhoea, toxicity or allergy occurred. Study 1 investigated the extent to which monitoring of antimicrobial prescribing is possible with the current data sources and the MAGNET dataset.

As described in Chapter 3, the PBS administrative dataset of dispensed prescriptions is not suitable for AMS monitoring. It does not include all GP prescribing – in 2011 about 7% of antibiotic prescriptions were private (off-label) prescriptions[83] which are not included (there is no data past 2011), and up to 25% of PBS data is from non-GP prescribers.[83] The PBS collects no data on the reason-for-prescription, the patient's co-morbidities, or clinical outcomes. It has been used in Australia for volume-based feedback to inform GPs if they are in the highest prescribing group in their region,[230] [236] but this does not identify where the GP could safely reduce antibiotic prescribing. For instance, GPs who sub-specialise in treating people with a high risk of sexually transmitted infections may appropriately be higher antibiotic prescribers; for them to reduce prescribing may harm patients. The MedicineInsight program[191] of GP electronic medical record surveillance is also unsuitable for AMS monitoring. It is voluntary, with only about 8% of Australian general practices contributing data.[204] It is unknown how representative these contributing practices are, apart from under-representing remote areas.[202 237] Patients who "infrequently" attend a general practice are not included.[6] "Infrequently" was not defined, nor was it stated why these were excluded. Patients are not linked across practices but data from the Practice Incentive Program for the 12 months ending 30 Nov 2017 showed that 53% of patients attended only one practice, 30% attended two practices, 11% three practices and 5% attended four or more practices.[202] Thus linking patients across practices may be useful. MedicineInsight does include private prescriptions and contains longitudinal general practice data. Its remit is to review medications and medical tests for quality improvement;[204] antibiotics are but one part of its scope. However it is also tasked in section 2.2.11 of Australia's AMR Implementation Plan with providing feedback to GPs on their antibiotic prescribing habits.[70] It is unknown if MedicineInsight has the capacity to be widely adopted across all general practices, their various clinical software programs - it currently extracts data from only two commonly used clinical software programs[202] (in Australia, practices supply their own preferred clinical software) - or if the NPS MedicineWise administering organisation has the capacity to provide regular analysis of antibiotic prescribing with feedback to all GPs. While MedicineInsight has potential, it is currently at too small a scale for use as required for AMS.

MAGNET was the dataset analysed in study 1. It comprised the deidentified electronic medical records from 50 general practices across Melbourne's eastern suburbs. As for MedicineInsight, it followed patients longitudinally, provided the date of prescription, name of the antibiotic, and the age and gender of the patient (amongst other information). However, MAGNET could follow a patient between participating practices. A comparison of data sets in included in Table 3. Study 1 analysed MAGNET data over five years, from 2010 to 2014 inclusive. From these data, it was seen that there was a preference for broad-spectrum antibiotics in this cohort of practices, with cefalexin, amoxicillin-clavulanic acid, roxithromycin, doxycycline and clarithromycin the most frequently prescribed antibiotics.[212] A decline in the prescribing rate over time was seen in age groups under 50 years, with the largest decline in those aged 1-19 years. There was little variation in the prescribing rate for patients aged 50 years and over.[212] There were winter peaks of prescribing in each of the five years, which suggests prescribing for winter respiratory illnesses.[212] However, it was not possible to assess the appropriateness of prescribing as a meaningful reason-for-prescription was found in only a minority (17.3%) of antibiotic prescriptions.[213] Some practices did not use this field at all and no practice used it for all antibiotic prescriptions.[213] MAGNET has been rolled out in PHNs as POLAR and claims to be the only program that can gather free-text information from the medical record to obtain a diagnosis.[211 238] This offers a potential source of information for assessment of antibiotic appropriateness, but its accuracy for

AMS would require verification, e.g. by comparing the computer generated outcome with completed reason-for-prescription fields or a manual record review. Software improvements are required to make the reason-for-prescription field fit within GP workflow[213] and be of use to GPs. Compulsion to use the field may have limited success without the improvements to workflow and usefulness to GPs. In Denmark, since 2011 doctors must enter a clinical reason to justify prescriptions. A survey from 2012-3 found that in 32% of prescriptions the reason was missing, but this varied between practices with a range from 10-90% and where the reason was recorded, approximately 26% were 'infection'. In 2014 the non-specific 'infection' option was removed, but missing indications were still approximately a third.[239] Another issue is that some electronic medical record software programs are not well designed to promote logical choice[240] or to extract data for use in quality measurements.[241] The (in)completeness of patient records has been identified as a cause of patient safety incidents and harm in primary care,[242] so there is an imperative beyond AMS for software enhancement. The interviewed Stakeholders suggested that the reason-for-prescription field may be used if it was linked to Therapeutic Guidelines,[9] patient information resources and could pre-populate a prescription. However infections, or infections with underlying conditions that do not fit within Therapeutic Guidelines parameters requires consideration.[243] Thus, GPs may need control to override when required.[244] Clearly, this is an area rich with opportunities for improvement in AMS and patient safety. Minimum standards may force the issue, but complexity science reminds us that changes should have input from users to help optimise outcomes.[187 223] Clearly, software improvements are urgently required. This is likely to need cooperation between software developers, GPs and the regulators who will oversee the monitoring and feedback. Rather than compelling GPs to use a software field that does not fit with in their workflow and is of little apparent use, changes to practice standards may be beneficial in putting pressure on software developers to improve the clinical software. For example, requiring the use of clinical software which provides a reason-for-prescription field which integrates with prescribing guidelines and patient information resources would not only provide the necessary data for monitoring, but would be useful for GPs. Again, GPs should have input into the design of clinical software.

Table 3 A comparison of prescribing data sources

Data set	Advantages	Disadvantages
PBS	Estimated to contain 90% community antibiotic prescriptions.	Excludes GP-written private prescriptions. No demographic data or reason for prescription available. Includes prescriptions from other community providers, hospital outpatients and discharged patients.
MAGNET/POLAR	Contains demographic and clinical data. Can track patients across participating practices.	Limited recording of reason for prescription. Needs a mechanism to allow for ongoing antimicrobial analysis and feedback. Cannot access data from all GP software. The MAGNET antibiotic study was a pilot project.
BEACH	16 years representative data. Provides demographic and clinical data and reason for prescription.	Survey based – intensive resources required. No longer funded; no data collected after 2016.
MedicineInsight	Contains demographic and clinical data. If expanded, potentially could track patients across participating practices.	Contains data from fewer than 10% of practices across Australia. Limited recording of reason for prescription. Needs a mechanism to allow for ongoing antimicrobial analysis and feedback. Cannot access data from all GP software.
RECENT	Provides longitudinal demographic and clinical data and reason for prescription.	Survey based – intensive resources required. Collects data from GP registrars only. Does not collect data from all registrars in all states.
Practice-based audit	All patient data available including reason for prescription.	May be subject to selection and analysis bias. No external/independent analysis available. Time intensive.

Diagnostic tests would be a useful surrogate marker for some infections (e.g. urine and sputum microscopy and culture for urinary tract infections and pneumonia respectively), more so if the result could be matched with a consultation record containing prescriptions. Few diagnostic tests are done in the general practice; the main one is a urine dipstick. In the MAGNET study we were unable to extract the laboratory results from the patients' records as they could not be de-identified. This may be amenable to an IT solution.

Stakeholders were clear that patient outcomes should be monitored. Outcomes may be assessed from MAGNET/POLAR and MedicineInsight if the patient returns to the same GP, but outcomes are not available in the PBS dispensed prescription dataset. MAGNET/POLAR currently has the advantage over MedicineInsight in that patients may be tracked across participating practices, i.e.

a patient who presents to one practice for assessment but presents to another participating practice when their condition worsens. Linkage with hospital admissions data is required to monitor if the patient was instead admitted to hospital or presented to a hospital emergency department. Ongoing monitoring of hospital admissions for serious infective conditions, e.g. pneumonia, mastoiditis, quinsy, meningitis, would be important to monitor for patients who were under-treated. Monitoring is also required for complications such as *C difficile* infections, anaphylaxis. Linkage of datasets carries the risk of information being identifiable,[245] but technology and data security plans may enable the management of this risk.[246] Linkage between GP and hospital data is urgently required to enable monitoring of patient outcomes as AMS programs are rolled out.

Monitoring of antimicrobial prescribing is likely to be done at a regional or national level. It was again notable, but perhaps not surprising, that there was no clear organisation or method nominated by Stakeholders to externally collect, analyse and feedback the prescribing data at any level of the health system. Stakeholders were concerned that external data collection and analysis should be a process trusted by GPs, with non-threatening feedback appropriate for the context of each practice. A new data gathering program that the interviewed stakeholders thought potentially could be exploited for monitoring is the Practice Incentives Program Quality Improvement Incentive (PIP QI). From 1 August 2019, accredited general practices are incentivised to submit a quality improvement dataset, the PIP QI, to their local PHNs.[247] The PIP QI only collects process level data from practices' clinical software, but it uses any available tool, such as inbuilt clinical software tools or externally provided software such as POLAR, to collect data sets. It also encourages practices to work with their clinical software provider to enable the collection of data, with practices given up to 12 months to find a solution.[247] The PIP QI reflects a collection mechanism that would enable the collection of data from all general practices, with the data being collected (and presumably held) by the PHNs. The first National AMR Strategy states that PHNs "may be well placed to support implementation of AMS initiatives in general practice,"[63] and the Stakeholders regarded PHNs as suitable organisations to work with GPs on AMS. However, if the PIP QI data set is to be exploited for AMS it needs clinical, not process level data. The PHNs may require regulatory approval and guidelines to permit the collection of deidentified clinical data, and the capacity, expertise and funding to enable the analysis, feedback and reporting of the data. Whether antimicrobial monitoring via the PIP QI would be acceptable to GPs, practices and PHNs and to what extent PHNs have the authority and capacity to manage or analyse this data would require research. Stakeholders were aware that PHNs vary in capacity; that what can be done at one PHN, like general practices, may not be viable at another. NPS MedicineWise through the MedicineInsight program is already conducting analysis on data from about 8% of practices[8] but is unlikely to have the capacity or funding for analysis on all practice data. Another data source under development by the Australian Institute of Health and Welfare

(AIHW) is the National Primary Health Care Data Asset.[248] Its aim is to produce high-quality data about the patient's journey. The need for data regarding the reason for encounter, the patient's diagnosis, treatment and outcomes are known.[249] Without adequate monitoring of antibiotic prescriptions and patient outcomes, there is little baseline data to inform and monitor AMS programs. Developing a secure data set which collects deidentified data from all general practices is an urgent priority. This should be automatically generated after agreement to participate.

