

Surgical Antimicrobial Prophylaxis Prescribing in Australia

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BPharm (Hons)

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Abstract

Background: Antimicrobial stewardship (AMS) programs are well established initiatives for the rationalisation and conservation of antimicrobial use. Surgical antimicrobial prophylaxis (SAP) has been identified as the most common indication for antimicrobial use in Australian hospitals, with low rates of appropriateness in both public and private hospitals. There is a paucity of literature targeting surgical AMS programs that are applicable to both sectors.

Aims: The aim of this PhD is to explore challenges in SAP prescribing and strategies for the optimisation of SAP prescribing in Australia. Developing an understanding of current SAP prescribing practices and factors that influence SAP prescribing decisions, informs a framework for surgical AMS. The framework aims to address identified issues and support implementation and sustainability of surgical AMS across all Australian hospitals.

Methods: A mixed-methods design integrating quantitative and qualitative research (within a pragmatic paradigm) constituted the overarching methodological approach in this thesis. Five projects were completed. In project 1, the implementability of the national SAP guidelines was assessed. In projects 2, 3 and 4, multiple logistic regression analyses were adopted across the Surgical National Antimicrobial Prescribing Survey dataset to investigate any potential association between patient, hospital and surgical factors' and SAP appropriateness. Finally, in project 5, a qualitative case study explored the phenomenon of SAP decision-making across the professional groups involved in SAP prescribing and administration, i.e., surgeons,

anaesthetists, theatre nurses and pharmacists. Barriers and enablers of prescribing decisions were identified through use of validated theoretical frameworks. Based on the integration and triangulation of all results, a framework for surgical AMS in Australia is proposed.

Results: There are limited surgical AMS interventions identified in the current literature, and a framework to support surgical AMS (and outcome measures such as surgical site infection surveillance) in Australia does not currently exist. SAP prescribing practices continue to demonstrate high rates of inappropriateness across a range of surgical specialties and surgical procedures. Identified targets for improvement include; procedural dose timing, post-procedural prescription duration, and surgical procedures with noted high rates of inappropriateness, broad-spectrum antimicrobial use, and SAP administration when not required. The qualitative research identified six themes in clinicians' perceptions about decision-making for antimicrobial use across surgical settings and highlighted the need for resources to support adequate documentation and communication about SAP prescribing decisions, engagement with senior clinicians who have significant influence upon their juniors' prescribing practices, and the need for meaningful data addressing common fears and misperceptions regarding SAP durations to generate prescribing behaviour change.

Conclusion: The surgical AMS framework provides a theoretical and evidence-based approach to improving patient quality of care and outcomes at a local level whilst also addressing the pressing issue of AMR at a national and global level. The

implementation of surgical AMS is critical for the optimisation of antimicrobial use across public and private surgical settings in Australia. The framework for surgical AMS focuses on three key strategies; engagement and collaboration with stakeholders, advocating for a multi-disciplinary collaboration; development, implementation and evaluation of meaningful data and outcome measures; and the adoption of a multi-faceted quality improvement program.

Declaration

This is to certify that:

(i) the thesis comprises only my original work toward the PhD except where indicated in the Preface,

(ii) due acknowledgement has been made in the text to all other material used,

(iii) the thesis is less than 100,000 words in length, exclusive of tables, figures, maps, bibliographies and appendices as approved by the Research Higher Degrees Committee.

A handwritten signature in black ink, appearing to read 'Cierano', with a stylized, cursive script.

Signed: Ms Courtney Erin Ierano

Date: 5th June 2020

Preface

Statement of contributions to jointly authored works contained in the thesis

The PhD candidate, Courtney Ierano, undertook the literature review and analysis for **Chapter 3**. Courtney Ierano drafted two publications that constitute this chapter under the guidance of the other co-authors. The names and roles of the co-authors for the publication *“Surgical antimicrobial prophylaxis”* are as follows: Dr Jo-Anne Manski-Nankervis, Dr Rodney James, Dr Arjun Rajkhowa and Dr Trisha Peel, who assisted in conception of this paper, and Professor Karin Thursky, who oversaw the paper’s publication. **Chapter 3** also included the publication of *“Surgical antibiotic prophylaxis - The evidence and understanding its impact on consensus guidelines”*.

The names and roles of the co-authors for this publication are as follows: Dr Trisha Peel and Dr Darshini Ayton, who assisted in the studies conceptualisation, development of the analysis plan and revision of the paper; Dr Arjun Rajkhowa and Associate Professor Caroline Marshall, who assisted in the paper’s revisions, and Professor Karin Thursky, who assisted in the development of the analysis plan, revision of the paper and oversaw the paper’s publication.

Courtney Ierano undertook project conception and design, data collection and analysis for all projects 1-5 completed across **chapters 7, 8, 9, 10 and 11** of this thesis. Courtney Ierano drafted these chapters and papers under the guidance of her supervisors and other co-authors.

Chapter 7 led to a published article, entitled: *“Evaluating the implementability of antibiotic surgical prophylaxis guidelines”*. The names and roles of the co-authors are as follows: Dr Trisha Peel, who assisted in the studies conceptualisation, development of the analysis plan and revision of the paper; Associate Professor Caroline Marshall, who assisted in the papers revisions, Dr Darshini Ayton, who assisted in the studies conceptualisation, development of the analysis plan, writing of the analysis and revision of the paper; and Professor Karin Thursky, who assisted in all the above and oversaw the paper’s publication.

Chapter 8 led to a published article, entitled: *“Appropriateness of surgical antimicrobial prophylaxis practices in Australia”*. The names and roles of the co-authors are as follows:

Professor Karin Thursky, Associate Professor Caroline Marshall, Ms Sonia Koning, Dr Rodney James and Dr Trisha Peel contributed to the studies conceptualisation and design. Professor Karin Thursky, Associate Professor Caroline Marshall, Dr Rodney James, Ms Sandra Johnson, Dr Nabeel Imam, Associate Professor Leon J Worth and Dr Trisha Peel assisted in the acquisition, analysis, or interpretation of data. Ms Sandra Johnson, Dr Nabeel Imam and Associate Professor Leon J Worth assisted with statistical analyses. Professor Karin Thursky, Associate Professor Leon J Worth and Dr Trisha Peel drafted the manuscript. All authors critically revised the manuscript and Dr Trisha Peel oversaw the paper’s publication.

Chapter 9 has been submitted to the Journal of Antimicrobial Chemotherapy-Antimicrobial Resistance and is pending review. The publication is entitled:

“Identifying targets for improvement using a nationally standardised survey: Surgical antimicrobial prophylaxis in orthopaedic surgery”. The names and roles of the co-authors are as follows: Professor Karin Thursky, Associate Professor Caroline Marshall, Dr Rodney James and Dr Trisha Peel contributed to the studies conceptualisation and design. Professor Karin Thursky, Associate Professor Caroline Marshall, Dr Rodney James, Ms Sandra Johnson, Dr Nabeel Imam, Associate Professor Leon J Worth and Dr Trisha Peel assisted in the acquisition, analysis, or interpretation of data. Ms Sandra Johnson, Dr Nabeel Imam and Associate Professor Leon J Worth assisted with statistical analyses. Professor Karin Thursky, Associate Professor Leon J Worth and Dr Trisha Peel drafted the manuscript. All authors critically revised the manuscript and Dr Trisha Peel oversaw the papers publication.

Chapter 10 has been submitted to the Journal of Antimicrobial Chemotherapy-Antimicrobial Resistance and is pending review. The publication is entitled: *“Factors associated with antimicrobial choice for surgical prophylaxis in Australia”*. The names and roles of the co-authors are as follows: Professor Karin Thursky, Associate Professor Caroline Marshall, Ms Sandra Johnson and Associate Professor Lisa Hall contributed to the studies conceptualisation and design. Professor Karin Thursky, Associate Professor Caroline Marshall, Dr Rodney James, Ms Sandra Johnson, and Associate Professor Lisa Hall assisted in the acquisition, analysis, or interpretation of data. Ms Sandra Johnson and Associate Professor Lisa Hall assisted with statistical analyses. Professor Karin Thursky, Associate Professor Caroline Marshall, Ms Sandra Johnson and Associate Professor Lisa Hall drafted the manuscript. All authors

critically revised the manuscript and Associate Professor Caroline Marshall oversaw the papers publication.

Chapter 11 led to a published article, entitled: *“Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals”*. The names and roles of the co-authors are as follows:

Professor Karin Thursky, Dr Trisha Peel, Associate Professor Caroline Marshall and Dr Darshini Ayton assisted in the conceptualisation and design of this research

Professor Karin Thursky, Dr Arjun Rajkhowa, Associate Professor Caroline Marshall and Dr Darshini Ayton assisted in data curation and investigation.

Dr Arjun Rajkhowa and Dr Darshini Ayton assisted with the formal analysis and data validation. All authors critically revised the manuscript and Dr Darshini Ayton oversaw the paper’s publication.

Statement of contributions by others to the thesis as a whole

I wish to acknowledge the significant contribution made to this thesis by my supervisors, Professor Karin Thursky, Dr Trisha Peel, Associate Professor Caroline Marshall, and Dr Darshini Ayton.

Professor Karin Thursky, Dr Trisha Peel, Associate Professor Caroline Marshall and Dr Darshini Ayton all played significant roles in the conceptualisation and design of all studies within this thesis and preparation of research into manuscripts for publication, and provided assistance with drafting of thesis chapters.

Additionally, Dr Arjun Rajkhowa, Project Manager for the National Centre for Antimicrobial Stewardship, also contributed significantly to the preparation of this research into manuscripts for publications, and provided assistance with the drafting and editing of thesis chapters.

As primary supervisor, Professor Karin Thursky has made a significant contribution in the ongoing and overarching review and guidance of this PhD thesis, and supported its progression from conception to publication.

Statement of work carried out in collaboration

None

Statement of work submitted for other qualifications

None

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None

Summary of candidate contribution per thesis chapter

Thesis Chapter	Publication title	Publication status- Journal (date)	Nature and extent of student contribution (%)
1.	Unpublished material not submitted for publication		Chapter design and completion (90%)
2.	Unpublished material not submitted for publication		Chapter design and completion (85%)
3.	Surgical antimicrobial prophylaxis	Published – Infection Disease & Health (14/11/2017)	Manuscript concept, design, creation and preparation (75%)
	Surgical antibiotic prophylaxis– The evidence and understanding its impact on consensus guidelines	Published – Australian Prescriber (22/06/2018)	Literature review and analysis, manuscript concept, design and preparation (80%)
4.	Unpublished material not submitted for publication		Chapter design and completion (90%)
5.	Unpublished material not submitted for publication		Chapter design and completion (75%)
6.	Unpublished material not submitted for publication		Chapter design and completion (75%)
7.	Evaluating the implementability of Antibiotic Surgical Prophylaxis	Published/ In Press- Infection Disease &	Study concept and design, data collection,

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11.	Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals	Published – PLOS ONE (14/11/2019)	Study concept and design, data collection, data analysis, manuscript preparation (70%)
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5. Ierano C, Thursky K, Peel T, Rajkhowa A, Marshall C, and Ayton D. Influences on surgical antimicrobial prophylaxis decision-making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals. *PLoS One*. 2019;14(11):e0225011. doi: 10.1371/journal.pone.0225011.
6. Ierano C, Rajkhowa A, Peel T, Marshall C, Ayton D, Thursky K. Antibiotic prescribing in surgery: A clinically and socially complex problem in Australia. *Infect Dis Health*. 2020; doi: 10.1016/j.idh.2020.04.004

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6. Ierano C. Perioperative antimicrobial prophylaxis and antimicrobial stewardship. Presented at Perioperative Medicine Special Interest Group Meeting 2018; 2018 Oct 26; Melbourne
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Public commentaries

1. Ierano C, Rajkhowa A and Thursky K. Antibiotic use too long in surgery. <https://pursuit.unimelb.edu.au/articles/antibiotic-use-too-long-in-surgery>

Public reports

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Table of Contents

Abstract	ii
Declaration	v
Preface.....	vi
Acknowledgements.....	xvii
Table of Contents.....	xix
List of tables and figures	xxiii
Abbreviations	xxv
Chapter 1: Introduction.....	1
1.1 Overview of thesis.....	1
1.2 Aims and objectives	2
1.3 Outline of thesis	2
Chapter 2: Antimicrobial resistance, stewardship, surgical prescribing and the Australian healthcare system	5
2.1. Introduction	5
2.2. A global perspective	5
2.3 The Australian response to AMR.....	11
2.4 Surgical antimicrobial prophylaxis prescribing in Australia	16
2.5 Chapter summary.....	22
Chapter 3: Surgical antimicrobial prophylaxis: An overview	23
3.1 Introduction	23

3.2	Aim	23
3.3	Surgical site infection prevention.....	24
3.4	Evidence-based medicine and surgical antimicrobial prophylaxis guidelines 34	
3.5	Principles of surgical antimicrobial prophylaxis.....	35
3.6	Adaptation of SAP principles for primary care.....	41
3.7	Australian guidelines for surgical antimicrobial prophylaxis	48
3.8	The evidence for surgical antimicrobial prophylaxis	50
3.9	Chapter summary.....	61
Chapter 4. Antimicrobial stewardship for surgical prophylaxis		63
4.1	Introduction	63
4.2	Antimicrobial stewardship for surgical antimicrobial prophylaxis	63
4.3	Chapter summary.....	81
Chapter 5: Theories, models and frameworks		83
5.1	Introduction	83
5.2	Rationale for theoretical models and frameworks.....	83
5.2	Utilisation of theories, models and frameworks.....	86
5.3	Theoretical Domains Framework (TDF)	88
5.4	The Capabilities, Opportunities, Motivators- Behaviour (COM-B) model and the Behaviour Change Wheel (BCW)	92
5.5	Mapping of the TDF to the BCW.....	94
5.6	The TDF, COM-B and BCW in the current literature	95
5.7	Mapping the current literature to the COM-B model.....	97

5.8	Chapter summary	108
Chapter 6: Methodology		110
6.1	Introduction	110
6.2	Research strategy	110
6.3	Mixed-methods research	112
6.4	Research design and quality issues	113
6.5	Researcher positionality	132
6.6	Ethics	133
6.7	Mixed-methods integration	135
6.8	Chapter summary	136
Chapter 7: Evaluating the implementability of antibiotic surgical prophylaxis guidelines		137
7.1	Introduction	137
7.2	Publication	137
Chapter 8: Appropriateness of surgical antimicrobial prophylaxis practices in Australia		149
8.1	Introduction	149
8.2	Publication	149
Chapter 9: Identifying targets for improvement using a nationally standardised survey: Surgical antimicrobial prophylaxis in orthopaedic surgery.....		164
9.1	Introduction	164
9.2	Submitted manuscript	165

Chapter 10: Factors associated with antimicrobial choice for surgical prophylaxis in Australia.....	197
10.1 Introduction.....	197
10.2 Submitted manuscript.....	198
Chapter 11: Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals	212
11.1 Introduction.....	212
11.2 Publication	213
Chapter 12: Discussions and conclusions: A framework for surgical antimicrobial stewardship.....	238
12.1 Introduction.....	238
12.2 Importance of surgical antimicrobial stewardship.....	238
12.3 Summary- addressing research questions.....	239
12.4 Development of a framework for surgical antimicrobial stewardship	243
12.5 Future directions and conclusions	256
References	259
Appendices	283

List of tables and figures

Chapter 2

Table 1: Summary of key findings from the Surgical National Antimicrobial Prescribing Survey 2018 report.

Chapter 3

Table 1: Adaptation and summary of the World Health Organisation's pre-, intra- and post-operative measures to prevent surgical site infections.

Table 2: Summary of Branch-Elliman *et al.* adjusted odds ratios demonstrating increased risk of acute kidney injury and *Clostridioides difficile* infection when SAP duration is prolonged.

Table 3: Summary of Australian and international guideline recommendations for the principles of surgical antimicrobial prophylaxis.

Chapter 4

Table 1: Potential targets to optimise surgical antimicrobial prophylaxis.

Table 2: Surgical antimicrobial stewardship interventions per the most recent Cochrane review.

Table 3: Summary of studies targeting surgical antimicrobial prophylaxis that were included in the Baysari *et al.* systematic review.

Chapter 5

Figure 1: Three aims of the use of theoretical approaches in implementation science and the five categories of theories, models and frameworks. Adapted from Nilsen 2015.

Table 1: Theoretical Domains Framework domains and theoretical constructs.

Figure 2: The Behaviour Change Wheel, COM-B model and Theoretical Domains Framework (TDF) domains. Reproduced with permission from Michie *et al.*

Figure 3: Links between the components of the ‘COM-B’ model of behaviour and the BCW ‘intervention functions’ and ‘policy categories’. Adapted from Michie *et al.*

Chapter 6

Figure 1: Timeline of PhD research projects from conception to publication/submission.

Figure 2: Mixed methods typology framework for this thesis. Adapted from Leech and Onwuegbuzie.

Table 1: Summary of data variables collected in the Surgical National Antimicrobial Prescribing Survey.

Table 2: Focus group sampling framework.

Table 3: Phases of thematic analysis.

Table 4: Summary of ethics approval required for projects 1 to 5.

Chapter 11

Figure 1: The six central themes to describe the influences on surgical antimicrobial prophylaxis prescribing and decision-making.

Chapter 12

Table 1: Summary of themes developed from project 5, mapped to Behaviour Change Wheel interventions and policies, and the proposed surgical AMS (SAMS) framework.

Figure 1: Framework for surgical Antimicrobial Stewardship (SAMS).

Figure 2: Theme 2: Developing and collecting meaningful data for action.

Figure 3: Theme 3: A multi-faceted quality improvement program - surgical AMS (SAMS).

Abbreviations

AA	Adjusted appropriateness
ACIPC	Australasian College of Infection Prevention and Control
ACSQHC	Australian Commission on Safety and Quality in Health Care
AGREE	Appraisal of Guidelines for Research and Evaluation
AIHW	Australian Institute of Health and Welfare
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
ASA	Australian Society for Antimicrobials
ASC	Ambulatory surgical centres
ASCCS	Antimicrobial Stewardship Clinical Care Standard
ASID	Australasian Society for Infectious Diseases
ASP	Antimicrobial stewardship programs
AURA	Antimicrobial Use and Resistance in Australia
BCW	Behaviour Change Wheel
CDC	Center for Disease Control
CDI	<i>Clostridioides difficile</i> infection
CDSS	Computerised decision support systems
CI	Confidence interval
COM-B	Capabilities, Opportunities, Motivators - Behaviour
CPG	Clinical practice guidelines
CPOE	Computerised provider order entry
EMM	Estimated marginal means
EMR	Electronic medical record
ENT	Ear/nose/throat
GLIA	Guideline Implementability Appraisal
GP	General practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAI	Healthcare-associated infection
HOPD	Hospital outpatient departments
HREC	Human Research Ethics Committee

ID	Infectious diseases
IR	Incidence ratio
IT	Information technology
ITS	Interrupted time series
LOS	Length of stay
MDRO	Multi-drug-resistant organism
NAPS	National Antimicrobial Prescribing Survey
NCAS	National Centre for Antimicrobial Stewardship
NHMRC	National Health and Medical Research Council
NHSN	National Health Services Network
NICE	National Institute for Health and Care Excellence
NRS	Non-randomised study
NSQHS	National Safety and Quality Health Service
POCEP	Point-of-care electronic prompt
RACGP	Royal Australian College of General Practitioners
RACS	Royal Australasian College of Surgeons
RCT	Randomised controlled trial
SAP	Surgical antimicrobial prophylaxis
SAMS	Surgical antimicrobial stewardship
SCIP	Surgical care improvement project
SHPA	Society of Hospital Pharmacists Australia
SSI	Surgical site infections
SWC	Surgical wound classifications
TDF	Theoretical Domains Framework
TG	Therapeutic Guidelines
UTI	Urinary tract infection
WHO	World Health Organisation
VICNISS	Victorian Healthcare Associated Infection Surveillance System

Chapter 1: Introduction

1.1 Overview of thesis

Surgical antimicrobial prophylaxis (SAP) is the most common indication for antimicrobial use in hospitals, but inappropriate practices are widely recognised and reported. Examples of inappropriate SAP include: incorrect timing prior to surgery, choice of antimicrobial, or extended usage in the post-operative period (1-8). Inappropriate use may lead to adverse consequences for both the patient and the healthcare system (9, 10). From a patient perspective, inappropriate antimicrobial use is associated with morbidity and mortality (9, 11-15). From a public health perspective, the emergence of antimicrobial resistance (AMR) imperils the future of surgery in our society (16). We need to ensure that antimicrobial use is optimised, and surgical antimicrobial use should be a key target of national antimicrobial resistance programs.

Antimicrobial stewardship (AMS) aims to increase appropriate antimicrobial use and subsequently optimise patient health outcomes (11, 17). AMS interventions can be tailored to suit a vast range of specific targets, including SAP.

Antimicrobial use in the surgical setting is a major problem that requires a multi-faceted and multi-disciplinary approach incorporating clinical knowledge, evidence-based practice, clinical guidelines, behaviour change theory, implementation science and health services research (18-25). Developing an understanding of these

components to build a framework to support AMS in the surgical setting is essential for successful optimisation of SAP (and, consequently, improvements in patient and healthcare outcomes).

1.2 Aims and objectives

The aim of this PhD is to explore challenges in SAP prescribing and strategies for the optimisation of SAP prescribing in Australia. More specifically, the objectives to achieve this aim are to:

1. Describe current SAP prescribing in Australian hospitals.
2. Describe current strategies for the optimisation of SAP prescribing in hospitals.
3. Identify and explore the underlying facilitators and barriers to appropriate SAP prescribing.
4. Propose a theoretically-informed framework for solutions to support sustainable AMS for SAP.

1.3 Outline of thesis

In **chapter two**, contextualisation of the problem of AMR from a global and Australian perspective, and the rationale for AMS and its targeting of SAP are provided.

A critical review of the current literature in relation to the evidence for SAP efficacy is provided in **chapter 3**.

Chapter 4 provides a summary of the current literature supporting AMS in the surgical setting and identifies any potential gaps in the evidence.

In **chapter 5**, the theories, models and frameworks adopted in this study (and the rationale for their use) are described.

The methodological approaches utilised in this PhD research program are described in **chapter 6**. We adopted a mixed-methods approach across five projects. This design (as opposed to a singular method) has enabled us to develop a stronger understanding of antimicrobial use in the surgical setting and its implications for stewardship and intervention design. Both quantitative and qualitative data analysed are of equal importance and complement each other. The methods for the five projects (particularly for data collection and analysis) are described in greater detail in each chapter.

In **chapter 7**, we present the findings of project 1, which explores the issue of guideline implementability. Project 1 is a quantitative guideline implementability appraisal of the Australian national guidelines for surgical prophylaxis utilising the validated Guideline Implementation Appraisal (GLIA) instrument (26).

Projects 2,3 and 4 are presented in **chapters 8, 9 and 10**. These chapters include quantitative analyses of the Australian Surgical National Antimicrobial Prescribing Survey (Surgical NAPS) datasets. These analyses provide greater insight into current SAP prescribing practices in Australia and identify problematic areas that may be viewed as targets for tailored AMS interventions.

Chapter 11 presents the findings from project 5 — a qualitative exploratory study. The facilitators and barriers to optimal SAP prescribing and guideline compliance are presented using the Theoretical Domains Framework (27) and the COM-B framework (28, 29).

Chapter 12 presents a synthesis of the findings from this research, contextualised with insights from the literature reviewed. Based on these findings, this chapter proposes AMS strategies and interventions that are better-suited for the surgical setting as well as a theoretically-informed framework for surgical AMS (SAMS). This chapter also presents the conclusions of this research, demonstrating the contributions it makes to theoretical and practical knowledge in the field of antimicrobial stewardship in the surgical setting, with recommendations for future research.

Chapter 2: Antimicrobial resistance, stewardship, surgical prescribing and the Australian healthcare system

2.1. Introduction

This chapter provides a brief overview of the issue of antimicrobial resistance from global and Australian perspectives, highlighting the importance of antimicrobial stewardship strategies for appropriate SAP prescribing and the consequences of not addressing the problem of inappropriate antimicrobial use.

2.2. A global perspective

2.2.1 Antimicrobial resistance and the global response

Antimicrobials are a powerful class of therapeutic agents and their use has markedly altered the treatment and prevention of infections. Since their discovery, antimicrobials have been used extensively; however, a significant proportion of use is not based on sound evidence and may be considered inappropriate (1-3, 5, 6).

Inappropriate antimicrobial use can have adverse consequences for patients; *Clostridioides difficile* infection (CDI), other healthcare-associated infections (HAIs), and allergies and toxicities associated with antimicrobial use can impact patient outcomes (9, 11, 12, 30-33). Additionally, inappropriate use contributes to the emerging threat of antimicrobial resistance (AMR). Infections with multi-drug-resistant organisms (MDROs) are associated with higher rates of mortality, and increased costs due to prolonged hospital admissions, expensive antimicrobial

treatments and contact tracing, infection control precautions and surveillance (13, 14, 34-36). The pipeline of new antimicrobials is limited, which means that there may be no effective treatments for patients with MDRO infections (37).

In 2014, the Lancet Commission on Global Surgery was established with an agenda to improve access and quality of surgery worldwide (38). This Commission identified 'ten needs for the provision of safe surgical and anaesthesia care', inclusive of antimicrobials and other critical medications for pain and anaesthesia (38).

In 2016, the United Nations held a General Assembly High-Level Meeting on Antimicrobial Resistance (AMR). This was the fourth time a health issue was discussed by the UN General Assembly, thus demonstrating the critical nature of the threat AMR presents globally. It was highlighted that no country, sector or organisation could address this issue alone (39). Countries present committed to developing national action plans on AMR based upon the 'Global Action Plan on Antimicrobial Resistance' (2015) (9), developed by the World Health Organisation (WHO) in conjunction with the Food and Agriculture Organisation of the United Nations and the World Organisation for Animal Health. Current investment into the development of new antimicrobials is minimal, and the process of drug discovery and development is intensive. Therefore, the conservation of current antimicrobials is of vital importance. Leaders pledged to promote regulation of antimicrobials and best practices, and support innovation in discovery and use of alternatives to antimicrobials and new technologies for diagnosis and vaccines (39).

The 'Global Action Plan on Antimicrobial Resistance' (2015) (40) outlines five key objectives within a One Health framework for action on AMR. A One Health approach entails the collaboration of multiple international and national stakeholders across sectors, including government, agriculture, human and veterinary medicine, environmental science, finance and society; it requires cross-sectoral coordination of activities aimed at minimising the burden of AMR (40). The optimisation of antimicrobial use in human and animal health is one of the action plans' key objectives, and the implementation of antimicrobial stewardship (AMS) programs is considered essential for the achievement of this goal (40).

The WHO Global Strategy for Containment of Antimicrobial Resistance (41) identifies the use of antimicrobials in the hospital setting (including for surgical prophylaxis) as a critical contributor to the global problem of antimicrobial misuse. The need for effective SAP use was highlighted in the first O'Neill Report on AMR (16), which discussed the prospect of a world where antimicrobials no longer work; in such a scenario, SAP would no longer work, and many procedures such as hip operations, which may prolong quality of life and one's contribution to the workforce, would be too risky to undertake (16). The 2016 O'Neill Report estimated that AMR would be responsible for 10 million excess deaths globally by 2050 if the current spread of AMR is not reduced (42). The report included recommendations about key areas for intervention and recognised that surveillance is a key component of infectious disease management (intervention four: 'improve global surveillance of drug resistance and antimicrobial consumption in humans and animals') (42). The report also supported capacity building among a range of health professionals to improve

antimicrobial stewardship (AMS) and infectious disease training to tackle the issue of AMR (intervention seven: ‘improve the number, pay and recognition of people working in infectious disease’) (42).

Three years later, the Chatham Institute published an update on and review of the O’Neill Report (42) and its impact, and progress on tackling AMR thus far (43). Despite its many successes, the 2019 review identified many areas for improvement, including the need to utilise digital technology to translate surveillance data into clinical decision-support tools for patient management, and the need to incorporate AMR-related training across a range of professionals’ education and develop a career pathway for progression and specialisation within AMS (43).

2.2.2 Antimicrobial stewardship in hospitals

AMS refers to “coordinated actions designed to promote and increase the appropriate use of antimicrobials” (1). AMS programs have been recognised internationally (40, 44) and nationally (11, 45, 46) as a key strategy for conserving the effectiveness of antimicrobials. AMS programs and interventions have not only optimised antimicrobial prescribing but subsequently reduced institutional rates of resistance, morbidity and mortality, as well as minimised health care and pharmacy costs, and consequences of antimicrobial use such as adverse drug reactions and toxicity (11).

A meta-analysis of 32 studies published between 1992-2014 demonstrated AMS programs reduced the incidence of *C. difficile* infections (32% reduction; incidence

ratio 0.68, 95% confidence interval [CI] 0.53–0.88; $P=0.0029$), the incidence of infections and colonisations with multi-drug-resistant Gram-negative bacteria (51%; IR 0.49, 95% CI 0.35–0.68; $P < 0.0001$), extended-spectrum β -lactamase-producing Gram-negative bacteria (48%; IR 0.52, 95% CI 0.27–0.98; $P=0.0428$), and methicillin-resistant *Staphylococcus aureus* (37%; IR 0.63, 95%CI 0.45–0.88; $P=0.0065$) (33).

AMS programs have been implemented globally for many decades (44). A global checklist was recently published (47) with core elements of AMS programs. However, these require adaptation to reflect a countries available resources and health priorities. For example, the WHO recently published a practical tool kit to support the development and implementation of AMS programs in low and middle income countries (48). Variations of AMS programs have been implemented internationally with a range of experiences reported in Latin America, Australia, many European countries, South Africa, Great Britain and North America (44).

Various AMS interventions have been proposed to improve antimicrobial prescribing for hospital inpatients. A Cochrane review (and its most recent update) (31, 49) identified interventions for the improvement of antimicrobial prescribing in hospital inpatients. These interventions were broadly classified as enabling or restricting (31).

The Cochrane review included 221 studies (58 randomised controlled trials [RCTs] and 163 non-randomised studies [NRS])(31) and utilised the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method to appraise the evidence. High-certainty GRADE evidence confirmed that interventions were effective in increasing compliance with antimicrobial policy by 15% (95% CI 14-

16%) across 29 RCTs. Meta-analysis of 14 RCTs also confirmed that interventions reduced the duration of total antimicrobial treatment by 1.95 days (95%CI -2.22 to -1.67) (31). Interventions that “increased means/reduced barriers to increase capability or opportunity” were defined as enabling interventions (enablement) by Davey *et al* (31).

Conversely, restrictive interventions aim to prevent inappropriate prescribing by placing strict limitations upon certain prescribing practices and aspects of antimicrobial use. Examples of such interventions include formulary restriction, pre-approval/authorisation by infectious diseases physicians/microbiologists or pharmacists prior to use, selective reporting of laboratory susceptibilities and automatic stop orders on antimicrobials (49).

The most recent Cochrane review demonstrated high-level evidence for both enabling and restrictive interventions that independently increased compliance with antimicrobial policies. Therefore, neither type of intervention could be proven to be superior. However, there was also high-level evidence to suggest that enablement enhances the efficacy of restrictive interventions. Enabling interventions that included the use of feedback were potentially more effective than those using enablement alone (moderate-certainty evidence) (31).

Similarly, multi-variable meta-regression of 91 interrupted time series (ITS) studies further supported the finding that both enablement and restrictive interventions independently improved compliance (31). It was concluded that testing the efficacy of AMS interventions against placebo for improved antimicrobial prescribing

practices was no longer warranted. The authors suggest future research is required to identify factors that influence AMS intervention efficacy, more specific optimal intervention regimens and the unintended consequences associated with restrictive interventions (31). This thesis aims to explore these potential factors and identify a targeted AMS strategy and intervention for SAP.

2.3 The Australian response to AMR

Australia is one of many nations that have adopted a One Health approach to combatting AMR. In 2013, the Australian Government Department of Health, with the Australian Commission on Safety and Quality in Health Care (ACSQHC), developed a co-ordinated surveillance system, 'Antimicrobial Use and Resistance in Australia' (AURA), targeting antimicrobial use and resistance in humans specifically. Following on from this, the ACSQHC has gone on to support programs aimed at improving the safety and quality of healthcare, i.e., infection control, antimicrobial use and medication safety programs (4, 8, 50-52). The most recent report noted an increase in hospital antimicrobial use with steady levels of inappropriate prescribing (50).

The Australian Government Department of Health released the First National Antimicrobial Resistance Strategy 2015-2019 (53), which provided a framework for the One Health approach to addressing AMR. The third objective was to advocate for the development of a nationally co-ordinated One Health surveillance system for AMR. In November 2018, leaders of the Australian Society for Antimicrobials (ASA), the Australasian Society for Infectious Diseases (ASID) and the Australasian College

of Infection Prevention and Control (ACIPC) published an advocacy statement calling for a 'National Coordinating Centre' on AMR, based upon the consensus of key representatives and stakeholders involved in the second National Antimicrobial Resistance Summit in Melbourne in 2017 (54). A recent commentary from Williamson *et al.* (55) highlights that this is yet to occur and reinforces the belief that this is critical for the Australian response to both emerging and endemic AMR threats (55).