Monitoring of data suggests the need for targets and the National AMR strategy 2020 states that "action plans should set clear targets and timeframes". However, patients in general practice may not have a clear diagnosis or may have multi-morbidities that affect guideline compliance and, as illustrated in Chapter 1, patients may have competing socio-economic priorities[178] or may not adhere to a treatment plan.[250] These factors may affect a GP's ability to reach an externally imposed target. GPs understand the processes and practices of general practice care and the types and sources of variation;[187] complexity science suggests that if targets are required, then GPs should be involved in the setting and measuring of any targets that will affect them.[187]

Stakeholders thought that when monitoring antimicrobial prescribing within a practice, a whole-of-practice, team-based approach to AMS was preferred over individual GPs monitoring their own prescribing. The ACSQHC's handbook on AMS indicates that an AMS team include at least a doctor and a pharmacist[73] but does not specify where this pharmacist should come from. A community pharmacist, like a GP, works in a private business so is unlikely to have the time or specific AMS training to be part of an AMS team in a general practice. Stakeholders spoke of the workforce incentive, available from 1 February 2020, that allows a non-dispensing pharmacist to be employed by a general practice.[251] However, it is the same funding stream as for practice nurses and other allied-health providers, so it is unknown how many pharmacists are likely to be employed or then used for AMS activities, or what ongoing AMS training the pharmacist may be able to access. In the Netherlands, GPs participate in regional focus groups where they discuss prescribing practices with pharmacists.[252] GP-pharmacist interactive group meetings have been found to be effective at reducing antimicrobial prescribing and increasing guideline adherence.[253] The workforce incentive funding stream has the potential to enable the employment of non-dispensing pharmacists, but ongoing AMS education will be required for the non-dispensing pharmacists to develop and maintain in-practice antimicrobial monitoring and feedback systems. Development of this AMS education is a priority.

6.2.1 Monitoring: Feedback to GPs on their antimicrobial prescribing

NPS MedicineWise provided an online AMS self-audit service for individual GPs with guidance on which patients to select, what to analyse, and provided instant peer comparison feedback with suggested actions. However, this is currently (July 2020) closed to new enrolments. Apart from a practice's voluntary participation in MedicineInsight (if they have a compatible clinical software system) or the visiting academic detailing service provided by NPS MedicineWise – for which AMS is but one of many topics provided[254] - there does not appear to be a mechanism for an individual GP or practice to readily obtain independent actionable feedback when internally monitoring antimicrobial prescribing. Feedback on antibiotic prescribing is likely to assist GPs to optimise patient outcomes. In the literature, it was unclear who is best placed to provide this feedback. Sweden's Strama AMS program, used "experts" and "local multiprofessional groups" to provide feedback.[120 122] Community multi-professional groups could be auspiced by PHNs or university-based research networks. Hospital funding is state based, so hospital staff such as infectious disease specialists are unlikely to be involved without separate funding provisions. In 2017 using volume-based PBS data, the Australian Chief Medical Officer wrote a generic letter to GPs who were in the top 30% of antibiotic prescribers in their region to inform them that they prescribed more antibiotics than their peers.[236] This reduced antibiotic prescribing, and was most effective when the letter came with the peer comparison in "a visual attention-grabbing graph."[236] However, there was no analysis of guideline concordance, no discussion of the practical issues faced by GPs, no description of strategies to promote alternatives to antibiotics for self-limiting infections and no measure of patient outcomes. The provision of these would require input from AMS experts and multi-professional groups and is likely to be resource intensive. Nevertheless, the provision of this level of information would be far more meaningful for GPs than volume-based feedback alone. The interviewed stakeholders perceived that this PBS volume-based feedback method could be flipped and used to identify GPs who prescribe antibiotics at a lower rate than their peers - i.e. used to identify positive deviance.[255-258] They suggested that these GPs could be interviewed to learn what techniques they use, and that knowledge used to inform other GPs. GPs could be supported to provide peer-led educational sessions. There could also be a mixture of group-based self-directed learning e.g. with the use of an RACGP approved learning module, invited experts or after a self-audit on antibiotic prescribing. However, modules would have to be funded, developed, hosted somewhere, and kept updated. Complexity science supports this by suggesting that clinicians do complex work, and they do most of it correctly. Building feedback loops may build a momentum for change,[179] which can be positive and reinforce a change or negative and modulate a change.[188 259] Feedback must take into account the needs and priorities of patients, which sometimes conflict with evidence-based care. The provision of external feedback, or wedging, may exhibit surprising outcomes.[186] What gets measured influences behaviour, and attempting to improve a measure or offer an incentive or penalty may offer a perverse incentive to do the wrong thing.[260] It also informs us that the quality and consistency of the data is important,[260] that key indicators are needed for monitoring and feedback,[260] that health professionals' confidence and trust in the data is important,[260] and that they must understand the concepts and mechanisms.[260] Providing GPs with informative, actionable feedback is an important part of AMS. Along with the monitoring system, a feedback mechanism for GPs and practices is urgently required; this could incorporate AMS tips from lower prescribing peers. Including peer comparisons is likely to be an educational incentive - as was seen in the 'Nudge vs Superbugs' intervention.[236]

In conclusion, there are no currently available general practice data sources that can adequately monitor antimicrobial prescribing for appropriateness, patient outcomes or provide adequate meaningful feedback to all GPs. Monitoring and feedback of antibiotic prescribing requires urgent development to enable AMS in general practice. This should be a priority for action. Capturing data from all practices, including the reason-for-prescription, clinical and social guideline modifiers and patient outcome data is likely to be important. SEIPS 2.0 human factors engineering provides insights that may assist with the development of monitoring. For instance, under tools and technology, this research suggests that the clinical record should fit into the GPs workflow with integrated guidelines and patient educational resources (as was suggested by the interviewed Stakeholders), it should include accountable justification and suggest alternatives to an antibiotic prescription where indicated. In the SEIPS 2.0 model, under organisation, is the fact that the general practice chooses to participate in a monitoring and feedback process. Under person, is the fact that the individual GPs are comfortable with the technology and monitoring processes. Finally in the external environment category of the SEIPS 2.0 is the acknowledgement of the need for a trusted external monitoring and feedback process.[261]

6.3 Monitoring of and feedback on AMR

Monitoring of AMR is described in objective 5 in the National AMR Strategy 2020[1], and is common across the literature. Data is needed to provide information about the prevalence of AMR organisms across Australia.[262] AMR monitoring is mostly managed by laboratories at the State and Territory level, and then collated and nationally reported by AURA.[6-8] While improving, there are data problems which include: different susceptibility testing systems in use,[16] not all laboratories being required to submit data,[16] not all patients with a suspected infection able to have a specimen collected and gaps caused by variable adoption of non-culture based technologies such as PCR. Stakeholders perceived that monitoring of AMR is a government responsibility which may require mandatory surveillance and data collection at the laboratory level to monitor resistance for general practice. Stakeholders thought that it may be useful for GPs to know local resistance patterns and recognised that variation in local resistance patterns may affect prescribing guideline applicability. AURA is the most likely source for this feedback. Improvements could include data collection from more laboratories, or possibly sentinel general practices, in each geographical area, more specimens to be collected from infections that are often empirically treated e.g. UTI, pneumonia/chest infections. Expert insight from infectious diseases specialists and/or clinical microbiologists would be required to advise when an antibiotic should no longer be used due to increased resistance and to provide a guideline concordant alternative. Complexity science would suggest caution in the provision of AMR data alone, as it could cause an unknown effect on antimicrobial prescribing as there is likely to be a feedback loop in the form of a non-linear interaction between the knowledge of AMR and the prescribing of antibiotics.[182 186]

6.3.1 Summary of recommendations on monitoring

Rigorous antimicrobial monitoring requires the details of each prescription – name of antimicrobial, dose, route, duration, reason-for-prescription along with any guideline modifiers such as co-morbidities, allergies, other therapies, the patient's age and for some patients, additional modifiers such as social circumstances. The illness' outcome is important to monitor for under-treatment or adverse events. This will require linkage of GP data with hospital data to monitor for presentations to the emergency department and/or admission to hospital. There is currently no system that can provide this data. There is potential for existing systems to supply some of this data, such as the PIP QI data being collected by the PHNs and the AIHW National Primary Health Care Data Asset, but neither are linked to hospital datasets. However, the problem of GPs not recording the reason-for-prescription in an extractable field remains. This is addressed further under consultation support below. The National AMR strategy 2020 calls for action plans to be "based on established research, data and modelling". Obtaining complete datasets for monitoring needs urgent attention; without baseline data, we cannot accurately target AMS initiatives or monitor the outcomes. Targets for GPs to meet regarding antimicrobial prescribing are not recommended due to the many factors that may affect the need for an antimicrobial prescription. Although targets may be successful, they need to be context specific and involve those being measured. Bombarding high prescribing practices with e.g. GP behavioural/educational interventions may lead to disengagement unless external factors are also managed. E.g. comorbidities, smoking, cultural demand for antibiotics, insufficient consultation time for patient education, lack of resources in formats appropriate for the population.

GPs and practices need feedback on how their prescribing compares against guidelines and their peers, along with recommended actions. There is currently no system that has the capacity to analyse all antimicrobial prescribing and feed summaries back to all GPs and practices. GPs may undertake a self-audit (but there is no encouragement for this), and there is no Australian process to guide the selection of patients, what to analyse, nor to obtain external feedback or advice. The National AMR strategy 2020 calls for action plans to "allow organisations to monitor progress and achievements". Again, these need urgent attention.

6.4 Education

6.4.1 Education of the public and patients

The published literature suggests that the general public do not have a good understanding about which conditions are treatable by antibiotics, why antibiotics are specific to individuals and conditions, the importance of taking the full course,[263-265] or what AMR is, its consequences and how it arises.[98] Public education was called for in a WHO report on AMR,[68] the JETACAR report of 1999,[65] the 2013 progress review,[66] and in Australia's first and second National AMR Strategies.[1 63] Studies have shown that GPs often perceive that patients expect antibiotics, which leads to increased inappropriate antibiotic prescriptions[100 266] and Australian parents have reported that they would see another doctor if they thought an antibiotic was needed for their child but it wasn't prescribed.[267] Hence there is an ongoing need for education of the public about AMR and AMS.