In addition to the AMR and antimicrobial use surveillance, the strategy highlighted the need for the implementation of effective AMS practices (53). Key Australian resources for the development and implementation of AMS programs are the ACSQHC, the National Centre for Antimicrobial Stewardship (NCAS) and state-wide services such as the South Australian Expert Advisory Group on Antimicrobial Resistance (SAAGAR) and New South Wales-Clinical Excellence Commission. In 2014, the Antimicrobial Stewardship Clinical Care Standard (ASCCS) was launched by ACSQHC as part of the National Safety and Quality Health Service (NSQHS) Standards (45), advocating for AMS programs to be implemented consistently in all hospitals and day-procedure services at a national level. The ASCCS consists of 9 quality statements that highlight the standard level of care for antimicrobial therapy that patients should receive. Quality statement 9, 'Surgical prophylaxis', advocates for prescribing adherence to the Australian *Therapeutic Guidelines: Antibiotic (TG: Antibiotic)* (56). It is aimed at reducing the inappropriate use of surgical antimicrobial prophylaxis (SAP), as this occurs at high and variable rates (30-90%, mainly due to incorrect timing and duration of antimicrobial use) (57).

The ACSQHC has also released multiple Antimicrobial Use and Resistance in Australia (AURA) reports (50-52), which support the ongoing development and implementation of AMS programs. The 2017 AURA report noted five key areas for action, including the need for improvement of appropriate SAP prescribing (52). The most recent AURA report did not relist SAP prescribing as a key area for action. However, the AURA National Coordination Unit has identified and promoted improvement actions for SAP prescribing and has committed to ongoing development of strategies and resources for implementation of improvement actions across both public and private sectors in Australia (50).

The Australian surgical and medical colleges do not currently have a proposed framework for AMR in the acute setting. The Royal Australian College of General Practitioners (RACGP) published their response to AMR in Primary Care in November 2017 (58). This publication included details of RACGP activities that would form a response to the First National AMR Strategy 2015-2019 (53), including a position statement on AMS (58). No frameworks have been reported from the Royal Australasian College of Surgeons (RACS). The RACS last published a position paper on infection control, 'Prevention of Healthcare-Associated Infection in Surgery', in 2015 (59), which was due for review 2018. The position paper acknowledged the global issue of AMR and endorsed multiple infection guideline documents that were developed by other national bodies, including the *TG: Antibiotic*. Most recently, in 2018, the RACS published an online news article about their collaboration with the ACSQHC to develop resources to support organisational improvement of SAP (60).

The Australian and New Zealand College of Anaesthetists republished in 2019 their 'Guidelines on Infection Control in Anaesthesia' (61), which also endorsed compliance with the *TG: Antibiotic*, but did not comment on AMR and stewardship specifically. Similarly, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists published a statement on SAP in obstetrics and gynaecology in 2016 (due for review in July 2019), which also included an endorsement of the *TG: Antibiotic* (62).

The delivery of AMS programs and interventions (and their success) varies immensely due to Australia's multifaceted healthcare system. Healthcare services operate in the public (all levels of government) and private (not-for-profit companies or organisations) sector.

Healthcare service delivery exists in many formats, including health promotion, primary healthcare, specialist services, emergency and acute admitted and non-admitted care in hospitals, day-stay facilities and home-based care, and subacute and non-acute services such as rehabilitation and palliative care (52, 63). Surgical services are provided across both public and private hospitals. In 2015-2016, private hospitals accounted for 67% of 2.2 million elective surgery hospitalisations in Australia (63).

All Australian hospitals are required to maintain national accreditation standards. The eight NSQHS Standards (45) were developed by ACSQHC in conjunction with the Australian Government and relevant private bodies to standardise and improve the quality of healthcare. Included in these standards is Standard 3: 'Preventing and

Controlling Healthcare-Associated Infection’, which highlights the core components and activities required for an accredited AMS program (Standards 3.15 and 3.16) (45). A notable criterion is the incorporation of core elements, recommendations and principles from the ACSQHCs’ Antimicrobial Stewardship Clinical Care Standard (ASCCS) (45, 46).

An advisory statement from the ACQSHC was later published in 2018 to update the NSQHS Standards and ensure surgical prophylaxis was addressed as part of hospital AMS programs. To ensure this requirement was met, the advisory statement advised monitoring the quality of SAP prescribing (64) using the following indicators from the ASCCS (46):

- Indicator 6a: Rate of documentation of clinical reason (or indication) for prescribing antibiotics;
- Indicator 9a: Surgical antibiotic prophylaxis in accordance with guidelines;
- Indicator 9b: Timely administration of prophylactic antibiotics prior to surgery; and
- Indicator 9c: Cessation of prophylactic antibiotics after surgery.

The advisory statement also endorsed the utilisation of the NAPS online auditing platform and the NAUSP for the monitoring of appropriateness and usage respectively (64).

In summary, there are a range of frameworks and government programs that highlight the need for AMS in the ongoing battle against AMR. For national

accreditation, both public and private hospitals require an AMS program that embeds the principles of the ASCCS and the *TG: Antibiotic* recommendations (56).

The development of sustainable AMS programs requires an understanding of the Australian healthcare system and its frameworks for action against AMR. SAP has been repeatedly identified as an area for action and improvement in Australia (50, 52). Development of targeted and tailored stewardship activities is warranted to further optimise antimicrobial usage and patient health.

2.4 Surgical antimicrobial prophylaxis prescribing in Australia

2.4.1 Surgical antimicrobial prophylaxis prescribers

When determining appropriate AMS interventions for surgical prophylaxis, one must consider the target prescribers and how to influence positive behaviour change, in addition to the key outcome measures for appropriate SAP. Additional research identifying who is responsible for SAP in Australian operating rooms (i.e., who prescribes, administers and reviews care) and assists in a supportive and prompting role will also assist with the development of tailored AMS SAP interventions. Currently, medical practitioners such as surgeons and anaesthetists can prescribe antimicrobials for surgery in Australia. Therefore, they are the primary targets for AMS interventions.

Non-medical prescribing by dentists, nurse practitioners, midwives, podiatrists and optometrists has been adopted with various prescribing models across multiple specialties (65). Nurse practitioners can prescribe antimicrobials and with adequate

upskilling have the potential to collaborate with other health professionals in the surgical setting to improve the use of SAP.

Pharmacists currently do not have prescribing privileges in Australia. There are examples in the literature where clinical pharmacists have been involved in the charting of medications in Australian hospital settings (66-70), though not exclusively in the surgical setting. The charting of medications in an inpatient hospital setting is different to prescribing, and as such pharmacists may play a supportive or active role in promoting guideline-compliant SAP charting (66).

A greater understanding of these varied health professionals' roles and whether they can collaborate together will provide direction for interventions that support multi-disciplinary and team-based decision-making to optimise SAP use. Project 5 aims to explore the roles and perceptions of these professionals.

2.4.2 Hospital National Antimicrobial Prescribing Survey (Hospital NAPS)

The Hospital National Antimicrobial Prescribing Survey (Hospital NAPS) (1-3, 5-7) is an audit tool developed by the Guidance Group at Melbourne Health and NCAS, and supported by the ASQHC, to provide a snapshot of current Australian antimicrobial prescribing. The Hospital NAPS is a key source of data on antimicrobial use and prescribing appropriateness reported as part of the AURA surveillance program (52). The most recent report (2018 data published in 2020) (7) included 324 hospitals and 26,714 prescriptions for 17,175 patients.

For comparison, the most recent Australian hospital statistics reveal that in 2017-2018, there were 1350 hospitals (693 public and 657 private hospitals) in Australia

(71). Thus, the Hospital NAPS is a reflection of approximately 23% of all Australian hospitals.

The Hospital NAPS identified surgical prophylaxis as the most common indication for antimicrobial use (at 14.1%)(7), similar to previous years (1-3, 5, 6). Of these surgical prophylaxis prescriptions, 39.5% were identified as inappropriate and 43.4% were identified as non-compliant with the *TG: Antibiotic* and/or local hospital guidelines (7). These rates of inappropriateness and non-compliance were observed as the highest for any given indication.

Excessive prescribing and usage of antimicrobials for SAP in hospitals (41), and continuation of SAP beyond the 12-24 hour post-operative time frame without clear clinical indication have been observed (41). Another key indicator from the Hospital NAPS is surgical prophylaxis given for >24 hours (1, 7). While best-practice guidelines suggest that <5% of SAP prescriptions should extend >24 hours, the 2018 data revealed a higher rate of prolonged SAP duration (at 28.0%), which was considered an improvement from 41.1% in 2013 (1, 7).

The Hospital NAPS classifies inappropriate use as use that is either suboptimal or inadequate and typically non-compliant with evidence-based clinical guidelines (1-3, 5-7). In Australia, the key clinical antibiotic prescribing guideline is the *TG: Antibiotic* (56, 57). In practice, hospitals may adapt this reference to produce their own local guidelines specific to their clinical setting. The use of guidelines should drive optimal SAP use; however, the above findings suggest this is not occurring. Exploration of

factors contributing to guideline non-compliance may help address this problem and improve appropriate antimicrobial usage.

The Hospital NAPS utilises a point-prevalence methodology, thus only capturing SAP patients if they received prophylaxis in the 24 hours prior to the audit date. Hence, it is already biased towards capturing patients on extended post-procedural prophylaxis.

Analysis of the Hospital NAPS 2014 report highlighted differences in SAP prescribing between public and private Australian hospitals (2, 72). In particular, private hospitals significantly used more SAP than public hospitals (46.9% vs. 9.6%; $P < 0.001$) (72). There was a non-significant difference in non-compliance with guidelines (37.9% in private hospitals vs. 46.5% in public hospitals). Notably, public hospitals had significantly higher rates of compliance with locally endorsed guidelines (17.5%) than private hospitals (6.8%) ($P < 0.001$). However, for some common surgical specialities and procedures, there was greater non-compliance with SAP guidelines in public hospitals, including for plastic surgery (73.4% in public hospitals vs. 38.0% in private hospitals; $P < 0.001$), general surgery (45.5% vs. 18.2%; $P < 0.001$) and orthopaedic surgery (45.0% vs. 37.4%; $P = 0.039$) (72).

A previous Australian study assessing antimicrobial use in private hospitals also identified low rates of SAP appropriateness. Only orthopaedic and neurosurgical procedures demonstrated appropriateness rates greater than 50%, in comparison to other specialties such as cardiothoracic surgery (25.0%), general surgery (20.5%) and plastic surgery (13.6%) (73); this is still considered suboptimal.

2.4.3 Surgical National Antimicrobial Prescribing Survey (Surgical NAPS)

The Hospital NAPS revealed concerning high rates of inappropriate SAP use (1-3, 5-7). In response to this concern, the NCAS developed a targeted Surgical NAPS audit tool. The Surgical NAPS tool adopts a longitudinal methodology to more accurately capture SAP prescribing and identify extended post-procedural prophylaxis. The Surgical NAPS has similar methodological limitations as Hospital NAPS, such as the potential for sampling and selection bias and the subjective nature of the auditing assessments. For example, each participating hospital was able to perform the surveys on the surgical units of their choice, thus allowing for non-randomisation and potential bias as they may have directed their surveys to targeted problematic or higher-volume surgical units (4, 8).

The Surgical NAPS 2018 report, published in December 2019 (8), presented an analysis of 5,637 surgical episodes from 109 hospitals, in which 4,525 initial procedural antimicrobial doses were prescribed (of which 36.0% were assessed as inappropriate). For prescribed procedural doses, where guidelines were available (n=4,345), 34.9% of doses were assessed as non-compliant (Table 1). Based on the available data, the surgical procedure groups most commonly with at least one antimicrobial prescribed were breast surgery (96.0%), orthopaedic (91.3%) and vascular surgery (85.4%). In comparison, dentoalveolar (59.1%), head and neck surgery (58.6%) and gastrointestinal endoscopic procedures (53.3%) were the procedure groups with the highest rates of inappropriateness (8). The most common reasons for inappropriate prescribing of procedural antimicrobials (n=1,212) were

‘incorrect timing’ (51.2%), ‘incorrect dose’ (23.28%) and ‘spectrum too broad’ (11.6%) (8).

Table 1 Summary of key findings from the Surgical National Antimicrobial Prescribing Survey 2018 report (8)

Measures	Procedural prophylaxis			Post-procedural prophylaxis		
	Total	Inappropriate		Total	Inappropriate	
	N	N	%	N	N	%
Surgical episodes						
- Antimicrobial prescribed	4,030	1,522	37.8	1,728	1,073	62.1
- No antimicrobial prescribed	1,606	97	6.0	3,086	56	2.4
Antimicrobial doses						
- Initial Procedural*/ Prophylaxis Post-procedural**	4,525	1,631	36.0	1,973	1,257	63.7
Guideline compliance	Total N	Non-compliant		Total N	Non-compliant	
		N	%		N	%
Guideline compliance (where guidelines were available)	4,345	1515	34.9	1,878	1,233	65.7

Key:

* Initial doses only applied to procedural doses

** Indication of prophylaxis only applied to post-procedural prescriptions

Post-procedural SAP data were also captured in the Surgical NAPS report (4, 8).

Overall, prescribed post-procedural SAP was inappropriate in 63.7% of 1,973 prescriptions (Table 1). For prescribed doses, where guidelines were available (n=1,878), 66.7% of post-procedural antimicrobial doses were assessed as non-compliant. The most common reasons for inappropriateness of post-procedural antimicrobials (n=574) were ‘incorrect duration’ (54.7%), ‘incorrect dose or frequency’ (37.6%) and ‘spectrum too broad’ (3.8%). Inappropriateness ranged from

37.5% (cardiac) to 100% (dentoalveolar). Other surgical procedure groups with high rates of inappropriateness include gynaecology (93.5%) and urological surgery (87.3%) (8).

Further analysis of the Surgical NAPS reports (4, 8) and the growing Surgical NAPS dataset is pending. Quantitative analyses of the Surgical NAPS dataset constitute projects 2, 3 and 4. The findings from these analyses will assist in the identification of current Australian SAP prescribing practices and include meaningful data that can provide direction for action in the form of guiding targeted AMS intervention development and implementation.

2.5 Chapter summary

There is a growing understanding of AMR as a serious threat, both globally and nationally. Multiple national and international organisations have developed policies and frameworks to support the fight against AMR, commonly in the form of AMS. Current Australian AMS policies support AMS at a national and hospital jurisdictional level, while the Australian online auditing platforms, the Hospital NAPS and Surgical NAPS from NCAS, enable hospitals to meet the required accreditation standards for AMS services.

Analysis of the Australian healthcare system and policies for AMS and AMR has identified current policy and practice gaps. The Australian surgical specialty response to AMR appears to be limited, with insufficient information on opportunities for

improvement and uptake of AMS strategies to address the issue of inappropriate SAP prescribing across all surgical specialties in both public and private sectors.

Chapter 3: Surgical antimicrobial prophylaxis: An overview

3.1 Introduction

This literature review first discusses SAP as an infection prevention measure and includes a summary of current national and international guidelines. The majority of this review focuses on examining the evidence behind prescribing guidelines, focusing in particular on the quality and recency of guidelines for selected surgical procedures with high frequency of SAP use, SSI incidence and the devastating outcomes when SSIs occur.

3.2 Aim

The aim of this literature review is to:

1. Demonstrate a thorough understanding of issues pertinent to SAP prescribing.
2. Establish context of SAP prescribing using national and international literature.
3. Examine the current literature on evidence for and prescribing rates of SAP.

3.3 Surgical site infection prevention

Surgical site infection (SSI) prevention includes many measures, one being the administration of antimicrobials, commonly referred to as surgical antimicrobial prophylaxis (SAP) (74). This is achieved by reducing the presence of microorganisms and their potential burden at the surgical site. SAP, among other strategies, is important for the reduction of SSIs. Research demonstrates that SSIs occur in approximately 2-13% of procedures in Australia (75-77) and place a significant burden on the Australian healthcare system in terms of costs (\$268 million per annum) (76). De lissovoy *et al.*'s analysis of 723,490 surgical hospitalisations in the US, with an SSI rate of 1% (n=6,891 cases), highlighted that SSIs have attributable costs such as costs associated with hospital length of stay. Increases of 406,730 hospital days and over \$900 million in costs were attributed to SSIs (78). Additionally, the researchers identified 91,613 readmissions for SSI treatment, which accounted for a further 521,933 days of hospital care (estimated to have cost \$700 million) (78).

The projected burden of primary total knee and hip arthroplasties in Australia for osteoarthritis is estimated to increase by 276% and 208% respectively by 2030 (79). This recent epidemiological modelling of the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) dataset, spanning 10 years (2003-2013), estimated a total cost of \$AUD5.32 billion to the Australian healthcare system (79). Arthroplasty has been identified as a high-cost surgery that is being performed with increasing frequency; in 2015, it was estimated that the direct costs for arthroplasty would exceed \$1 billion AUD per year (80). The additional costs of

preventable post-operative complications such as SSI contributed a further \$97 million (80).

There is currently an extensive body of literature in support for SAP and its efficacy for reduction of SSIs in addition to post-operative pneumonia and urinary tract infections (UTIs) (57). The quality of the literature varies, ranging from high-quality RCTs, systematic reviews and meta-analyses to lower-quality cohort studies and expert consensus reviews. However, Australian data continue to suggest high rates of inappropriate SAP prescribing (1-8).

There is a suite of recommended measures for the prevention of SSIs. Table 1 provides a summary of the WHO recommendations for pre-, intra- and post-operative measures to prevent SSIs (81, 82). The recommendations varied in strength (conditional to strong) and evidence quality (very low to moderate). All recommendations regarding SAP were strong with moderate-quality evidence.

Table 1 Adaptation and Summary of the World Health Organisations' pre-, intra- and post-operative measure to prevent surgical site infections (81, 82)

Pre-operative Recommendations	Summary of Recommendations	Strength of recommendations (quality of evidence)
Peri-operative discontinuation of immunosuppressive agents	Immunosuppressive agents should not be discontinued before surgery.	Conditional (very low)
Enhanced nutritional support	Consider oral or enteral multiple nutrient enhanced nutritional formulas in underweight patients undergoing major surgical operations.	Conditional (very low)
Pre-operative bathing	Patients should shower/bathe prior to surgery with either a plain or antimicrobial soap.	Conditional (moderate)
Decolonisation with mupirocin ointment, with or without chlorhexidine	Patients with known nasal carriage of <i>Staphylococcus aureus</i> should receive peri-operative intranasal mupirocin 2% ointment with or without a chlorhexidine body wash.	Strong (moderate) for cardiothoracic and orthopaedic procedures Conditional (moderate) for all other types of surgery
Mechanical bowel preparation and use of oral antimicrobials	Both are recommended for use in combination for adult patients undergoing elective colorectal surgery.	Conditional (moderate)
	Mechanical bowel preparation without antimicrobials is not recommended.	Strong (moderate)
Hair removal	Not recommended. If necessary, clipping is preferred, and shaving is discouraged.	Strong (moderate)
Optimal timing for SAP administration	SAP administration should be before surgical incision when indicated.	Strong (low)
	SAP administration should occur within 120 minutes before incision and include	Strong (moderate)

	consideration of the antimicrobial half-life.	
Surgical hand preparation	Recommended antimicrobial soap and water or alcohol-based hand rub before wearing sterile gloves.	Strong (moderate)
Surgical site skin preparation	Recommended alcohol-based antiseptic solutions based on chlorhexidine	Strong (low to moderate)
Antimicrobial skin sealants	Not recommended for use for the purpose of reducing SSIs.	Conditional (very low)
Intra- and Post-Operative Recommendations	Summary	Strength of recommendations (quality of evidence)
Peri-operative oxygenation	For patients undergoing general anaesthesia with endotracheal intubation; should receive 80% fraction of inspired oxygen intraoperatively and if feasible, in the immediate post-operative period (2-6 hours).	Strong (moderate)
Normothermia	Warming devices are recommended for patient body warming in the operating room.	Conditional (moderate)
Protocols for intensive perioperative blood control	Protocols are recommended for both diabetic and non-diabetic adult patients.	Conditional (low)
Normovolaemia	Recommended intra-operative goal-directed fluid therapy.	Conditional (low)
Drapes and gowns	Recommended either sterile disposable non-woven or sterile reusable woven drapes and surgical gowns.	Conditional (moderate to very low)
	Not recommended to use plastic adhesive incise drapes with or without antimicrobial properties.	Conditional (low to very low)
Wound-protector devices	Consider use in clean-contaminated, contaminated and dirty abdominal surgical procedures.	Conditional (very low)

Incisional wound irrigation	Consider use of an aqueous povidone-iodine solution before closure in clean and clean-contaminated wounds.	Conditional (very low)
	Antimicrobial incisional wound irrigation before wound closure is not recommended.	Conditional (low)
Prophylactic negative pressure wound therapy	Recommended on primarily closed surgical incisions with high-risk wounds.	Conditional (low)
Antimicrobial-coated sutures	Triclosan-coated sutures are recommended in all surgery types.	Conditional (moderate)
Laminar airflow ventilation systems in the operating room	Not recommended for patients undergoing total arthroplasty.	Conditional (low to very low)
Antimicrobial prophylaxis in the presence of a drain	Not recommended to continue due to presence of a drain for the purpose of preventing SSIs.	Conditional (low)
Optimal timing for wound drain removal	Remove when clinically indicated. No evidence to recommend an optimal and exact time.	Conditional (very low)
Wound dressings	No type of advanced dressings is recommended over standard dressings on primarily closed surgical wounds.	Conditional (low)
Post-operative SAP	Not recommended to prolong SAP after completion of the operation.	Strong (moderate)

The efficacy of guideline-compliant SAP as an SSI prevention measure was observed in an Australian retrospective observational study of 1019 patients who underwent hip or knee arthroplasty (83). According to this study, 38.7% received guideline-compliant SAP, and the overall SSI rate was 2.7%; but there was a significant difference ($P < 0.01$) in SSI rates between those who received guideline-compliant (1.7%) and non-compliant SAP (5.0%) (83).

There is emerging evidence that even a single dose of antimicrobials for surgical prophylaxis may be associated with patient harm. Most recently, a US multicentre retrospective cohort study of the Veteran Affairs healthcare system demonstrated that the prolongation of SAP did not reduce SSIs but was associated with a higher adjusted odds ratio of developing *CDI* and acute kidney injuries (AKI) for both cardiac and non-cardiac procedures (10) (Table 2).

Table 2 Summary of Branch-Elliman *et al.* (10) adjusted Odds Ratios demonstrating increased risk of acute kidney injury and *Clostridioides difficile* infection when SAP duration is prolonged

Duration (hours)	Adjusted Odds Ratio (aOR) (95% CI)		
	Acute kidney injury – cardiac surgery	Acute kidney injury – non cardiac surgery	<i>Clostridioides difficile</i> infection
24-<48	1.03 [0.95-1.120]	1.31 (1.21-1.42)	1.08 (0.89-1.31)
48-<72	1.22 (1.08-1.39)	1.72 (1.47-2.01)	2.43 (1.80-3.27)
>72	1.82 (1.54-2.16)	1.79 (1.27-2.53)	3.65 (2.40-5.55)

Therefore, SAP is an important infection prevention measure and its appropriate use would minimise patient harms associated with antimicrobial exposure and reduce the risk of resistance.

3.3.1 Risk factors for surgical site infections

It is important to note that there are many risk factors for SSIs that influence their incidence. These factors include basic infection control measures, surgeon technique and experience, procedure duration, hospital environment, pre-operative preparation, perioperative management and patient factors (e.g., underlying medical conditions, age, previous infections/colonisations) (84-92). These factors can influence the classification of the surgical wound and subsequently the use of SAP.

The surgical wound classification (SWC) was developed by the United States Center for Disease Control and Prevention (CDC) (93, 94) to pre-emptively identify patients at risk of surgical site infection and provide a rationale for the use of SAP. While all surgical procedures may carry a risk of SSIs, the extent and type of the SSI can vary. There are four classes: 1) Clean, 2) Clean-contaminated, 3) Contaminated, and 4) Dirty-Infected (93, 94).

The US 2013 Clinical practice guidelines for antimicrobial prophylaxis in surgery (85) and the UK's National Institute for Health and Clinical Excellence (NICE) clinical guideline (95) for surgical site infections recommends that SAP be used in the following circumstances: clean surgery involving the placement of a prosthesis or implant; clean-contaminated surgery; and contaminated surgery. The use of antimicrobials for dirty procedures or where there is an established infection is classified as treatment rather than prophylaxis. It is not recommended routinely for clean non-prosthetic or uncomplicated surgery (85, 95). In Australia, the *TG: Antibiotic* recommendation for surgical prophylaxis (56) does not explicitly refer to

the above definitions but highlights the importance of using SAP only if there is a significant risk of post-operative infections, or if there would be serious consequences if such an infection were to occur.

Counter to this rationale for SAP, in a review of meta-analyses examining 21 different surgical procedures, Bowater *et al.* (96) postulated that SAP is universally associated with reduced incidence of SSIs, regardless of surgery type or wound classification. All surgical procedures carry some form of risk for SSIs, and, therefore, it is reasonable to assume that the administration of SAP would reduce that risk. However, a limitation of such a review is that for each surgical procedure, the risk type or pathogens and the type of SAP vary. Along with the other external factors previously described, the risk reduction can vary. Additionally, this review lacked an assessment of publication bias.

An overall blanket endorsement of SAP for all procedures would not only drive unnecessary use but also increase the risk of CDI, other HAIs, allergies and toxicities that are associated with antimicrobial use (9, 11, 12, 30-33). In circumstances where antimicrobial use is not warranted, the use of antimicrobials is more likely to cause harm from unintended consequences such as adverse effects and development of resistance. Antimicrobial overuse and inappropriate use contribute to antimicrobial resistance (97), thus efforts should be made to rationalise antimicrobial use. This applies to SAP, and encouraging unjustified antimicrobial use for SAP would not be appropriate.

Therefore, factors that influence decision-making about SAP include the efficacy of SAP as an SSI prevention measure, the clinical indication for SAP and the risks associated with antimicrobial use (both to the patient and globally in terms of AMR).

3.3.2 Classification, incidence and impact of surgical site infections

The United States Center for Disease Control and Prevention (CDC) define surgical site infections as:

“infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure or within 90 days if prosthetic material is implanted at surgery” (94).

SSIs are classified as superficial, deep, or organ/space as per the CDC National Healthcare Safety Networks (NHSNs) criteria (93, 94).

The incidence and impact of SSIs on both the patient and healthcare system are significant (98-101), thus warranting their prevention via appropriate SAP.

SSIs occur after 2-13% of procedures in Australia and vary according to the surgical procedure performed (75-77). Of these SSI cases, approximately half were considered preventable (102, 103). The costs associated with SSIs have been estimated as \$268 million per annum in Australia (76). Point-prevalence surveys on HAIs across the UK and Europe have found similar rates of SSIs, which accounted for 15.7% (England) (104), 18.6% (Scotland) (105) and 19.6% (Europe) (106) of all HAIs.

The type of surgical procedure performed will influence the risk of SSIs. Colorectal SSI rates are consistently ranked as one of the highest SSI rates per surgical procedure (5-30%) (107-109). These higher rates may be explained by the nature of the procedure as colorectal procedures are considered contaminated surgeries (78, 109).

SSIs are currently the most common and most costly HAI in the US (110). In 2013, a meta-analysis of costs and financial impact of five HAIs in the US found SSIs the 3rd most costly HAI on a per case-basis (\$20785 USD) (111). However, in terms of total annual costs of all five infections (\$9.8billion, 95%CI, \$8.3-1.5billion USD), SSIs contributed the most to this overall cost with 33.7% (~\$3.3billion USD) (111).

These increased costs of SSIs are largely based on increased length of stay (LOS) and attributable hospitalisation costs. Thus, SAP has a very large role to play in the reduction of SSIs and its consequences, including costs and patient outcomes.

Attributable hospitalisation costs of SSIs were found to increase in parallel with the LOS (78). There are many attributable costs of SSIs in addition to LOS costs, but these will vary according to the type of procedure and pathogens (110). Therefore, the true costing of SSIs' economic burden is a complex issue. Despite this, the current literature recognises that SSIs have a significant financial impact on both patients and the healthcare system.

3.4 Evidence-based medicine and surgical antimicrobial prophylaxis guidelines

Patients deserve optimal health services that are based on the best available evidence. Evidence-based clinical practice guidelines are one aspect of such services and have the potential to improve healthcare processes and patient outcomes (112). A systematic review of effectiveness and efficacy of guideline dissemination and implementation strategies found that 86.6% of the 235 studies reviewed had observed improvements in care (113).

Evidence-based medicine as defined by Sackett *et al.* is the '*conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients*' (114). Evidence-based medicine requires the combination of practitioners' individual clinical expertise with the best available external clinical evidence. Use of either alone is insufficient and creates gaps in the provision of optimal healthcare. Grimshaw *et al.* (115) suggest that the basic unit of knowledge translation should usually be up-to-date systematic reviews or other syntheses of research findings.

Clinical-based practice guidelines ideally consist of two key components; a foundation of evidence in the form of a systematic review; and recommendations that are extrapolated from the former in combination with expert opinion to account for context (116). The *TG: Antibiotic* (56) is the key clinical guideline regarding antimicrobial use in Australia. Multiple international guidelines regarding SAP prescribing and SSI prevention also exist and complement the general Australian

recommendations (81, 82, 85, 117-119). A comparative summary of the broad recommendations between these guidelines is presented in the following section.

3.5 Principles of surgical antimicrobial prophylaxis

SAP prescribing is complex and involves multiple principles. These principles pertain to elements such as indication, antimicrobial choice, dose, route of administration, timing of administration and duration. When SAP guidelines are developed, they are commonly structured around these principles (56, 85, 117). Additionally, when SAP prescriptions are assessed for appropriateness, these elements are common data points and are accounted for in appropriateness and compliance assessments (1-8).

The strength of evidence for SAP efficacy varies greatly by procedure type. Thus, no one uniform regimen can be recommended. This leads to an extensive range of guidelines, which may be difficult for physicians to use in actual practice as multiple variables can influence uptake (120, 121).

Table 3 provides a summary of the Australian and International guidelines recommendations in relation to these key prescribing principles.

Table 3 Summary of Australian and international guideline recommendations for the principles of surgical antimicrobial prophylaxis

Guideline – Author [Country]	Evidence Review Methodology	Principles of SAP Prescribing			
		Indication	Antimicrobial, Dose and Route	Timing	Duration
<i>Therapeutic Guidelines:</i> <i>Antibiotic – Antibiotic Expert Group (56)</i> [Australia]	- Expert consensus review - No grading of evidence	- Specific to procedure groups - Generally, indicated if: = significant risk of post-operative infection = post-operative infection has serious consequences.	<u>Antimicrobial:</u> - Cefazolin is preferred drug for the majority of procedures. - Avoid using broad-spectrum antimicrobials. - Modified according to patient and environmental factors. <u>Route:</u> - Almost always intravenous (IV).	- Short-acting antimicrobials (i.e., cefazolin); administered no more than 60 minutes before surgical incision. - Longer-acting, antimicrobials (i.e., vancomycin) administered no more than 120 minutes before surgical incision. - Vancomycin requires a slow infusion but surgical incision can occur before the	- Single-dose (i.e., no post-operative doses) for the vast majority of clean and clean–contaminated procedures. - Post-operative SAP doses can be considered (IV or oral) but should not continue beyond 24 hours for the following: cardiac, total knee arthroplasty, extensive neck dissection for malignancy, debulking or reconstructive surgery for head/neck malignancy, laryngectomy, and breast reconstruction or augmentation surgery. - Applying antimicrobials (e.g.,

				infusion is completed.	ointments, solutions, powders) to the surgical incision to prevent SSIs are not recommended.
<i>Clinical practice guidelines for antimicrobial prophylaxis in surgery – Bratzler et al. (85) [United States]</i>	- Expert consensus - Levels of evidence and recommendations graded as per American Society of Hospital Pharmacists guideline recommendations (122)	Specific to procedure groups (refer to guideline).	<u>Antimicrobial:</u> - For most procedures, cefazolin is the drug of choice. - Active against the most common surgical-site pathogens. - Narrowest spectrum of activity required for efficacy <u>Route:</u> - For a majority of procedures IV is preferred	- Within 60 minutes before surgical incision. - Timed to provide serum and tissue concentrations exceeding the minimum inhibitory concentration at time of incision, and for procedure duration.	- Post-operative SAP is not necessary for most procedures. - Duration should be less than 24 hours for most procedures.
<i>Antibiotic prophylaxis in surgery – Scottish</i>	- Expert consensus from guideline development and	Specific to procedure groups (refer to	<u>Antimicrobial:</u> - Must cover the expected pathogens for	- Within 60 minutes before skin incision and as close to time of	- Single dose of SAP with a long enough half-life to achieve activity throughout the operation is

Intercollegiate Guidelines Network (117) [Scotland]	review groups, specialist and editorial review.	guideline).	operative site. - Narrow spectrum, less expensive antimicrobials preferred <u>Route:</u> - Intravenous	incision as practically possible. - Vancomycin IV infusions should start 90 minutes prior to skin incision.	recommended. - Up to 24 hours of SAP should be considered for arthroplasty.
<i>New WHO recommendations on preoperative measures (81) and intraoperative and post-operative measures (82) for surgical site infection prevention: an evidence-based global perspective – Allegranzi et al. (81, 82) [World Health</i>	- Adoption of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methods (123). - Expert panel review for recommendation development.	No comment	No comment	Administration of SAP (depending on the type of operation) within the 120 min before the incision, while considering the half-life of the antimicrobial.	Recommends against the prolongation of SAP administration after completion of the operation for the purpose of preventing SSIs

Organisation, Switzerland]					
<i>Centers for Disease Control and Prevention guideline for the prevention of surgical site infection – Berríos-Torres et al. (118) [United States]</i>	Modified GRADE for evaluating evidence quality and determining the strength of recommendations (124, 125).	Administer SAP only when indicated based on published clinical practice guidelines	No comment	- Timed for establishment of bactericidal concentration of the agent in the serum and tissues when the incision is made - No further refinement of timing can be made for preoperative antimicrobial agents based on clinical outcomes.	For clean and clean-contaminated procedures; no additional SAP doses after the surgical incision is closed in the operating room, even in the presence of a drain.
<i>Surgical site infections: prevention and</i>	- Committee consensus review - GRADE	- Clean surgery involving the placement of a	<u>Choice:</u> - Use local antimicrobial formulary	- Single dose of SAP intravenously on starting anaesthesia.	- Do not use topical antimicrobial agents for surgical wounds that are healing by primary intention

<i>treatment</i> – National Institute for Health and Clinical Excellence (NICE) (119) [United Kingdom]	methodology - Guideline development as per NICE manual (126).	prosthesis or implant - Clean- contaminated surgery - Contaminated surgery.	- Consider potential adverse effects	- Give a repeat dose of SAP when the operation is longer than the half- life of the antimicrobial given.	to reduce the risk of surgical site infection. - Single dose peri-operatively and no comment specifically referring to post-operative SAP.
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3.6 Adaptation of SAP principles for primary care

3.6.1 Synopsis

The general principles of SAP prescribing also apply outside the acute setting and in primary care. Current practice allows general practitioners (GPs) to complete minor procedures, the majority of which do not require SAP (127). The *General practice activity in Australia report (2015-2016)* (128) reviewed the Medical Benefits Scheme general practice service items claimed for 965 GPs over a one-year period. It reported 97,398 encounters with 150,279 'problems managed'. Procedural treatments accounted for 17.6% of all GP encounters and 11.4% of all problems managed (128). Over half of these procedural treatments were excisions (17.4%), local injections (14.5%) and dressings (14.4%). Rates of SAP use and appropriateness across these encounters are not clear.