Public health campaigns were included in many of the AMS frameworks examined in study 2, but the campaigns were not well described.[68 73 120 122 175 217 218 224 226-228 235 268] Australia's NPS MedicineWise and earlier bodies have delivered public AMS campaigns concerning upper respiratory tract infections (RTI) with associated reductions in antibiotic use and increased consumer awareness about appropriate use of antibiotics,[74 76 269] but there was no public campaign during the autumn or winter of 2019 nor autumn of 2020. The interviewed Stakeholders suggested that government-sponsored public health messages should be ongoing and that the Consumers Health Forum could be involved in developing the campaigns. They acknowledged that this would require significant funding and working with communities at the community level. Belgium and France, like Australia, use more antibiotics than the OECD average. [8 82] Public health campaigns there have reduced antibiotic expenses more than the cost of the campaign.[270] A local social marketing approach was cost-effective at reducing antibiotic prescribing rates.[271] In future cost-effectiveness studies, the future cost of antimicrobial resistance should be considered[24] and patient outcomes included.[272]

A survey study of 60 campaigns from 47 countries found all but 12 campaigns targeted both the public and physicians, including parents, teachers, GPs, paediatricians, and pharmacists. Most campaigns (46, 77%) focussed on RTI, 15 campaigns focussed on urinary tract infections and six on sexually transmitted infections. While only 24 campaigns were evaluated, some were associated with a reduction in overall antibiotic use. In Europe, campaigns between 1997-2007 were associated with a 6.5-28.3% drop in antibiotic use. The authors recommended that messages should address public misconceptions, legislative changes and be appropriate for local context and popular understanding, as no message was considered “universal”.[273] A systematic literature review of 14 public campaigns with an estimated 74-75 million participants found that multifaceted campaigns targeting both clinicians and the public using a variety of formats and repeated messages over a long duration about RTIs were successful in reducing antibiotic prescribing.[128] However, there were also conflicting pharmaceutical company messages promoting over the counter products, and public health messages encouraging the early detection and treatment of diseases. Thus, messages are complex and audiences may interpret them differently, in ways not fully understood.[274] It has also been observed that campaigns may increase knowledge, but they do not always change behaviour.[275] Complexity science may be able to offer insights into campaigns;[259] for example, incorporating behaviour change science into interventions and allowing for adaption to context and needs.[189] Ongoing evaluation of campaigns is recommended.

Australia has a multicultural population with, in 2018, 7.3 million migrants (29% of the population), from every country of the world.[276] Prescribing practices differ across the world, so Stakeholders perceived a need for reliable information in community languages on the internet and social media. Messages in all languages need to be clear and account for poor health literacy[277] and for those who have limited vision or hearing, so a range of video/pictures/written information and/or access to health professionals who speak community languages is suggested. Education for health literacy and antibiotic use was suggested in the literature[68 73 122 217 218 226] and by stakeholders, starting at school level.[214] There are models for school AMS education in Europe’s eBug program,[278] and Canada’s Do Bugs Need Drugs program.[279 280] No similar programs currently operate in Australian schools. Introducing a school-based AMS education would require collaboration between the Commonwealth Department of Health and the state- and territory-based education departments. Programs are likely to need tailoring to the differing curriculum requirements of the six states and two territories.

GPs are called upon to educate patients about the appropriate use of antibiotics[73 175 218 226 234 235] and the treatment and management of self-limiting infections,[73 217 218 226 227 233-235 268] with their main resources being patient information leaflets and waiting room posters. It was not clear from the literature what should be included in these, or who should develop and evaluate them regarding literacy level, language and cultural appropriateness. It has been suggested that doctors underestimate the patient desire for information. [281] Stakeholders suggested the use of informational material playing on waiting room screens.

In conclusion, targeted multifaceted public health AMS campaigns have been successful in Australia and elsewhere; but they may need the input of relevant bodies with multi-cultural expertise and evaluation to ensure messages have been targeted and understood across society.

6.4.2 Education for health professionals

The high prescribing rates of the broad-spectrum antibiotics cefalexin and amoxicillin-clavulanic acid is a serious concern. A cross-sectional survey of GPs in 2011-12 showed that only 24 out of 730 (3%) respondents believed broad-spectrum antibiotics increased AMR, and 6% believed that prescribing the narrowest spectrum antibiotic increased AMR. Further, 70% of respondents stated they would often or always prescribe a narrow-spectrum antibiotic.[100] An educational program around antibiotic spectrum and its contribution to resistance is warranted.

AMS education for GPs was called for in the literature,[68 73 122 175 217 218 224 226-228 233 235 268] with a need for it to be provided independently from pharmaceutical marketing.[68 73 217 218 226 268] Six papers also called for education for general practice team members but did not describe the content in any more detail.[73 122 175 217 235 268] No mandatory education programs were described, nor was it clear who should develop, deliver or evaluate this education. As described in Chapter 1, interventions with education have produced mixed outcomes and may be successful in one setting but not in another. Passive education or provision of educational material alone had limited impact but providing multi-faceted interventions and tools to change behaviour may promote more change.[125] Stakeholders perceived that health professional education endorsed by a professional college, supplied by medical specialists or PHNs was well regarded and trusted. The question was raised about whether the current NPS MedicineWise GP AMS education modules are at the breadth and depth required.

A human factors engineering approach suggests that education is secondary to system design; to be used when a system solution cannot be found.[161] This may explain why some educational programs have limited impact. Higher order interventions are to: eliminate the hazard, create barriers, mitigate the consequences and finally, to educate to prevent or avoid the hazard.[161] As an example, to reduce unnecessary antibiotic prescribing for an acute upper RTI, patients could be immunised to prevent influenza (elimination of hazard), provided with community resources (e.g. pharmacy advice) to self-manage a self-limiting infection so that they do not need to present to general practice. An example of a barrier is the regulation of fluroquinolone antibiotics which require an authority prescription. Other barriers could include the GP's use of watch-and-wait or delayed prescribing strategies. Mitigating the consequences of prescribing would include unit dispensing and the safe disposal of leftover antibiotics. Finally, education could be provided to complement the above. It may be informative if papers reporting the outcomes of AMS interventions also reported the availability and use of community barriers and mitigating factors.

6.5 Consultation support

From the literature, consultation support included access to prescribing guidelines,[68 73 120 122 175 217 218 226 228 233 235 268] electronic decision support, [73 175 217 218 228 233 235 268] access to expert advice,[73 217 218 226 228 235] appropriate use of microbiology testing and reporting[68 73 122 217 218 226 228 233 268] (including selective reporting of antimicrobial susceptibilities in line with guideline recommendations)[73 175 217 218 228 233 282] and patient information resources to support shared decision making.[73 122 175 217 218 227 228 233 235 268] The components considered valid and feasible by Stakeholders were integration of prescribing guidelines and patient information resources into clinical software to improve decision support, and selective reporting of antimicrobials in microbiology reports.

Australia has national antibiotic guidelines (Therapeutic Guidelines[9]) for use in all clinical settings, including general practice.[9] However, they are not well followed by all GPs, especially for RTIs.[85] This may be due to perceived patient demand for antibiotics even when none are warranted, the lack of integration of the guidelines into the clinical software and/or the guideline's access fee.[283] (The latter two are human factors barriers to its use.[161]) Product information, on the other hand, is integrated into GP clinical software and available without fees, but Stakeholders regarded it as potentially outdated for some antibiotics and potentially driving inappropriate antibiotic use. Stakeholders regarded Therapeutic Guidelines as very appropriate for GPs to use but reported that the problem was getting GPs to use it. Stakeholders perceived that behaviour change interventions would encourage its use; human factors engineering would add in the reduction of barriers.[161] In 2019 to further assist GPs, Therapeutic Guidelines released a free one page document: Antibiotic Prescribing in Primary Care: Therapeutic Guidelines Summary Table 2019.

It may take regulatory changes to force clinical software suppliers to integrate TG into their software.

Regarding access to expert infectious diseases advice to guide antibiotic use, France has described a telephone support service for GPs.[228] Sweden has described clinical experts who work with prescribers to provide audit and feedback information and to promote guideline adherence.[122] The European Centre for Disease Prevention and Control, has recommended that infectious disease specialists should be available for consultation and for review and feedback on prescribing.[214] Study 3's interviewed stakeholders commented that they, and possibly the wider GP community, tend to rely on hospital experts – sometimes with relationships built from when they were part of the hospital system. This is partly reliant on goodwill, but the patient may also be later referred to that hospital for management. Apart from referring a patient to a hospital or specialist, there is no other formal existing support mechanism for GPs to access expert advice.

Selective reporting of antimicrobial susceptibility results for pathogens identified in microbiology specimens was seen as a priority by Stakeholders in study 3, and has been shown to improve prescribing guideline concordance.[284 285] This selective reporting of only the narrowest spectrum antibiotics to which the organism is susceptible is an example of a human factors engineering barrier.[161] Stakeholders also perceived that GPs may want regular updates on the selection of appropriate microbiology tests and interpretation of results. Pathology/microbiology expert advice may be obtained by GPs from a local private pathology provider or a hospital laboratory, but Stakeholders perceived there is little standardisation of information. The Royal College of Pathologists of Australia was viewed as a suitable developer of standardised information. The ordering and interpretation of laboratory investigations was one of the five causes of patient safety incidents identified in a WHO international Delphi exercise of iatrogenic harm in primary care,[242] so there would appear to be an imperative to assist GPs with this.

Patient information resources for use with patients were desired and Stakeholders suggested that the NPS MedicineWise patient resources could be more widely used. However, these are only available in English and are not integrated into clinical software. The ACSQHC has a handful of resources integrated into Therapeutic Guidelines, but these have not been subject to publicly available external evaluation and may not be available to non-prescribers e.g. nurses or pharmacists. Making patient information widely available e.g. through the PHN Health Pathways was suggested by Stakeholders. Government funded health services were named as potential developers of additional patient information resources. Another suggested source was the guideline developers themselves i.e. when a prescribing guideline is developed, a patient facing resource is also developed. The (unanswered) question arose about how resources would be kept current if they were integrated into clinical software.

All guidance and resources must be kept current which requires ongoing monitoring by practice staff. Guidance and resources should be regularly reviewed and updated by relevant national bodies; this requires expert advice with funding to update and distribute.