Access to and compliance with the *TG: Antibiotic* are not mandatory for GPs. Auditing of antimicrobial use in Australian general practice is currently being undertaken by NCAS researchers who have adapted the Hospital NAPS to develop a General Practice NAPS. A report of the pilot study is pending.

Review of patients post-operatively and management of post-operative wounds commonly occur in the general practice setting (129). Patients may be discharged after their surgical procedures with post-operative SAP and then require follow-up with their GP. Upon iterative review, it was identified that the principles for SAP in theory remained the same for acute and primary care but did require adaptation. A

manuscript was prepared and tailored to suit a GP readership about how GPs can apply these principles to optimise their SAP prescribing and the importance of their roles in AMS, surgical site infections and wound management.

3.6.2 Published Manuscript: Surgical antimicrobial prophylaxis

Surgical antimicrobial prophylaxis

SUMMARY

Surgical antimicrobial prophylaxis is the most common indication for antimicrobial use in Australian hospitals. However, it is associated with high rates of inappropriate use.

Effective use of antimicrobials to prevent infection is essential to reduce risks associated with surgical procedures. Efforts need to be made to maximise the quality of surgical antimicrobial prophylaxis prescribing.

Procedural prophylaxis (before or during surgery) is not indicated for all surgeries, especially minor procedures. Post-procedural prophylaxis, including the use of topical antimicrobials, is rarely indicated yet frequently prescribed.

The Therapeutic Guidelines: Antibiotic is a key reference for all Australian prescribers.

GPs can have a significant role in optimising surgical antimicrobial prophylaxis and reducing the burden of inappropriate antimicrobial use.

Introduction

Surgical antimicrobial prophylaxis refers to the use of antibiotics for the prevention of surgical site infections,¹ and does not include preoperative decolonisation or treatment of established infections. It is the most common indication for antimicrobial use in Australian hospitals. However, 40% of prescriptions were found to be inappropriate in the 2015 National Antimicrobial Prescribing Survey, which analysed 22 021 prescriptions from 281 hospitals.² Inappropriate use, such as extended duration of surgical prophylaxis (e.g. 5 days of cefalexin at discharge), contributes to the overall burden of antibiotic use in the community and exposes patients to adverse reactions and *Clostridium difficile* infections.

Optimal prescribing in surgical prophylaxis is ideally concordant with the Therapeutic Guidelines: Antibiotic³ or local guidelines (as endorsed by the Antimicrobial Stewardship Clinical Care Standard).⁴ Prescribing of prophylaxis occurs in acute and primary care. However, current data on the extent of prescribing in primary care are lacking.

Antimicrobial stewardship

Antimicrobial stewardship is defined as 'coordinated actions designed to promote and increase the appropriate use of antimicrobials',² and is considered an important strategy for the conservation of the effectiveness of antibiotics. Since 2011, it has been one of the compulsory criteria for hospital accreditation.⁵ Appropriate surgical antimicrobial prophylaxis prescribing is part of the national Antimicrobial Stewardship Clinical Care Standard, which was released in 2014.⁴ This standard was developed for hospital and

general practice prescribers and patients. Monitoring antimicrobial use and resistance is a requirement of the National Safety and Quality Health Service Standards.⁶

Significant improvement in prescribing practices (potentially attributable to antimicrobial stewardship programs) in hospitals has been observed by auditing tools such as the National Antimicrobial Prescribing Survey.² Despite identifying surgical antimicrobial prophylaxis prescriptions as a key area of concern, the 2015 Survey found a decline in the proportion of surgical prophylaxis prescriptions extending greater than 24 hours.² Further improvements are still required to meet the best-practice target of less than 5%.²

The 2016 Surgical National Antimicrobial Prescribing Survey solely focuses on surgical prophylaxis prescribing.⁷ Its results highlight ongoing concerns regarding inappropriate procedural and post-procedural prescribing (43.4% and 46.5% respectively) in Australian hospitals. Procedural prophylaxis was defined as any antimicrobial prescribed immediately before or during the surgery, while post-procedural prescribing refers to antimicrobials given after the procedure. Where guidelines were available, 41% of procedural and 62% of post-procedural prophylaxis was non-concordant with guidelines (see Table).⁷

Appropriate surgical antimicrobial prophylaxis

The key elements of appropriate surgical antimicrobial prophylaxis prescribing include the correct indication, antimicrobial, drug dose, route, timing of administration and duration.

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Table 2016 Surgical National Antimicrobial Prescribing Survey results

Key assessments	Procedural prophylaxis*	Post-procedural prophylaxis
Overall inappropriateness of prescribed antimicrobials	43.4% [†] (1384/3189)	46.5% [‡] (1032/2218)
Prescribed antimicrobials non-compliant with guidelines (where guidelines were available)	41% [†] (1211/2954)	62% [‡] (894/1442)
Surgical episodes where antimicrobial prophylaxis was prescribed but not indicated	10.6% (281/2641)	40.3% (503/1248)

* antimicrobials prescribed immediately before or during the surgical procedure

[†] procedural antimicrobials measured in doses

[‡] post-procedural antimicrobials measured in prescriptions (or courses)

Source: Reference 7

Right indication

All surgical procedures carry a risk of infection. However, the benefit of prescribing prophylaxis must be balanced against the potential risks of antimicrobial use, including allergic reactions, antibiotic-associated *C. difficile* and antibiotic resistance.

The 2016 Surgical National Antimicrobial Prescribing Survey found procedural antimicrobial prophylaxis was prescribed but not indicated in 10% of surgical procedures, and post-procedural prophylaxis was prescribed but not indicated in 40% of procedures (see Table).⁷

Prophylaxis is not indicated for clean non-prosthetic-associated procedures as defined by international guidelines.^{3,8,9} It is more likely to be indicated for procedures where:

- the incidence of surgical site infections tends to be high, for example, colorectal surgery
- the consequences of infection are significant, for example, surgery with implanted material such as arthroplasty and cardiac valve surgery.

Overall, there is insufficient evidence to support surgical prophylaxis for minor procedures, and prophylaxis in general practice is usually not warranted.^{3,9-11} If a patient has an associated infection (e.g. ingrown toenail, or abscess with cellulitis), an appropriate course of antibiotics should be given but this would not be considered prophylaxis. Key practice points for prescribing appropriate surgical antimicrobial prophylaxis in primary care are listed in the Box.

For dental procedures, guidelines recommend that antimicrobial prophylaxis may be appropriate for surgery in immunocompromised patients, and for surgical removal of a bone-impacted tooth or periapical surgery in a patient with a history of recurrent infections.^{3,8,12}

Box Best-practice surgical antimicrobial prophylaxis in general practice

Do not prescribe surgical antimicrobial prophylaxis without an appropriate indication

Avoid topical antimicrobials for surgical procedures

Use the eTG for specific information regarding optimal drug, dose, route and timing³

Query long-term use of post-procedural antibiotics with the initial prescriber or surgical team

Avoid prescribing ongoing supply of topical and oral antimicrobials without a clear indication from the initial prescriber

Monitor for surgical complications such as superficial, deep and organ space infections, and discuss with the surgeon or treating hospital

The presence of catheters or surgical drains is not an appropriate indication for prolonging surgical prophylaxis.¹³ This use is not supported by current evidence and may increase the risk of adverse events associated with antimicrobial use.⁸

Right antimicrobial

The choice of antimicrobial is ultimately influenced by the surgical procedure and associated risk factors. It should provide coverage of the expected microbiological flora at the incision site.¹⁴ This is further influenced by multiple patient-specific risk factors including:

- pre-existing infection
- recent antimicrobial use
- known colonisation with a resistant organism
- prolonged hospitalisation
- prostheses
- weight¹⁵⁻¹⁷

- renal function
- allergy status
- comorbidities
- immunosuppression.

For the majority of procedures, a first-generation cephalosporin, such as cefazolin, remains the preferred antimicrobial for prophylaxis.^{3,14,18} Uptake of this recommendation was shown across current Australian practice in the 2016 Surgical National Antimicrobial Prescribing Survey, with cefazolin being the most commonly prescribed antimicrobial for procedural (69%) and post-procedural prophylaxis (57%). However, 50% of the post-procedural cefazolin prescribing was deemed inappropriate.⁷

Right dose

When indicated, a single defined dose of antibiotic(s), for example, 2 g intravenous cefazolin, is sufficient for most procedures.^{3,14} This dose may be influenced by patient-related risk factors such as age, renal function and weight.¹⁵⁻¹⁷

Right route of administration

Parenteral administration (intravenous or intramuscular) is the preferred route for surgical antimicrobial prophylaxis. However, there are exceptions, including intracameral use for ophthalmic procedures,^{3,19} oral antibiotics for transurethral resections of the prostate³ and surgical terminations of pregnancy,^{3,20} and oral amoxicillin before certain dental procedures for endocarditis prophylaxis.^{3,12,21}

Within the acute setting, the 2016 Surgical National Antimicrobial Prescribing Survey identified intravenous administration as the most common route for procedural (94.2%) and post-procedural antimicrobials (64.5%). Oral administration accounted for 20.4% of post-procedural antimicrobials, however only 18.4% of oral administrations were deemed appropriate.⁷

Topical prophylaxis

Overall, there are conflicting data regarding the benefits of topical antimicrobial prophylaxis,²² and it is currently not indicated for most wounds, especially those resulting from clean procedures. The most recently updated Centers for Disease Control and Prevention guidelines for the prevention of surgical site infections also advise against the application of topical prophylaxis.⁸ Despite insufficient evidence, antibiotic ointments and creams are frequently used for topical prophylaxis.²³

Antimicrobial prophylaxis should not be used as a stopgap for inadequate infection prevention measures. Similarly, topical prophylaxis should not be a substitute for good surgical closure technique and

dressing management, particularly in cases where wounds are hard to seal and dress.

The most recent Cochrane review proposes that topical prophylaxis 'probably' prevents surgical site infections when compared to antiseptics or no topical antibiotic use.²⁴ However, when comparing topical antibiotics to no topical antibiotic use, the number needed to treat for one additional beneficial outcome was 50. It is important to note that this Cochrane review of trials from 1967 to 2014 found a considerably high risk of bias. The authors could not draw conclusions regarding the influence of topical antibiotics on antibiotic resistance and wound healing.

An earlier review on topical prophylaxis in dermatological procedures concluded that there was no significant difference between topical antimicrobials and petrolatum or paraffin for postsurgical wound infections.²⁵ An Australian study found that topical chloramphenicol for high-risk suture wounds produced only a moderate absolute reduction in infection rate that was statistically but not clinically significant.²⁶ An earlier Australian randomised controlled trial including 1801 surgical wounds found no significant benefit from mupirocin or paraffin ointments before occlusive dressings when compared to no ointment use.²⁷

Antimicrobial resistance

High use of topical prophylaxis may increase the risk of antimicrobial resistance. A New Zealand study has correlated increasing use of topical fusidic acid with a rapid clonal expansion of fusidic acid-resistant *Staphylococcus aureus*.²⁸

Topical mupirocin is commonly indicated for decolonisation of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA). Increased use has been associated with 'emergence of resistance through enhanced selective pressure and cross-transmission'.²⁹ A Korean drug utilisation review found an increase in mupirocin consumption correlated with increases of low- and high-level mupirocin resistance in MRSA infections.³⁰

Unrestricted use of mupirocin, in particular for wounds and pressure sores, is strongly associated with increased resistance.²⁹ Fortunately, in Australia, mupirocin is a Schedule 4 prescription-only medicine so both GPs and hospital prescribers have a significant role in reducing its inappropriate use.

Right timing of administration

Appropriate surgical prophylaxis achieves antimicrobial serum and tissue concentrations that exceed the minimum inhibitory concentration for the most probable organisms at the surgical site during the procedure.¹⁴ Appropriate timing of antimicrobial administration is crucial to prevent effective surgical site infection.

ARTICLE

Surgical antimicrobial prophylaxis

Incorrect timing of prophylaxis before or during a procedure was the most common factor in inappropriate prescribing in the 2016 Surgical National Antimicrobial Prescribing Survey (45.7%).⁷

Most guidelines, including Therapeutic Guidelines: Antibiotic, recommend that preoperative intravenous antibiotics be given within 60 minutes of incision.^{3,8,14,31-34} More recently, the World Health Organization recommended administration within 120 minutes of incision.³⁵ For caesarean sections, evidence supports antimicrobial prophylaxis before cord clamping rather than afterwards.^{36,37}

Right duration

A single preoperative dose is adequate for the majority of procedures. Post-procedural doses of intravenous antibiotics (up to 24 hours) are only required in defined circumstances, such as some cardiac and vascular surgeries, and lower limb amputation.³⁸⁻⁴⁰

The 2016 Surgical National Antimicrobial Prescribing Survey found that incorrect duration was the most common factor in inappropriate post-procedural antimicrobial prescribing (73.7%).⁷ Prophylaxis should not extend beyond 24 hours, regardless of the surgical procedure. Intravenous and oral antibiotic prophylaxis offer no benefit beyond this period.³

Post-procedural antimicrobials may be initiated in the acute setting but can be reviewed and re-assessed during follow-up with the GP. It is essential that the surgical team clearly communicates with the GP about post-procedural antimicrobial use (usually in the discharge summary).

A recent retrospective cohort study included 1488 patients who received at least 24 hours of parenteral or oral antibiotic therapy. The study identified 20% (n=298) of these patients experienced at least one antibiotic-associated adverse event, and 20% (n=56) of those adverse events were associated with non-clinically indicated antibiotic regimens.⁴¹ The authors stated for every 10 additional days of antibiotic therapy, there was a 3% increased risk of adverse events.⁴¹

Conclusion

It is important that all prescribers conserve the usefulness of available antibiotics through the practice of appropriate antimicrobial prescribing. GPs and surgeons play a role in reducing inappropriate surgical antimicrobial prophylaxis by only prescribing prophylaxis when indicated.

Further research into surgical antimicrobial prophylaxis prescribing is warranted to tailor future antimicrobial stewardship interventions for these targeted areas and to ensure that there are appropriate guidelines tailored for general practice that are available at the point of care. ◀

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3.6.3 Summary

GPs have a significant role in optimising surgical antimicrobial prophylaxis and reducing the burden of inappropriate antimicrobial use. The key principles of SAP prescribing are relevant to both acute and primary care; however, SAP prescribing varies due to the differing levels of care undertaken and procedures performed in the two settings. Further research and auditing of surgical procedures in primary care will support greater understanding of current Australian practices.

3.7 Australian guidelines for surgical antimicrobial prophylaxis

The *TG: Antibiotic* (56) is a key guideline for the prescribing of antimicrobials in Australia and is endorsed by the ASCCS (46). National policies recommend that *TG: Antibiotic* be adopted or referred to in the development of Australian AMS programs.

There is an assumption that when clinicians prescribe according to clinical practice guidelines (CPG) such as the *TG: Antibiotic* (56), they are practicing evidence-based medicine. However, the two terms are not synonymous as CPGs can vary in quality (112, 130, 131). The *TG: Antibiotic* (56) guideline is an example of a CPG that must grapple with lower-quality evidence; due to this, its recommendations are developed via expert consensus review by the 'Antibiotics Expert Group'.

The guidelines are regularly reviewed every four years by the expert group. The expert group includes a range of medical experts in the field of infectious diseases, microbiology and surgery, who have acknowledged the inclusion of "evidence-poor"

recommendations within the guidelines (132). The guidelines were updated (Version 16 (56)) in April 2019 (mid-candidature). It should be noted that research and assessments conducted prior to this refer to Version 15 (57).

The quality of the current evidence may be perceived as questionable by prescribers, the end users of such guidelines, and thus influence their agreement and compliance with its recommendations. Despite this limitation, the guidelines are considered best-practice and previous versions received endorsement from peak national bodies (e.g., ASID, RACS and the Society of Hospital Pharmacists of Australia (SHPA)) (57). The most recent update, Version 16, notes the developers are no longer seeking guideline endorsements (56).

Optimal antimicrobial prescribing in Australia is considered to be prescribing that is compliant with the *TG: Antibiotic*. Therefore, utilisation of the *TG: Antibiotic* has become a key performance indicator for hospitals and a targeted area for AMS strategy development. However, guideline non-compliance continues to be observed (1-8).

A review of the current evidence base for SAP and its implications for the *TG: Antibiotic* current SAP recommendations has been published as part of this thesis (see section below, 3.8).

3.8 The evidence for surgical antimicrobial prophylaxis

3.8.1 Synopsis

The evidence base for SAP is vast and covers an extensive range of surgical procedures. A critical review of the current evidence was required in the early stages of this PhD to ensure I had a background level of understanding of the challenges associated with SAP research and how these impact on the Australian prescribing landscape. Ongoing review of the literature led to the publication of a discussion article that reviewed the current level-1 evidence for SAP across a range of common procedures and how these have been incorporated into the Australian *TG: Antibiotic surgical prophylaxis* recommendations (57).

3.8.2 Published Manuscript: Surgical antibiotic prophylaxis - the evidence and understanding its impact on consensus guidelines

The supplementary data published with this manuscript can be found in Appendix 2.



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Discussion paper

Surgical antibiotic prophylaxis – The evidence and understanding its impact on consensus guidelines

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Abstract *Background:* Surgical site infections are complications of surgical care that may be prevented with appropriate surgical antibiotic prophylaxis (SAP). SAP is the most common indication for antimicrobial use in Australian hospitals; however, it is associated with high rates of inappropriate use.

Inappropriate SAP is associated with adverse consequences for both the patient and the community. The underlying reasons for inappropriate use, however, are not well delineated. Potential factors include the quality of the evidence base regarding SAP use and available guidelines.

Methods: The literature review focused on research classified as having Level 1 evidence according to the National Health and Medical Research Council (NHMRC) evidence hierarchy. Findings were then compared to the current Australian recommended guidelines (Therapeutic Guideline: Antibiotic Surgical Prophylaxis).

Results: Overall, 50 systematic reviews (SR) and meta-analysis (MAs) were identified for the review. The evidence examined highlights that first-generation cephalosporins are the antimicrobial agents of choice and single-dose prophylaxis is effective for the majority of surgical procedures included in this review. There is limited evidence pertaining to a specific optimal antimicrobial, dosing and timing. Thus, there is no overarching Level 1 evidence combining all elements for an optimal SAP regimen (i.e., choice of agent, dose, route and duration) to support individual Therapeutic Guideline: Antibiotic recommendations, although there may be Level 1 evidence for the individual elements.

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Conclusions: Considerable evidence supports the use of SAP; however, there are gaps in the evidence behind recommendations for the most appropriate SAP regimen for different surgical procedures. Expert consensus guideline development aims to narrow these gaps, but guideline implementability and uptake are influenced by multiple factors including the comprehensiveness of the evidence. Further research is warranted to examine guideline implementability and uptake, and to identify problematic areas surrounding surgical prophylaxis prescribing.

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Highlights

- Surgical site infections are complications of surgical care that may be prevented with appropriate surgical antibiotic prophylaxis (SAP). SAP is the most common indication for antimicrobial use in Australian hospitals; however, it is associated with high rates of inappropriate use.
- Inappropriate SAP is associated with adverse consequences for both the patient and the community. The underlying reasons for inappropriate use, however, are not well delineated. Potential factors include the quality of the evidence base regarding SAP use and available guidelines.
- The evidence for SAP across a range of surgical procedures can vary in quality. Recommendations for SAP encompass multiple surgical procedures and combine many elements of antimicrobial prescribing, i.e., indication, antimicrobial agent, dose, route, timing and duration. The broad nature of these recommendations may reflect the lack of overall Level 1 evidence (per the National Health and Medical Research Council hierarchy). This may be a barrier to uptake of and compliance with guidelines such as *Therapeutic Guidelines: Antibiotic*.

Introduction

Surgical antibiotic prophylaxis (SAP) refers to the utilisation of antibiotics for the prevention of surgical site infections (SSIs) [1]. SSIs impact on both the patient and health care system through increased mortality and morbidity, prolonged hospital admission, reduced quality of life and additional financial costs for ongoing inpatient and outpatient treatment [2].

There is an extensive body of literature demonstrating the efficacy of SAP for the prevention of SSI [3–47]. Optimal use of antimicrobials in the operative setting includes prescribing the correct antimicrobial when indicated and adhering to the recommended drug dose, route and timing of administration, and duration [1,6,48]. The strength of the evidence for SAP efficacy varies greatly for different procedures and there is a wide range of guidelines available to assist clinical practice. The quality of the evidence behind these recommendations may influence prescriber perceptions, agreement with the guidelines, and their consequent prescribing behaviours [49–52].

In Australian hospitals and general practice, *Therapeutic Guidelines: Antibiotic (TG: Antibiotic)* [3] is the recommended guideline for the prescribing of antimicrobials, including SAP [53,54]. Guideline use is reinforced in the national *Antimicrobial Stewardship Clinical Care Standards* [55]. Based on data from the *National Antimicrobial Prescribing Survey (NAPS)* [56] and the *Surgical National Antimicrobial Prescribing Survey (SNAPS)* [57], SAP is the most common indication for antimicrobial use in Australian

hospitals, accounting for 15.5% of antimicrobial prescriptions [56]. Notably, prescriptions for SAP also have the highest rate of inappropriate use (40.5%) [56].

This discussion aims to explore the quality of the literature for SAP that informs the current *TG: Antibiotic Surgical Prophylaxis* [3] recommendations and identify potential gaps between the evidence and these recommendations.

Literature search

The literature review focused on research classified as having Level 1 evidence according to the National Health and Medical Research Council (NHMRC) evidence hierarchy [58]. Level 1 evidence includes systematic reviews (SR) and meta-analyses (MA) of randomised controlled trials (RCTs); this was extended to include SR/MAs that reviewed both RCTs and non-RCTs.

The review involved keyword searches of three electronic databases (MEDLINE, EMBASE and Google Scholar). Key search terms such as 'anti-bacterial agents', 'antibiotic prophylaxis', 'antimicrobial', 'antimicrobial prophylaxis', 'operation', 'postoperative complications', 'prophylaxis' and 'surgical wound infection' were used to focus the search on SAP for common surgical procedures. Further specific searches were conducted in relation to commonly performed surgical procedures in Australia [59], including cataract, orthopaedic, cardiac, colorectal, and obstetric and gynaecological procedures. Selection criteria included

Level 1 evidence-based research conducted in humans that examined the impact of SAP on SSIs and patient outcomes.

A manual search of the reference lists of identified articles and recent review articles was also conducted. Studies included in the review were published in English from January 1965 to June 2017. The *Therapeutic Guideline: Antibiotic Surgical Prophylaxis* [3] references were reviewed and a hand searching technique was applied to identify further literature.

Findings from the literature search were then compared to the current Australian recommended guidelines (*Therapeutic Guideline: Antibiotic Surgical Prophylaxis*) [3]. The current guidelines were then reviewed in relation to the presence or lack of Level 1 evidence across the multiple elements of antimicrobial prescribing, i.e., indication, dose, route, timing and duration [48].

Findings

Overall, 50 SR and MAs were identified for the review [9–47,60–70]. Appendix 1 summarises the characteristics of the included reviews. Reviews included were published

between 1990 and 2017. The majority of the reviews included RCTs only (94%). All RCTs and non-RCTs included in the reviews were published between 1965 and 2016. Eleven of the reviews included research published in the last five years (22%). Approximately 40% of these reviews were in relation to SAP for abdominal procedures (see Appendix 1).

Table 1 summarises the Level I evidence [58] for SAP efficacy, the primary literature sources and the evidence-based recommendations regarding some of the elements of SAP prescribing (antimicrobial agent and duration). Noted differences include arthroscopic procedures in which there was no Level 1 evidence to support a recommendation of SAP for SSI prevention (Table 1). With regard to cataract procedures, there was only one systematic review that exclusively included RCTs ($n = 4$ RCTs), and the evidence supported the specific use of intracameral (IC) cefuroxime as opposed to any other antimicrobial agent or route of administration (Table 1). The evidence also highlights that first-generation cephalosporins are the antimicrobial agents of choice and single-dose prophylaxis is effective for the majority of procedures included in this review.

Table 1 Summary of current level 1 evidence for surgical prophylaxis for various surgical procedures.

Surgery type	Level 1 evidence ^a for SAP efficacy in reducing SSIs	Primary literature sources	Evidence based antimicrobial agent	Evidence based effective duration
Cataract surgery	Yes	SR/MAs [9–11]	Intracameral cefuroxime	Single dose
Arthroplasty, hip & limb fractures	Yes	SR/MAs [12–17]	1st Gen Cephalosporin	Single dose
Arthroscopy	No	<Level 3 [72–78] Expert Opinion [79–81]	1st Gen Cephalosporin	Single dose
Spinal procedures	Yes	SR/MA [18]	1st Gen Cephalosporin	Single dose
Cardiac procedures	Yes	SR/MAs [19–22]	1st Gen Cephalosporin	24–48 h
Cardiac device insertion	Yes	SR/MA [23]	1st Gen Cephalosporin	Single dose
Appendicectomy	Yes	SR/MAs [24,25]	Aerobic (1st Gen Cephalosporin) + anaerobic cover	Single dose
Colorectal procedures	Yes	SR/MA [26]	Aerobic (1st Gen Cephalosporin) + anaerobic cover	Single dose
Laparoscopic cholecystectomy	Inconclusive ^d	SR/MAs [27,60–66]	1st Gen Cephalosporin	Single dose
Open cholecystectomy	Yes	SR/MA of biliary tract surgery [28]	1st Gen Cephalosporin	Single dose
Inguinal hernia repair	Inconclusive ^e	SR/MAs [29–32,67–70]	1st Gen Cephalosporin	Single dose
Termination of pregnancy	Yes	SR/MAs [33–35]	PO doxycycline	Single dose
Caesarean section	Yes	SR/MAs [36–41]	1st Gen Cephalosporin	Pre-cord clamp; single dose
Elective hysterectomy, abdominal hysterectomy (AH) & vaginal hysterectomy (VH)	Yes	SR/MAs [42–45]	1st Gen Cephalosporin + anaerobic cover for VH	Single dose
Vascular surgery ^b	Yes	SR/MA [46]	1st Gen Cephalosporin	Single dose
Plastic surgery ^c	Yes	SR/MA [47]	1st Gen Cephalosporin	Single dose

Abbreviations: SR = Systematic review; MA = Meta-analysis; IC = Intracameral; 1st Gen Cephalosporin = First generation cephalosporin e.g. cefazolin and cefalexin.

^a Level 1 Evidence: Evidence obtained from a systematic review of all relevant randomised controlled trials [58].

^b Peripheral arterial reconstruction.

^c Clean breast surgery and contaminated surgery of the hand or the head and neck.

^d Eight studies were included; one in support of SAP, six against SAP and one inconclusive.

^e Eight studies were included; four in support of SAP, three against SAP and one inconclusive.

Indication

Level 1 evidence demonstrates SAP reduces the incidence of SSIs for the following procedure types examined: cataract [9,11], arthroplasty, hip and limb fractures [12–16], spinal [18], cardiac [19–23,71], appendicectomy [24,25], colorectal [63–66], biliary procedures [28], surgical termination of pregnancy [33–35], caesarean sections [36–39,41], abdominal hysterectomy [43,44], vascular surgery (peripheral arterial reconstruction) [46], and plastic surgery [47] (Table 1).

Conflicting evidence for SAP efficacy was reported for laparoscopic cholecystectomy [27,60–66] and inguinal hernia repair [31,32,69,70]. The most recent Cochrane systematic review regarding inguinal hernia repairs [69] included 17 RCTs from 1973 to 2011 and noted a difference in infection rates between the prophylaxis and control groups of 3.1% and 4.5%, respectively (odds ratio [OR] 0.64, 95% CI 0.50–0.82) [69]. However, the authors reported that whilst there may be a benefit, the dataset was not strong enough to either recommend universal use or advise against its use [69]. Additional reviews published prior to [32,70] and after [29–31,67,68] this Cochrane review [69] have offered conflicting results due to differing methods of analysis and interpretation of the data [68] (see Table 1).

Antimicrobial agent

First-generation cephalosporins are the preferred class of antimicrobials for SAP and are supported by Level 1 evidence for the following surgical procedures: cataract [9,11], arthroplasty, hip and limb fractures [12,14,15], spinal [18], cardiac [19–23,71], and caesarean sections [36,37]. However, the superiority of one first-generation cephalosporin over another has not been demonstrated.

The Cochrane review of SAP for colorectal surgery included 260 RCTs with over 60 different antibiotics [26]. Multiple pooled analyses demonstrated that regimens with both anaerobic and aerobic coverage significantly reduced SSI rates when compared to either anaerobic coverage only (15 studies; RR: 0.44; 95% CI: 0.29–0.68; $P = 0.0002$) or aerobic coverage only (19 studies; RR: 0.47; 95% CI 0.31–0.71; $P = 0.0004$) [26]. There were no Level 1 studies demonstrating superiority of broad-spectrum monotherapy regimens using agents such as piperacillin–tazobactam and third- and fourth-generation cephalosporins [6,26] over dual-therapy regimens, i.e., the currently recommended cefazolin and metronidazole [3].

Timing of administration

Limited studies have assessed the optimal timing of administration. The exception to this is for caesarean procedures, where there are a number of studies examining this aspect of SAP prescribing [38–41]. Traditionally, SAP was withheld until after umbilical cord-clamping due to the potential risks of antibiotic transfer to the neonate and consequent impact on their unestablished gut flora [38]. However, the most recent Cochrane review noted there was a reduction in both endometritis (RR 0.54; 95% CI 0.36–0.79; high quality evidence) and wound infection (RR

0.59; 95% CI 0.44–0.81; high quality evidence) when intravenous SAP was given pre-operatively as opposed to after neonatal cord clamping [38].

Duration

Numerous reviews were unable to demonstrate that multiple doses were superior to single-dose SAP for a range of orthopaedic [13,14,16], abdominal [25,28], and gynaecological procedures [42].

There is limited evidence to support postoperative doses of intravenous antibiotics (up to 24 h) in defined circumstances, such as some cardiac and vascular surgeries [20,21,46,82]. The review by Stewart et al. [46] of SAP for peripheral arterial construction suggested no additional benefit when SAP was prolonged for more than 24 h (RR 1.28; 95% CI 0.82–1.98; $P = 0.28$) (Table 1).

Earlier literature promoting single-dose prophylaxis has been questioned in relation to cardiac surgery given its unique risks, i.e., longer length of surgical procedure, use of cardiopulmonary bypass and indwelling chest catheters, and the high rates of morbidity and mortality associated with sternal SSIs [21,83]. Level 1 evidence suggests extended SAP durations may be of benefit [20,21,84]. Mertz et al. [21] demonstrated SAP with a duration of greater than 24 h may be more efficacious than shorter regimens; and Lador et al. [20] proposed there may be a 'possible advantage' to prolonging SAP up to 48 h post-operatively.

Discussion

The evidence for surgical antibiotic prophylaxis

The majority of the published reviews demonstrated that SAP, when indicated, reduced the risk of SSIs [9,10,12–29,31–47]. Table 1 shows that the majority of the TG: Antibiotic recommendations, particularly regarding the class of antimicrobial agent and effective duration, are supported by some form of Level 1 evidence. Exceptions do exist, which points to the importance of consensus-based decision-making for guideline development. Whilst SRs and MAs provide the highest quality of evidence [58], they are inherently limited by the quality of the studies that they include. Statistical and clinical heterogeneity, in terms of study design, sample size, age of publication and inclusion/exclusion criteria, influence quality study. Unique to the topic of SAP, many SRs and MAs are clinically heterogeneous in terms of the antimicrobials examined and their dosing, formulation, administration time, dosing frequency and duration. Thus, these reviews cannot confirm the superiority of any one SAP regimen, and caution is required while interpreting their findings.

Consequently, there is no overall Level 1 evidence combining all elements for an optimal SAP regimen (i.e., choice of agent, dose, route and duration) to support individual TG: Antibiotic [3] recommendations, although there may be Level 1 evidence for the individual elements.

Earlier literature discussing and summarising SAP recommendations suggests there is insufficient evidence to propose an optimal detailed SAP regimen for any specific surgical procedure [85–87]. A recent review summarises

the current US consensus guidelines but does not discuss the evidence behind such recommendations [88]. Similarly, Munckhof [1] and Sartelli et al. [86] provide generalised and non-procedure-specific recommendations regarding key principles of SAP prescribing but do not discuss the quality of the evidence behind them.