6.6 Pharmacy and nursing approaches

Pharmacy and nursing approaches to supporting AMS in general practice were not well described in the literature. Pharmacist review of prescriptions and advice to consumers and health professionals were the most frequently described approaches.[73 214 217 218 226 228 235] Other approaches included ensuring an adequate supply of antibiotics,[68 73 122 218 224] unit dispensing, where the exact amount of medication is supplied,[218 227 228 233] and safe disposal of leftover antibiotics.[218] Pharmacists in Australia may only prescribe a very limited range of topical antimicrobials (e.g. eye drops containing chloramphenicol). The term 'pharmacist' here refers to community pharmacists unless otherwise specified. Stakeholders with pharmacist backgrounds suggested that patients may be told that they should visit their GP for antibiotics; those with GP backgrounds perceived that patients had been told they needed antibiotics (including for conditions like a viral URTI or a cough). AMS needs an integrated approach so that messages are consistent across sectors and patients receive consistent advice wherever they present for triage. Pharmacist review of antibiotic prescriptions is limited as they do not have all the necessary information about the patient, including most importantly the indication for use. Unit dispensing currently depends on the GP writing the exact amount on the prescription and the pharmacy being willing to break packs. Communication between GPs and community pharmacists was considered necessary for delayed prescribing strategies to be successful, but the feasibility of this was considered problematic. (Australians may visit any GP and any pharmacist.) However, a survey of Queensland pharmacists found that 60% of those surveyed would not dispense a delayed prescription that was presented to the pharmacy within 24 hours of seeing a doctor.[286] Stakeholders could not see a role for community pharmacists to offer antimicrobial prescribing advice to GPs beyond alerts about prescription errors or medication shortages. Communication problems between health care professionals have been identified as a cause of patient harm,[242] so any improvements to the communication process between GPs and community pharmacists may be beneficial. Potential roles for pharmacists in AMS could include interactive GP-pharmacist group meetings with shared education to promote e.g. consistency of messaging in local communities (which could include shared patient information resources), and updates on the pharmacokinetics and pharmacodynamics of antimicrobials and their spectrum.[253]

Australians have reported retaining leftover antibiotics for use the next time they have similar symptoms or giving them to other people, and disposing of leftover antibiotics in household waste or pouring liquids down the sink.[287] There is poor awareness of the free *Return of Unwanted*

Medicines program in pharmacies.[287] Human factors engineering would support the promotion of unit dispensing (eliminating the hazard of leftovers) and the *Return of Unwanted Medicines* program (mitigation of consequences).

General practice nurses (as against nurse practitioners) do not have prescribing rights and are widespread in Australian general practice. In 2015 there were 12,746 practice nurses in Australia,[288] whereas in March 2020, there are 2,017 nurse practitioners in Australia,[289] mostly employed in acute care settings.[290] Community-based nurse involvement was mainly limited in the literature to phone hot lines and patient triage.[122 175 235] Triage by practice nurses was viewed by stakeholders as potentially useful, but currently unfunded. Nurse triage may add a human factors engineering barrier between the patient and an antibiotic prescription if they educate the patient e.g. about self-management strategies for self-limiting infections.[161] Thus, practice nurses in general practice are potentially an untapped resource for AMS. Many will be involved in activities such as educating new mothers or reviewing elderly patients. In those circumstances, talking about infections, infection prevention and antibiotic use may be very useful. Similarly, wound care nurses, aged care nurses, and other specialist areas (e.g. maternal child/family health nurses, diabetes educators) may all be useful members of an AMS team.

6.6.1 Summary of recommendations

AMR/AMS education for the public and health professionals, consultation support, and pharmacist and nurse involvement may all assist GPs to safely reduce antimicrobial prescribing in general practice. Funding should be resumed for ongoing public education campaigns including in a range of community languages and formats. The *Return of Unwanted Medicines* program should be promoted. NPS MedicineWise, the Consumers Health Forum of Australia and local community groups may be suitable partners to develop appropriate messages to reach people across Australia's diverse community. Due to the multiple providers of health professional education, the provision of consistent messages, and messages consistent with public health campaigns may require oversight by a centralized Commonwealth-level group. This group ideally needs the technical expertise to assess appropriate content and the capacity to reach across the multiple sources of content and the multiple healthcare sectors. Input from professional colleges is recommended. Evaluation of education modules will help to ensure there is an appropriate breadth and depth of effective education. Education should be free of pharmaceutical marketing and is likely to be more effective if barriers to antimicrobial prescriptions are also used (e.g. pharmacy triage and advice for self-limiting infections).

Consultation support in the form of integrated prescribing guidelines and patient educational material that pops up when a GP enters a diagnosis would not only assist GPs but provide the reason-for-prescription data for monitoring. Research is being undertaken on this,[291] and a system (preferably automated) for updating resources would be useful in any future roll out. The issue of patients who do not fit guideline criteria is also to be addressed.[243] Prescribing and expert advice for GPs, in a manner that suits their workflow, is an area worthy of further exploration in Australia. Selective reporting of antimicrobial susceptibilities is to be encouraged, or mandated.

Improved communication between community pharmacists and GPs, particularly around delayed prescriptions and watch-and-wait tactics may be useful. Local PHNs may be able to promote this e.g. with combined educational sessions. Pharmacists have a key role in patient triage and self-management of self-limiting infections; education modules on this may assist, along with the provision of patient education material. Unit dispensing should be encouraged, which may require adjustments to pack-based fees.

The inclusion of community-based nurses in AMS is largely unexplored in Australia, but they interact with the public in many roles (e.g. practice nurses, wound care, maternal and child/family health nurses). Apart from phone hot lines and patient triage, they could have an important role in patient education. Further research is needed to ascertain their needs.

6.7 Research

The need for AMS research was widely recognised in the literature [68 73 122 175 217 218 227 233 235 268] and by the interviewed Stakeholders. This includes the need for translation of evidence into practice using behaviour change science, along with the recognition of the context and culture across general practice; [73 175 217 218 225 226 233] and that a “one size fits all” approach to AMS implementation is not appropriate.[73 217] The use of human factors engineering would bring a systems analysis approach to AMS that is likely to be of use; also complexity science for adapting to context.[189]

The scoping literature review described the quantity of research in general practice AMS, identified gaps that can be addressed through ongoing research and mapped the key concepts that underpinned AMS. One paper was published in 2001, the other 15 were published between 2012 and 2018. There is limited literature, with limited time for follow up publications in this emerging field to fully measure the success of these strategies. However, two papers were an evaluation of Sweden’s success over 20 years with their Strama program.[120 122] Other measures of success may be found in the volume of antibiotic prescribing in general practice. Four papers were from the UK, which is below the OECD average.[82] A more serious limitation of the scoping review, which is included in the paper, is the restriction to English language papers as several of the lowest antibiotic prescribing nations are non-English speaking.[82]

As noted in Section 6.1, there is a lack of identified accountability for AMS in general practice, so research direction is likely to remain ad hoc. There is no specific funding, so research into AMS in general practice is likely to remain limited to bodies such as university Departments of General Practice or Centres of Research Excellence to apply for funding and direct their own research. This also makes it difficult to roll out improvements beyond the research network. There is a need to identify research gaps and then fund the research into these gaps and implement solutions. An accountable body would greatly assist this process.

Areas in need of research identified in this thesis include: establishing priorities and what assistance may be necessary to introduce AMS to general practice; to what extent regulatory or policy changes would assist; integrating Therapeutic Guidelines and patient information into the clinical record in a format that is useful and timely to the GP which provides a standardised reason for prescription; what patient information is required and in what formats and languages and where to host them; how to obtain datasets to analyse antimicrobial prescribing and how to collect and compare these with patient outcome data (including hospitalisations); in what format GPs would prefer feedback on their antimicrobial prescribing and patient outcome data; how to obtain antimicrobial resistance data from all laboratories and how to feedback that data with local interpretation - which recognises the often empirical treatment provided to general practice patients (i.e. specimens may be collected only after a treatment failure); how to contextualise and evaluate interventions to the different needs of general practices across Australia; what educational interventions are needed and in what formats for GPs, their staff, pharmacy staff and the public; and the role of the community pharmacy in supporting AMS.

6.8 The framework as a whole

General practice AMS is in its infancy in Australia, with only a small pool of experts. The 12 senior and expert stakeholders each discussed this framework for an average 54 minutes. Apart from being unable to interview the practice nurse expert in the timeframe, I identified only one other key stakeholder/organisation, but they refused interview stating that “The (named organisation) is not in the best place to help with your query regarding AMS in general practice and we recommend you contact RACGP and ACRRM. Professional colleges were represented in the interviewed stakeholders. The Stakeholders regarded this proposed AMS framework as comprehensive, with the six components considered feasible and valid for Australian general practice. The detailing of the individual sub-components was viewed as providing a link between the seven objectives of Australia’s National AMR Strategy 2020 and an action. However, Stakeholders considered that the framework required an implementation process with priorities, incentives and an integrated approach. Stakeholders’ priorities were components that could be embedded into systems and those that would provide maximum impact. These included a national

AMS action plan with accountability; ideally the establishment of a national coordinating body to cover AMR and AMS across all healthcare sectors; regulatory changes (such as the default on antibiotic prescriptions changed to zero repeats, pack sizes to match Therapeutic Guidelines recommendations, computerised decision support with integrated access to guidelines for GPs; ongoing coordinated national education strategies; and research to investigate which changes have an impact, including at the practice level. Leadership and accountability for AMS in Australian general practice need clarification and/or improved awareness. This includes clarification of the roles for the Department of Health Office of Health Protection, the professional colleges, the ACSQHC, NPS MedicineWise, and the PHNs. A proposed governance structure clarifying the roles for AMS in general practice is outlined in Figure 3. An incentive to engage GPs is required. This could be in the form of a PIP QI to participate in Table 4 sets out the detail of the individual components and sub-components of the framework along with the Stakeholder's suggestions for responsibility in the Australian context and maps them against the objective and priority areas for action in Australia's National AMR Strategy 2020 and beyond.[1] Ideally, once resources and standards are available, each practice would appoint a person to drive AMS. This does not have to be a GP and could be the practice manager or practice nurse. AMS implementation would be helped if it was required for accreditation.

Asked how they would define success, Stakeholders nominated short- and long-term goals. In the short-term, increased prescribing guideline adherence (a process measure); improved patient outcomes and/or no increase in hospitalisations. They also spoke of outcomes for the GP of increased support leading to improved professional satisfaction. The long-term goal was a decrease in AMR, or at least, no increase in AMR. Implicit in these goals is the successful monitoring of and feedback on antimicrobial prescribing and AMR. As described in section 6.2, monitoring for prescribing guideline adherence is not currently possible for all practices and should be a priority action area. An interim measure may be to e.g. analyse and promote narrow- versus broad-spectrum antimicrobial prescribing. Patient outcomes in the form of local hospital admissions data may be possible for selected conditions e.g. a time trend of the number of patients admitted with pneumonia, mastoiditis, bacterial meningitis, so that GPs can see if they are rising in response to reduce antimicrobial prescribing. This would need negotiation for access with each state and territory government.

This framework may also offer a framework for the development and reporting of AMS interventions. The identification of the health system components that interact with AMS, and the human factors engineering analysis, may help to explain otherwise hidden factors that may cause an AMS intervention to succeed in one setting but fail in another setting.