With the example of SAP for hip and knee arthroplasty, due to the lack of RCT data demonstrating the superiority of an antimicrobial agent or duration, guidelines incorporate evidence from lower-level studies for antimicrobial choice [12,15,17,89–95] and preferred duration [13,14,16,17].

Antimicrobial agent and dose

An ideal antimicrobial agent provides coverage of the expected microbiological flora at the site of incision [6]. SRs and MAs have not been able to demonstrate the superiority of any one antibiotic or regimen. This is largely due to the clinical heterogeneity, in terms of the antimicrobial agents and regimens that were examined, of these reviews and the methodological flaws of the studies that were included [18,20,26]. First-generation cephalosporins remain the antimicrobial class of choice in national and international guidelines [5,6]. This is largely due to the lack of evidence for one antimicrobial over another [5,6]. Recommendations regarding the optimal antimicrobial agent are also influenced by pharmacokinetic principles, local availability and cost. Broad-spectrum monotherapy agents are widely discouraged due to the ongoing development of antimicrobial resistance [6].

Studies providing evidence regarding the dosage strength of antimicrobials were clinically heterogeneous throughout the literature examined. There is no Level 1 evidence supporting a specific dosage strength for any of the recommended antimicrobials for SAP. There is conflicting, lower-level evidence supporting the benefits of increased dosing of cefazolin in obesity [96–99]. Such evidence has been perceived as insufficient to change the current dosage recommendation of cefazolin 2 g [3].

Timing of administration and re-dosing

Effective surgical prophylaxis should achieve antimicrobial serum and tissue concentrations that exceed the minimum inhibitory concentration (MIC) for the most probable organisms at the surgical site for both the time of incision and duration of the procedure [6]. Our research reviewed the literature by surgical procedure, and found no Level 1 evidence to support an optimal time for SAP. In terms of SAP across multiple procedures, the literature regarding specific optimal surgical antimicrobial timing also remains inconclusive [4,7].

A recent World Health Organisation (WHO) SR of 13 observational studies (across a range of surgical procedures) noted that administration <120 min prior to incision is the optimal SAP administration timing, compared to >120 min (combined OR: 5.26; 95% CI: 3.29–8.39; moderate quality evidence) [4]. Furthermore, there was no significant difference in terms of SSI risk when comparing

other administration times (<60 min vs 60–120 min; and <30 min vs 30–60 min) [4].

Additionally, the recent WHO guidelines strongly recommended against prolonged surgical antimicrobial prophylaxis [100]. A MA of 69 RCTs found no difference in SSI incidence between a single dose of prophylaxis at the time of incision and continuing prophylaxis in the postoperative period (OR 0.89; 95% CI 0.77–1.03) [100].

Similarly, a MA of 21 RCTs ($n = 14,285$) was undertaken to inform the CDC guideline update [7] and demonstrated high GRADE [101] evidence that there was no benefit in continuing SAP after the wound is closed in the operating room (OR 1.19; 95% CI 0.94–1.50; $P = 0.15$) [7].

Thus, evidence suggests a single dose at the time of surgery is as effective as multiple post-operative courses and prophylaxis should not extend beyond 24 h, regardless of the surgical procedure.

Lower-level evidence for the re-dosing of SAP in prolonged procedures exists, but is also heterogeneous and dependent on the selected antimicrobial's half-life. Current guidelines [3,5,6] advocates re-dosing if the procedure's duration is longer than two half-lives of the antimicrobial [83,102–104], or if there is excessive blood loss [105,106]. The half-life of cefazolin in adults with normal renal function is 1.2–2.2 h, with a recommended redosing interval of four hours as per the American Society of Health-System Pharmacists' (ASHP) SAP guidelines [6].

Guidelines aim to bridge the gap between evidence and best-practice [107,108]. This discussion highlights that recommendations simply cannot always be derived from the highest levels of evidence and developers must also consider lower levels of evidence, pharmacokinetic principles and the Australian setting to make practical recommendations.

Consensus-based guidelines and methodologies

National and international infectious diseases guidelines utilise expert consensus methods for their recommendations [5,6,8,109–111]. Lee and colleagues analysed the overall quality of evidence of 41 of the Infectious Diseases Society of America (IDSA) guidelines [112]. Within the 41 guidelines, 4218 individual recommendations were identified and only 14% were classified as having Level 1 evidence, 31% as Level 2 and 55% as Level 3 evidence [112], as per the IDSA evidence-grading system [113]. Similar findings were reported in Khan et al. [114] analysis of 4182 recommendations from 42 current IDSA guidelines (14.8% Level 1, 29.7% Level 2 and 55.5% Level 3 evidence) [114].

The recently updated Centers for Disease Control and Prevention (CDC) guidelines for SSI prevention [7] provide evidence-based recommendations that are classified using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology, which provides a systematic and explicit approach to judging evidence quality [101]. The updated guidelines propose that a single dose of SAP prior to skin incision is required for clean and clean-contaminated procedures (Category IA—strong recommendation; high-quality evidence) [7].

The National Institute for Health and Clinical Excellence's (NICE) SSI guidelines also propose that SAP is only indicated for clean surgery involving placement of a

prosthesis or implant, clean-contaminated surgery and contaminated surgery [8]. The guidelines were developed from the NICE guideline development manual [115], which supports the use of a variety of research methods for guideline development.

Additionally, the ASHP SAP guidelines adopt the IDSA evidence-grading system and note that clean procedures (i.e., head and neck) that do not include the placement of a prosthesis or implant do not warrant SAP, as there is limited evidence to support its use (Strength of evidence = B) [6]. Thus, different guidelines [3,6–8] employing various methods have reached similar conclusions regarding the appropriate indications for SAP.

Lack of evidence and guideline disagreement as barriers to guideline uptake

Australian data suggest that SAP prescribing is being performed inappropriately and not in compliance with the current Australian guidelines [56,57]. Guideline non-compliant SAP prescribing occurs at a high rate, but even more so post-procedurally (62%, as compared to 41% for procedural SAP) [57]. The issue of guideline non-compliance is not unique to Australia and has been reported in many other countries [116–121]. However, the underlying reasons for such findings have not been clearly delineated.

The quality of SAP evidence, and subsequent guideline development, implementation and awareness, is one of many potential factors that influence appropriate SAP prescribing. Qualitative research has identified and highlighted social factors such as prescriber etiquette, the influence of professional hierarchy and fear of disapproval from colleagues that influence antibiotic decision-making for SAP [49,122–125]. This discussion, however, focuses on only one component, i.e., evidence quality and its application in the current guidelines.

A lack of overall Level I evidence for each current guideline recommendation may cause disagreement amongst prescribers and is a potential barrier to guideline uptake [49,50,52,107,108]. The included literature on SAP is broad and conflicting, across a range of surgical procedures. The evidence included in this discussion is predominantly based on historical studies, some dating as far back as 1965. Additionally, the literature includes an assessment of a range of antimicrobials [20,26], many of which are not available in Australia, and, therefore, not applicable to current Australian prescribers.

Other factors pertaining to surgical procedures that may further expand the gap between the evidence behind the Australian guidelines and actual practice include advances in surgical practice, lack of data describing the downstream consequences of antimicrobial use such as adverse effects [12,26,33,36–38] and the emergence of antimicrobial resistance, and study eligibility criteria that specifically exclude participants who are critically ill or at higher risk of SSIs, such as participants with diabetes mellitus, obesity, or procedures with known prolonged surgery durations [126–128].

Therefore, the guideline development process relies heavily upon expert consensus and requires developers to

critically examine the literature and factor in the aforementioned issues to provide concise recommendations that reflect the current evidence. When high-quality evidence is sparse, it is important that guideline developers provide some form of comment or recommendation, even if considered weak [129]. Transparency of evidence, regardless of its strength, is essential and facilitates guideline acceptance and subsequent uptake [130]. Similarly, transparency of how the recommendations were arrived at and made, i.e., what evidence was used, and what methods were employed, is of equal importance [52,130,131].

Limitations

The key limitation of this discussion paper is that it does not provide a complete overview of surgical prophylaxis for all surgical procedures. This review is non-systematic and does not aim to provide high-quality, evidence-based recommendations regarding SAP regimens. The expansive literature on this topic extends even further when one considers all the different surgical procedures. This review was based on a comparison of recommendations to Level I evidence only, as this is considered the highest standard of evidence [58]; thus, it is not an exhaustive review of all SAP literature.

Conclusions

SSIs are complications of surgical care that may be prevented with appropriate SAP. Considerable evidence supports the use of SAP; however, there are gaps in the evidence behind recommendations for the most appropriate SAP regimen for different surgical procedures. The aim of expert consensus discussions during guideline development is to narrow these gaps, but guideline implementability and uptake are influenced by multiple factors, including the comprehensiveness of the evidence. This discussion is not an appraisal of the guidelines but a summary of the evidence for SAP recommendations and how this may influence guideline acceptance and uptake.

Research in the form of guideline appraisals, assessment of implementability, and exploration of prescriber perceptions and behaviour may identify additional facilitators and barriers to guideline use, and inform future development, review and implementation strategies. These strategies would aim to enhance guideline compliance and improve antimicrobial use to optimise patient health care outcomes and reduce the impact of inappropriate use on the patient and the community, and on the development of antimicrobial resistance.

Ethical considerations

As this is a discussion paper, ethical approval is not required.

Authorship statement

CI – conducted data analysis, developed analysis plan, wrote analysis, drafted and revised paper.

TP – developed analysis plan, revised paper.

DA — developed analysis plan, revised paper.

AR — revised paper.

CM — revised paper.

KT — developed analysis plan, revised paper.

Conflicts of interest

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Appendix A. Supplementary data

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3.8.3 Summary

The findings from the published review suggest that the quality of the current evidence may be perceived as questionable by prescribers. Prescribers are the end users of such guidelines, and this may influence their agreement and compliance with guideline recommendations. This review provided direction for projects 1 and 5. Project 1 includes an assessment of guideline implementability, validity and strength of evidence behind the recommendations. Poor guideline compliance may reflect issues with validity. Project 5 aims to identify various perceptions about current SAP prescribing practices and guidelines, thus providing further insight into current SAP prescribing behaviour and facilitators and barriers of appropriate SAP prescribing, and inform potential AMS interventions.

3.9 Chapter summary

Antimicrobials are frequently prescribed inappropriately for SAP in Australia (1-8). AMS interventions have proven efficacy in improving antimicrobial use (31). An understanding of evidence and guidelines for SAP is required to support the development of Australian AMS interventions. Tailored interventions specifically for SAP are warranted and should address the key facilitators and barriers of optimal prescribing behaviour.

The uptake of guideline recommendations is a primary outcome measure in the AMS literature (31) and for Australian prescribing surveys such as the Hospital NAPS (1-3, 5-7) and Surgical NAPS (4, 8). Ongoing analysis of the Surgical NAPS dataset will form

projects 2, 3 and 4; and will illuminate current practices and trends in SAP prescribing in Australia. This will support the direction for targeted SAP interventions.

Chapter 4. Antimicrobial stewardship for surgical prophylaxis

4.1 Introduction

This literature review discusses current AMS interventions targeting the surgical setting and SAP, and identifies any potential gaps and solutions to optimise SAP.

4.2 Antimicrobial stewardship for surgical antimicrobial prophylaxis

Antimicrobial stewardship (AMS) services need to accommodate the needs of different settings (e.g., public vs. private; metropolitan vs. regional), as well as multiple targets for appropriate use (e.g., correct dose, indication and duration) (31, 133, 134). Table 1 provides a summary of issues around SAP prescribing as identified in the current literature. These issues may be considered as potential targets for future AMS interventions.

Table 1 Potential targets to optimise surgical antimicrobial prophylaxis

• Guideline compliance (1-8, 135-138). • Guideline awareness (135, 139, 140). • Guideline implementability (135, 140). • Documentation of administration time (1-8). • Documentation of indication (1-8, 138). • Duration of SAP (1-8, 137, 138, 141). • Social, cultural, organizational and behavioural factors influencing SAP i.e., prescribing etiquette (18-22, 140, 142-147).
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AMS interventions cover an array of domains within the field of antimicrobial use. The Australian Hospital NAPS (1-3, 5-7) and Surgical NAPS (4, 8) have demonstrated high levels of inappropriate SAP (39.5%) (7). Thus, specialised AMS interventions tailored to suit the context of the specialised and unique environment of the theatre and the highly specialised clinical staff (surgeons and anaesthetists) may be required. While most surgeons are aware of the problem of AMR, many underestimate its relevance to their own hospital and practice (148). AMS interventions involving collaboration and engagement with the surgical team may help to address this issue.

Table 2 highlights the eleven AMS interventions for SAP that were included in the most recent Cochrane review (31). The majority (9 of 11) of interventions were conducted as interrupted time series interventions (149-157), compared to two randomised controlled trials (158, 159).

Table 2 Surgical antimicrobial stewardship interventions as per the most recent Cochrane review

Audit and feedback (149-151, 153, 154).
Educational meetings with dissemination of guidelines (150, 151, 155, 158); antimicrobial policy (149, 152); educational materials (153, 154, 159) and evidence base (150).
Educational outreach by academic detailing (153, 158).
Physical reminders, e.g., posters and brochures (149, 153, 155, 159); electronic prompts (156, 157).
Restriction by expert approval (155).

(31)

4.2.1 Guideline implementation and dissemination

Common surgical AMS interventions adopt an educational approach; however, these interventions are only effective if knowledge of the guidelines and appropriate prescribing is the key driver for inappropriate prescribing. Qualitative evidence suggests there are additional barriers and facilitators relating to social and organisational constructs (18, 20, 160).

Australian prescribers are required to refer to the *TG: Antibiotic* surgical prophylaxis recommendations (per the national hospital standards established by the ACSQHC) or their locally developed practice guidelines (which should reference this key guideline resource) (46). Development of clinical practice guidelines (CPG) and their implementation and dissemination are examples of AMS interventions. In addition, the requirement to refer to and abide by these guidelines to meet hospital accreditation standards implies a level of restriction. Uptake of guidelines is a key outcome measure for appropriate SAP prescribing, thus critical appraisal of their implementability is warranted and forms the focus of project 1.

Implementability refers to the characteristics that predict the ease with which such guidelines and their recommendations are actually implemented (161). Therefore, when appraising CPGs, one must not only consider their quality but also their implementability.

The implementability of a guideline may influence the prescriber's capacity and opportunity to utilise such a resource. Difficulties arise when implementing

evidence-based guidelines into routine daily practice and attempts to do so have generated mixed results (113). One of the most consistent findings from clinical and health services research is that translating evidence into policy and practice is challenging (115). In attempts to address this, use of an implementation science methodology may promote the uptake of research findings (162), and thus maximise optimal health outcomes and minimise inappropriate care.

Guideline quality appraisal using the 'Appraisal of Guidelines For Research and Evaluation' (AGREE II) (163, 164) instrument highlights that many CPGs are generally of a lower quality, with notable room for improvement (112). While guideline quality is of high importance, it does not necessarily correlate with successful guideline implementation. Consequently, the implementation of CPGs varies immensely, and is influenced primarily by intrinsic guideline factors; for example, guideline ambiguity, incompleteness and inconsistency may reduce guideline implementability (161). Further, considerable time and resources are required for guideline development and implementation, and so it is unsurprising that guideline compliance is often poor.

Guideline implementability can be appraised utilising an internationally recognised and validated instrument known as the Guideline Implementability Appraisal (GLIA) (161). GLIA is an instrument designed to assess guideline implementability by 'systematically highlight[ing] barriers to implementation' (161). The GLIA tool consists of 9 dimensions that incorporate 31 questions. The dimensions account for factors that can facilitate or restrict a guideline's implementability and potential

uptake. The 9 dimensions include: global considerations, executability, decidability, validity, flexibility, effect on process of care, measurability, novelty/innovation, and computability (161). Current research supports utilisation of the GLIA instrument after guideline implementation to identify barriers and enablers influencing guideline uptake (165-167). To date, implementability assessments of SAP guidelines have not been published. **Chapter 7** presents the findings from project 1 of this study, an appraisal of the implementability of the *TG: Antibiotic surgical prophylaxis* recommendations with the GLIA instrument. **Chapter 11** also discusses issues of guideline implementability within the context of the qualitative research conducted in project 5.

4.2.2 Audit and feedback

Hospital audits have been conducted to assess SAP use, in terms of guideline compliance and appropriateness, both nationally (137, 168-172) and internationally (136, 138, 173-182). These audits have highlighted target areas for SAP interventions, such as incorrect pre-procedural timing of administration, broad-spectrum antimicrobial choice and prolonged SAP durations post-procedurally. Audits of SAP use are informative and should guide how feedback is provided to prescribers. Challenges around the timely delivery of feedback and how this can then inform the design and implementation of a targeted surgical AMS intervention remain.

Australian research

Further research on the contexts of SAP prescribing will help identify appropriate targets of surgical AMS interventions in Australia. The ongoing Surgical NAPS survey supports audit and feedback for SAP prescribing in Australia (4, 8). Analysis of the data collected from the Surgical NAPS enables identification of prescribing patterns across hospital services and surgical procedures, which can be used to tailor feedback provided to local hospitals and surgical specialties. Other publications utilising Hospital and Surgical NAPS data have highlighted potential targets for ongoing AMS interventions, including in regional and remote hospitals (183), and private hospitals (73), and settings such as cardiac and colorectal surgery (141).

International research

Large audits of SAP use have recently been reported internationally and highlight a range of factors influencing SAP prescribing. A large multicentre national (US) Veterans Health Administration retrospective cohort study examined 153,097 outpatient surgeries in the top five surgical specialties: general surgery, urology, ophthalmology, ear/nose/throat (ENT) surgery and orthopaedics (184). The authors aimed to determine if there was an association between facility type (and its complexity) to SAP prolongation, i.e., greater than 24 hours of incision closure (184). There were 7,712 outpatient surgeries with prolonged SAP (50.%) (184). This rate varied by facility type and surgical procedure, e.g., ENT procedures had higher rates of prolonged use in complex facilities such as hospital outpatient departments (HOPDs) in comparison to smaller ambulatory surgical centres (ASCs) (9.2% vs. 6.3%,

respectively, $p=0.01$) (184). Comparatively, general, orthopaedic and eye surgeries were associated with lower rates of prolonged SAP in HOPDs than ASCs. However, only general surgery was significantly lower (0.55% vs. 2.87%, respectively, $p<0.001$). The overall findings suggest that larger, more complex facilities were less likely to be associated with prolonged SAP durations, and this may be because they are more likely to have services that support evidence-based practice and guideline compliance, such as AMS teams, pharmacy reviews and policy interventions. The authors advocated that such services and policies should be adapted to lower complexity facilities with less resources to support ongoing quality improvement in patient care and safety.

A Chinese prospective multicentre survey including 14,525 clean and clean-contaminated surgical procedures examined adherence to the Chinese National Antibiotic Guidelines and identified that the following factors were independently associated with inappropriate SAP: age, hospital type, hospital size, surgical discipline and surgical duration (185).

Both Ou *et al.* (185) and Branch-Elliman *et al.* (184) successfully demonstrated associations between a range of factors and SAP appropriateness/guideline compliance through the use of multivariate logistic regressions. Recommendations were made to improve SAP prescribing. However, there was no discussion of how this audit data was then fed back to prescribers and whether this informed the design of further quality improvement projects. This limitation appears quite common in the current literature (174, 178, 186-188).

Vitrat *et al.* (189) described the failure of an audit and feedback model to improve SAP guideline compliance in a poster presentation at the International Conference on Prevention and Infection Control Convention in 2015. The authors audited 124 surgical interventions at a tertiary French hospital in 2013 at two scheduled time points (T1 and T2), presented the results to surgeons and anaesthetists with a focus on negative performance outcomes, and provided support to improve these gaps in care. One-year later, they performed an identical audit (56 interventions, T3) and analysis to assess the impact of the intervention. Overall guideline conformity was higher at T1 and T2 (both 60%), compared to 54% in T3. Guideline conformity in relation to timing of administration (within 30 minutes of incision) was lower post-feedback (30% T1 and T2 compared to 14% T3). However, all audits (T1, T2 and T3) revealed similar non-conformity to guidelines in regard to SAP duration, with 100% of all audited surgical interventions receiving SAP for greater than 24 hours. This study is limited by the small volume of SAP audited but highlights that audit and feedback alone may not be effective in improving the quality of SAP prescribing.

The Cochrane review of interventions for improving antimicrobial prescribing in hospitals identified that feedback as an intervention was included in 4 (17%) of 23 RCTs and 20 (47%) of 43 ITS studies involving enabling interventions. When this occurred, the adjusted effect increased (10.88; 95%CI: 7.16-19.32), with moderate-certainty evidence (31). It is important to note that none of the four RCTs included interventions that targeted SAP. However, five of the 20 included ITS studies that involved feedback strategies targeted SAP (150, 151, 153, 155, 156); these concluded that feedback was beneficial. Of note, there were only nine ITS studies targeting SAP

that were included in the Cochrane review (31). We consider the fact that audit and feedback has been found to be a beneficial intervention in ITS studies an important finding.

4.2.3 Information technology

There is increasing uptake of information technology (IT) in Australian healthcare. Therefore, the development of computerised decision support systems (CDSS) presents another avenue for AMS interventions. CDSS provides 'access to electronically stored knowledge that may aid patients, carers and service providers in healthcare decision-making' (190). The provision of clinically appropriate information to the user aims to reduce error and improve accuracy. Examples of CDSS include mobile applications containing guidelines, electronic prompts, electronic approval systems and automatic stop-orders.

A systematic review of 45 articles demonstrated that information technology (IT) interventions increased appropriate use of antimicrobials in the hospital setting (pooled RR: 1.49, 95%CI: 1.07–2.08) (191). The IT interventions were categorised into four main types: (1) stand-alone CDSSs, (2) decision support embedded within a hospital's electronic medical record (EMR) or computerised provider order entry system (CPOE), (3) computerised antimicrobial approval systems and (4) surveillance systems. However, due to heterogenous study design and outcome measures, the authors were unable to provide meaningful comparisons between the various IT interventions types (191). The authors concluded that although these IT interventions could improve antimicrobial prescribing, there is a need for ongoing

research, specifically '*high -equality, systematic multi-site comparative studies*' (191) to support hospital services with their decisions regarding which IT interventions are most effective and worth implementing in their institutions.

However, the systematic review only included three studies that looked at the use of IT interventions for SAP (Table 3); one of which did not demonstrate any SAP improvement, as the use of SAP was already deemed guideline compliant (192). Other non-antimicrobial measures were improved through the use of electronic decision support.

Table 3 Summary of studies targeting surgical antimicrobial prophylaxis that were included in Baysari *et al.* (191) systematic review

Author (year)	SAP Target/ Outcome Measure	Intervention	Key findings
Haynes <i>et al.</i> (193), 2011	Duration	Decision support with CPOE*/EMR**	Intervention hospital: Increased timely discontinuation of SAP (38.8% vs. 55.7% (p < 0.001). Control hospital: No significant change (55.9% vs. 56.9%).
May <i>et al.</i> (192), 2014	Choice of antimicrobial agent, Duration	Decision support with CPOE/EMR	No change in either appropriate choice of antimicrobial agent and duration. (100% pre and 100% post-intervention).
Evans <i>et al.</i> (194), 1990	Duration	Electronic surveillance system	Reduction in patients receiving excessive doses/duration (50% pre- vs. 44% post-intervention, p<0.001). Reduction in duration of excessive doses (4.7 days pre- vs. 2.9 days post-intervention, p<0.001).

*CPOE= computerised physician order entry

**EMR= Electronic medical record

The systematic review from Baysari *et al.* (191) included research up to March 2015. Most recently, Rittman *et al.* (195) published a systematic review of CDSS and their role in AMS. Of the 45 included studies, only 1 targeted SAP (196). Okumura *et al.* (196) conducted a cross-sectional study that evaluated the impact of CDSS to improve the use of cefazolin for SAP and the cost-savings associated with this improved use. The study was conducted over 12 years, 3 years pre-CDSS implementation and 9 years post-CDSS implementation. Prior to CDSS implementation, the cost of 84,283 cefazolin vials was USD 44,722.99. After the implementation of CDSS, there was a reduction in antimicrobial use from 6.31 defined daily doses/100 bed days to 2.15 ($p < 0.05$). The authors calculated that if CDSS had not been implemented, the cost of cefazolin may have reached USD 116 998.07, and, therefore, the intervention provided potential cost savings of USD 50,433.39 (196).

The benefits of developing and implementing 'point of care electronic prompts' (POCEPS) was also demonstrated by Schwann *et al.*'s (156) prospective observational study. The POCEP was developed to support compliance with the US Surgical Care Improvement Project core measure (SCIP 1) of timely SAP administration within 60 minutes of surgical incision, and was embedded in the hospital network's existing intra-operative automated anaesthesia information management system. A total of 19,744 procedures were included in the study; 9,127 pre-intervention and 10,617

post-intervention. The study demonstrated that implementation of the POCEP increased compliance with the SCIP1 indicator (62% pre-intervention to 92% post-intervention, $p<0.001$). Improvement in SAP timing was also associated with a reduction in SSI rates between the pre-intervention period (1.1%) and the initial post-intervention period of 6 months (0.8%, $p=0.004$), 12 months (0.7%, $p<0.001$) and 24 months (0.5%, $p<0.001$) (156).

Another US cohort before-and-after study examined the efficacy of a CDSS intervention that provided initial dosing recommendations for SAP and an intra-operative reminder for re-dosing of SAP (197). The use of CDSS for SAP was considered successful, with an improvement of 17.1% (5% CI: 8.1-26.1; $p<0.001$) for intra-operative redosing (51.4% pre-intervention vs. 68.5% post-intervention) (197). Jacques *et al.* (198) also reported a similar increase in intra-operative redosing following their CDSS intervention, a computerised prompt (20% pre-intervention vs. 58% post-intervention; $p<0.001$).

Implementation of a multidisciplinary program based on health technology improved SAP guideline adherence in a Spanish prospective pre-post study (199). The program was targeted at the orthopaedic department and consisted of three phases and multiple components:

1. Pre-intervention:

- a. development of a multidisciplinary team,
- b. updating of guidelines, and
- c. analysis of adherence to new recommendations;

2 Study intervention:

- a. embedding guideline recommendations in the computerised physician order entry (CPOE) system, with links to dose and renal function alerts,
- b. educational activities regarding evidence-based SAP practices, and
- c. pharmacy-led training sessions on CPOE use and alerts; and

3. Post-intervention:

- a. pharmacist-based patient care monitoring, and
- b. analysis of adherence to protocol recommendations in the post-intervention group (199).

A small sample size of 83 orthopaedic patients was included in the study (40 pre-intervention, 43 post-intervention). There was an improvement in overall guideline adherence in the intervention group (pre: 76.7% vs. post: 89.9%; $p=0.039$). When comparing individual components of the SAP recommendations, the intervention group consistently demonstrated an improvement in adherence, including in antimicrobial duration (75.0% vs. 97.7%), post-surgery dosage (55.0% vs. 76.7%) and timing of administration (57.5% vs. 72.1%). The intervention group also reported significantly less SSIs (3 vs. 0, $p>0.05$). The study also collected data on other outcome measures; the intervention group demonstrated a reduced length of stay (1 day) and reduction in 30-day readmissions by 15% ($p=0.038$) (199). The study is novel in its ability to describe the impact on the quality of SAP from a bundle of interventions that adopts a multi-faceted approach with a range of methods, incorporating information technology, auditing and education. In the era of electronic prescribing, the use of CPOE has many potential future applications, and

could be enhanced through being linked to CDSS regarding body-weight and renal function in real time.

4.2.4. Bundles of care and multi-faceted quality improvement programs

As discussed above, there are multiple types of AMS interventions that have been adopted across hospital inpatients, and for optimising surgical prophylaxis specifically. Evidence from the most recent Cochrane review highlights that most interventions are multifaceted; enabling interventions are more successful when paired with feedback (adjusted effect: 10.88; 95% CI: 7.16-19.32) and restrictive interventions (adjusted effect: 38.6; 95% CI: 18.94-57.78) (31).

The development and implementation of 'bundles of care' for the purposes of quality improvement of patient outcomes is becoming more widespread. Bundles of care are commonly developed to reduce surgical site infections; appropriate SAP is a common component and they have been shown to be effective (108, 200-204). However, the true efficacy of each individual component, such as appropriate SAP, cannot be defined, and thus it is important to acknowledge that AMS and infection prevention interventions cannot rely on one sole method and need a multifaceted approach.

A successfully implemented US multifaceted quality improvement program was recently described by O'Sullivan *et al.* (205). The program consisted of:

- development and implementation of intraoperative 'Antibiotic Administration Guide', developed and reviewed by pharmacy and the AMS committee;

- notification and education about the project for anaesthesia providers, surgeons, nurses and pharmacists;
- increased accessibility of the 'Antibiotic Administration Guide' in the hospitals electronic health record system;
- engagement with surgical service chiefs to ensure project support;
- electronic prompt/reminder on the anaesthesia record 15 minutes before the next scheduled antibiotic redosing time; and
- audit of the SAP redosing data and monthly reporting to hospital executives to facilitate peer accountability and feedback (205).

A total of 13,695 surgical procedures were included in the study. The authors conducted a time-series analysis that demonstrated that the program improved compliance of intra-operative re-dosing significantly (incidence rate ratio: 1.16; $p=0.002$) (205).

The New Zealand national orthopaedic surgical suite infection improvement program was first implemented in 2013 and promoted adherence to evidence-based practices to reduce SSIs (206). Over the years, there have been multiple changes to the SAP recommendations and guidelines, including a change from flucloxacillin and gentamicin back to a first-generation cephalosporin-based regimen in 2015. Morris *et al.* (207) examined if there was an association between SAP timing of administration and the rate of SSIs, and also if the updated recommendations in 2015 led to a change in practice. This research included 46,360 hip and knee arthroplasties from 1st July 2013 to 31st December 2017. The program adopted a

three-pronged approach including: 1) establishment of a nationwide surveillance system 2) implementation of practice change interventions; and 3) monitoring changed practices and their effects, and providing feedback (208).

Clindamycin was recommended over vancomycin for patients with a cephalosporin allergy as it was associated with better compliance of timing. The authors demonstrated that clindamycin was given on time 96% of the time (as opposed to 70% for vancomycin), and over time, the use of clindamycin increased from <50% to 75% ($p<0.0001$) (208). Overall, the authors demonstrated that when SAP was administered on time (<60 minutes of incision), as opposed to late or early, the SSI rate was significantly reduced (OR: 0.52; 95%CI 0.34-0.78, $p<0.003$) (208). In summary, a multifaceted quality improvement project that targeted appropriate SAP and linked these measures with clinically relevant outcome data such as SSI rates was found to be effective.

In Australia, there is no centralised, nationwide surgical site surveillance system. Recently, in May 2019, the NHMRC, in conjunction with the ACSQHC, published the '*Australian Guidelines for the Prevention and Control of Infection in Healthcare*' (209). The guideline details recommended evidence-based processes across pre-, intra- and post-operative settings, including for the use of SAP. However, the guidelines do not address the concept of a surgical bundle of care, which has previously demonstrated success in reducing SSIs nationally (108) and internationally (200-204, 206-208). The lack of recommendations regarding surgical bundles of care was also noted in a recent commentary on the new guidelines (210).

In summary, bundles of care facilitate a multi-faceted approach to improving quality of patient care, including in appropriateness of SAP prescribing. The development and tailoring of these systems to focus in greater detail on SAP recommendations and interventions, while including both auditing and feedback, will close the loop of interventions development and implementation, supported by evaluation, refinement and further interventions to improve SAP use and quality of care.

4.2.5. Use of behaviour change techniques and interventions for antimicrobial stewardship

AMS programs are developed to improve antimicrobial use and subsequently modify prescriber behaviour. Therefore, effective AMS strategies for SAP need to consider the relevant context of such behaviour and the adaptation of behaviour change interventions from other healthcare scenarios (211).

Davey *et al.* (211) conducted a systematic review to review existing applications of behaviour change techniques and interventions to improve antimicrobial prescribing in hospitals. Key techniques identified by the authors were goal-setting, self-monitoring, and feedback and action planning.

The review included 116 studies with 123 interventions. The use of behaviour change techniques in these interventions was described as poorly reported. Goals were set in all interventions; however, they were not considered to be specific. Self-monitoring was only reported in 0.8% (n=1) while action planning was reported in 2.4% (n=3). Comparatively, feedback was reported in 13.8% (n=17) interventions.

The authors recommend that future AMS intervention research should provide greater details on methods and refer to behaviour change techniques to enhance understanding of which behaviour change interventions are most appropriate to improving antimicrobial use in the hospital setting. This could then be used to better understand antimicrobial prescribing behaviour in the surgical setting and lead to the development of more appropriately targeted interventions for SAP stewardship.

The use of behaviour change interventions for antimicrobial prescribing was reported by Rawson *et al.* (212), who analysed 311 antimicrobial stewardship and resistance abstracts that were presented at major UK scientific research conferences in 2015. The interventions were categorised and mapped to the Behaviour Change Wheel framework (28). Only 18% (n=56) of antimicrobial stewardship and resistance abstracts described behaviour change interventions. Of these, 71 behaviour change functions were identified. The most commonly reported was the policy category of 'guidelines' (16/71), followed by 'service provision' (11/71) (212).