Figure 4 Proposed governance structure for AMS in general practice

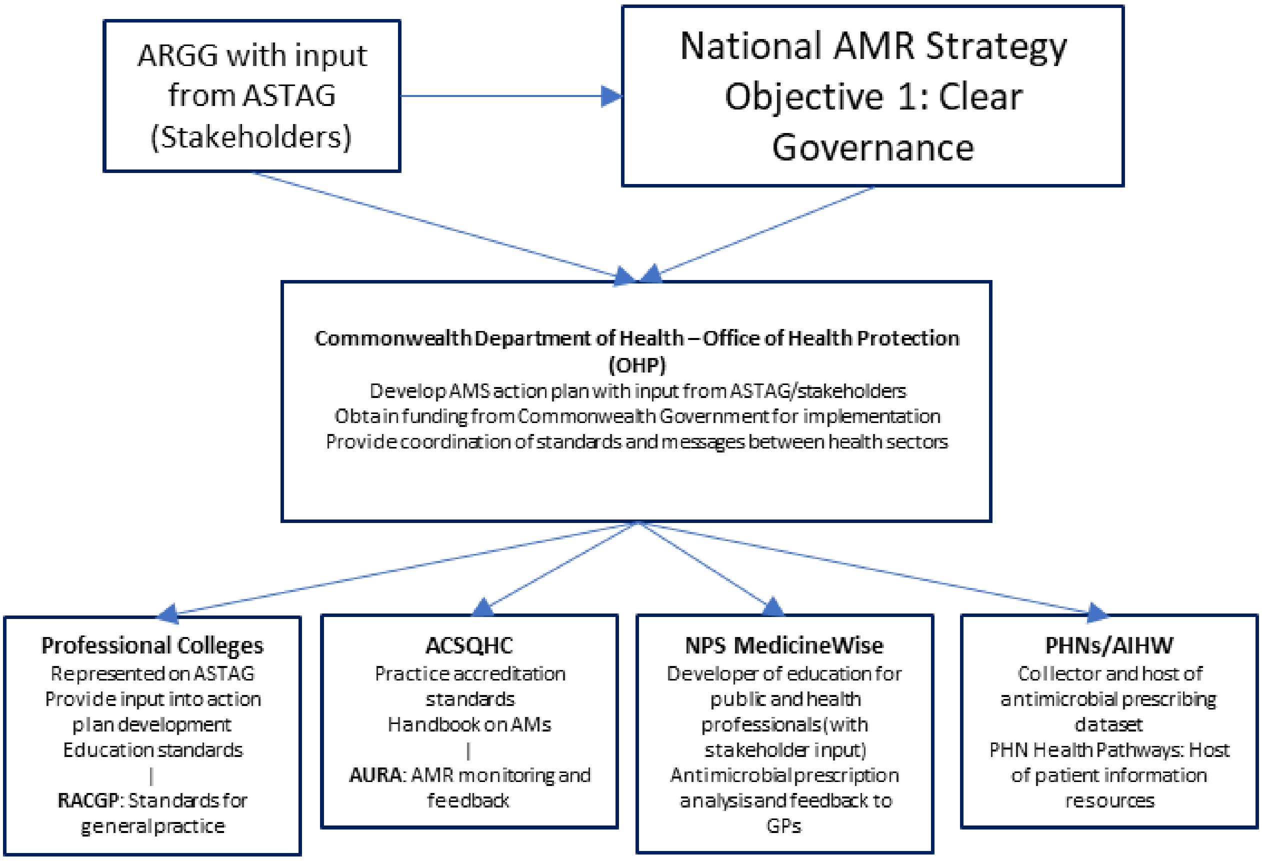

Table 4 Mapping of the AMS framework to the National AMR Strategy 2020

Items that Stakeholders considered a priority are **highlighted in blue**. The framework component is provided in bold **[component name]**

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
1. Clear governance for antimicrobial resistance initiatives 1.1. Create sustainable funding for combatting antimicrobial resistance based on evidence of economic and societal costs and benefits of different approaches in all sectors.	1.1. AMR likely to cost significant part of health budget. Funding and incentives required to implement AMS in general practice. **[Governance: funding]**	1.1. Commonwealth government responsible for funding.	1.1 Funding is critical to AMS success[68 73 122 217 218]
1.2. Develop, implement and/or maintain sector-specific action plans.	1.2. **Develop and implement an action plan with accountability and priorities for AMS in general practice**. **[Governance: action plan]**	1.2. **National coordinating body**. Department of Health - Office of Health Protection for oversight and coordination of the national AMS action plan, with input from professional colleges. Encourage a team-based approach at the practice level.	1.2-1.4. Accountability, communication, coordination and regulation were recommended in the JETACAR[65] and subsequent reports.[66 67]
1.3. Maintain and expand linkages and opportunities between stakeholders across all sectors to provide a nationally coordinated approach to combatting antimicrobial resistance.	1.3. Consistency of messages across health sectors. **[Governance]**	1.3. **National coordinating body** to coordinate messages and standards across sectors, professional colleges to tailor messages to members.	
1.4. Monitor and review regulatory measures (legislated and other) relevant to antimicrobial usage and resistance.	1.4. **Regulations: antimicrobial agents to be available by prescription only; removal of automatic repeats on antimicrobial prescriptions; reduction of the 12-month expiry on antibiotic prescriptions (except where indicated by guidelines); increased controls on private prescriptions; availability of unit dispensing**. **[Governance: Regulations]**	1.4. Commonwealth government and authorised bodies.	

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
2. Prevention and control of infection and the spread of resistance.	Prevention and control of infection is beyond the scope of this thesis. **Prevention and control of AMR was viewed by Stakeholders as the long-term goal for AMS in general practice.**		2. AMR is a globally recognised serious health problem.[24 68] 2. The prevention and control of AMR is a goal of AMS. [62]
2.1. Adopt evidence-based and nationally consistent standards for infection prevention and control and biosecurity.			2.4. The spread of AMR should be measured to enable its management.[292] Awareness of AMR should be improved.[68]
2.2. Maximise compliance with best-practice infection prevention and control and biosecurity measures through adherence to applicable legislation, targets and accreditation standards.			2.4 The AURA reports provide Australian AMR data.[6-8]
2.3. Promote disease prevention practices to reduce infections and subsequent use of antimicrobials.			
2.4. Share information on emerging antimicrobial resistance trends to inform responses.	2.4 Feedback on AMR: There is currently no system to collate, analyse and report local/regional data to GPs. **[Monitoring of and feedback on AMR]**	2.4. AURA is the best placed organisation to provide complete local/regional AMR reports to GPs.	

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
3. Greater engagement in the combat against resistance. 3.1. Develop and implement a coordinated, One Health communication strategy, as well as monitoring and evaluation, to support whole-of-society awareness and behavioural change. 3.2. Strengthen public and political awareness to champion and improve the understanding of the importance of combatting antimicrobial resistance. 3.3. Create new and different key antimicrobial resistance messages that resonate with society. 3.4. Drive education and training initiatives across all relevant sectors and increase accessibility to evidence-based best-practice information.	3.1. A One Health communication strategy is beyond the scope of this thesis. This framework supports a communication strategy that integrates and evaluates messages across the health and public sectors. **[Governance]** 3.2. **Public education campaigns about AMR/AMS. [Education: Education of the public and patients]** Recognise AMR as a priority need for action/include on the national risk register. **[Governance: AMR included on the national risk register]** 3.3. **Use a variety of formats and community languages**; seek community input; develop school based AMS programs. Inform the public about self-management of self-limiting infections and the appropriate use and disposal of antibiotics. Train community-based nurses to deliver AMS education. **[Education: Education of the public and patients]** 3.4. Health professional AMS education to include GPs, community pharmacists, community-based nurses at prevocational, specialty training and continuing education levels. Use of behaviour change science. **[Education: Education of health professionals]**	3.1. Department of Health – Office of Health Protection. 3.2. Government sponsored public health messages, developed with NPS MedicineWise and the Consumers Health Forum and designed for evaluation; integrated with health professional education and resources. 3.3. Community group input including those representing diverse community languages. Collaboration between Departments of Health and Education regarding the introduction of school based AMS education. Evaluation of programs. 3.4. Involvement of professional colleges and relevant experts to develop health professional education; PHNs to assist with delivery at local levels.	3.1. A One Health approach is supported by the WHO.[68] 3.2 Awareness of AMR is Objective 1 in the Global action plan on AMR.[68] and called for in the JETACAR report[65] Education is called for in the handbook AMS in Australian health care.[73] 3.3; 3.4 Previous AMR/AMS campaigns have been associated with reductions in antibiotic use and increased consumer awareness of AMR.[74 76 269]

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
4. Appropriate usage and stewardship practices. 4.1. Ensure that coordinated, evidence-based antimicrobial prescribing guidelines and best-practice supports are developed and made easily available and encourage their use by prescribers.	4.1. Therapeutic Guidelines and relevant guidelines integrated into the clinical software, along with patient education materials, so that when a GP enters a diagnosis a guideline, a pre-populated prescription, any alerts and an information resource pop up. Patient information resources to be made widely available to other health professionals and the public. Availability of point of care tests, allergy testing, expert advice. **[Consultation support]** To encourage use: Education (See also 3.4 above)	4.1 Integrated decision support: Software developers, GPs, researchers; research funders. Point of care tests: Pathology kit developers and RCPA (kit standards). Allergy testing: Specialists. Expert advice: Medical microbiologists, AMS pharmacists and infectious diseases physicians.	4.1 Australia has nationally- and RACGP-endorsed Therapeutic Guidelines.[9]
4.2. Develop and implement effective mechanisms to monitor, reward and enforce compliance with standards and best-practice approaches for appropriate and judicious antimicrobial use.	4.2. Standards for general practices to include an AMS policy and program by which practices are accredited. Develop a monitoring system for extracting, analysing and reporting on antimicrobial prescribing data which includes patient outcomes; must be a process trusted by GPs. Enforced data targets not recommended. [**Governance: Accreditation and a practice level AMS policy and program; Monitoring of antimicrobial prescribing]**	4.2 RACGP set general practice standards and ACSQHC regulates the accrediting agencies. 4.2 & 4.3. Department of Health to develop a monitoring system, possibly in partnership with NPS MedicineWise, PHNs, and/or AIHW. Analysis and feedback may involve NPS MedicineWise. (Targets not recommended) Policy changes should involve professional colleges and professional representatives.	4.2 Approximately 90% of Australian general practices are accredited to RACGP standards. [117] 4.3 Accurate data is necessary to inform policy and actions and tailor to the setting. Feedback to GPs is part of this response.[73]
4.3. Use data on antimicrobial usage to inform antimicrobial stewardship policy and support the development of targeted, timely and effective responses.	4.3. Antimicrobial prescribing data to be fed back to GPs with local and national peer comparisons and with recommendations and resources for best-practice approaches to improvement. **[Monitoring: Feedback to GPs on their antimicrobial prescribing]**		