The lack of consideration of behavioural and social influences on the development of AMS interventions was also highlighted by Lorencatto *et al.* (213). The authors proposed four key areas where application of behavioural and social science can support the development of effective and sustained behaviour change in relation to antibiotic prescribing:

1. defining behavioural problems and their context,
2. adopting a theory-driven and systematic process for intervention design,
3. researching how to improve implementation and sustainability of interventions,

and

4. maximising learning by undertaking detailed intervention reporting to contribute to the growing body of evidence for behaviour change interventions (213).

There is increasing awareness of the importance of understanding prescribing behaviour for optimising AMS interventions. Rzewuska *et al.* (214) recently published a position paper on the need to prioritise behaviour in AMS research. Ten research topics were identified, three of which were considered to be specifically relevant to this doctoral research, in particular project 5 (b). These include:

- “ - Comprehensively identifying barriers and facilitators to implementing antimicrobial stewardship programs (ASP) and clinical recommendations intended to optimise antibiotic prescribing.*
- Identifying actors (‘who’) and actions (‘what needs to be done’) of ASPs and clinical teams.*
- Investigating the role and impact of government and policy contexts on ASPs” (214).*

4.3 Chapter summary

Antimicrobials are frequently prescribed inappropriately for SAP in Australia (1-8). AMS interventions have proven efficacy in improving antimicrobial use (31). An understanding of the Australian healthcare system, policies for AMS, evidence and guidelines for SAP, and the various aspects of decision-making and prescribing are required to support the development of an Australian AMS intervention. Interventions tailored to specifically suit the needs of surgical settings are required

and these should address the key facilitators and barriers of optimal prescribing behaviour. Qualitative studies, in particular those that are developed using theoretical frameworks, are effective in identifying such facilitators and barriers, and should ideally inform future surgical AMS interventions (18). Surgical AMS interventions should also align with such theoretical frameworks to ensure they target the relevant drivers of the prescribing behaviour they aim to improve (20).

Guideline implementability has been identified as a key area for review, as uptake of guideline recommendations is a primary outcome measure in the AMS literature (31) and Australian prescribing surveys such as the Hospital NAPS (1-3, 5-7) and Surgical NAPS (4, 8). An appraisal of the implementability of the *TG: Antibiotic surgical prophylaxis* recommendations will form the basis of project 1.

Ongoing analysis of the Surgical NAPS dataset will inform projects 2, 3 and 4, which will describe current practices and trends in SAP prescribing in Australia. This will support the identification of targeted SAP interventions.

The current literature also identifies a need for further research into the drivers of SAP prescribing behaviour (see 4.3.4). Theory-informed qualitative research undertaken in project 5 aims to provide context to the current state of SAP prescribing in Australia. Project 5 aims to inform the development of potential theory-informed and targeted AMS interventions to optimise SAP prescribing.

Chapter 5: Theories, models and frameworks

5.1 Introduction

This chapter describes the implementation science theories that have guided this research. As highlighted in **chapters 2, 3 and 4**, surgical antimicrobial prophylaxis (SAP) prescribing is an area of importance within the field of antimicrobial stewardship (AMS). Improved understanding of this phenomenon (SAP prescribing behaviour) is required, and this can be facilitated by the application of the theoretical models and frameworks described below. This chapter also describes a range of qualitative research that has been undertaken to identify factors influencing SAP prescribing. These factors have been mapped to the chosen framework for this thesis.

5.2 Rationale for theoretical models and frameworks

The issue of AMR is not only a biological problem but also a social one, shaped by many cultural, political, economic and environmental factors. Smith (215) suggests the way we, as the public and healthcare professionals, understand and value the use of antimicrobials is a key social influence on AMR. Such a social problem requires social solutions (215).

Antimicrobial prescribing and decision-making is a multifactorial process involving socio-cultural, environmental, organisational and behavioural influences. The Australian *Therapeutic Guidelines (TG: Antibiotic)* is the national clinical antimicrobial prescribing guideline recommended by the Australian Commission on Safety and

Quality in Health Care (ACSQHC), and provides recommendations for SAP prescribing (45, 46). Despite the development of these expert consensus-based and evidence-based guidelines, Australian data demonstrate high rates of inappropriate and guideline non-compliant SAP prescriptions (1-8). In order to improve this, improved understanding of the various underlying contexts and behaviours that are shaping current suboptimal decision-making and practices is required.

Systematic reviews of interventions and their implementation demonstrate that some interventions can be effective in changing healthcare professionals' clinical behaviour (216-219), but, as previously discussed, inconsistencies in reported efficacy exist, and this may be due to a multitude of factors, including a lack of theoretical ground, i.e., explanation of how and/or why the intervention works (220).

Charani *et al.* (20) conducted a systematic review of behaviour change strategies to influence antimicrobial prescribing in acute care. Five qualitative and five quantitative studies were included. The qualitative research demonstrated the impact of behavioural and social determinants on prescribing. Conversely, the quantitative research that reported interventions to optimise antimicrobial prescribing did not use implementation science theory to inform the design or choice of the interventions implemented. The authors concluded that to ensure a greater understanding of prescribing behaviours and to improve the quality of potential interventions, one should consider the application of behavioural and theoretical science theories (20).

The inclusion of theory-based assessment in interventions for behaviour change enables the identifications of barriers and facilitators of desired outcomes, thus assisting with intervention implementation and evaluation design (221). As noted by Charani *et al.*, such interventions have relevance to the field of AMS (21) and guideline implementability (57).

The Theoretical Domains Framework (TDF)(27) and the Capabilities, Opportunities and Motivators of Behavior (COM-B) model (which is a part of the Behaviour Change Wheel (BCW) (28, 29)) have been applied extensively across a range of clinical and non-clinical quality and behaviour change interventions (222-227) (see section 5.6). McIsaac and colleagues (228) suggested that combining the TDF and BCW delivered a stronger theoretical approach to implementation research.

Given its broad clinical application and linkage to additional models such as the BCW, the TDF was considered the most appropriate and relevant determinant framework to achieve the main aim of this thesis, i.e., to explore the underlying barriers and enablers of appropriate SAP prescribing behaviour.

The theories adopted across this research provide structure and clarity to the thesis design and data analysis (229, 230). Improvement in the implementation of clinical guidelines and SAP prescribing is dependent on prescriber behaviour change. Adopting the TDF and linked models (BCW) streamlines thematic analysis and enhances rigour. This combined methodology facilitates the identification of the issues (barriers and enablers of SAP prescribing) and then links this analysis to potential solutions, i.e., the development of a targeted stewardship intervention that

is theory-informed and more likely to be sustainable (which is a secondary aim of this thesis) (221, 231).

5.2 Utilisation of theories, models and frameworks

When resources such as clinical guidelines are developed to guide and support prescribing behaviour, the implementability of these resources can vary. Campbell and colleagues (232) proposed that applying theoretical models to behavioural change intervention development may improve the implementability and efficacy of interventions. Grimshaw and Eccles (233) also suggest that interventions targeting healthcare professionals' behaviour and organisational behaviour are more likely to be effective if they are grounded in behavioural theory.

Nilsen (234) proposed three key aims for adopting a theoretical approach in implementation science: describing/guiding the translation of research into practice; understanding/explaining influences on implementation outcomes; and implementation evaluation (Figure 1). Further to this, Nilsen described how different theories, models and frameworks may be applied to achieve these aims (Figure 1).

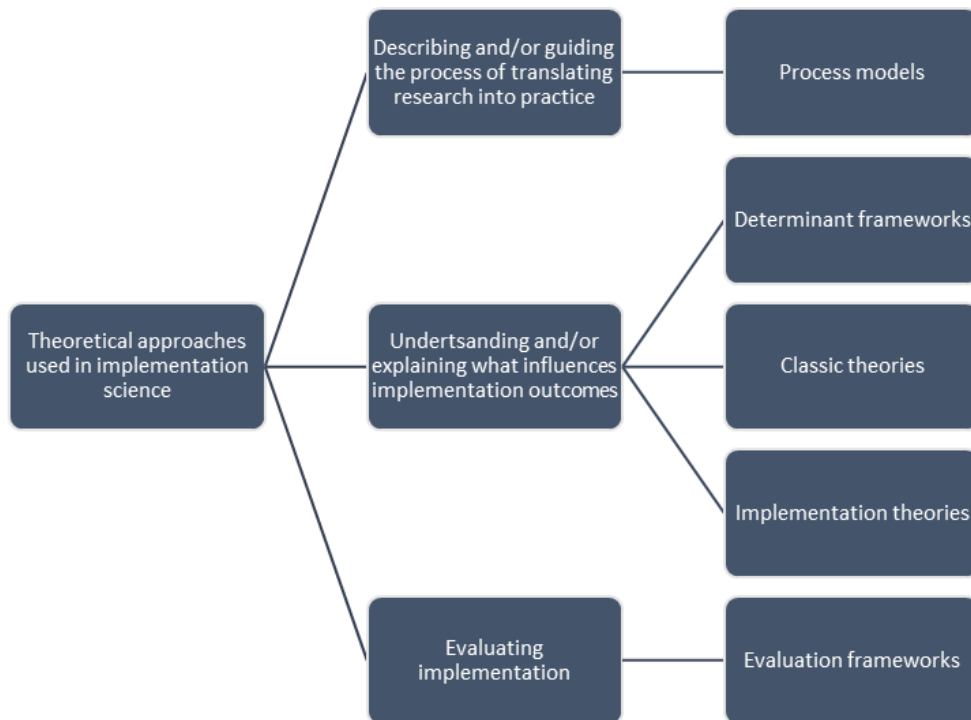


Figure 1 Three aims of the use of theoretical approaches in implementation science and the five categories of theories, models and frameworks. Adapted from Nilsen 2015 (234)

Using Nilsen’s formulation (234), the overarching aim of this thesis is to explore the underlying enablers and barriers to appropriate SAP prescribing. To achieve this aim, we need to better understand the underlying factors and behaviours that influence and determine SAP prescribing.

Nilsen (234) proposes that the use of determinant frameworks will facilitate this research. The TDF (27), COM-B Model and BCW are the chosen determinant frameworks (see Figure 1) that have guided the data collection and analysis components of the thesis.

5.3 Theoretical Domains Framework (TDF)

The TDF (27) provides a theoretical approach to behavioural change interventions. The framework was developed over six stages and was agreed upon via consensus from three expert groups: health psychology theorists, health services researchers and health psychologists (221). The theoretical constructs identified were considered to be useful for addressing two key objectives: ‘to study the implementation of evidence-based practice and to develop strategies for effective implementation’ (221). Lipworth *et al.* (235) conducted a thematic synthesis of fifty qualitative studies in which the TDF was found to be useful in the identification of barriers and enablers of clinical quality interventions (235).

The original TDF (221) underwent validation and refinement. The updated TDF (27) consists of 84 constructs, which are then categorised into 14 domains (Table 1). A systematic review comparing the degree of concordance between domains and constructs of both the original (2005) (221) and the updated TDF (2012) (27) included fifty publications, and the domain ‘environmental context and resources’ was identified as the most frequently assessed domain (n=42, 84%), followed by ‘beliefs about consequences’ (74%) and ‘social influences’ (66%). Comparatively, ‘reinforcement’ (12%) and ‘intention’ (14%) were the least commonly assessed domains.

Table 1 Theoretical Domains Framework domains and theoretical constructs (27)

Domain (definition)	Theoretical Constructs
1. Knowledge (An awareness of the existence of something)	- Knowledge (including knowledge of condition/scientific rationale) - Procedural knowledge - Knowledge of task environment
2. Skills (An ability or proficiency acquired through practice)	- Skills - Skills development - Competence - Ability - Interpersonal skills - Practice - Skill assessment
3. Social/professional role and identity (A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting)	- Professional identity - Professional role - Social identity - Identity - Professional boundaries - Professional confidence - Group identity - Leadership - Organisational commitment
4. Beliefs about capabilities (Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use)	- Self-confidence - Perceived competence - Self-efficacy - Perceived behavioural control - Beliefs - Self-esteem - Empowerment - Professional confidence
5. Optimism (The confidence that things will happen for the best or that desired goals will be	- Optimism - Pessimism - Unrealistic optimism

attained)	- Identity
6. Beliefs about Consequences (Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation)	- Beliefs - Outcome expectancies - Consequents - Characteristics of outcome expectancies - Anticipated regret
7. Reinforcement (Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus)	- Rewards (proximal/distal, valued/not valued, probable/improbable) - Incentives - Punishment - Consequents - Reinforcement - Contingencies - Sanctions
8. Intentions (A conscious decision to perform a behaviour or a resolve to act in a certain way)	- Stability of intentions - Stages of change model - Transtheoretical model and stages of change
9. Goals (Mental representations of outcomes or end states that an individual wants to achieve)	- Goals (distal/proximal) - Goal priority - Goals (autonomous/controlled) - Goal/target setting - Action planning - Implementation intention
10. Memory, attention and decision processes (The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives)	- Memory - Attention - Attention control - Decision making - Cognitive overload/tiredness
11. Environmental context and resources (Any circumstance of a person's situation or environment that discourages or	- Environmental stressors - Resources/material resources - Organisational culture/climate

encourages the development of skills and abilities, independence, social competence and adaptive behaviour)	- Salient events/critical incidents - Person × environment interaction - Barriers and facilitators
12. Social influences (Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours)	- Social pressure - Social norms - Group conformity - Social comparisons - Group norms - Social support - Power - Intergroup conflict - Alienation - Group identity - Modelling
13. Emotion (A complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event)	- Fear - Anxiety - Affect - Stress - Depression - Positive/negative affect - Burn-out
14. Behavioural regulation (Anything aimed at managing or changing objectively observed or measured actions)	- Self-monitoring - Breaking habit - Action planning

The TDF is useful for assessing barriers and enablers of behavioural change interventions. However, like any theoretical framework, it still has some challenges that must be overcome to enhance its application in the implementation of healthcare and clinical quality interventions. Phillips *et al.*'s (236) mixed-methods research examined the experiences, attitudes, and perspectives of ten health

professionals regarding their use of the TDF across a range of healthcare implementation projects. Three main themes highlighted were:

1. reasons for use: increased confidence, broader perspective, and theoretical underpinnings;
2. challenges using the TDF: time and resources, operationalisation of the TDF; and
3. future use of the TDF (236).

Phillips and colleagues argued that there was overwhelming support for the TDF and for future application of this framework (236). Formalised training and the adoption of practical guidelines for the TDF were recommended by participants to improve its use in future research (236). Further studies in which the TDF has been applied have since been published (222-227); some studies have also linked the TDF to the previously described Behaviour Change Wheel (inclusive of the COM-B model) (28) and the Behavior Change Technique Taxonomy (237).

The TDF domains may be interpreted as barriers or enablers of behaviour change and can inform the development of tailored strategies to influence the desired behaviour, i.e., optimal and evidence-based SAP prescribing.

5.4 The Capabilities, Opportunities, Motivators- Behaviour (COM-B) model and the Behaviour Change Wheel (BCW)

The Capabilities, Opportunities, Motivators-Behaviour (COM-B) model was developed as a simplified version of the TDF. The COM-B model identifies perceived

barriers and enablers of implementation for interventions and subsequent behaviour change. The COM-B model was developed by Michie *et al.* (28) via a systematic review of 19 frameworks for behaviour change interventions. The COM-B model categorises the complexity of behaviour into three domains: the physical and psychological 'capabilities' (C) of the individual; the social and environmental 'opportunities' (O) that facilitate or negate behaviour; and the reflective and automatic 'motivators' (M) that energise and direct behaviour (28).

Michie and colleagues (28) further identified nine intervention functions that link to the COM-B model and seven categories of policy that might enable such interventions. These components were then combined into one resource known as the 'Behaviour Change Wheel' (BCW) (28)(Figure 2). Reference to the BCW is inclusive of the COM-B model.

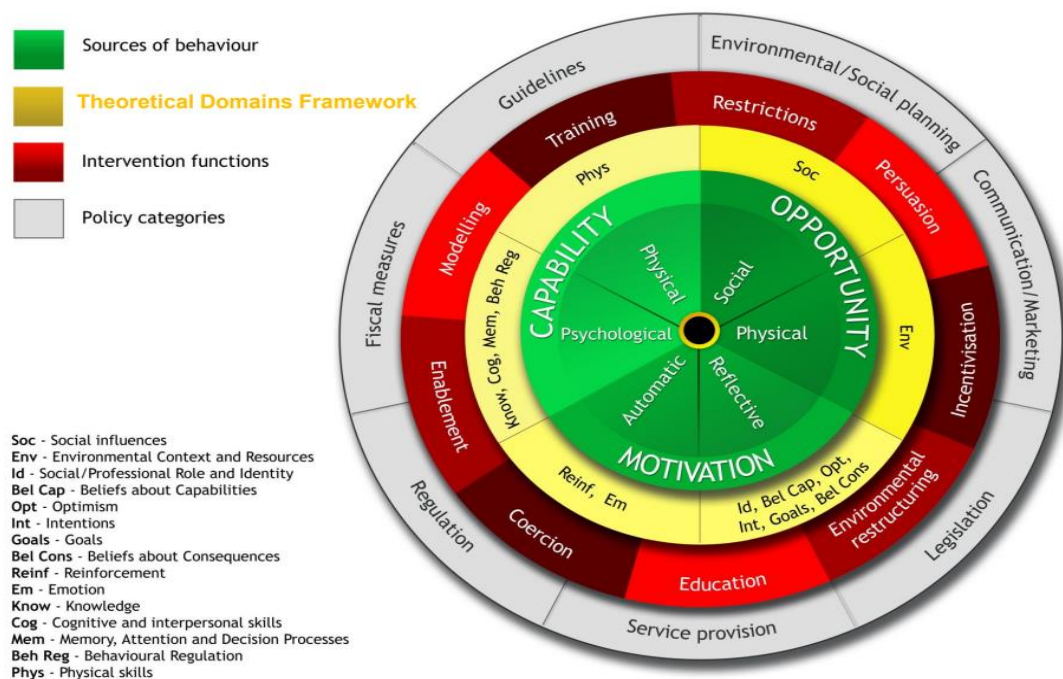


Figure 2 The Behaviour Change Wheel, COM-B model and Theoretical Domains Framework (TDF) domains. Reproduced with permission from Michie *et al.* (28, 29).

5.5 Mapping of the TDF to the BCW

The TDF domains have been linked to the BCW (and COM-B) as illustrated in Figure 2, and current literature (222-227). The BCW provides the foundations of a decision-making process that connects the underlying theory-driven behaviour to a theory-inspired intervention (28). Thus, the interventions developed will target the desired behaviour change. Figure 3 illustrates which BCW interventions are linked to both the COM-B models of behaviour and the BCW policy categories. The TDF domains also correspond to the COM-B models of behaviour and subsequently the BCW interventions and policy categories. I believe this combined analytic framework would be beneficial for further research on this topic.

For example, the TDF domain ‘skills’ might be considered as a barrier to appropriate SAP prescribing behaviour. This is then mapped to the ‘physical capability’ model of behaviour (COM-B). Figure 3 suggests an appropriate type of intervention to address this would include ‘training’-based action. This intervention may be supported by various policies such as ‘guidelines’ to develop SAP skills and ‘regulation’ of SAP prescribing skills development training.

Figure 3 Links between the components of the ‘COM-B’ model of behaviour and the BCW ‘Intervention Functions’ and ‘Policy Categories’. Adapted from Michie *et al.* (28,29).

	BCW Intervention Functions								
	Education	Persuasion	Incentivisation	Coercion	Training	Restriction	Environmental Restructuring	Modelling	Enablement
COM-B Model of Behaviour Sources									
Physical Capability					✓				✓
Psychological Capability	✓				✓				✓
Physical Opportunity						✓	✓		✓
Social Opportunity						✓	✓		✓
Automatic Motivation		✓	✓	✓			✓	✓	✓
Reflective Motivation	✓	✓	✓	✓					
BCW Policy Categories									
Communication/Marketing	✓	✓	✓	✓				✓	
Guidelines	✓	✓	✓	✓	✓	✓	✓		✓
Fiscal			✓	✓	✓		✓		✓
Regulation	✓	✓	✓	✓	✓	✓	✓		✓
Legislation	✓	✓	✓	✓	✓	✓	✓		✓
Environmental/ Social Planning							✓		✓
Service Provision	✓	✓	✓	✓	✓			✓	✓

Thus, application of the TDF in project 5 will not only facilitate the identification of barriers and enablers of appropriate SAP prescribing but will also facilitate further research applications by linking to the COM-B and BCW for the proposal of relevant theory-informed/inspired AMS interventions.

5.6 The TDF, COM-B and BCW in the current literature

Since its inception, the TDF has been used to investigate a range of implementation problems across healthcare settings nationally and internationally (238, 239).

Examples include:

- nurse engagement with antimicrobial stewardship (222) and electronic medication management systems (240);
- uptake of services/recommendations such as temporary work modifications for 'return to work' goals (241), sexual health service use amongst university students (223), and disease-modifying rheumatic drug use (225);
- decision-making for pre-operative testing (242), computed tomography pulmonary angiography orders (243);
- understanding of clinical practices such as hand hygiene (244), primary care management of paediatric respiratory infections (224), prescribing errors (245), and adverse drug reaction reporting (246);
- implementation of guidelines pertaining to blood transfusions (247), diabetes and hypertension (248), diagnostic imaging (249), antenatal corticosteroid use (250), preconception care (251), and stroke management (252).

Other non-clinical applications of the TDF include questionnaire development (253, 254); development of guidance for data extraction and synthesis of evidence for qualitative systematic reviews (255); evaluation of health promotion resources to identify which determinants (barriers) were successfully addressed (256); and evaluation of the acceptability of a hospital falls prevention program (257).

Application of the TDF has facilitated development of theory-based interventions (258-260) and also linkage to other theory-based frameworks and models, including the Behaviour Change Wheel(BCW) (inclusive of the COM-B model) (28) and the Behavior Change Technique Taxonomy (237).

Most recently, Cowdell *et al.* (261) conducted a systematic review and narrative synthesis of how the TDF and BCW have been applied to the development of health behaviour interventions. Ten studies were included and covered the topics of sexual health and contraception (262); smoking (263, 264); diet and exercise (265-270); and hypertension (271). The authors noted that more recent studies were more likely to have taken a systematic approach to the application of the TDF. The number of included studies was low, thus there was limited evidence for firm conclusions regarding the efficacy of applying the TDF and BCW. Therefore, the authors made tentative recommendations in supporting the use of the BCW as a sufficient process for the development of targeted behavior change interventions.

5.7 Mapping the current literature to the COM-B model

The COM-B (and TDF) model is the model chosen to inform the design and analysis of the qualitative research undertaken in **chapter 11**. However, not all qualitative research adopts the same theoretical models and frameworks, or may not use one at all. The following section reviews the current literature regarding antimicrobial decision-making and maps their respective findings to the domains of the COM-B model; the physical and psychological ‘capabilities’ (C) of the individual; social and environmental ‘opportunities’ (O); and reflective and automatic ‘motivators’ (M) (28, 29).

5.7.1 Capabilities

Capability is defined as “*individual’s psychological and physical capacity to engage in the activity concerned*” (28, 29). Activities associated with SAP include decision-making, prescribing and administration.

Physical capability

Physical capability refers to skills for SAP prescribing and administration. Suboptimal antimicrobial use in Australia is directly shaped by prescriber behaviour. Prescribing skills are commonly taught during junior doctor training. Safe and appropriate prescribing requires sound clinical assessment and decision-making before a prescription is provided (272).

Charani *et al.*’s (21) qualitative study on the surgical prescribing pathway in the UK highlighted the perception that surgeons viewed antimicrobial management (and prescribing) as a peripheral role. They considered it a lower priority than surgical technique and thus delegated the role of antimicrobial management to others (21). The authors noted this lack of priority was compounded by a lack of expertise in antimicrobials (21).

SAP administration is considered a physical skill that anaesthetists and nursing staff may perform as result of this delegated antimicrobial management (21). There is limited literature regarding the development of nurses’ and anaesthetists’ skills for SAP administration. A Nigerian ‘knowledge, attitudes and practice’ study on nurse-anaesthetists identified there was a need to improve SAP practices by increasing

knowledge and communication between the nurse-anaesthetists and the surgeons, and developing protocols for nurse-anaesthetist to follow (273).

Psychological capability

Decision-making for SAP is a complex process and includes a range of factors such as clinical knowledge. Decision-making is largely influenced by external factors such as the presence of guidelines and hierarchical structures within the workforce.

Knowledge of and attitudes towards guidelines influence compliance and optimal SAP prescribing. Hulscher *et al.* (160) reported behavioural aspects such as prescriber knowledge and attitudes as key determinants of antimicrobial prescribing.

Pulcini *et al.*'s (274) survey of junior doctors in Scotland and France reported limitations in their knowledge regarding antimicrobial prescribing and resistance. The authors reported that advice from pharmacists, microbiologists and senior colleagues were statistically significant factors that influenced how they prescribed ($p<0.001$) (274). Guidelines were acknowledged as a key influence, but this was not statistically significant ($p=0.18$) (274). The need for further knowledge of antimicrobials and AMS education across medical professionals, spanning undergraduate and post-graduate education, has been highlighted in the current literature as a means to support appropriate antimicrobial prescribing (275-277).

Guideline non-compliance in SAP prescribing (1-8, 135, 137-139) and general clinical practice (140) has been frequently reported. Barriers to physician adherence to clinical practice guidelines were identified in a systematic review of 76 articles (22).

These barriers were organised into a framework consisting of the following seven groups: lack of familiarity, lack of awareness, agreement with specific guidelines and guidelines in general, outcome expectancy, self-efficacy, motivation/inertia of previous practice and presence of external barriers. Similarly, a literature review of barriers to evidence-based practice in primary care (142) identified barriers such as availability of evidence, lack of relevance to practice and lack of dissemination of evidence and guidelines.

Numerous qualitative studies describe a common prescriber perception that guidelines may not be appropriate for their individual patient and use this to justify their guideline non-compliance (278, 279). Such perceptions may also exist among Australian health professionals in the operating theatre, such as surgeons, anaesthetists, nurses and pharmacists, and are described in project 5 in **chapter 9** of this thesis.

Guideline non-compliance has also been reported across Australian antimicrobial audits and reports (1-8, 73, 137). Greater understanding of perceptions regarding current guidelines and evidence may provide insight into the current state of guideline non-compliant SAP prescribing (1-8).

5.7.2 Opportunities

Opportunity is defined as *“all the factors that lie outside the individual that make the behaviour possible or prompt it”* (28, 29). The types of opportunities have then been broadly sub-divided into those that are social and physical.

Social opportunities

Socio-cultural influences of hierarchy are well documented in the fields of medicine and surgery (280-283). Subsequently, hierarchy also bears influence on SAP decision-making and prescriber behaviour (284). Qualitative research suggests senior colleagues exert a significant influence on antimicrobial prescribing in the acute setting (20, 23, 143-145, 278).

A qualitative study of 30 physicians identified the behaviour of those in training were greatly influenced by their supervisors when it came to antimicrobial prescribing (143). Additionally, the physicians in training at times would think about questioning the antimicrobial prescribing of their colleagues but would avoid comment or critique due to barriers such as infrequent face-to-face encounters, professional hierarchy and the awkwardness of these conversations (143).

The opinions of one's peers may have a greater impact upon antimicrobial prescribing than local guidelines and policy (146). Schouten *et al.* (146) conducted 18 semi-structured interviews of residents, consultants, microbiologist and a clinical pharmacist across three Dutch hospitals. The authors identified that guideline non-compliance for empirical antimicrobial prescribing was mainly influenced by physicians' negative attitudes towards the guideline (146). Charani *et al.* (19) also identified in their qualitative study involving 39 health professionals across four London hospitals that senior physicians prefer a culture of autonomous decision-making that is based upon their personal knowledge and experience rather than local policy and guidelines. This disagreement with guidelines and a social culture

that encourages following senior colleagues' advice create a cumulative effect of further guideline non-compliance among junior prescribers (146). This hierarchy-informed behaviour has been described as 'prescriber etiquette' (19).

Prescriber etiquette refers to a set of culturally-determined rules that shape antimicrobial prescribing behaviour (19). Prescribing etiquette facilitates a culture of 'non-interference' where prescribers are reluctant to alter or critique the prescribing of another physician. Similarly, in terms of hierarchy, a junior physician would be less likely to query or change the prescribing of a senior physician.

Physical opportunities

Physical opportunities relate to the environment and resources available. The surgical pathway is unique as SAP administration can occur before, during and after the surgical procedure. This represents three very different environments and may be complicated further by the various health professionals and their roles in SAP decision-making. The lack of financial resources to support availability of health professionals (pharmacists in particular) to perform their role and be advocates for AMS was identified in an Australian qualitative study as a barrier to AMS implementation (285).

Strong organisation/facility commitment, also referred to as 'institutional buy-in', is a core element of hospital antimicrobial stewardship programs in the US (286) and Australia (11). An organisational culture that is supportive of AMS is likely to develop when hospital directors and stakeholders collaborate and engage with senior

clinicians to develop local policies that endorse appropriate SAP and guideline compliance. A qualitative study including fifteen AMS pharmacists and six physicians in the US explored factors that influence the implementation of AMS strategies (287). The need for leadership and institutional buy-in was identified as a facilitator of AMS interventions due to the fact that leadership buy-in can facilitate multidisciplinary collaboration and consensus regarding policies and guidelines (287). Similarly, a qualitative study on influences on AMS implementation in low- and middle-income countries highlighted participants' concern over a lack of 'concrete' support for AMS in national and institutional policies (288).

The uptake of guidelines, CDSS and additional AMS interventions are largely dependent on the hospital's resources, including IT infrastructure, access to electronic guidelines, and development of protocols such as 'enhanced recovery after surgery' (289, 290) and 'time-out' (291, 292). Lack of access to IT resources was identified as a barrier to AMS interventions in a US qualitative study involving AMS pharmacists and physicians (287).

5.7.3 Motivators

Michie *et al.* (28, 29) define motivation as *"the brain processes that energise and direct behaviour, inclusive of; habitual processes, emotional responding, and analytical decision-making"*. This has then been subcategorised into automatic and reflective motivation.

Automatic motivation

Automatic processes of motivation are those developed and driven by emotions (28, 29). A common emotion that influences antimicrobial prescribing and is highlighted in the literature is fear.

A prescriber's fear of contributing to AMR does not appear to outweigh their fear of causing direct harm to their patients by leaving potential infections untreated. A US study of thirty inpatient physicians demonstrated that concerns about AMR and the potential for antimicrobial adverse effects were not influential considerations in their antimicrobial decision-making (143).

There appears to be minimal ownership of individual contributions to AMR. A US mixed-methods study assessed clinician perceptions about the extent of AMR as a problem across four healthcare facilities (293). The authors demonstrated that clinicians were significantly more likely to perceive that AMR was a problem nationally than in their own institution (95% vs. 77%; $P=0.001$) or practice (95% vs. 65%; $P=0.002$).

Broom *et al.*'s (23) Australian qualitative study involving surgeons and anaesthetists noted that prolonged SAP administration was justified by physicians as an act of benevolence (23). Broom *et al.* (24) also highlighted the application of low-evidence-based practices such as antibiotic-soaked grafts and prostheses, and antibiotic solutions for wound irrigation were also justified as having a low risk of harm and providing increased 'surgical comfort' in terms of reassurance regarding prevention

of complications. A lack of understanding of one's contribution to AMR and the concept that prolonged antimicrobial use does not cause harm may influence antimicrobial decision-making.

A qualitative study of the influences on AMS implementation in low- and middle-income countries highlighted that fear of '*treatment failure*' and '*retribution from senior physicians*' had a negative impact on antimicrobial prescribing behaviour, particularly among junior physicians (288). Broom *et al.* similarly proposed that guideline non-compliant prescribing occurs due to the fear of disapproval from colleagues (23, 24).

Comparatively, an Italian mixed-methods study that explored health professionals' attitudes regarding SAP use in children (294) proposed guideline non-compliance was influenced by a fear of medical malpractice, in which guideline compliance was not perceived to be an adequate legal safeguard if patients experienced adverse events such as SSIs.

Reflective motivation

Reflective motivation is defined as '*brain processes that involve planning and evaluation*', i.e., they are intentional (28, 29). Establishment and identification of roles for SAP prescribing and decision-making are represented by this COM-B domain.

In relation to SAP prescribing, the prescriber's behaviour is the target of behaviour change interventions. In the surgical setting, as there are multiple professionals

involved in the surgical pathway, who the prescriber is needs to be clarified. A recent qualitative study incorporating face-to-face interviews with ethnographic observations identified perceptions that antimicrobial management was a peripheral role and a low priority for surgeons (21). The hierarchical nature of professional relationships in surgery settings was also highlighted in this study; however, the study noted that hierarchies shifted based upon the availability of senior surgeons. The overall decision for SAP was left to the consultant, but the choice of antimicrobial, route and timing were left to junior staff. Thus, AMS interventions should ideally target both senior surgical consultants and junior surgeons but with different approaches to reflect the varying roles they have in SAP decision-making.

Charani *et al.* noted the role of the anaesthetist was not clearly defined but acknowledged anaesthetists' supportive role in SAP prescribing. It was observed that anaesthetists had a higher awareness of the need for SAP and would remind surgical staff of this (21). Anaesthetists then have an assumed responsibility for antimicrobial management (295), which places them in an unclear position of authority. A review from Gifford *et al.* (296) highlighted anaesthetists' role in prevention of post-operative infection, which included responsibility for SAP. Anaesthetists are involved in the surgical care of patients and SAP is generally given at the same time as induction anaesthesia (56, 57). Appropriately timed and targeted SAP can reduce the risk of SSIs, thus highlighting the important role anaesthetists can play in optimisation of SAP (296). Knox *et al.* (137) support the notion of anaesthetist involvement in AMS for SAP as anaesthetists "*commonly administer antibiotic prophylaxis autonomously on the surgeons' behalf*" (137), and that it would be wise

to have a multidisciplinary and collaborative effort involving both surgeons and anaesthetists (as key target prescribers for SAP interventions).