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
5. Integrated surveillance and response to resistance and usage.	One Health is beyond the scope of this thesis.		
5.1. Create a sustainably funded national One Health surveillance system that integrates human, animal, food and environmental usage and resistance data.	5.1 Surveillance of GP prescribing and AMR data. However, community AMR data is incomplete. **[Monitoring of and feedback on AMR]**	5.1 Department of Health to develop a antimicrobial prescription monitoring system, possibly in partnership with NPS MedicineWise, PHNs, and/or AIHW. 5.1 AURA collates AMR data. Expansion to collect all community AMR data is recommended.	5.1 Surveillance of usage and resistance is widely recommended.[68 73 218] 5.1 Remove interoperability barriers; prioritise funding.[73]
5.2. Develop and regularly review lists of priority organisms and associated antimicrobials.	5.2 Lists of priority organisms and antimicrobials are published.[8]	5.2. Priority lists are the responsibility of the Australian Commission on Safety and Quality in Health Care.	
5.3. Implement national alignment of laboratory testing practices and reporting for antimicrobial resistance.	5.3. Implement selective reporting of identified pathogens from clinical specimens. **[Monitoring of and feedback on AMR]**	5.3. RCPA for laboratory standards relating to reporting	5.3 Selective reporting encourages narrow-spectrum prescribing.[73]
5.4. Use evidence-based surveillance and monitoring data to inform actions and responses to contain antimicrobial resistance.	5.4. Mandated collection of AMR. Feed local AMR data back to GPs with information on local AMR and their antimicrobial prescribing data (from action item 4.3 – to be developed). **[Monitoring of and feedback on AMR]**	5.4. State and territory governments to mandate collection of AMR data. AURA to collate, analyse and feedback on local AMR. Integrated feedback to be developed (see action item 4.3). Office of Health Protection with stakeholder input to oversee response.	5.4. Monitoring of AMR and antimicrobial usage will aid knowledge of their links.[292]

National AMR Strategy Objectives with identified priority areas for action[1]	AMS Framework Components and Subcomponent(s)	Responsibility	Evidence for intervention
6. A strong collaborative research agenda across all sectors. 6.1. Set a flexible national antimicrobial resistance research and development agenda that strives for innovation. 6.2. Coordinate and share research and development activities. 6.3. Seek and maintain dedicated funding for the national research and development agenda, including private and public investment partnerships. 6.4. Support the translation of research findings into new approaches, applications and policies to combat antimicrobial resistance.	6.1. AMR research is beyond the scope of this thesis. 6.2. **AMS research across all sectors in which GPs work**, including general practice, aged care, rural hospital, Aboriginal and Torres Strait Islander health services. **[Research]** 6.3. Funding for AMS research in general practice. **[Governance: Funding; Research]** 6.4. **Identification of gaps in evidence. Translation of evidence into practice using behaviour change science, along with recognition of the context and culture across general practice; a "one size fits all" approach to AMS implementation in general practice is not appropriate**. **[Research]** Planning for the release of new antimicrobials. **[Governance: Regulations]** Human factors engineering to bring a person-centred systems approach to AMS research; complexity science will assist with adapting to context. **[Research]**	6.2. Researchers in relevant sectors. 6.3. Research funding bodies e.g. National Health and Medical Research Council; Medical Research Future Fund. 6.4. Researchers collaborating with GPs and professional colleges. Professional education providers to educate health professionals about new antimicrobials.	6.2. Objective 2 of the Global Action Plan is Strengthen the knowledge and evidence base through surveillance and research.[68] 6.2 Coordination of research and activities reduces duplication.[73] 6.3 Professional associations and scientific societies should promote and conduct relevant research.[214] 6.3 NHMRC funds four Centres of Research Excellence.[73] 6.4 Translation of research into new policies and approaches.[68 73]
7. Strengthen global collaboration and partnerships.	Global collaboration and partnerships are beyond the scope of this thesis; except to note that Australia may be able to learn from other countries' interventions in general practice AMS, and to share our experiences.		

Table 5 Leadership and role summary for the framework

Framework Component	Leader	Role; Output
Governance	Office of Health Protection (OHP) with input from ASTAG and stakeholders. (See also Figure 3)	Liaison between health sectors including hospital, general practice, aged care and other sectors where GPs work to ensure consistency of messages and standards; remove duplications.
		Develop and implement an action plan for AMS in general practice.
Monitoring	OHP with input from stakeholders including Professional Colleges, ACSQHC, PHN/AIHW, NPS MedicineWise.	Develop an antimicrobial prescription monitoring system that is trusted and accepted by GPs and their patients.
Education	Public: NPS MedicineWise with Consumers Health Forum and input from community groups.	Public education about AMR and appropriate use of antimicrobials. Develop patient information about AMR and appropriate use of antimicrobials in a range of formats and languages.
	Health professional: Professional colleges in liaison with OHP and ASTAG/ARGG.	Health professional education about AMR with AMS strategies to promote the appropriate use of antimicrobials. Professional colleges to ensure educational standards are met. Liaison to ensure consistency of messages between sectors.
Consultation support	Researchers, GPs and software companies.	To research integrated decision support and incorporate it into clinical software.
Pharmacist and nurse approaches	Office of Health Protection with input from professional colleges.	Pharmacist triage and advice. Nurse triage and patient education.
Research	Researchers with GP/professional college/relevant input.	Research the gaps in evidence; translate findings into practice using behavioural science theory.

6.9 Adding to the SEIPS 2.0 human factors engineering approach to AMS in general practice

The fifth paper for this thesis aims to add to the knowledge about the SEIPS 2.0 human factors engineering approach to AMS in general practice. A summary of the main points is collated below.

This research has added to the existing SEIPS 2.0 human factors engineering[170 172] for AMS in general practice[175] as described in Chapter 2's Figure 2 and Table 1. To the external environment are added a national AMS action plan with accountability/leadership and multi-level and multi-disciplinary (including GP) input and response; inclusion of AMR on the national risk register/recognition of AMR as a national priority; regulations around antimicrobial prescribing and dispensing, such as zero automatic repeats on antibiotic prescriptions and unit dispensing; accreditation of practices and/or prescribers to AMS standards; expansion of public health campaigns to include languages and cultures present in the population.

In the work system there is added access to clinical and AMS experts who assist GPs with expert advice, but their responsibilities and the communication between expert and GP are still to be studied. The community pharmacist is added with their knowledge and attitudes to AMS. There are relationships, trust and communication between patient and community pharmacist, and between the GP and community pharmacist. For example, the pharmacist may contact the GP about prescribing errors or alerts (e.g. antibiotic shortages); and delayed prescribing strategies would be enhanced with improved communication between GP and community pharmacists. The pharmacist may advise and resource a patient with a self-limiting infection so that they are able to manage without a GP consultation, thus eliminating the chance of an antibiotic prescription – a higher order intervention in complexity theory. The general practice may also employ a non-dispensing pharmacist, who becomes part of the general practice work system with tasks, roles and relationships. Under tools and technologies - the objects used to do the work[172] - this research has included the need to keep updated the clinical decision support systems which integrate prescribing guidelines and patient education materials. For organisation – the structure and organising of a general practice[172] – this research adds the practice level AMS policy and program; and the provision to staff of AMS/AMR/antimicrobial drug education which is independent from pharmaceutical company marketing. Tasks are specific actions including their complexity and sequence.[172] The community pharmacy has tasks of (unit) dispensing, explaining safe disposal of leftover antibiotics to the patient and communicating with the GP. Referring a patient for antibiotic allergy testing is added to a GP's tasks. The physical environment of a general practice may now include patient education information on waiting room screens. An outcome for the GP is increased AMS support.

Under processes is the process that pharmacists undertake to dispense an antimicrobial prescription and advise a patient, to triage a patient and choose to refer (or not) to a GP, a choice of unit dispensing or not, a choice of when to dispense a delayed prescription. There are processes for nurse triage and patient education e.g. choosing which information best suits the patients' needs.

For outcomes, there are outcomes for the nurses and pharmacists e.g. patients return to the pharmacy for repeat business, professional satisfaction for nurses with an enhanced role.

These additional human factors engineering may help to explain differences in the outcomes of AMS interventions. Analysis of systematic and ethnographic reviews of AMS interventions demonstrates that no one intervention is applicable to all practices,[129] that no combination of interventions was found to be superior;[293] and that the culture/context of the general practice is important.[129 130] Cultural determinants include patient health seeking behaviour, their previous experience and awareness of antibiotics, the GPs training, antibiotic awareness and practice context.[130] The factors contributing to high antibiotic use are poorly understood,[294 295] there is recognition that antibiotic prescribing is complex and influenced by factors including the GPs, other providers, the system and the patients and that these are mutually dependent.[295] No studies reported AMR outcomes[127] or took these into account when interpreting outcomes.[296] There is no good evidence about the effectiveness or cost-effectiveness of interventions in reducing AMR.[297] Interventions were not designed to measure patient outcomes.[127] There was a lack of evaluation of government AMS programs.[298] Systematic reviews found that local barriers to change should be addressed,[125] that interventions should be beneficial to implement in practice,[299] that interventions should be broader than targeting single conditions in sing age groups,[293] and that multifaceted interventions should target all key stakeholders.[300] There was a call for research to discover which elements of multi-faceted interventions were the most effective.[125] A strength of this thesis is that human factors engineering and complexity science offer insights into these factors.

As described in Chapter 1, there is variation in prescribing between GPs and practices. Patients may differ between practices and regions with their undiagnosed conditions, co- or multi-morbidities, perceptions, varying health literacies and languages and cultures. The resources available to the community (e.g. pharmacist advice, information in community languages) or to GPs (e.g. integrated decision support; availability of prescribing guidelines) may differ. Thus, there is no 'one-size-fits-all' AMS intervention. Some interventions, such as passive education, have had limited effects.[125 301] Of the multi-faceted interventions, it has been difficult to determine which intervention is most responsible for the success of the intervention.[125 127] Human factors engineering and complexity science would suggest that GPs need a range of tools and technologies that they may use as the situation demands, in a supportive practice with a team approach to AMS. Similarly, pharmacists and nurses.

Working to eliminate the hazard, creating a barrier or mitigating the consequences are higher order interventions than education alone.[161] For example, a community with good health literacy and support for managing self-limiting infections has reduced the need for patients to present to the GP, where they may exert pressure for an antibiotic prescription. An intervention in this community or their general practice has a greater chance of success than in a community which has few supports and relies on a GP consultation for most self-limiting infections.

6.10 Strengths and Limitations

This research is the first to articulate a comprehensive AMS framework for Australian General Practice and propose it as a set of actionable components mapped against the objectives of Australia's National AMR strategy 2020. By incorporating a human factors engineering approach it may also assist in the development and reporting of AMS intervention by providing a framework to study the background setting which may affect compliance with the intervention.