As previously discussed in **chapter 2**, nurse practitioners have the potential to prescribe along the surgical pathway and pharmacists currently do not. However, both have active roles regarding SAP administration and review along the surgical pathway.

There is limited literature detailing the roles of nurses and pharmacists as antimicrobial stewards in the operative setting. Prado *et al.* evaluated the impact of a peri-operative SAP protocol and demonstrated the importance of the hospital pharmacist's role as an AMS steward (297). The pharmacist's role pertained to protocol education and implementation, and managerial roles that optimised the ordering, dispensing, administering and documenting of pre-operative SAP (297). The intervention evaluation demonstrated an increase in appropriate indications for SAP (from 56.4% pre-intervention to 100% post-intervention) (297).

Charani *et al.*'s qualitative study proposed a solution to the poorly co-ordinated antimicrobial management practices identified. They proposed the development of a dedicated clinical role with responsibility for ensuring patients receive appropriate antimicrobial management throughout the surgical pathway within the surgical team (i.e., pharmacist, nurse or surgical trainee) (21).

For an AMS program and intervention to be successful, a multidisciplinary effort is required. Further research to understand the behaviour of and relationships

between surgeons, anaesthetists, theatre nurses and pharmacists with regard to SAP is warranted for the development of tailored SAP interventions. Project 5 will aim to provide a greater understanding of such behaviour using two theoretical frameworks, the TDF (27) and COM-B model (28).

5.8 Chapter summary

In summary, the utilisation of theoretical frameworks from implementation science is advantageous for this thesis, in particular project 5. These frameworks provide structure to and enhance the rigour and validity of the research design and analysis. Most importantly, adopting a theory-based approach provides both researchers and readers greater insight into the underlying behaviours and any barriers and enablers that influence appropriate surgical prophylaxis prescribing.

The utilisation of the TDF facilitates application of other theoretical approaches such as the COM-B and BCW, and may subsequently assist with the development of targeted and more appropriate AMS interventions to improve SAP prescribing (linking theory-based research to theory-informed interventions). The current literature regarding antimicrobial prescribing behaviour can be mapped to the domains of the COM-B model (section 5.7). However, this review is not exclusive to SAP prescribing, and greater exploration of the influences of SAP decision-making is warranted.

In conclusion, the application of these theoretical frameworks supports two of the overarching aims of this thesis, which are to: (1) identify and explore the underlying

facilitators and barriers to appropriate SAP prescribing, and (2) propose a theoretically-informed framework for solutions to support sustainable AMS for SAP.

Chapter 6: Methodology

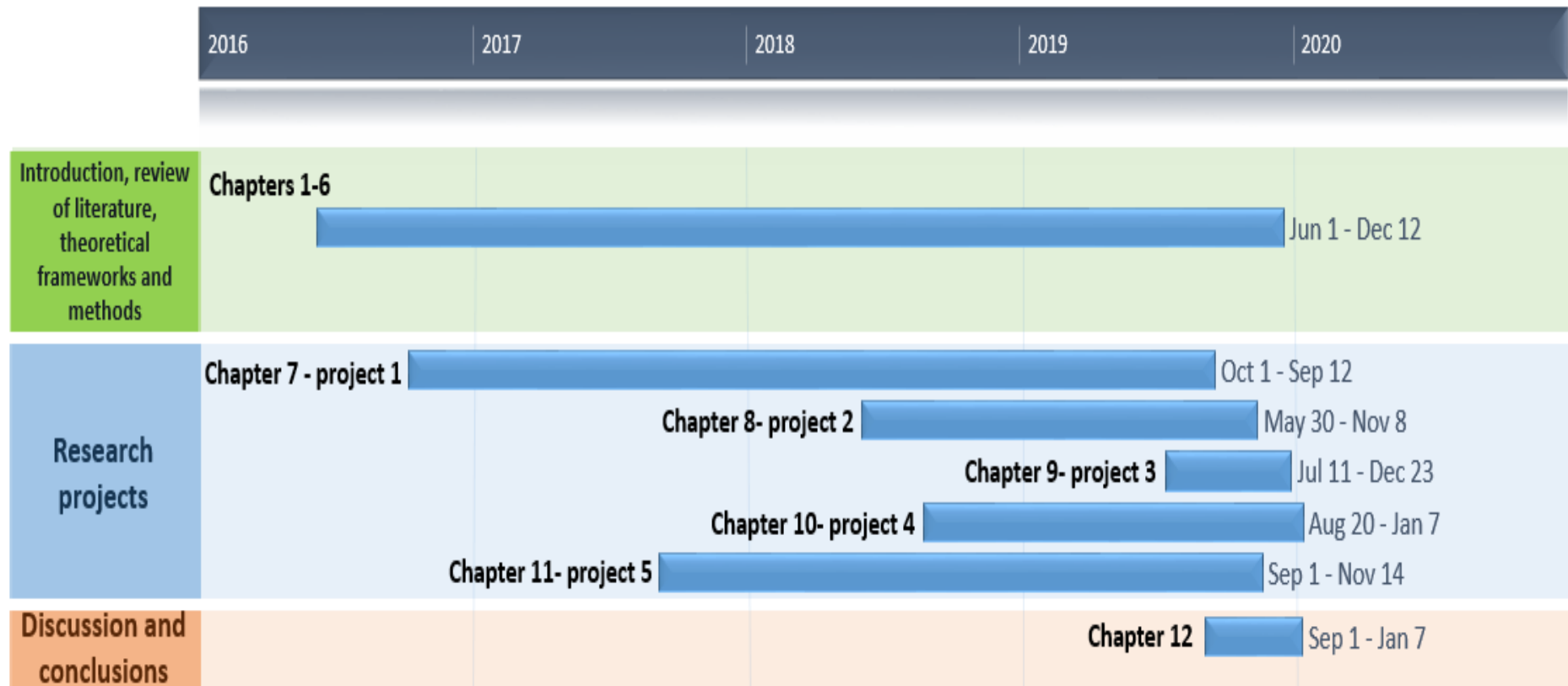
6.1 Introduction

This chapter details the methodological approach of this PhD research and provides a rationale for the selection of the methods employed across the multiple projects.

6.2 Research strategy

An initial review of the current literature identified how the Australian government, healthcare system and policies and frameworks shape SAP prescribing practices (**Chapter 2**). This was supplemented with a critique of the evidence for SAP and its limitations (**Chapter 3**) and an examination of AMS interventions that currently existing for hospital inpatients and across surgical settings (**Chapter 4**). **Chapter 5** included a discussion of theoretical frameworks and how these facilitate improved understanding of behaviour and inform behaviour change, with a review of qualitative research focusing on antimicrobial prescribing. Based on a review of the literature, this PhD study has adopted a mixed-methods approach including quantitative (**Chapters 7 to 10**) and qualitative projects (**Chapter 11**), the data from which are triangulated to inform a proposed framework for surgical AMS (**Chapter 12**). Figure 1 illustrates the timeline of projects from conception to publication/thesis submission.

Figure 1 Timeline of PhD research projects from conception to publication/submission



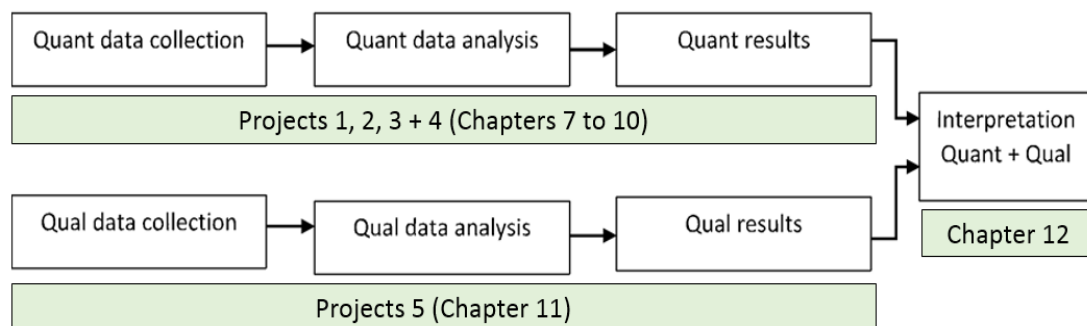
6.3 Mixed-methods research

Mixed-methods research involves the combination of both quantitative and qualitative research. Leech and Onwuegbuzie (298) developed a typology framework for mixed-methods research focusing on three dimensions:

1. mixing (partial or full),
2. timing (concurrent or sequential); and
3. emphasis (dominant or equal) (298).

Based upon this framework, my research adopts a partial, concurrent and equal design (Figure 2).

Figure 2 Mixed methods typology framework of this thesis. Adapted from Leech and Onwuegbuzie (298)



Both qualitative and quantitative studies were conducted concurrently throughout the study. The overall analysis consists of partial mixing of both methods, in which the qualitative analysis iteratively provided insight and an explanatory context to the ongoing quantitative analysis generated in **Chapters 7 to 10**. Both methods are of equal importance and complementary to one another.

Mixed-methods research is advantageous in health services research as it enables researchers to review the problems (i.e., inappropriate SAP prescribing) from a range of perspectives and contextualise findings using complementary data. For example, the quantitative analyses in **Chapters 7 to 10** enable a description of current SAP prescribing across Australian hospitals. Complementing this, the qualitative work undertaken in **Chapter 11** aims to provide a 'how' and 'why' context to the current practices and problem identified.

Additionally, the adoption of a mixed-methods design aims to enhance the strengths of both quantitative and qualitative methodologies while minimising their weaknesses (299), thus potentially enhancing the rigour and validity of the findings of this research (300).

The combination of quantitative and qualitative research approaches in this study facilitates the development of a more complete understanding of the problem of inappropriate SAP prescribing. A thorough understanding of inappropriate SAP prescribing in Australia may also provide clarity surrounding potential solutions, i.e., AMS interventions and strategies.

6.4 Research design and quality issues

Mixed-methods research can adopt a range of research paradigms or 'world views'. Pragmatism has been identified as the most suitable paradigm for research using mixed methods (301-303) and the social sciences (304). Pragmatism as a research paradigm is premised on the concept that to answer a particular research problem, one should adopt whatever philosophical or methodological approach is best suited

(305), thus placing greater emphasis on the research questions as opposed to the methods. This PhD program aims to improve SAP prescribing in Australia. To achieve this, the research projects are focused around three key questions:

1) What are the current SAP prescribing practices across Australia and are these influenced by patient, hospital and surgical factors? (projects 2-4).

2) What are the underlying facilitators and barriers to appropriate SAP prescribing? (projects 1 and 5).

3) Can this information be applied to develop a theoretically-informed framework for solutions to support sustainable AMS for SAP? (projects 1-5).

This section provides further detail on the rationale for methods that could not be included in journal publications but are critical for the understanding of these projects' conception and design.

6.4.1 Project 1: Guideline implementability

Rationale for evaluating guideline implementability with the Guideline Implementability Appraisal instrument

A variety of guideline appraisal tools have been developed to improve guideline quality. Forty tools were assessed in a recent systematic review (112). The review described indicators for guideline quality such as evaluation of evidence (88%), presentation of guideline content (85%), "transferability" (83%), "independence" (80%) "scope" (75%) and "information retrieval" (73%) (112).

The dissemination and implementation of a clinical practice guideline (CPG) is just as important as its content. Without an implementation plan, the potential benefits of a CPG may not be realised. Thus, the authors highlighted that these quality dimensions require greater focus for the development of high-quality CPGs (112).

Siering *et al.*'s (112) systematic review identified the Appraisal of Guidelines, Research and Evaluation (AGREE) II tool (131) as the most ideal tool for comprehensive guideline appraisals in English. However, such comprehensive appraisals are not always warranted, thus appraisal tool selection may be determined by the research questions, the nature of the guideline, and the time and resources available for guideline appraisal (26).

Upon examination of the literature and consultation with key stakeholders and guideline developers, it was discussed that the AGREE II tool (131) may not be an appropriate tool for project 1, as the national antibiotic guideline, *TG: Antibiotic* (57), did not adopt a graded methodology and would automatically fail one of the key criteria, thus skewing the results. As such, it was decided that a focus on guideline implementability was of greater interest than the grading of evidence, as this would be reviewed in the literature review of this thesis (see **Chapter 2**).

Guideline quality appraisal via the AGREE II instrument highlights that many CPGs are generally of a lower quality (112). While guideline quality is of high importance, it does not necessarily correlate with successful guideline implementation. Thus, guideline implementability warrants its own evaluation.

Guideline implementability can be appraised utilising an internationally recognised and validated instrument known as the Guideline Implementability Appraisal (GLIA) (26, 161). This tool is designed to 'systematically highlight barriers to implementation' and consists of 9 dimensions that incorporate 31 questions. The dimensions account for factors that can, therefore, both facilitate or reduce a guideline's implementability and potential uptake.

The first section of GLIA consists of nine questions that address the guideline as a whole; these questions are classified as global considerations. The second section consists of 21 questions that are grouped into eight dimensions, focusing on the intrinsic characteristics of the guideline. These dimensions include global considerations, executability, decidability, validity, flexibility, effect on process of care, measurability, novelty/innovation, and computability (26) The computability dimension is optional and was included in this appraisal as the electronic version (rather than the print version) of the guidelines was appraised. The GLIA instrument is both a paper-based tool as well as an online electronic resource known as eGLIA (26).

The GLIA instrument can be utilised during guideline development to identify intrinsic factors that can be addressed prior to the implementation of guidelines (306). Other research includes utilisation of the GLIA instrument post-guideline implementation to identify barriers and enablers influencing their uptake (165-167); however, none of this literature examines SAP guidelines. This research utilises the GLIA tool in a post-guideline implementation setting.

The evaluation of the implementability of the *TG: Antibiotic* surgical prophylaxis recommendations is novel research that is of importance for gaining greater understanding of SAP prescribing behaviour. Utilisation of a validated tool such as GLIA promotes methodological rigour of this research and its application post-guideline implementation will facilitate structured feedback to guideline developers.

Feasibility study

To ensure feasibility of the project, a pilot study was conducted by two appraisers, researcher CI and an external stakeholder, an ID physician. The pilot appraisal included the application of section two (21 questions) of the GLIA appraisal to each 17 subsections of the guideline.

The pilot appraisal identified two key issues that were thought to negatively influence project participation and results: 1) prolonged duration to complete the appraisal (greater than four hours); and 2) the 17 subsections of the guidelines were similar in intrinsic factors such as structure, formatting and presentation.

Long duration surveys and appraisals have been associated with response burden and, therefore, reduced response rate (307-309). Given that the intrinsic properties of these subsections were noted to be similar and that the GLIA appraisal measures these intrinsic factors, the authors decided it was feasible to combine these sections into one 'recommendation' for the appraisal, i.e., participants would only be required to answer the 21 questions of GLIA's 2nd section once, as opposed to an additional 17 times.

The GLIA developers recommend follow-up with all appraisers to seek full agreement with responses (26). The feasibility study identified that this process would be time-consuming and a deterrent for recruitment, especially with a larger number of appraisers. The GLIA project was identified as a preliminary and exploratory project for this thesis and achieving 100% agreement on all GLIA questions was not required to identify issues with *TG: Antibiotics'* implementability. Exploration of guideline implementability and compliance was also proposed for project 5.

6.4.2 Projects 2-4: Surgical National Antimicrobial Prescribing Survey (Surgical NAPS)

To provide context to the analysis of the Surgical NAPS datasets, this section details the development of the Surgical NAPS (4, 8) methodology and reporting that goes beyond what is described in subsequent publications (**Chapters 8 to 10**).

Survey design

The pilot survey (4) was developed in 2015 by the Hospital NAPS team (Guidance Group, Royal Melbourne Hospital) after the hospital-wide point-prevalence survey consistently demonstrated high levels of inappropriateness for prescriptions related to surgical prophylaxis (1-3, 5-7). The survey was co-designed through stakeholder consultation from a range of specialities (i.e., infectious diseases, AMS, infection control, anaesthetics, surgery) and in collaboration with the Victorian state-wide body undertaking surgical site infection surveillance and surgical prophylaxis surveys (Victorian Healthcare Associated Infection Surveillance System (VICNISS)),

supplemented by a systematic literature review. User feedback facilitated survey refinement prior to development and pilot of the web-based survey.

The Surgical NAPS surgical 'procedure system/group' list was developed from the Royal Australasian College of Surgeons' (RACS) Morbidity Audit and Logbook Tool Procedure List (310) and the Fellow of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists' Logbook Procedure List and Classification List (311).

Data collection and collation

The Surgical NAPS was launched in April 2016. Auditors registered with the Hospital NAPS were notified and asked to participate in the Surgical NAPS. Additional recruitment methods included marketing across social media platform Twitter® by NCAS and the ACQSHC, and an advertisement in the RACS publication 'Surgical News' (312).

Data were collected between 18th April and 3rd November 2016 for the 2016 pilot Surgical NAPS report. The dataset for project 2 (**Chapter 8**) was extended to include data collected until June 2018 as this was reflective of the time project 2 was initiated. Projects 3 and 4 had the Surgical NAPS data included until April 16th, 2019. This timepoint was reflective of when the *TG: Antibiotic* guidelines were updated from Version 15 (57) to Version 16 (56). It was identified by authors that analysis of data beyond this timepoint would be difficult to compare as guideline recommendations had been altered and, therefore, comparisons of guideline

compliance and appropriateness would be inaccurate. Table 1 summarises the numerous patients, hospital, surgical and antimicrobial variables collected in the Surgical NAPS dataset which contribute to the structure of reporting and benchmarking.

Data were collected by trained auditors according to a standardised method and data collection form (4, 8) (Appendix 1). Auditors were primarily pharmacists, nurses and infectious diseases physicians. Auditors at each site were provided with structured education and online training to ensure consistency of methodology. Ongoing support, including the provision of advice from NAPS clinical support team (experienced stewardship pharmacists, infectious diseases clinicians, and microbiologists), was also available by phone and email throughout the survey period to guide auditors, specifically with appropriateness assessments. All data from registered sites were entered into the Surgical NAPS online portal. Auditors are also able to use their own data to generate local reports and contribute to benchmarking reports, where data can be compared to hospitals of similar type (based on the Australian Institute of Health and Welfare (AIHW) peer groups). This facilitates targeted local feedback by auditors to prescribers and other stakeholders within their health service.

Table 1 Summary of data variables collected in the Surgical National Antimicrobial Prescribing Survey (4, 8)

Patient factors	Hospital factors	Surgical procedure factors	Antimicrobial factors		
			Existing therapy	Procedural doses	Post-procedural prescriptions
Patient identification number	Hospital name	Surgery date	Antimicrobial		
Date of birth/ Age	Hospital audit	Surgery start and stop time	Route		
Gender	AIHW Peer Group	Initial or subsequent surgery	Dose		
Height	ABS Remoteness	Elective or emergency surgery	Date and time of last dose	Repeat dose required, but not given	Frequency
Weight	State/ Territory	Presence of trauma		Documentation of administration time	Indication

Renal function	Funding	Removal/ insertion of prosthetic material		Initial or repeat dose	Start and End dates and times
Allergies		Excessive blood loss		Guideline Compliance	
Risk factors		Surgeon code		Appropriateness	
Admission/ Discharge Dates		Anaesthetist code		Reason for inappropriateness	
American Society of Anaesthesiologists (ASA) physical status score		Time of first incision			
Free text for surgical or clinical notes, microbiology, radiology		Wound Classification			

Statistical analyses

Projects 2, 3 and 4 employ descriptive and statistical analyses to describe SAP prescribing patterns across Australian hospitals and to identify factors that influence appropriateness. The following section provides a more detailed explanation of the novel statistical methods used in **Chapters 8 to 10**. All statistical analyses were conducted using Stata version 14.1 (StataCorp LP, College Station, TX, USA).

Mixed-effects logistic regressions

The Surgical NAPS data is complex and includes multiple variables that are potential influencers of SAP prescribing. Univariate and multivariate logistic regression models were adopted across projects 2, 3 and 4 to identify whether the relevant patient, hospital and surgical factors were significantly associated with appropriateness.

The dataset required removal of observations in which appropriateness was deemed 'not assessable'. This created a binary model of two outcomes, 'appropriate' or 'inappropriate'. Initially, a maximal model with all relevant patient, hospital and surgical variables was included. Model selection was determined by likelihood ratio tests and residual plots to assess the goodness of fit of the model.

Mixed-effects logistic models fit with unique hospital identifiers as random intercepts, provided the best fit to the data, and were selected. As previously discussed, each hospital had the flexibility to complete the Surgical NAPS to the methodology and surgical unit that suited them best. Therefore, a hospital's unique identifier represented the most appropriate choice of random intercept for this

model. Adoption of this model proposes that the appropriateness (dependent variable) for each observation (data entry) is then predicted by the hospital identifier that varies across the independent variables (patient, hospital and surgical factors) included in the model.

Estimated marginal means

The Surgical NAPS dataset includes both continuous (e.g., age) and categorical variables (e.g., surgical procedure group, antimicrobial). Upon review of the crude appropriateness of the data and the multivariate analyses, it was identified that the dataset represented an unbalanced population, due to flexibility of the survey methodology. Calculation of the estimated marginal mean enabled the 'weight' of the individual observations to be increased to accommodate any missing observations. Application of the estimated marginal means, therefore, delivered an equal-weighted average across all independent variables (e.g., age, remoteness, presence of trauma). This was then reported as an 'adjusted appropriateness' (AA) with 95% confidence intervals. This method aims to adjust for any biases created by the varying subgroup sizes in the independent variables and to provide a balanced measure of appropriateness in an unbalanced sample. Reporting adjusted appropriateness values facilitates greater confidence in our analyses as the value is adjusted for the variations in our sample that could have been viewed as a limitation. Our application of adjusted appropriateness is novel to the literature on antimicrobial appropriateness assessments.

Limitations

The Surgical NAPS (4, 8) report highlights limitations to the reports methods and findings and highlight that these should be taken into account when examining the results. Refer to the published reports for further details (4, 8). The Surgical NAPS also collects data on 30-day outcomes, including surgical site infections, morbidity and mortality. However, this component was not mandatory, and the findings are too limited to provide meaningful insights. Additional resources and support are required to facilitate the uptake of this component of the Surgical NAPS.

6.4.3 Project 5: Influences on surgical antimicrobial prophylaxis prescribing and decision-making

Chapter 11 (project 5) provides the qualitative component to this mixed-methods thesis and aims to provide an explanation to the current practices identified in the Surgical NAPS datasets. Key methodologies not described in the publication in **Chapter 11** are detailed here.

Project 5 is an exploratory, multi-site, collective qualitative case study consisting of focus groups designed to explore the phenomenon of the decision-making regarding SAP prescribing and guideline compliance among multiple health professionals across two contexts, public and private Australian hospitals. This study design facilitated comparisons across the two cases and at multiple levels within each case, i.e., across multiple health professions and surgical specialties.

Sampling frameworks

Sample sizes for qualitative research are ideally estimated by determining how many interviews or focus groups are enough to reach data saturation. The answer to such a question is not clearly defined and heavily dependent on the context of the project (313, 314). Data saturation is reached when the ability to gain further new information (i.e., code development) has been achieved and when additional coding is no longer attainable (315, 316).

There is no 'one size fits all' methodology for achieving data saturation (313). However, certain strategies may be employed to facilitate data saturation (313, 315, 317, 318). This research adopted an iterative approach to data collection and sample size pending the saturation of qualitative data. An initial sample size of sixteen focus groups was proposed. The transcripts of the focus groups were reviewed iteratively, prior to subsequent focus groups. Newly identified concepts were examined in the following focus groups (317, 319). If data saturation was not achieved, additional recruitment was considered.

Sixteen purposively sampled focus groups is larger than the rule of thumb of three to six focus groups proposed by Guest and colleagues (320). However, the purpose of a qualitative case study is to gain a depth of knowledge surrounding chosen phenomena (in this case, the phenomenon of decision-making for SAP prescribing), and, to achieve this, multiple perspectives needed to be explored.

This research aimed to explore different groups of health professionals' perspectives across both private and public hospitals. Thus, a larger a sample size of sixteen focus groups may be justified to support achievement of data saturation.

The minimum number of participants for each focus group was set at four participants as supported by the current literature (317, 321). However, this was subject to the availability of participants. In circumstances where four participants were recruited but fewer than four attended, the focus group still proceeded. In circumstances where four participants could not be recruited, a semi-structured paired interview was conducted instead.

An initial sampling framework targeted fewer surgical specialties with focus groups duplicated across for public and private hospitals. Table 2 highlights the finalised sampling framework, in which modifications included greater focus on different surgical specialty groups rather than a focus on public and private hospitals. This change was made primarily due to the difficulty in co-ordinating focus groups in the private sector. Additionally, the initial focus groups revealed that most health professionals had experience across both sectors and could provide commentary on practices across both cases.

Table 2 Focus group sampling framework

Health Profession	Public Hospital 1	Public Hospital 2	Private Hospital	Total
Surgeons- cardiothoracic	1			1
Surgeons- orthopaedics		1		1
Surgeons- vascular			1	1
Surgeons- plastic and reconstructive		1		1
Surgeons- colorectal		1		1
Surgeons- neurological		1		1
Surgeons- urological		1		1
Surgical Registrars/Residents		1		1
Anaesthetists	1	1	1	3
Theatre Nurses	1		1	2
Pharmacists	1		1	2
Total	4	7	4	15

Thematic analysis

Thematic analysis via deductive coding was the key analytical method used in project 5. The phases of thematic analysis determined by Braun and Clarke (322) (Table 3) formed the structure of the analysis, but were modified to reflect the utilisation of frameworks for deductive coding. This was then followed by inductive coding for emerging themes. Adoption of Braun and Clarke (322) (Table 3) increased methodological rigour, and findings were validated with double-coding (20% of all transcripts).

Table 3 Phases of thematic analysis (322)

Phase (322)	Description of the process	Project 5 process	Completed by
1. Familiarizing yourself with your data.	Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.	-Focus groups conducted, recorded and field notes taken.	CI, AR, DA, KT and CM
		- Focus group recordings transcribed by hired transcriber.	Transcriber
		- Data de-identified imported into data management software NVivo11® and was de-identified.	CI
2. Generating initial codes.	Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code	Modified inductive and deductive coding to the TDF. 20% of focus group transcripts were double coded to promote consistency and rigour.	CI (AR 20%)
3. Searching for themes.	Collating codes into potential themes, gathering all data relevant to each potential theme.	- Deductive coding enabled identification of common themes proposed by the TDF (42). - Concurrent inductive coding facilitated development of new/emerging themes and sub themes to the TDF. - NVivo coding comparison reports for double coded transcripts generated for discussion and reflection of data (323).	CI (AR 20%)

4. Reviewing themes.	Checking if the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic 'map' of the analysis.	- TDF themes identified in Phase 3 were then mapped to the COM-B model.	CI
		- New/emerging themes discussed by research team. Agreement on all new/emerging themes to be reviewed and mapped to the COM-B.	CI, AR, DA
5. Defining and naming themes.	Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme.	Relevant and dominant themes were identified through consensus among 3 researchers. Factors for consideration of relevance and dominance include: frequency of belief/domain across focus groups, presence of conflicting beliefs/domains and perceived strength of that belief/domain upon impacting behaviour (242). Only 10 of the 14 TDF domains were considered relevant and were mapped to the COM-B	CI, AR, DA
6. Producing the report.	The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature,	- Development of six key themes mapped to the COM-B was proposed by the lead researcher CI.	CI
		- Refinement and consensus on the 6 themes and respective sub themes.	CI, AR, DA, KT, TP, CM
		- Compelling quotes were extracted from NVivo® to represent	CI, AR

	producing a scholarly report of the analysis.	the identified themes and subthemes.	
		- Selected quotes were edited for clarity and tabled to their respective themes to facilitate the results and discussion of the manuscript in Chapter 11 .	CI, AR, DA

As discussed in **Chapter 5**, the TDF and COM-B model form the foundation for data collection and analysis of this research project. Application of theoretical frameworks promotes academic rigour and supports the development of theory-driven AMS interventions.

Key limitations described in **Chapter 11** include the small hospital sample size (three Victorian metropolitan hospitals); thus, the study is not truly representative of all Australian hospitals and states. Additionally, not all surgical specialties were included, and the inclusion of their niche insights and concerns would have enhanced our findings.

6.5 Researcher positionality

Guidelines on reporting standards for qualitative research include recommendations about reporting of the researchers' roles, which may help contextualise explanation of the research design, and data collection, triangulation and analysis (324-326). My interest in undertaking research on antimicrobial stewardship in tertiary hospitals, and on surgical antimicrobial prophylaxis prescribing specifically, was influenced by my experience as a clinical and antimicrobial stewardship pharmacist, through which I gained insights into antimicrobial prescribing behaviours in acute care. My supervisory team comprised experienced infectious diseases physicians, AMS experts, infection prevention surveillance consultants and qualitative researchers. The qualitative research undertaken throughout this doctoral study was informed by the research team's expertise and professional insights. This research is considered

to be a form of ‘insider research’ as the research team had the capacity to share in participants identity, professional roles and clinical experiences (327).

This PhD research is part of a larger body of work at the National Health and Medical Research Council-Centre of Research Excellence - the National Centre for Antimicrobial Stewardship (NCAS) at the University of Melbourne. NCAS is a research collaboration that adopts a One Health approach to optimising antimicrobial use across both human and animal health settings. NCAS researchers have adopted mixed-methods approaches to research on antimicrobial use and AMS interventions across a range of settings, including aged care homes (328-332); rural and regional hospitals (183, 333, 334); general practice (224, 335, 336); paediatrics (337); private hospitals (72, 73, 338); tertiary hospitals (antifungal use and stewardship) (339); and veterinary and agricultural settings (340-347).

6.6 Ethics

Ethics approvals were required throughout the course of my thesis. Table 4 provides a summary of ethics approvals obtained in relation to each project.

Table 4 Summary of ethics approval required for projects 1 to 5.

Project	Ethics Type and Approval details
1	Minimal Risks Ethics approved by the University of Melbourne, School of Population and Global Health, Human Ethics Advisory Group (Ethics ID:1648127.1).
	Ethics approval included consent for participation and potential publication.
2	The collection and analysis of data from Surgical NAPS was approved by Melbourne Health Human Research and Ethics Committee (approval number QA2013066). Individual ethics approval was not required for these projects. Ethics approval was covered under the original ethics application for the piloted Surgical NAPS
3	
4	
5	Ethical approval granted following low-risk review from: - Alfred Hospital Human Research Ethics Committee (HREC) on the 11/10/2017[HREC/17/143]. - Epworth HealthCare HREC on the 30/10/2017
	Local governance approval - Alfred Health [local project number: 469-17] - Epworth HealthCare [local project number: EH2017-270] - Melbourne Health (Ethics approval inclusive of Alfred Health HREC approval) [local project number: 2017.346]
	Ethics approval included consent for participation and potential publication.

Projects 1 and 5 required minimal risk, low-risk ethics reviews. The main concerns considered to be of negligible risk were:

- disclosure of sensitive personal information, i.e., potential loss of confidentiality due to focus group format (project 5);

- data confidentiality (project 1 and 5); and
- reputational harm, depending on the responses given (project 5).

Risks were mitigated with the adoption of password-protected software accounts, Qualtrics® for project 1 and NVivo® for project 5. All data were stored on a password-protected University of Melbourne computer, which was stored within NCAS at the secure Doherty Institute and was only accessed by the researchers.

Additionally, all data across projects were de-identified. In project 5, only information pertaining to profession (e.g., surgical specialty or clinician type) and sector (e.g., public or private) were noted when describing participants.

The main risk associated with conducting focus groups in project 5 was the potential loss of confidentiality. While we could not truly control this, the Project Information Statement (Appendix 6) and the introductory statement of the focus groups included a clause advising participants to respect each other and to not share information provided by and break the confidentiality of other participants outside the focus group.

6.7 Mixed-methods integration

Integration of quantitative and qualitative research has the potential to increase the value of mixed-methods research (301, 348). The qualitative data from project 5 about SAP prescribing behaviour can validate and provide context to the prescribing behaviour identified in projects 2-4. Similarly, the quantitative data from projects 1-4

may reflect the factors and influences identified in our qualitative research from project 5.

Creswell and Clark (301) proposed four methods for the integration of mixed-methods research, connecting building, merging and embedding. The quantitative research of projects 2, 3 and 4 was designed and developed iteratively, but, in terms of integration of quantitative and qualitative research, a merging integrations method was adopted. The merging of both methods occurs in **Chapter 12**, where the findings from all projects are triangulated to propose a theoretically-informed framework for surgical AMS (SAMS). This chapter utilises the quantitative data to identify areas for targeted quality improvement and the qualitative data to provide an explanation of the underlying behavioural influences, and how to appropriately address these in a meaningful and sustainable interventional framework.

6.8 Chapter summary

In summary, a review of the literature generated much discussion when designing the structure and methodological approach for this mixed-method thesis. This approach was considered appropriate for achieving the objectives of this thesis, which are to identify and describe the current state of SAP prescribing in Australia (**Chapters 8 to 10**), explore the underlying facilitators and barriers to appropriate SAP prescribing (**Chapters 7 and 11**), and, subsequently, identify characteristics of a practical and sustainable AMS intervention for SAP (**Chapter 12**).

Chapter 7: Evaluating the implementability of antibiotic surgical prophylaxis guidelines

7.1 Introduction

This chapter provides insight into the challenges of guideline implementation. **Chapter 3** explored the evidence for SAP that informs current guidelines. However, there are multiple factors that influence its implementation. The implementation of SAP guidelines and providing feedback on SAP prescribing (in relation to these guidelines) is a key example of an AMS intervention that has been adopted across Australia. An evidence gap was identified around the need to assess how implementable these guidelines are and if this influenced appropriate SAP prescribing. This chapter explores the intrinsic factors that influence guideline implementation via the use of the Guideline Implementability Appraisal (GLIA) instrument. The rationale for this instrument was discussed in **Chapter 6**. Identifying barriers and facilitators of guideline implementability is meaningful for guideline developers and implementers at national and local levels. Extrinsic factors also bear influence on guideline implementability and are explored in **Chapter 11**.

7.2 Publication

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.journals.elsevier.com/infection-disease-and-health/>

Research paper

Evaluating the implementability of Antibiotic Surgical Prophylaxis guidelines

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KEYWORDS

Guideline
implementability;
Surgical antimicrobial
prophylaxis;
Guideline compliance

Abstract *Background:* Current Australian data highlight guideline noncompliant prescribing of antimicrobials for surgical prophylaxis. The study aim was to evaluate the implementability of the Australian national surgical prophylaxis (SAP) guidelines to identify facilitators for and barriers to compliance.

Methods: Key stakeholders appraised the surgical prophylaxis guidelines using the Guideline Implementability Appraisal (GLIA) tool. Questions with 100% agreement for the response 'Yes' were identified as facilitators and those with 100% agreement for 'No', a barrier. Questions that did not receive 100% agreement, but had a majority (40–60%) 'Yes' or 'No' consensus were considered as borderline facilitators and barriers respectively.

Results: Ten appraisals were completed. Guideline recommendations were rated as easily identifiable and concise and were thus facilitators for implementation. The ability to measure guideline adherence and outcomes, and recommendations that were consistent with guideline user abilities and beliefs were also identified as facilitators. Borderline facilitators related to the clarity of the recommendations and whether they were explicit in what to do and in what circumstances. Evidence quality underpinning recommendations (validity), inflexibility of recommendations (flexibility) and the lack of patient data at the point of use (computability) were identified as borderline barriers to implementation. No recommendation reached agreement as being a barrier.

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Conclusion: The GLIA appraisal demonstrated overall implementability of the current Australian national surgical prophylaxis guidelines. Facilitators (i.e., measurability) and borderline facilitators highlight strengths of the current guideline. Borderline barriers (i.e., validity, flexibility and computability) may negatively impact upon implementability. Guideline developers should consider these dimensions to optimise guideline uptake and consequently patient care. © 2019 Australasian College for Infection Prevention and Control. Published by Elsevier B.V. All rights reserved.

Highlights

- Appraisal of Australian surgical antimicrobial prophylaxis guidelines implementability.
- Current guidelines demonstrated overall implementability.
- Facilitators such as measurability highlight the guidelines strengths.
- Borderline barriers such as validity and flexibility require ongoing development.
- Guideline developers/implementers should consider these factors to improve uptake.

Introduction

Surgical antimicrobial prophylaxis (SAP) aims to reduce the occurrence of surgical site infections (SSIs) and their impact on both the patient and the health care system. SSIs occur after 2–13% of procedures in Australia and rates vary according to the surgical procedure [1–3]. Of these SSI cases, approximately half were considered as preventable [4,5].

SAP is the leading indication for antimicrobial prescriptions in the Australian hospital setting and also has the highest rate of inappropriate use (43.1%) [6]. According to the Surgical National Antimicrobial Prescribing Survey (Surgical NAPS), overall inappropriateness of antimicrobial prescriptions was similar for perioperative (43.4% of antimicrobial doses) and post-operative (46.5% of antimicrobial courses) prophylaxis [7].

SAP guideline non-compliance is not unique to Australia and has been reported in the international literature [8–13]. Despite the development of numerous interventions to improve antimicrobial prescribing in the surgical setting [14–24], there remains a gap between evidence, guideline recommendations and clinical practice [25].

Clinical practice guidelines aim to promote high quality and appropriate healthcare [26,27]. Potential benefits include enhanced knowledge, attitudes and behaviour of the prescriber, which may then optimise patient outcomes [28]. However, guideline development does not guarantee successful implementation, and, consequently, may not mitigate suboptimal care.

Various methods have been developed to assess guideline quality and implementability [29–32]. The Guideline Implementability Appraisal (GLIA) instrument [33] is an internationally recognised and validated tool for assessment of a guideline's intrinsic characteristics [32]. The GLIA instrument was developed to provide feedback about a guideline's implementability to two distinct audiences; the guideline authors, and individuals/policy makers who choose guidelines for application within a health care delivery system [32].

The national guidelines (Australian Therapeutic Guidelines (TG): Antibiotic Surgical Prophylaxis chapter [34]) are recommended to support appropriate and evidence-based prescribing of SAP for Australian health professionals under the Antimicrobial Stewardship Clinical Care Standard [35] (where

SAP should be prescribed in accordance with the national guidelines in addition to the patients clinical condition); and the National Safety and Quality Health Service Standards which mandate access to the endorsed national guidelines for national hospital accreditation [4]. Access to the guidelines is online via paid subscription to Therapeutic Guidelines® or via free access for public hospitals. Targeted users are principally prescribers, but other health professionals such as pharmacists and nurses may refer to guidelines for their own clinical practice and review.

Development of the national guidelines is based upon expert-consensus from their 'Antibiotic Expert group' which is made up of writing groups of clinicians charged with reviewing the literature across each of the domains and providing consensus-based recommendations. It is independent from both government and commercial sponsorship. Experts are selected carefully to minimise conflicts of interest [36].

The 'Antibiotic Expert Group-C' that developed the assessed national guidelines includes experts from the multiple subspecialties of medicine and surgery, general practice and pharmacy [37]. These experts are representative of almost all states (except Tasmania) and territories of Australia. To our knowledge, the national guidelines [34] have yet to be appraised by guideline implementability appraisal tools. This study evaluated the implementability of the national guidelines for surgical prophylaxis (TG: Antibiotic Surgical Prophylaxis chapter) using the validated Guideline Implementability Appraisal (GLIA) instrument. This evaluation identifies potential facilitators and barriers to the national guidelines implementation that may contribute to the current state of non-compliant SAP prescribing [7,38]; The findings from this study also endeavour to inform future research for SAP guideline development and implementation.

Methods

Aim

To evaluate the implementability of the national guidelines for surgical prophylaxis (TG: Antibiotic Surgical Prophylaxis chapter) using the validated Guideline Implementability Appraisal (GLIA) instrument.

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Clinical practice guideline

The electronic version of the national guidelines was selected for review to enhance appraiser accessibility. The national guidelines consist of a section containing general principles (Recommendation 1: General principles of surgical prophylaxis) followed by 17 additional subsections addressing surgical prophylaxis for the following surgical procedures: abdominal, gastrointestinal endoscopic, breast, burns, cardiac, implantable cardiac device insertion, dermatological, head and neck, lower limb amputation, neurosurgery, obstetric and gynaecological, ophthalmic, orthopaedic, plastic, thoracic, urological, and vascular.

Feasibility of the individual appraisals for all 17 subsections was assessed in a pilot appraisal by one author and one external infectious diseases consultant. The time taken to complete the pilot appraisal was approximately 4 h. The subsections were noted to be similar in terms of intrinsic factors, i.e., structure and presentation, and vary in terms of specific recommendations. Overall the pilot appraisal revealed that the content was of a high volume and repetitive. It was agreed by the authors *a priori*, that appraisal of each recommendation was not feasible as it would be time consuming and impact on response rate. Therefore, these 17 subsections were appraised as one recommendation. Thus, this appraisal refers to two pre-defined recommendations: 1. General principles of surgical prophylaxis, and 2. Surgical prophylaxis for specific surgical procedures.

Appraisal instrument

The GLIA instrument measures intrinsic characteristics of guidelines, and includes a manual, which was provided to assist appraisers. The first section of GLIA consists of nine questions that address the guideline as a whole; these questions are classified as global considerations (Table 1). The second section consists of 31 questions that are grouped into eight dimensions, focusing on the intrinsic characteristics of the guideline (Table 2).

The computability dimension is optional and was included in this appraisal as the electronic version of the

guidelines were appraised as opposed to the print version. All questions have four response categories; 'Yes', 'No', 'Unsure' (?) and 'Not Applicable' (N/A) (Table 3).

The GLIA instrument was manually entered into Qualtrics® — an online survey database. Additional space for comments explaining why the recommendation did not meet the criteria, similar to the original GLIA instrument, was included. 'Yes' responses did not require explanation or comment.

Recruitment of appraisers

Purposive sampling was employed to recruit key stakeholders across public and private sectors in the state of Victoria, Australia, and to ensure representation from relevant areas of surgery, anaesthesia, infectious diseases, infection control and antimicrobial stewardship. GLIA developers recommend at least two appraisers [32,33] however, a target of six to twelve appraisers was considered adequate to represent the different areas of expertise. Recruitment was an ongoing process until an appraisal from each stakeholder was achieved. Participants were recruited via email with a letter of invitation including details of the study and ethics approval. Those who consented to participate via email were provided with a personalised Qualtrics® survey link to complete the appraisal. Participants who completed the appraisal received a \$100 online gift voucher as a token of appreciation for their time.

Analysis

Questions that received 100% agreement with an answer of 'Yes' were identified as facilitators [F] and those with 100% agreement of 'No' identified as a barrier [B]. Questions that did not receive 100% agreement but had a majority (40–60%) 'Yes' or 'No' consensus were considered borderline facilitators [BF] and barriers [BB] respectively. The application of the use of borderline facilitators and barriers as analytic categories has been reported elsewhere [39]. Free text comments were included in the appraisal to discuss 'No', '?' and 'N/A' responses. Iterative review of open text responses provided illustrative quotes to support the GLIA results.

Table 1 GuideLine implementability appraisal (GLIA) global considerations: Questions 1–9 [33].

1.	Does the guideline clearly define the target patient population?
2.	Does the guideline clearly define its intended audience (i.e., types of providers)?
3.	Are the settings in which the guideline is to be used clearly described?
4.	Do the organization(s) and author(s) who developed the guideline have credibility with the intended audience of the guideline?
5.	Does the guideline suggest strategies for implementation or tools for application e.g., a summary document, a quick reference guide, educational tools, patients' leaflets, online resources or computer software?
6.	Is it clear in what sequence the recommendations should be applied?
7.	Is the guideline internally consistent, i.e., without contradictions between recommendations or between text recommendations and flowcharts, summaries, patient education materials, etc.?
8.	Are all recommendations easily identifiable, e.g., summarized in a box, bold text, underlined, etc.?
9.	Are all recommendations (and their discussions) concise? (Longwinded explanations impair implementability.)

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Table 2 Guideline implementability appraisal (GLIA) dimensions: Questions 10–30 [33].

Dimension	Definition	Questions
Executability	Exactly what to do.	10. Is the recommended action (what to do) stated specifically and unambiguously? 11. Is sufficient detail provided or referenced (about how to do it) to allow the intended audience to perform the recommended action?
Decidability	Precisely under what conditions to do something e.g. age, gender, clinical findings, laboratory results.	12. Would the guideline's intended audience consistently determine whether each condition in the recommendation has been satisfied? 13. Are all reasonable combinations of conditions addressed? 14. If this recommendation contains more than one condition, is the logical relationship (ANDs and ORs) between conditions clear?
Validity	The degree to which the recommendation reflects the intent of the developer and the strength of evidence.	15. Is the justification for the recommendation stated explicitly?
Flexibility	The degree to which a recommendation permits interpretation and allows for alternatives in its execution.	16. Is the quality of evidence that supports each recommendation stated explicitly? 17. Is the strength of each recommendation stated explicitly? 18. Does the recommendation specify patient characteristics (such as coincident drug therapy and common co-morbid conditions) that require or permit individualization? 19. Does the recommendation specify practice characteristics (such as location and availability of support services) that require or permit modification?
Effect on process of care	The degree to which the recommendation impacts upon the usual workflow in a typical care setting.	20. Can the recommendation be carried out without substantial disruption in current workflow? 21. Can the recommendation be pilot tested without substantial resource commitment?
Measurability	The degree to which the guideline identifies markers or endpoints to track the effects of implementation of this recommendation.	22. Can adherence to this recommendation be measured? 23. Can outcomes of this recommendation be measured?
Novelty/Innovation	The degree to which the recommendation proposes behaviours considered unconventional by clinicians or patients.	24. Can the recommendation be performed by the guideline's intended users without acquisition of new knowledge or skills? 25. Is the recommendation consistent with existing attitudes and beliefs of the guideline's intended audience? 26. Is the recommendation consistent with patient expectations?
Computability	The ease with which a recommendation can be operationalized in an electronic information system.	27. Are all patient data needed for this recommendation available electronically in the system in which it is to be implemented? 28. Is each condition of the recommendation defined at a level of specificity suitable for electronic implementation? 29. Is each recommended action defined at a level of specificity suitable for electronic implementation? 30. Is it clear by what means a recommended action can be executed in an electronic setting, e.g., creating a prescription, medical order, or referral, creating an electronic mail notification, or displaying a dialog box?

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Table 3 Types of guideline implementability appraisal (GLIA) responses [33].

Response	Rationale
Yes (Y)	The recommendation meets this criterion fully.
No (N)	The recommendation does not meet this criterion.
Unsure (?)	Appraiser is unable to address this question because of insufficient knowledge or experience in this area
Not Applicable (N/A)	Criterion is not applicable to this recommendation

Results

Fifteen participants were recruited iteratively, with ten appraisals completed (response rate: 66.7%) that represented all targeted stakeholders; three infectious diseases physicians, one surgeon, one infection control consultant, three anaesthetists and two antimicrobial stewardship pharmacists. Five surgeons did not respond to complete the appraisal.

Overall, the GLIA appraisal supports the implementability of the current guideline; with 66.1% of all responses 'Yes' (n = 510).

Facilitators of global considerations

Global considerations (Q1–9) (Table 1) were rated by the appraisers in relation to the guideline in its entirety.

Identifiable and concise recommendations

Appraisal of the overall guideline demonstrated that the recommendations were perceived to be easily identifiable (Q8) and concise (Q9). All ten appraisers considered these global considerations (Q8 & 9) as facilitators (100% 'Yes'). 'Yes' responses did not prompt for explanation or comment (see Methods).

Borderline facilitators of global considerations

Target patient population

The target patient population was adequately described according to eight appraisers (Q1: 80% 'Yes'). Opposing appraisers commented that whilst the population was not "actually defined ... it was implicit e.g. patients having surgical procedures for surgical prophylaxis" (Appraiser 2) and "assumed for hospital patients" (Appraiser 4).

Credibility of guideline authors

Eight of the appraisers believed that the guideline authors were credible (Q4: 80% 'Yes'). One appraiser did not believe they had sufficient experience to rate this item and Appraiser 5 did not believe the authors accurately reflected all surgical specialty groups stating "limited surgical staff (e.g. orthopaedics) included in Expert Group. Not all specialties represented."

Guideline setting

Five appraisers believed that the setting for the guideline was well described with the remaining five disagreeing (Q3: 50% 'Yes' and 50% 'No'). Therefore, this domain is both a

borderline facilitator and a borderline barrier. Half the appraisers felt the setting was not adequately described and this is demonstrated by the following quotes:

"Not stated - I'm sure intended to be used in any setting where the described infections are seen and treated - hospital, primary care, community." – Appraiser 2.

"I assume the PRIMARY setting is acute care hospitals." – Appraiser 4.

"Implied that hospital-based practice is setting." – Appraiser 5.

"Assumed to be for acute patients, but could be outpatients or inpatients." – Appraiser 7.

Clear sequence of recommendations to be applied

Appraisers were either in support of the sequencing of recommendations (Q6: 60% 'Yes') or believed this was not an applicable question to the guideline as a whole (Q6: 40% 'N/A').

Guideline is internally consistent

The majority of the appraisers found the guidelines were internally consistent; that is without contradictions between recommendations and other resources such as flow charts and summaries (Q7: 90% 'Yes').

Borderline barriers of global considerations

Guideline audience

The majority of the appraisers noted the guideline did not clearly define its intended audience/users; thus, it is considered a borderline barrier (Q2: 60% 'Yes'). Those who disagreed commented that the audience was "not explicitly defined" (Appraiser 9) or "stated" (Appraisers 2 and 5). Despite this lack of specificity, appraisers suggested that the implied users were "clinicians (including generalist/specialist prescribers and pharmacists) working in hospitals" (Appraiser 4), "health professionals prescribing antibiotics" (Appraiser 2), "surgeons and anaesthetists" (Appraisers 5 and 8); and "pharmacists" (Appraiser 8).

Strategies for implementation

Implementation strategies and tools to assist guideline application were lacking according to appraisers (Q5: 60% 'No'); thus, identifying this global consideration as a borderline barrier.

Appraisers noted there was "no mention of these strategies re surgical prophylaxis" (Appraiser 6) nor was a "summary provided" (Appraiser 5). Two appraisers acknowledged the presence of "online resources" (Appraiser 8) including "references provided and some flow charts and links" (Appraiser 7).

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Facilitators and borderline facilitators of guideline recommendations

The eight dimensions were assessed for both recommendations 1 (general principles of surgical prophylaxis), and 2 (surgical prophylaxis for specific surgical procedures) (Table 2).

Measurability

All appraisers agreed that adherence to the recommendations was measurable (Q22: 100% 'Yes') and thus is a facilitator for guideline implementation. Similarly, most of the appraisers concurred that the ability to measure the outcomes of guideline adherence also facilitated implementation (Q23: 90% 'Yes').

Novelty/innovation

Novelty and innovation was considered either a facilitator or borderline facilitator across all questions and recommendations (Q24–26). Both recommendations were thought to be implementable without the intended user acquiring new knowledge or skills (Q24: 90–100% 'Yes'). Eight appraisers achieved consensus that both recommendations were consistent with the attitudes and beliefs of the intended users (Q25: 80% 'Yes'). Those that disagreed believed that the guidelines may not reflect surgeons' views based on non-adherent practices they may have witnessed. Issues pertaining to potentially non-adherent SAP use are illustrated in the quotes below and include; incorrect antimicrobial, duration, lack of indication and intraoperative re-dosing.

"No - many surgeons have alternative views on whether antibiotics should be used (default is to request antibiotics even for clean superficial procedures) and which antibiotics should be used." – Appraiser 2.

"Duration (and sometimes choice) of prophylaxis is still often based on a particular surgeon's beliefs that are inconsistent with Therapeutic Guidelines. Not all anaesthetists are aware of the re-dosing recommendation. Certain surgeons love to apply topical antibiotics to surgical sites in theatre/afterwards." – Appraiser 6.

Flexibility

The ability to modify recommendations to suit the patient characteristics was considered a borderline facilitator (Q18: 60% 'Yes'). However, disagreement was noted by appraisers who suggested such flexibility was limited (see Borderline Barriers).

Executability and decidability

Appraisers believed there was considerable detail provided to ensure the recommendations could be executed in a consistent manner and that users could clearly identify how and when to do so; with consensus as a facilitator ranging between 60 and 90%. Thus, both the dimensions of executability (Q10–11) and decidability (Q12–14) were identified as borderline facilitators.

Exceptions were noted by appraisers regarding executability, particularly for the first recommendation (General principles of surgical prophylaxis), in which less directive instructions reflected by the words "may", "should" and

"consider"; allow for user autonomy and potential variation in SAP prescribing. Examples are illustrated in the following quotes:

"Dosing issues related to obesity are confusing. There are no suggested doses for cefazolin in obesity. Are dose recommended for [vancomycin and gentamicin] for body mass or lean body mass? This should be explicitly stated because we frequently do arthroplasty or [Coronary artery bypass graft] (CABG) on 140 kg patient so dose would range from 400 mg to 700 mg for [gentamicin] for example." – Appraiser 1.

"Dosage adjustment may be necessary" in obesity but there are no further details given. 'Excessive blood loss' requiring antibiotic re-dosing is not defined. Dosing of teicoplanin as an alternative to vancomycin is not detailed." – Appraiser 6.

Similarly, this terminology caused disagreement amongst appraisers when assessing the recommendations decidability. Appraiser 1 suggested that this may allow guidelines users to interpret such recommendations to justify their "preformed opinion by applying their own definitions, such as for 'Significant Risk of Postoperative Infection'" and may contribute to the "uncertainty or debate about situations not requiring prophylaxis - especially for breast surgery, upper [gastrointestinal] (GI) and urologic surgery" (Appraiser 2).

Various health professionals utilise the guidelines and, therefore, there may be differences in user knowledge and how they interpret recommendations:

"ID Physicians are not surgeons, so I have found it tricky interpreting the Head and Neck Surgery section re 'prophylaxis should be considered for procedures that involve incision through oral, nasal, pharyngeal or oesophageal mucosa ...'. Does this include turbinoplasty? What about turbinectomy?" (Appraiser 6).

Effect on process of care (EPOC)

Guideline implementation did not have a negative impact upon the surgical setting's existing workflow (Q20–21 range: 80–90% 'Yes'). One appraiser noted an exception regarding vancomycin administration, which "almost always complicates workflow in anaesthesia" (Appraiser 1).

Borderline barriers of guideline recommendations

None of the GLIA dimensions received 100% 'No' agreement, thus there were no identified barriers. Borderline barriers (>40% 'No' consensus) were identified across three dimensions; validity, flexibility and computability.

Validity

Overall, this GLIA appraisal supported the notion that the guideline's validity or lack thereof was a borderline barrier to its implementation. Nine appraisers noted that evidence quality was not stated explicitly (Q16); "references are present, but no grading of their quality" (Appraiser 6). Appraiser 9 acknowledged that "a sense of the quality of evidence is evident, but not using a particular metric".

Appraisers noted that whilst references were present (Appraisers 3, 6 and 8), inclusion of evidence quality is "not a feature of the Therapeutic Guidelines" (Appraiser 6);

and if it was, it would be a "very long document" (Appraiser 1). Consequently, the guidelines may "become less practical and more unwieldy" (Appraiser 2), complicating its implementation. It was also noted that given the current literature for SAP, it might not be possible to include such explicit referencing as "evidence is either poor or extrapolated from limited studies" (Appraiser 1).

Mixed opinion was generated by appraisers when assessing recommendation justifications (Q15), with 60% 'Yes' consensus for recommendation 1 and 60% 'No' consensus for recommendation 2. Appraiser 2 suggested the provision of the references at the end of the online chapter may represent some sort of justification and highlighted that guideline users are "trusting appropriate expert review of the provided literature". Conversely, Appraiser 8 noted that it was "not clear which reference refers to which recommendation" thus questioning this component of guideline development.

Flexibility

The flexibility of the guideline's recommendations and its allowance for alternatives also generated mixed opinion amongst the appraisers with a range in 40–70% 'No' consensus for the 3 questions in this dimension (Q17–19) across both recommendations. The strength of each recommendation was not explicitly stated (Q17); appraisers again noted that this was "not a feature of the Therapeutic Guidelines" (Appraiser 6). However, the formatting of the guidelines enabled identification of stronger recommendations by using green highlighted boxes; in comparison, to "in text discussion ..." to provide additional information and "... give the sense of strength of the recommendation" (Appraiser 9).

Mixed opinion was demonstrated when assessing whether the recommendations specified patient (Q18) or practice (Q19) characteristics that required individualization. Both were considered borderline barriers across both recommendations (Q18 mean score: 40% 'No'; Q19 mean score: 45% 'No'). Only quotes reflecting a lack of patient characteristics were provided and are demonstrated below:

"The issue of SSI prophylaxis in the setting of the patient already on antibiotics needs more attention, particularly with regard to dosing intervals of coincident antibiotics" – Appraiser 1.

"No. Recommendation based on procedure, hypersensitivity and if [resistant] organisms likely" – Appraiser 3

Computability

Six appraisers reported a lack of electronic patient data available to support recommendation implementation (Q27: 60% 'No'). However, this was deemed to be dependent on accessibility of data and the information technology (IT) infrastructure of the guideline user's work place as demonstrated by the following quotes:

"Current levels of IT in my workplace would not allow decision support to prompt appropriate surgical prophylaxis." – Appraiser 2.

"Depends on what electronic systems are in place at a given facility. Some hospitals have electronic data on patients' weight, [body mass index] (BMI), renal function, allergies, current medications, etc, but many do not." – Appraiser 6.

"This will be hospital dependent, and often not the case." – Appraiser 7.

"The information may exist, and indeed in electronic location, but not at the treating institution (perhaps in Drs rooms)." – Appraiser 9.

Additionally, searching for these patient data may be time consuming and would disrupt the existing work flow; for example, patient history of colonisation for multi-drug resistant organisms.

"It would not be usual to comprehensively look for evidence of past colonisation with [methicillin-resistant *Staphylococcus aureus*] (MRSA) before every routine surgery." – Appraiser 1.

"For instance, patient factors that increase risk of [multi-resistant organism] (MRO) colonisation need to be specifically sought." – Appraiser 9.

Discussion

Our research is the first implementability study of the national guidelines for surgical prophylaxis. Overall, these SAP recommendations were found to be intrinsically implementable for general daily practice. However, borderline facilitators and barriers do exist.

Multiple intrinsic and extrinsic factors may influence guideline implementability, quality and consequently uptake. Gupta and colleagues [40] advocate an increased focus on improving the intrinsic qualities of guidelines, rather than solely extrinsic factors. Suboptimal intrinsic components of guidelines, particularly format and content, may also influence guideline implementation [27,41,42]. A systematic review including 41 studies identified intrinsic characteristics of the guideline, including utility, access, structure and local applicability, as key barriers to implementation [25]. Thus, highlighting the relevance of an intrinsic appraisal tool such as GLIA.

Our GLIA appraisal highlights the importance of intrinsic qualities as facilitators for guideline implementability. Within the national guidelines, green highlighted boxes surround the recommendations to make them more readily identifiable. Additional information is also provided, but not highlighted. The electronic version is also text-searchable, thus supporting identification of specific recommendations. The recommendation structure is concise and consistent throughout the guideline. Sequentially, the recommendation includes the drug, dose, (paediatric dose), route, timing and duration (if applicable). For example, the recommended surgical prophylaxis for cardiac surgery is:

cephazolin 2 g (child: 30 mg/kg up to 2 g) IV, within the 60 min (ideally 15–30 min) before surgical incision, then 8-hourly for up to 2 further doses [34].

Measurability as a facilitator has been reported elsewhere [41]. Compliance with the current guidelines is currently observed with ongoing data collection from the annual Surgical NAPS. We recommend that health service organisations provide resource and financial support for the ongoing review and measurement of SAP guideline compliance. Ongoing utilisation of Surgical NAPS will further support measurability of guideline compliance, provide

comparative site data for benchmarking, and identify areas of concern requiring specific interventions [7]. We recommend that health service organisations provide resource and financial support for the ongoing review and measurement of SAP guideline compliance.

Flexibility as both a facilitator and barrier of guideline implementability has been described in the literature [39,41,43–46]. Our appraisal noted the paucity of evidence and its consequent lack of recommendations for specific patient and practice characteristics may impact upon guideline implementation e.g. guidance for patients on concomitant antimicrobials. Similarly, Fischer and colleagues' scoping review of guideline implementability barriers and strategies [47] noted that a 'focus on patients with single disease entities' and 'exclusion of patients with complex disease entities' were considered barriers to implementation [47]. Consideration of these patient factors e.g. obesity, and acknowledging the strength of evidence may enhance the flexibility of the recommendations and consequent implementability [47]. We acknowledge that not every patient factor can be accommodated into a guideline recommendation. However, we would suggest that guideline developers consider including factors that are specific to the surgical procedures that have evidence to support any modified recommendations.

The national guidelines do not adopt a grading method to assess the evidence behind their recommendations. References are included online at the end of the section, but do not directly link recommendations to the specific evidence underpinning them. This may impact on the end-user's assessment of the guideline.

Our appraisal identified that the lack of evidence grading (i.e. validity) was considered a borderline barrier. This was also observed by Fisher and colleagues' scoping review on barriers to guideline implementation [47]. Comparatively, another GLIA appraisal [39] noted the opposite, where structured evidence reporting and linkage of evidence quality assessments alongside its recommendations were considered as facilitators.

In a counter argument, given the wide range in evidence quality, our appraisers have also suggested the grading and explicit justification of the recommendations may be impractical and negate implementation rather than enhance it. Thus, the adoption of evidence-based gradings has the potential to both enhance and complicate guideline implementability. Suggested strategies we propose are; an increase in transparency of the guidelines development and evidence based methodology, explicit grading of evidence quality or referencing and further guideline appraisals [47,48].

Ongoing advancements in health and technology have seen the emergence of electronic tools which appear to improve efficiency and appropriateness of care and the safety and quality of prescribing [49,50].

Our GLIA appraisal supports this need for integration by identifying computability as a borderline barrier [35]. A proposed strategy could include the provision of readily available electronic access to patient information and guidelines and electronic decision support tools, which may provide further support to prescribers and minimise impact on workflow in the theatre setting. Additionally, access via smartphones and tablets and connection to computerised

decision support systems or electronic medical records may also enhance guideline computability and implementability [47]. We recommend future updates to the national guidelines to include a focus on increasing electronic usability.

Guideline implementability may be enhanced with the development of additional implementation resources and tools [51]. The website for the national guidelines includes a video tutorial to support ease of use but does not provide information for workplaces to implement the guidelines into practice. Our appraisal identified the lack of resources and tools as a borderline barrier. There is ongoing research on what constitutes a desirable guideline implementation tool, and one component is the need for stakeholder and target user input [52]. We advocate the development of implementation resources that are adaptable to the various health services that are intended users of the guidelines.

Similarly, stakeholder input has been considered essential for guideline development [30]. Our appraisal supports the notion that the guideline's authors have credibility with the intended audience of the guideline, and this can be considered a borderline facilitator (Q5). However, the SAP guidelines encompass multiple surgical procedures and surgical specialities. Whilst the credibility of the guideline authors is recognised, the authors may not accurately represent all the surgical craft groups in Australia. Our findings suggest further engagement of surgeons from a range of surgical craft groups to assist with guideline development at the national level, but also for local guideline variations and their subsequent implementation.

Limitations

Modifications to the GLIA appraisal were made to assist with participant engagement (see Methods). The main modification was the summation of the guidelines into two recommendations, general principles and specific surgical procedures. Ideally, each recommendation would be appraised individually. This modification reduced the appraisal time required to support the participant completion rate but did not allow for differentiation of the recommendations for the multiple surgical procedures.

The developers of the GLIA instrument encourage appraisers to discuss any divergent responses to try and achieve consensus [32]. Due to the exploratory nature of this study, the authors opted to report the appraisers' views individually. Achieving full agreement of appraisers would have allowed greater clarification of facilitators and barriers.

This small exploratory sample size may not be representative of all clinician perspectives; however, it is important to note that large sample sizes are not warranted for guideline appraisals, with GLIA developers recommending two to three appraisers [32, 33]. It is not compulsory for guideline appraisals to be completed by end users; however, we wanted to provide the opportunity for engagement of multiple relevant stakeholders. Despite this, we believe our engagement with surgeons was sub-optimal. This complements the existing qualitative research in Australia [53] and the UK [54] that have also demonstrated poor engagement of surgeons in SAP

prescribing, guideline compliance and research. This research is a preliminary study for a larger qualitative research project that will include a greater recruitment of clinicians, in particular surgeons across a range of craft groups, to gain insight on barriers to and facilitators of appropriate and guideline complaint SAP prescribing in regard to both intrinsic (i.e., implementability) and extrinsic (i.e. social, environmental) factors.

Our sample size only included health professionals located within one state of Australia, Victoria. We acknowledge this as a limitation as this may have introduced a level of bias, as each Australian state and territory may have different policies and processes in regard to infection, prevention and control, and SAP. For example, the South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR) have developed their own evidence-based, peer-reviewed guidelines [55] that are designed to be used in conjunction with the national guidelines. For future research into guideline implementability we would recommend inclusion of all Australian states and territories to generate data that is reflective of national implementation.

Since, the completion of our data collection and analysis, the national guidelines have been updated [56]. We believe our findings are broadly translatable and provide beneficial feedback about implementability to the guideline developers and healthcare policy makers who are currently in the process of implementing these updated guidelines into practice. We advocate for additional research into the implementability of the recently updated guidelines to facilitate comparison with our findings.

This research only evaluates intrinsic factors that influence guideline implementability. Theoretical frameworks [42,57,58] provide a structured approach to identifying and understanding determinants that influence implementation and behaviour such as guideline non-compliance [59–62]. These frameworks consider extrinsic factors such as the environment/setting and the guideline user (their capabilities, opportunities and motivators). The decision-making process for SAP prescribing is complex and multifactorial. It is unlikely that guideline implementability is the sole issue pertaining to inappropriate SAP prescribing rates.

Conclusions

The GLIA appraisal demonstrates that the national SAP guidelines are overall implementable. Facilitators (i.e., measurability) and border facilitators (i.e., novelty/innovation, flexibility, executability, decidability and EPOC) highlight the strengths of the current guideline, and stakeholders who use the guidelines should consider interventions that further strengthen such factors.

Borderline barriers warrant further research on their influence for guideline implementability and non-compliance. Potential strategies include adopting explicit and transparent evidence-based methodology, assigning 'strengths' to recommendations, inclusion of patient and practice characteristics that support flexibility, further engagement with multiple surgical craft groups and integration of electronic guidelines with the users' electronic health platform.

There may be opportunities to enhance the implementation of the national guidelines. We advocate future research to identify optimal implementation strategies and exploration of extrinsic factors that may provide insight to the current state of guideline non-compliance and inappropriate SAP prescribing. This may then inform future interventions to optimise SAP prescribing and consequently enhance its benefits for both patient safety and care and the healthcare system.