The qualitative interviews with 12 key Stakeholders provided important insights and validation of the proposed framework components and important extensions in relation to implementation. The Stakeholders were in a variety of senior roles, from a limited pool of potential interviewees, but those who accepted the invitation may not be typical of those who were not interviewed. Although six GPs were among the Stakeholders interviewed in this research, they may not be typical of all GPs. Some of the suggestions for AMS, while acceptable to GP experts who have a broad knowledge about AMR and the urgent need for AMS, may be unacceptable to a GP who doesn't perceive that AMR is affecting their patients or practice. No practice nurses were interviewed, so their perceptions of their proposed role in patient triage and education is not known. Despite this there was little disagreement in Stakeholders views. The capacity and willingness of the named organisations and professional bodies to participate in the recommended roles was not examined. Input from those affected by changes is essential, consideration may be required of how best to support these roles.

It was beyond the scope of this thesis to examine infection prevention and control; however, it is a vital component of AMS and preventing an infection is a high order barrier to an antimicrobial prescription. Additionally, other primary care settings were not included. Caution is suggested when extending these findings to other primary care settings (e.g. dentists). The research was limited to settings where systemic antibiotics are limited to prescription only; the findings may not be applicable in countries where antibiotics are available over the counter. The availability of unregulated antimicrobials via the internet may become an issue if the public perceive that they need antibiotics but AMS has reduced their prescribed availability for self-limiting infections.

The COVID-19 pandemic has affected the community and general practice in many ways. This includes the reduction in influenza and RSV infections due to improved public health measures,[302 303] which may help to reduce unnecessary antibiotic prescribing for viral respiratory tract infections. The Medicare Benefits Schedule has introduced a temporary telehealth item to promote an uptake in telephone and internet-based triage and automated prescription services. The extent and impact of these on antimicrobial prescribing is unknown. State and Commonwealth budgets have also been damaged e.g. by increased unemployment which has increased government income support, reduced taxation income and the additional expenditure on hospital care and PPE provision and disposal. This is likely to affect future spending in many areas. The impacts of SARS-CoV-2 on AMR are still to be studied.

The strengths and limitations of individual studies have been reported in each publication (Chapters 3, 4 and 5).

6.11 Conclusions and implications

AMS aims to reduce inappropriate antimicrobial prescribing and improve patient outcomes. Australia's first[63] and second[1] national AMR strategies and other reports into AMR[65 66 304] contain strong imperatives for general practice to introduce AMS, yet AMS in general practice is still immature. This research offers an actionable framework, mapped against Australia's National AMR Strategy 2020, to progress the introduction of AMS into general practice, with additional insights from key Stakeholders regarding its feasibility, validity and implementability for Australian general practice. It has identified six main components for AMS: governance, monitoring, education, consultation support, pharmacy and nurse support, and research. There are two major hurdles to surmount in Australia: the lack of a clear organisation or leader with accountability to drive the implementation of AMS into general practice, and a system to monitor all general practice antimicrobial prescribing and patient outcomes. Stakeholders were not aware of any organisation taking accountability for the introduction of AMS into general practice, and the roles of the ACSQHC and the Office of Health Protection in general practice AMS were not clear. To enable the targeting of AMS initiatives, monitoring of antimicrobial prescribing requires measures of prescribing guideline concordance and patient outcomes across all general practices. Linkage with hospital data will enable identification of patients who present to emergency departments or who are admitted to hospital. To assist GPs to reduce inappropriate prescribing while maintaining patient safety, GPs require feedback on their antimicrobial prescribing with peer comparisons and specific actions for improvement that considers the demographics of their practice population. There is no currently available system that has the capacity for this monitoring and feedback across all general practices and needs urgent development. It is also important that this is a process that is trusted by GPs; complexity science informs us that GPs should have input into the development of the process and the feedback to GPs.

General practices are mostly small private businesses and will not want to risk losing patients to another practice by refusing a real or perceived demand for unnecessary antibiotics. Human factors engineering approaches suggest barriers and mitigation responses are important. These may include improved community support for self-management of self-limiting infections (e.g. pharmacy triage and advice); unit dispensing and safe disposal of leftover antibiotics to reduce the circulation of unused antibiotics; and nurse-led education at the general practice. Regular public awareness and education campaigns may also help to reduce the demand for inappropriate antibiotic use across the community. NPS MedicineWise has run successful public campaigns, but ongoing funding to enable ongoing campaigns in a variety of community languages, formats and media may reach a wider audience. Research and evaluation will help to inform which languages, media and formats may be most beneficial. Patient education materials for use by GPs with their patients exist on the NPS website and in Therapeutic Guidelines but are limited to the English language. The extent of evaluation of these is not clear, including whether additional topics or languages are wanted, whether patients understand the information provided, if it answers their questions and if they know under what circumstances they should seek further medical help. Integrated decision support would assist GPs by providing easy access to recommended prescribing guidelines and approved patient education resources. This will require consideration of how these can be kept updated across all the brands of clinical software. Consideration should be given to establishing a formal support mechanism for GPs to access expert advice. Access to a range of resources is recommended for GPs to use as required for individual patients.

The role of community pharmacies and nurses in AMS has been largely unexplored, but this research has highlighted their roles in patient triage and education, including around self-limiting infections. The role of the community pharmacy in delayed prescribing strategies and to what extent communication between GP and community pharmacy may support delayed prescribing strategies need exploration.

The 5th edition standards[114] by which general practices are accredited do not mandate AMS and accreditation is not compulsory. The resource guide[118] that accompanies the standards does provide some AMS resources, but not in a structured program format. A draft practice-level policy, and a practice-level program with three introductory levels have been included in Appendices 3 and 4 to assist general practices to implement AMS. As AMS in general practice matures further levels may be added.

This research has successfully identified a potential framework for AMS in general practice that links the objectives of the National AMR Strategy 2020 with actions. It has highlighted that accountable leadership and monitoring of antimicrobial prescribing are areas for urgent development and that ongoing research and evaluation are required.

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Appendices

Appendix 1 The MAGNET dataset and cleaning

The data source

The data source was the Melbourne East Monash General Practice Database (MAGNET). MAGNET was a research platform launched in 2013 to provide a deidentified general practice data source for primary care research. The research was a collaboration between Monash University and the Inner East Melbourne Medicare Local (IEMML); IEMML is now part of the Eastern Melbourne PHN. MAGNET contained deidentified field data from the clinical software records of 50 general practices across Melbourne's eastern suburbs. It did not contain any patient notes or progress notes. Practices signed a consent agreement for the extraction and informed patients, who had the ability to opt out of the data collection.[210]

Ethics approval for this quantitative analysis was granted by the Monash University Human Research Ethics Committee, CF12/1057 – 2012000504, with an extension approved until 4 May 2022.

Data cleaning

The data came as two data sets, one containing the medication data and the other the consultation visit data. The datasets required extensive cleaning. Duplicate entries were removed. One practice contained no medication or visit data and five practices had only partial medication datasets. The 44 practices with complete medication datasets were analysed for their antibiotic prescriptions. The medications had been classed according to the Anatomical Therapeutic Chemical Classification System (ATC) prior to receipt of the dataset, but some mistakes were found. For example, trimethoprim had been classed in combination with sulphamethoxazole, so we searched in the antibiotic name fields and found trimethoprim alone. Amoxicillin with clavulanate was grouped three different ways. This information was passed back to the MAGNET owners. Repeats on the original prescription were not included as some are issued automatically by clinical software and not all repeats are dispensed.[83] Of these 44 practices, five had incomplete consultation visit data so were eliminated before merging the two datasets.

Stata 13.1 (StataCorp) was used for cleaning and analysis of the data. Merging was done by month and year only as some prescriptions did not match a visit day. This was likely due to broken linkages occurring in the data warehouse (personal communication). Where a prescription did not match a month of visit, the age recorded at the closest month of visit was used as a proxy, where there were no other visits recorded in that year the age was recorded as missing. Patient ages that were less than zero or greater than 99 years were analysed as missing. The 39 practices with merged medication and consultation visits were analysed for antibiotic prescription by patient age.

Data analysis

Descriptive statistics – counts and percentages - were performed on the antibiotic prescriptions, and on antibiotic prescriptions by patient age. Reason-for-prescription field: Some practice software allowed free text entries, others used pre-coded entries, but there was more than one coding system used. Free text entries included question marks, typographical errors, symptoms (e.g. fever, cough) instead of diagnoses, and non-infectious conditions (e.g. asthma; presumably concurrent illnesses). An infectious disease physician (KB) provided input into which reason-for-prescription related to which diagnosis.

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Appendix 2: The participant explanatory statement; consent form and interview guide for the key Stakeholder interviews

The explanatory statement

Project ID: 20721
Project title: Qualitative exploration of antimicrobial stewardship in Australian general practice, including a model framework.

Chief Investigator: Professor Danielle Mazza Department of General Practice Phone: 03 99024512 Email: Danielle.Mazza@monash.edu	**Co-Investigator:** Associate Professor Kirsty Buising National Centre for Antimicrobial Stewardship Phone: 03 93429401 Email: Kirsty.buising@mh.org.au	**PhD Student: Lesley Hawes** Phone: 03 99024468 Fax: 03 9902 4300 Email: Lesley.Hawes@monash.edu

You are invited to take part in this study. Please read this Explanatory Statement in full before deciding whether or not to participate in this research. If you would like further information regarding any aspect of this project, you are encouraged to contact the researchers via the phone numbers or email addresses listed above.

What does the research involve?

The quality of antibiotic prescribing in general practice must be improved to optimise outcomes for patients with infectious diseases. This requires the implementation of antimicrobial stewardship (AMS) in general practice - for which there is currently no detailed Australian framework. The researchers in this study have reviewed the published literature and developed a potential framework for AMS in general practice. However, this framework is international and requires input from key stakeholders about their experiences and needs in the Australian context. The aims of this research are to explore current AMS practices in general practice, identify the extent to which any other components may be implemented and to determine what will be required to implement these.

If you are willing to participate in this study, the student researcher will contact you to organise a time for a telephone interview. The semi-structured interview will be a conversation that explores your personal experiences with antimicrobial stewardship in general practice. It is expected to take up to an hour and will be audio recorded.

Why were you chosen for this research?

We are sending you this Explanatory Statement because you have been identified as someone who may have experience with, or relevant insights into, AMS in general practice.

Source of funding

This research is funded by the NHMRC via a grant to the National Centre for Antimicrobial Stewardship. There are no declarable conflicts of interest.

Consenting to participate in the project and withdrawing from the research

If you are willing to participate, please return the signed consent form to Lesley.Hawes@monash.edu or Fax: 03 9902 4300). You will then be contacted to arrange an interview time. By returning the consent form, it is implied that you have read through the explanatory statement and consent to participating in the study.

You may withdraw from the study at any point from signing the consent form to the completion of the interview. If you discontinue the study following the interview, your transcript will not be used in the data analysis. It will not be possible to withdraw once we have commenced analysis of your de-identified transcript.

If you choose not to participate, you may simply ignore this explanatory statement and the consent form.

Possible benefits and risks to participants

Our findings will further develop a framework to guide the development of AMS in general practice. The benefits for general practice will be improved support for quality antibiotic prescribing. The benefits to the community will be optimal management of patients' infections, and in the long term, a lower risk of a bacterial infection being antibiotic resistant.
We do not anticipate that your participation in the study will cause you any inconvenience or discomfort. Collected data will be de-identified, thereby minimizing the risk of loss of confidentiality.

Payment

If you participate in this research, you will be offered a $150 gift voucher as reimbursement for your time. This will be emailed or posted to you after the interview. You may keep the gift card once it has been sent to you even if you withdraw from the study and we do not use your transcript.

Confidentiality

The interview will be audio-recorded, and recordings will be transcribed through an external transcription service with a strict confidentiality agreement. All interview transcripts will be de-identified using a code number to maintain confidentiality. No identifiable information will be included in presentations and publications resulting from the study.

Storage of data

All data collected will be stored at the Department of General Practice in a locked filing cabinet and/ or password protected computer. Only the researchers involved in this study will have access to the data. All study materials will be confidentially destroyed five years from the date of thesis submission.

Results

Each participant will be provided with a transcript of their interview for review and amendment prior to data analysis. We expect to present deidentified findings from the study at conference(s) and publish our findings in a peer-reviewed journal. Abstracts of conference presentations relating to our study or links to journal publications will be directly shared with you via email or post.

Complaints

Should you have any concerns or complaints about the conduct of the project, you are welcome to contact the Executive Officer, Monash University Human Research Ethics Committee (MUHREC):

Executive Officer
Monash University Human Research Ethics Committee (MUHREC)
Room 111, Chancellery Building D,
26 Sports Walk, Clayton Campus
Research Office
Monash University VIC 3800
Tel: +61 3 9905 2052 Email: muhrec@monash.edu Fax: +61 3 9905 3831

Thank you,

Professor Danielle Mazza
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Director, SPHERE NHMRC Centre of Research Excellence in Women's Sexual and Reproductive Health in Primary Care https://www.spherecre.org/

The consent form

Project ID: 20721
Project title: Qualitative exploration of a model framework for antimicrobial stewardship in Australian general practice
Chief Investigator: Professor Danielle Mazza, Head, Department of General Practice, Monash University
I have been asked to take part in the Monash University research project specified above. I have read and understood the Explanatory Statement and I hereby consent to participate in this project.

I consent to the following:	Yes	No
Interview	☐	☐
Audio and/or video recording during the interview	☐	☐

Name of Participant:

Preferred contact details (phone and email) and any preferred days or times for interview:

Participant Signature:

Date:

The semi-structured interview guide

Interview guide

Thank you for participating in this interview. Before we start, can I confirm that it is OK with you if I record our discussion; and do you have any questions about this research?

First a bit of background

1. What can you tell me about your interest or experience in antimicrobial stewardship?
2. What do you think is required to improve antibiotic prescribing in general practice?

Now I will take 2-3 mins to explain the model framework and then I will ask you for your comments on it.

3. What is your overall impression of this framework?
4. How well does each component reflect what you understand about AMS?
5. Is it plausible?
6. Does anything not ring true?
7. Do you know of any other models?
    a. How do they differ from this model?
8. To what extent are each of these components currently being done?
9. To what extent do you think the other components are implementable?
    a. What needs to be done to make it happen?
10. Who is, or should be, responsible for each of these components?
11. What do you think may happen if all this came to be?
    a. E.g. Intended and potential unintended effects
    b. E.g. changes in: clinical outcomes;
    c. resistance/C diff rates;
    d. care-related quality outcomes e.g. guideline adherence, documentation?
    e. Measures e.g.: Patient, practice, state level?
    f. Timeframe – long or short?

You are doing really well, there's not much more to go.

12. Are there any gaps in this framework?
13. What would you prioritise?
14. How do we measure success?

Last question

15. Is there anything missing that we haven't discussed?

Thank you so much for your time and for sharing your thoughts. I will send you a transcript of this interview. You can amend or withdraw up to two weeks after you receive the transcript. After then your responses will have been de-identified.

Are you allowed to accept the gift voucher?

Appendix 3 Sample Antimicrobial Stewardship Policy

Name of Practice

Version number	
Effective from	
Review date	
Approved by	

Antimicrobial stewardship

Antimicrobial stewardship (AMS) aims to optimize clinical outcomes while minimising unintended consequences of antimicrobial use including toxicity, the selection of pathogenic organisms (such as *Clostridioides difficile*), and the emergence of antimicrobial resistance.[62]

An AMS program is the coordinated actions designed to promote and increase the appropriate use of antimicrobials and is a key strategy to conserve the effectiveness of antibiotics.[63]

Aim of this policy

The aim of this AMS policy is to provide a framework for optimal antimicrobial prescribing in this practice.

Standards and Guidance

The following standards and guidance underpin antimicrobial stewardship:

- RACGP Standards for general practices, 5th edition[114]
- Antimicrobial Stewardship Clinical Care Standard[4]
- Antimicrobial stewardship in Australian health care[73]
- Therapeutic Guidelines[9] and/or Australian Medicines Handbook[305] and/or other locally relevant antimicrobial prescribing guideline.
- Australian Government: Antimicrobial Resistance website[306]
- [*Insert any other relevant local standards*]

Principles

This practice will:

1. Implement an antimicrobial stewardship program.
2. Provide Therapeutic Guidelines[9] or other relevant guidelines for antimicrobial prescribing.
3. Promote clinical care in accordance with the Australian Antimicrobial Stewardship Clinical Care Standard.[4]
4. Provide education and resources to GPs, staff and patients about optimal antibiotic use.
5. Promote infection prevention and control to GPs, staff and patients.
6. [*Insert any other relevant actions*]

Expected outcomes

Improved patient outcomes (e.g. fewer *C. difficile* infections, fewer allergic or other antimicrobial drug reactions, reduced costs to patients, increased knowledge about appropriate use of antibiotics).

Improved prescribing of antibiotics (e.g. increased guideline concordance, increase in narrow spectrum prescribing, reduced antibiotic prescribing for viral/self-limiting upper respiratory tract infections, increased prescription review after microbiology and/or pathology results are known).

Reduced selection pressure for multi-resistant bacteria (e.g. reduction of, or no increase in, community antimicrobial resistance).

Appendix 4 Sample Antimicrobial Stewardship Program

Name of General Practice

This antimicrobial stewardship (AMS) program is based on the Australian Commission on Safety and Quality in Health Care (ACSQHC) 2018 guidebook *Antimicrobial stewardship in Australian health care.*[73]

Bronze level AMS Program

- The institution of an antimicrobial stewardship (AMS) policy and program will be discussed at a staff meeting.
- This practice will provide RACGP Standards endorsed prescribing guidelines such as Therapeutic Guidelines[9] and/or the Australian Medicines Handbook,[305] and/or other locally relevant antibiotic prescribing guidelines.
- Education on the use of the practice's approved antibiotic prescribing guidelines will be provided to at least one full time equivalent (FTE) GP per year.
- This practice will promote clinical care in accordance with the Australian Antimicrobial Stewardship Clinical Care Standard[4] as provided in the RACGP Standards for General Practices Resource Guide.[118]
- This practice will promote infection prevention and control to GPs, staff and patients in accordance with RACGP Standards.[114]

Silver Level AMS Program

This practice will provide the Bronze level AMS program plus:

- An AMS policy and program have been implemented; details may be found at [insert place]
- The AMS policy and program will be discussed at least annually at a staff meeting.
- This practice will provide patient education resources regarding appropriate antibiotic use and/or symptomatic management of self-limiting infections.
- All staff on induction will receive education on the use of the practice's approved antibiotic prescribing guidelines and the use of patient education resources.
- Ongoing AMS education is provided to at least one FTE GP per year.

Gold Level AMS Program

- This practice will provide the Silver level AMS program plus:
- The AMS program will be included on the agenda at every staff meeting.
- All staff on induction will receive education on the practice's AMS policy and program.
- This practice participates in the monitoring of antimicrobial prescribing. Details may be found at [insert place]
- All staff receive education on the use of prescribing guidelines and/or patient education resources at least annually.

Optional

Feedback from the monitoring of prescribing is provided to prescribers. (If available; highly recommended.)

A delayed prescribing and/or a watch-and-wait strategy for [insert condition(s) e.g. acute upper respiratory infections] has been introduced. This involves

- education to all staff about when a delayed prescription or a watch-and-wait strategy for [insert condition(s)] may be appropriate;
- an annual review of the practice's delayed prescribing/watch-and-wait policy with at least one pharmacist and GP.

Sample Resources

Provide details on which resources will be promoted and how/where they may be accessed.

Sample Resource	Details
Antibiotic Prescribing Guidelines	
Therapeutic Guidelines (TG) (requires subscription)	On desktop, Log in details: Phone app: Download from: Log in details: Free printable summary table available from https://tgldcdp.tg.org.au/fulltext/quicklinks/GPSummary_v11.pdf
Australian Medicines Handbook (requires subscription)	On desktop, Log in details:
Other locally relevant guideline	
Sample consultation strategy	
Australian Government. Antimicrobial Resistance website: www.amr.gov.au	www.amr.gov.au/what-you-can-do/general-practice www.amr.gov.au/what-you-can-do/general-practice/prescribing-antibiotics
Patient education resources	
Therapeutic guidelines	(For selected respiratory tract infections; also available at ACSQHC below)
Australian Commission on Safety and Quality in Health Care (ACSQHC): Decision support tools for patients	www.safetyandquality.gov.au/our-work/partnering-consumers/shared-decision-making/decision-support-tools-patients
NPS MedicineWise: Patient information resources	Nose, throat, lungs: www.nps.org.au/consumers/respiratory-tract-infections-rtis-nose-throat-and-lungs For parents/carers of children: www.nps.org.au/consumers/what-every-parent-should-know-about-coughs-colds-earaches-and-sore-throats
TARGET Antibiotics Toolkit (UK) Includes patient education leaflets	www.rcgp.org.uk/clinical-and-research/resources/toolkits/amr/target-antibiotics-toolkit.aspx
CDC (USA) Common Illnesses	www.cdc.gov/antibiotic-use/community/for-patients/common-illnesses
Staff education about the use of antimicrobial prescribing guidelines	
On induction	By whom; Date
Annually to all staff	By whom; Date
Monitoring of antimicrobial prescribing	
In house	By whom; how often; details of what is monitored; feedback process
NPS MedicineInsight practice-level audit	www.nps.org.au/medicine-insight Date:
External monitoring	Details:

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