Ethical considerations

Minimal Risks Ethics approved by the University of Melbourne, School of Population and Global Health (MSPGH) Human Ethics Advisory Group (HEAG). Ethics ID:1648127.1 Ethics approval included informed consent for participation and potential publication.

Authorship statement

CI- conducted data analysis, developed analysis plan, wrote analysis, drafted and revised paper. DA-developed analysis plan, wrote analysis, revised paper. TP- developed analysis plan, revised paper. CM-revised paper. KT-developed analysis plan, wrote analysis, revised paper.

Conflicts of interest

Nothing to declare.

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Provenance and peer review

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Chapter 8: Appropriateness of surgical antimicrobial prophylaxis practices in Australia

8.1 Introduction

This chapter demonstrates the efficacy of the Surgical NAPS online auditing platforms ability to describe SAP prescribing practices across Australia. The Surgical NAPS facilitated novel assessments of appropriateness of Australian prescribing practices and delineated rates of appropriateness for both procedural and post-procedural SAP. This research project has highlighted the benefits of using SAP auditing data to identify potential targeted areas of action for surgical AMS (SAMS) interventions, such as timely procedural administration and documentation of timing, post-procedural duration and surgical specialty groups. This project adopted an estimated marginal means statistical analysis to account for a range of patient, hospital and surgical factors, which once factored in, appropriateness of SAP was still low. Thus, highlighting that there is much room for improvement of SAP prescribing in Australia. This chapter sets the scene of Australian SAP prescribing and informed the directions of projects 3, an in-depth analysis of the orthopaedic procedures audited in the Surgical NAPS dataset and project 4, an in-depth analysis of antimicrobial choice for procedural SAP.

8.2 Publication

The supplementary data published with this manuscript can be found in Appendix 3.



Appropriateness of Surgical Antimicrobial Prophylaxis Practices in Australia

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Abstract

IMPORTANCE Surgical antimicrobial prophylaxis (SAP) is a common indication for antibiotic use in hospitals and is associated with high rates of inappropriateness.

OBJECTIVE To describe the SAP prescribing practices and assess hospital, surgical, and patient factors associated with appropriate SAP prescribing.

DESIGN, SETTING, AND PARTICIPANTS Multicenter, national, quality improvement study with retrospective analysis of data collected from Australian hospitals via Surgical National Antimicrobial Prescribing Survey audits from January 1, 2016, to June 30, 2018. Data were analyzed using multivariable logistic regression. Crude estimates of appropriateness were adjusted for factors included in the model by calculating estimated marginal means and presented as adjusted-appropriateness with 95% confidence intervals.

MAIN OUTCOMES AND MEASURES Adjusted appropriateness and factors associated with inappropriate prescriptions.

RESULTS A total of 9351 surgical episodes and 15 395 prescriptions (10 740 procedural and 4655 postprocedural) were analyzed. Crude appropriateness of total prescriptions was 48.7% (7492 prescriptions). The adjusted appropriateness of each surgical procedure group was low for procedural SAP, ranging from 33.7% (95% CI, 26.3%-41.2%) for dentoalveolar surgery to 68.9% (95% CI, 63.2%-74.5%) for neurosurgery. The adjusted appropriateness of postprocedural prescriptions was also low, ranging from 21.5% (95% CI, 13.4%-29.7%) for breast surgery to 58.7% (95% CI, 47.9%-69.4%) for ophthalmological procedures. The most common reason for inappropriate procedural SAP was incorrect timing (44.9%), while duration greater than 24 hours was the most common reason for inappropriate postprocedural SAP (54.3%).

CONCLUSIONS AND RELEVANCE High rates of inappropriate procedural and postprocedural antimicrobial use were demonstrated across all surgical specialties. Reasons for inappropriateness, such as timing and duration, varied according to the type of SAP and surgical specialty. These findings highlight the need for improvement in SAP prescribing and suggest potential targeted areas for action.

JAMA Network Open. 2019;2(11):e1915003. doi:10.1001/jamanetworkopen.2019.15003

Key Points

Question What are the current surgical antimicrobial prophylaxis prescribing practices in Australia, and what factors are associated with their appropriateness?

Findings This quality improvement study of 9351 surgical episodes found high rates of inappropriate procedural and postprocedural antimicrobial use across various hospital, patient, and surgical factors. The most common reason for inappropriate procedural use was incorrect timing, while duration greater than 24 hours was the most common reason for inappropriate postprocedural use.

Meaning These findings suggest that the identified hospital, patient, and surgical factors should be considered as targets for development of tailored interventions to ensure appropriateness of surgical antimicrobial prophylaxis prescriptions.

+ [Invited Commentary](#)

+ [Supplemental content](#)

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November 8, 2019 1/15

Welfare hospital peer groups categorizes similar hospitals based on shared characteristics and services provided, with a range of categories for both public and private hospitals.

Data Collection and Collation

The Surgical NAPS audit was conducted annually between January 1, 2016, to June 30, 2018. Survey participation was voluntary and could be completed prospectively or retrospectively. Hospitals could adopt a convenience sampling method to audit either a targeted surgical specialty or all procedures conducted during a specific period.

Trained auditors collected data according to a standardized method and data collection form¹⁷ (eFigure 1 in the [Supplement](#)). Auditors were primarily pharmacists, nurses, and infectious disease physicians who were provided with structured education and online training to ensure consistency of methods. All data from registered sites were entered in the Surgical NAPS online audit platform. Ongoing support and advice from a central clinical support team was also available by phone and email to guide auditors, specifically with appropriateness assessments.

Appropriateness was assessed by surgical episode and by each prescription given for the surgery. Three categories of antimicrobial prescriptions were defined for each surgical episode: procedural, postprocedural, and existing (eTable 1 in the [Supplement](#)). Guideline compliance was assessed against the national guidelines⁸ or local site-based guidelines available at the time of assessment. A summary of the guideline's recommendations for the general principles of SAP prescribing is included in eTable 2 in the [Supplement](#). Appropriateness was a composite measure based on antibiotic choice, timing of administration, dose, duration, and repeat dosing applying the standardized Appropriateness Assessment Guide (eFigure 2 in the [Supplement](#)). For example, incorrect dosing may refer to a strength that is not consistent with the guidelines or is not clinically appropriate for that specific patient in regard to his or her body weight or renal function.

The purpose of this study was to assess the quality of SAP prescriptions in terms of appropriateness. Surgical episodes and prescriptions in which no antimicrobials were prescribed, existing antimicrobial therapies only, or prescriptions deemed not assessable were therefore excluded from the statistical analysis. Our statistical analysis also excluded repeat doses that were indicated but not given and postprocedural prescriptions with a treatment indication or an indication that was not assessable ([Figure 1](#)).

As a sensitivity analysis, crude overall appropriateness of the surgical episode was calculated and compared when antimicrobials were and were not prescribed for either procedural or postprocedural SAP.

For univariable and multivariable analysis, exclusions were doses deemed not assessable or subvariables with missing, low, and/or disproportionate numbers. The top 10 prescribed antimicrobials accounted for more than 90% of the data, and the remaining antimicrobials were classified as "other."

Statistical Analysis

Data are presented descriptively, with categorical data presented as frequencies and percentages. Antimicrobial doses were stratified into procedural and postprocedural surgical prophylaxis.

Logistic regression models were used to identify hospital, patient, and surgical factors associated with appropriateness. Model fitting was started with the maximal model, including all relevant factors. Model selection was performed using a likelihood ratio test, and model fit assessed by residual plots. Mixed-effects logistic models fit with unique hospital identifiers as random intercepts provided the best fit to the data and were selected.

Crude estimates of appropriateness were adjusted for factors included in the model by calculating estimated marginal means, presented as adjusted appropriateness (AA) with 95% confidence intervals. These means are generated by estimating the outcome (ie, appropriateness) from the model and calculating an equal-weighted average across all subgroups. Here, the aim is to adjust for any biases caused by varying subgroup sizes in our sample.

Two-tailed tests were conducted, and a *P* value of less than .05 was considered statistically significant. Statistical analysis was conducted with Stata statistical software version 14.1 (StataCorp LP).

Results

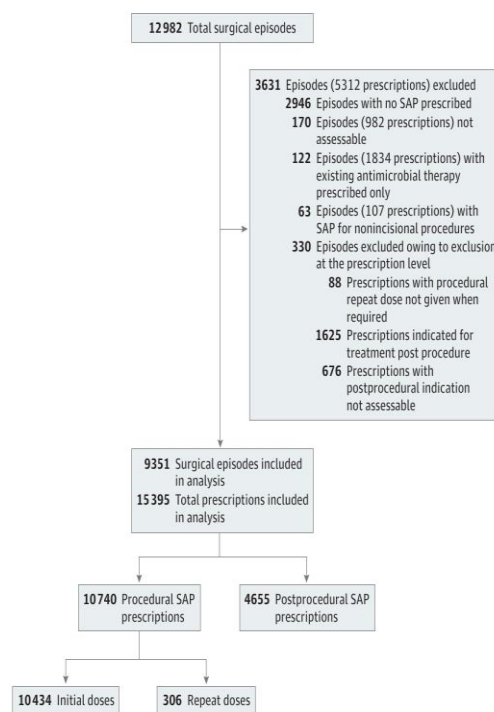
Overall, there were 156 contributing hospitals representing 22.5% of Australian hospitals with the capacity to perform elective procedures (256 public and 437 private hospitals).^{21,23-25}

In total, data on 12 982 surgical episodes were reviewed, including 6872 female patients (52.9%), 6069 male patients (46.8%), and 41 surgical episodes (0.3%) classified as other; median (range) patient age was 56.5 (0-105) years. Figure 1 provides an overview of included and excluded surgical episodes and antimicrobial prescriptions. There were 3631 surgical episodes excluded from statistical analysis. The remaining 9351 surgical episodes were included in statistical analysis (Figure 1).

A combined total of 15 395 prescriptions (10 740 procedural and 4655 postprocedural) were analyzed. Crude appropriateness of total prescriptions was 48.7% (7492 prescriptions). Hospitals located in Victoria (27.4%) and New South Wales (24.8%) were the largest contributors and accounted for more than half the prescription doses reviewed (eTable 3 and eTable 4 in the Supplement). Public hospitals accounted for 57.5% of the data set in comparison with private hospitals (42.5%). Orthopedic (31.9%) and abdominal (15.2%) surgery were the most commonly audited surgical procedure groups.

Our sensitivity analysis demonstrated a high overall appropriateness per surgical episode when no SAP was prescribed (2767 procedures [93.9%]). Comparatively, overall appropriateness was

Figure 1. Workflow Summary of Surgical National Antimicrobial Prescribing Survey Analysis



SAP indicates surgical antimicrobial prophylaxis.

reduced when at least 1 antimicrobial was prescribed for SAP (3727 procedures [39.9%]). Inversely, inappropriateness per surgical episode when no SAP prescriptions occurred was low (3.9%), compared with 54.1% when an episode included at least 1 prescription for SAP.

Procedural Prescriptions

Of all 10 740 procedural prescriptions, 615 (5.7%) were not assessable for appropriateness. eTable 3 in the [Supplement](#) describes the crude and adjusted appropriateness values for all the variables studied. All factors were included in the multivariable model. **Figure 2** illustrates the crude and adjusted appropriateness for each surgical procedure group. The AA of each surgical procedure group was low, ranging from 33.7% (95% CI, 26.3%-41.2%) with dentoalveolar surgery to 68.9% (95% CI, 63.2%-74.5%) for neurosurgery. Similarly, the range of AA across antimicrobial prescriptions was also low (eTable 3 in the [Supplement](#)). Ceftriaxone prescriptions accounted for the lowest AA (13.3% [95% CI, 8.4%-18.2%]; 261 prescriptions) and ceftioxin prescriptions for the highest AA (68.3% [95% CI, 58.0%-78.5%]; 77 prescriptions). Ceftriaxone is not recommended at all by national guidelines and ceftioxin is considered a second-line alternative recommendation for specific abdominal procedures.⁸ Cefazolin, the most commonly recommended antimicrobial agent for SAP, had an AA of 64.7% (95% CI, 61.1%-68.3%; 7991 prescriptions) (eTable 3 in the [Supplement](#)).

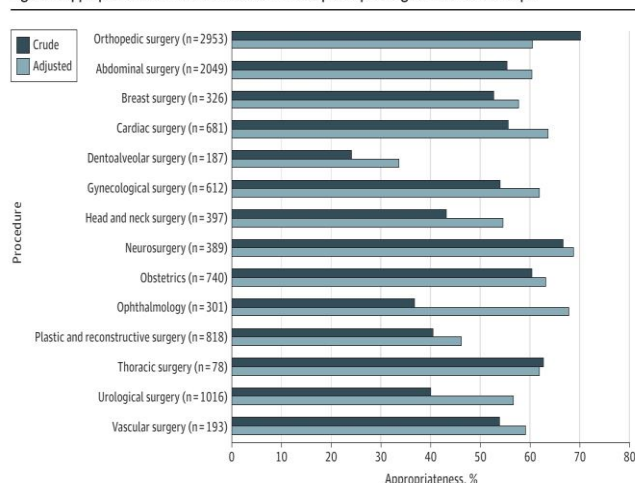
Patient factors such as sex (AA range: 59.1%-59.2%) and age (AA range: 55.0%-61.4%) demonstrated similar AA rates across their respective subvariables. This was similar for surgical factors such as initial vs subsequent admission (AA range: 59.0%-63.0%), surgery classification (AA range: 58.7%-69.8%), and presence of trauma (AA range: 58.7%-66.0%), prosthesis (AA range: 55.7%-65.4%), or excessive blood loss (AA range: 59.0%-65.9%) (eTable 3 in the [Supplement](#)).

Subanalysis compared acute hospital peer groups based on their funding type (ie, public or private groups A, B, and C). Significant differences in appropriateness were identified in only 1 comparison, between public acute group B and private acute group B ($\chi^2 = 4.03$; $P = .04$).

Postprocedural Prescriptions

A total of 4523 postprocedural surgical prophylaxis prescriptions (97.2%) were included for statistical analysis (132 prescriptions [2.8%] were not assessable). eTable 4 in the [Supplement](#) shows the crude and adjusted appropriateness values for all the hospital, patient, and surgical variables that were included in the multivariable model.

Figure 2. Appropriateness of 10 740 Procedural Prescriptions per Surgical Procedure Groups



After adjustment for these risk factors, AA was low across the hospital variables of state or territory (range: 30.4%-54.6%) and remoteness (range: 42.2%-52.5%) and the patient variables of sex (range: 42.5%-43.6%) and age (range: 40.2%-46.7%) (eTable 4 in the [Supplement](#)).

Figure 3 illustrates the crude and adjusted appropriateness for each surgical procedure group. All surgical procedure groups were associated with a low AA, ranging from 21.5% (95% CI, 13.4%-29.7%) for breast surgery to 58.7% (95% CI, 47.9%-69.4%) for ophthalmological procedures. Orthopedic surgery was the most commonly audited procedure group (1954 prescriptions [42.0% of postprocedural prescriptions]) and demonstrated a low AA (47.0% [95% CI, 41.0%-53.1%]). Overall, 38 different antimicrobials were prescribed for postprocedural surgical prophylaxis, with AA ranging from 26.8% for amoxicillin (95% CI, 15.8%-37.7%; 79 prescriptions) to 49.3% for cefazolin (95% CI, 43.6%-55.0%; 2752 prescriptions) (eTable 4 in the [Supplement](#)).

Subanalysis of comparable acute hospital peer groups based on their funding type (ie, public or private groups A, B, and C) did not demonstrate significant differences between the respective cohorts (ie, public acute group A vs private acute group A).

Reasons for Inappropriateness

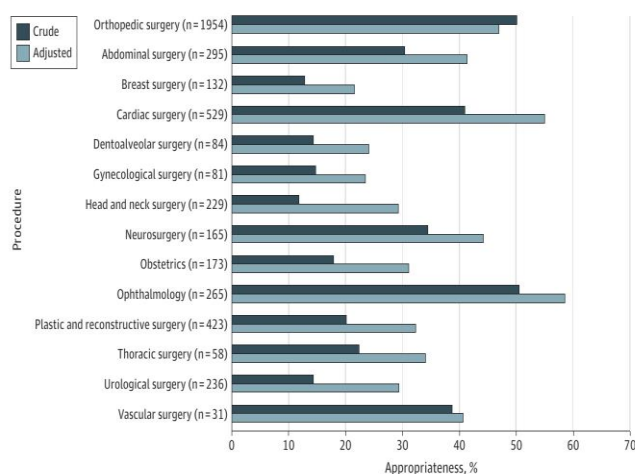
For procedural prescriptions, 11.7% (1252) were prescribed when procedural SAP was not deemed to be required. For the 9488 procedural prescriptions that were clinically indicated, 33.7% (3195) were inappropriate, with 1 or more reasons for inappropriateness documented (3543 total reasons). A total of 134 of 156 health care facilities (85.9%) contributed to this data subset. Surgical procedure groups with the largest proportion of contributing health care facilities were abdominal (60.4%) and orthopedic (55.2%) procedures. Comparatively, ophthalmology (6.7%) and thoracic (7.5%) surgery had the lowest contribution of different health care facilities.

The reasons for inappropriateness per surgical procedure group are presented in [Table 1](#). The most common reasons for inappropriate prescriptions were incorrect timing (44.9%), incorrect dose (26.1%), and/or spectrum too broad (15.9%). Only 65.6% of surgical episodes included a documented incision time.

Of all 4655 postprocedural surgical prophylaxis prescriptions, 60.2% (2801) were deemed inappropriate. The most common reason for inappropriateness was SAP administered when not required (as per guidelines) (61.5% [1724]).

For the remaining 1077 postprocedural prescriptions (38.5%), multiple reasons for inappropriateness could be applied to each prescription (1312 total reasons).

Figure 3. Appropriateness of 4655 Postprocedural Prescriptions per Surgical Procedure Groups



Ninety-eight health care facilities contributed to this data subset. Surgical procedure groups with the largest proportion of contributing health care facilities were orthopedic (66.4%) and plastic and reconstructive (26.5%) procedures. Comparatively, dentoalveolar (2.0%) and ophthalmology (6.1%) surgery had the lowest contribution of different health care facilities.

The reasons for inappropriateness per surgical procedure group are presented in **Table 2**. Incorrect duration (greater than 24 hours) (54.3%), incorrect dose and/or frequency (28.6%), and spectrum (too broad) (7.5%) accounted for more than 90% of all reasons (Table 2).

Discussion

The Surgical NAPS captures real-world prescribing behaviors for SAP across a broad range of procedures, hospital peer groups, and locations from both public and private hospitals. Our analysis has identified key targets for AMS programs, particularly related to timing and duration of SAP. An important finding of this study is that overall rates of appropriateness were low in the surveyed population. Comparatively, when SAP was not prescribed, high rates of appropriateness were demonstrated. Thus, patients not receiving SAP at all were considered a low priority target for SAP optimization.

Our data reveal that there are some interesting differences in rates of appropriateness across surgical specialties in Australian hospitals. Importantly, we did not demonstrate a significant difference between public and private hospital peer groups.

Inappropriate SAP prescribing has consistently been reported in both Australian²⁶⁻²⁹ and international³⁰⁻⁴¹ literature with a broad range; Ou et al⁴⁰ reported a 9.4% overall rate of appropriateness, while Hohmann et al³⁹ reported an overall compliance rate of 70.7%. The Surgical NAPS data demonstrated SAP appropriateness rates of 53.6% for procedural prescriptions and 36.9% for postprocedural prescriptions, with 48.7% as the combined overall rate of appropriateness. Definitions of appropriateness, compliance, and concordance vary in the literature; thus,

Table 1. Reasons for Inappropriateness of Procedural Prescriptions per Surgical Procedure Group

Surgical Procedure Groups	No. (%)		Types of Reasons for Inappropriateness							
	Health Care Facilities	Inappropriate Prescriptions ^a	Total Reasons for Inappropriateness ^b	Timing ^c	Dose	Broad Spectrum	Narrow Spectrum	Route	Allergy Mismatch	Microbiology Mismatch
Total	134	3195	3534	1588 (44.9)	923 (26.1)	561 (15.9)	279 (7.9)	88 (2.5)	50 (1.4)	45 (1.3)
Orthopedic surgery	74 (55.2)	700 (21.9)	755 (21.4)	360 (47.7)	218 (28.9)	120 (15.9)	31 (4.1)	11 (1.5)	13 (1.7)	2 (0.3)
Abdominal surgery	81 (60.4)	719 (22.5)	789 (22.3)	392 (49.7)	166 (21.0)	116 (14.7)	99 (12.5)	2 (0.3)	8 (1.0)	6 (0.8)
Breast surgery	32 (23.9)	92 (2.9)	79 (2.2)	41 (51.9)	23 (29.1)	3 (3.8)	1 (1.3)	7 (8.9)	3 (3.8)	1 (1.3)
Cardiac surgery	21 (15.7)	204 (6.4)	233 (6.6)	113 (48.5)	42 (18.0)	59 (25.3)	12 (5.2)	ND	3 (1.3)	4 (1.7)
Dentoalveolar surgery	24 (17.9)	78 (2.4)	95 (2.7)	14 (14.7)	28 (29.5)	42 (44.2)	7 (7.4)	ND	1 (1.1)	3 (3.2)
Gynecological surgery	43 (32.1)	176 (5.5)	199 (5.6)	101 (50.8)	64 (32.2)	16 (8.0)	13 (6.5)	1 (0.5)	2 (1.0)	2 (1.0)
Head and Neck surgery	45 (33.6)	97 (3.0)	98 (2.8)	37 (37.8)	32 (32.7)	3 (3.1)	22 (22.4)	1 (1.0)	3 (3.1)	ND
Neurosurgery	31 (23.1)	96 (3.0)	107 (3.0)	47 (43.9)	35 (32.7)	9 (8.4)	11 (10.3)	3 (2.8)	2 (1.9)	ND
Obstetrics	42 (31.3)	215 (6.7)	243 (6.9)	153 (63.0)	54 (22.2)	9 (3.7)	11 (4.5)	1 (0.4)	9 (3.7)	6 (2.5)
Ophthalmology	9 (6.7)	60 (1.9)	77 (2.2)	6 (7.8)	23 (29.9)	25 (32.5)	ND	22 (28.6)	1 (1.3)	ND
Plastic and reconstructive surgery	62 (46.3)	226 (7.1)	247 (7.0)	111 (44.9)	83 (33.6)	16 (6.5)	22 (8.9)	5 (2.0)	4 (1.6)	6 (2.4)
Thoracic surgery	10 (7.5)	17 (0.5)	18 (0.5)	11 (61.1)	6 (33.3)	ND	ND	1 (5.6)	ND	ND
Urological surgery	70 (52.2)	457 (14.3)	528 (14.9)	170 (32.2)	124 (23.5)	140 (26.5)	47 (8.9)	34 (6.4)	1 (0.2)	12 (2.3)
Vascular surgery	19 (14.2)	58 (1.8)	66 (1.9)	32 (48.5)	25 (37.9)	3 (4.5)	3 (4.5)	ND	ND	3 (4.5)

Abbreviation: ND, no data.

^c Timing was only assessable for procedural prescriptions.

^a Inappropriate prescriptions when surgical antimicrobial prophylaxis was indicated.

^b Rationale for the reasons for inappropriateness are described in eFigure 2 in the Supplement: Surgical National Antimicrobial Prescribing Survey Appropriateness Assessment Guide.

interpretation of comparisons requires caution. Our development and application of appropriateness assessments is, to our knowledge, novel in the current literature as it accounts for circumstances in which guideline-noncompliant prescriptions may in fact be appropriate in relation to the prescription's context.

Surgical Specialties

The comparison of surgical specialty SAP prescribing is relatively sparse in the current literature, as many assess guideline compliance^{34,37-42} as opposed to appropriateness. However, compliance does not infer appropriateness.

Orthopedic surgery was the most commonly audited surgical procedure group, accounting for 31.9% of all prescriptions. Our findings are consistent with the literature, in which orthopedic surgery has demonstrated low SAP guideline compliance^{34,37,39,40} ranging from 24.1%³⁷ to 44.4%.³⁴

We have identified that all surgical procedure groups demonstrated low AAs across procedural and postprocedural prescriptions. We believe low AAs may have the potential to adversely affect patient care and outcomes. All surgical procedure groups require ongoing support and AMS interventions tailored to their common reasons for inappropriateness to optimize SAP prescribing.

A Chinese prospective multicenter study⁴⁰ assessed the quality of SAP for 14 525 clean and clean-contaminated elective surgical procedures (orthopedic, vascular, gynecologic, and intestinal) and excluded emergency and contaminated and/or dirty procedures. Quality of SAP prescriptions was measured as adherence to the Chinese national guidelines, similar to our methods. Orthopedic surgery was also used as the reference group and gynecological surgery demonstrated significantly high rates of inappropriateness in comparison (odds ratio, 1.60; 95% CI, 1.37-1.88; $P < .001$).⁴⁰ Comparatively, the Surgical NAPS data included 156 hospital sites and emergency and contaminated or dirty procedures. These observations were similar to our results for postprocedural prescriptions, but not to our results for procedural prescriptions.

Table 2. Reasons for Inappropriateness of Postprocedural Prescriptions per Surgical Procedure Group

Surgical Procedure Groups	No. (%)			Types of Reasons for Inappropriateness						
	Health Care Facilities	Inappropriate Prescriptions ^a	Total Reasons for Inappropriateness ^b	Incorrect Duration ^c	Dose or Frequency ^c	Broad Spectrum	Narrow Spectrum	Route	Allergy Mismatch	Microbiology Mismatch
Total	98	1077	1312	712 (54.3)	375 (28.6)	99 (7.5)	48 (3.7)	47 (3.6)	10 (0.8)	21 (1.6)
Orthopedic surgery	65 (66.4)	423 (39.3)	499 (38.0)	273 (54.7)	192 (38.5)	16 (3.2)	8 (1.6)	3 (0.6)	6 (1.2)	1 (0.2)
Abdominal surgery	25 (25.5)	52 (4.8)	55 (4.2)	34 (61.8)	6 (10.9)	7 (12.7)	8 (14.5)	ND	ND	ND
Breast surgery	12 (12.2)	48 (4.5)	51 (3.9)	44 (86.3)	7 (13.7)	ND	ND	ND	ND	ND
Cardiac surgery	15 (15.3)	247 (22.9)	399 (30.4)	206 (51.6)	89 (22.3)	33 (8.3)	23 (5.8)	27 (6.8)	3 (0.8)	18 (4.5)
Dentoalveolar surgery	2 (2.0)	12 (1.1)	11 (0.8)	ND	ND	10 (90.9)	1 (9.1)	ND	ND	ND
Gynecological surgery	8 (8.2)	14 (1.3)	16 (1.2)	9 (56.3)	3 (18.8)	3 (18.8)	ND	1 (6.3)	ND	ND
Head and Neck surgery	17 (17.3)	38 (3.5)	22 (1.7)	10 (45.5)	5 (22.7)	4 (18.2)	ND	3 (13.6)	ND	ND
Neurosurgery	14 (14.3)	55 (5.1)	75 (5.7)	43 (57.3)	29 (38.7)	ND	1 (1.3)	1 (1.3)	1 (1.3)	ND
Obstetrics	10 (10.2)	23 (2.1)	25 (1.9)	11 (44.0)	5 (20.0)	ND	2 (8.0)	7 (28.0)	ND	ND
Ophthalmology	6 (6.1)	38 (3.5)	32 (2.4)	14 (43.8)	1 (3.1)	17 (53.1)	ND	ND	ND	ND
Plastic and reconstructive surgery	26 (26.5)	49 (4.5)	43 (3.3)	21 (48.8)	13 (30.2)	3 (7.0)	3 (7.0)	2 (4.7)	ND	1 (2.3)
Thoracic surgery	9 (9.2)	17 (1.6)	22 (1.7)	10 (45.5)	8 (36.4)	1 (4.5)	1 (4.5)	1 (4.5)	ND	1 (4.5)
Urological surgery	19 (19.4)	47 (4.4)	44 (3.4)	27 (61.4)	9 (20.5)	5 (11.4)	1 (2.3)	2 (4.5)	ND	ND
Vascular surgery	9 (9.2)	14 (1.3)	18 (1.4)	10 (55.6)	8 (44.4)	ND	ND	ND	ND	ND

Abbreviation: ND, no data.

^c Duration and frequency were only assessable for postprocedural prescriptions.

^a Inappropriate prescriptions when surgical antimicrobial prophylaxis was indicated.

^b Rationale for the reasons for inappropriateness are described in eFigure 2 in the Supplement: Surgical National Antimicrobial Prescribing Survey Appropriateness Assessment Guide.

Reasons for Inappropriateness and Potential Impact

Timing

Incorrect timing was a common reason for inappropriate procedural prescriptions in our surveyed population and the existing literature.^{28,31,33,40,43} It is well established in the current literature that the timing of SAP is associated with rates of SSI.⁴⁴⁻⁴⁶ Controversy remains when recommending an optimal time frame. The World Health Organization guidelines advocate for administration within 120 minutes of incision time.⁴⁶ Current Australian guidelines recommend antimicrobials with a short half-life (eg, cefazolin) be administered 60 minutes before incision and those with a longer half-life (eg, vancomycin) be administered 120 minutes before incision.⁹

Assessment of appropriate timing depends on the incision time. The Surgical NAPS identified suboptimal documentation of incision time; thus, caution is required when interpreting findings in relation to timing. The Surgical NAPS online reporting and public report¹⁷ provides ongoing feedback to auditors and highlights this as an area in need of improvement. Implementation of electronic medical records and theater management systems in Australian hospitals are likely to enhance documentation in terms of legibility, completeness, and consistency.⁴⁷⁻⁵⁰ This may support more accurate assessments of timing in relation to first incision.

Duration

The Surgical NAPS is the first national survey for SAP that has demonstrated widespread use of extended antimicrobial durations after surgery in Australian hospitals. We believe this use is underestimated, given that the survey permitted up to 24 hours of antibiotics, and not just a single dose, in keeping with published quality indicators.^{16,51}

Prolonged duration of antimicrobial use is associated with increased risk of adverse effects, such as *Clostridioides difficile* (formerly *Clostridium difficile*) infection and contributes to the burden of antimicrobial resistance.⁵²⁻⁵⁴ The observational 4-year cohort study by Harbarth et al⁵⁵ of 2641 patients undergoing cardiac surgery confirmed that compared with short SAP (<48 hours), prolonged SAP (>48 hours) was not associated with a decreased risk of SSI (adjusted odds ratio, 1.2; 95% CI, 0.8-1.6) and was associated with an increased risk of acquired antibiotic resistance (adjusted odds ratio, 1.6; 95% CI, 1.1-2.6).

Most recently, a multicenter national retrospective cohort study⁵⁶ of patients in the US Veterans Affairs health care system captured data from 79 058 patients who underwent a range of surgical procedures (cardiac, orthopedic, colorectal, and vascular). The study⁵⁶ demonstrated that longer durations of prophylaxis did not lead to additional SSI reduction and were associated with increases in acute kidney injury and *C difficile* infection.

Recent national and international guidelines^{9,11,12} advocate for single-dose prophylaxis only. Despite the growing evidence advocating for shorter durations and demonstrating harm associated with extended antimicrobial use, duration was identified as the most common reason for inappropriate postprocedural SAP, which mirrors the literature.^{28,30-32,34,37,40,57} Our data also highlighted prolonged SAP durations prescribed across a range of procedures in which there was no evidence to support such use.

Retrospective assessments identified postoperative SAP that extended from the operative theater to the ward and discharge prescriptions. Therefore, SAP interventions should not solely target the operating theater and should include recovery and general wards.

AMS Interventions

The systematic review by Davey et al⁵⁸ demonstrated strong evidence that interventions targeted at antibiotic use among hospital inpatients were associated with increased antibiotic policy compliance and durations. Eleven of the 159 studies (6.9%) with intervention outcomes targeted SAP. Common interventions targeted reducing excessive use.⁵⁹⁻⁶¹ Enabling interventions were found to "increase the means and reduce barriers to enhance capability and opportunity"⁵⁸ and were considered the most effective intervention type compared with restrictions of use by expert approval.⁶² Examples

of enabling interventions include audit and feedback,^{59-61,63-65} educational outreach,^{63,66} and clinical decision support systems.⁶⁷⁻⁶⁹

Adoption of clinical decision support systems may improve evidence-based antimicrobial use.⁶⁹ We support implementation of clinical decision support systems with a variety of interventions such as feedback⁵⁸ from the Surgical NAPS audits to synergistically improve SAP prescribing, feedback, and subsequent outcomes for patients and the health care system.

Limitations

This study has some limitations. First, participation in the Surgical NAPS is voluntary; thus, our results may not be generalizable across all hospitals. Second, auditor flexibility to perform convenience sampling introduced respondent bias due to the variation in data collected. A mixed-effects regression model was used to account for the intrahospital correlations; however, the effects of an unbalanced survey design may persist. Third, variability of appropriate assessments is probable, as one auditor's interpretation may have differed from another. To minimize this, an assessment rubric and support from the central clinical support team were available. After completion of the first Surgical NAPS report in 2016,¹⁷ developers completed a small validation study and demonstrated a 6.7% disagreement rate when comparing assessments by local auditors with those conducted by the NAPS support team. This was deemed acceptable for this type of self-auditing by nonexperts; however, larger validation studies may be warranted.

In addition, there were limited data on clinical outcomes, as this component of the current survey was not mandatory. We support the introduction of mandatory outcome fields and the need for outcome data to provide greater insight and meaning for surgeons. We believe these data are required to drive change in prescribing behaviors. However, collection of data such as SSIs after admission is complex and would require additional systems and resources.

Conclusions

The Surgical NAPS data have identified high rates of inappropriateness for procedural and postprocedural SAP. Low and wide variation in appropriateness was noted across hospital and surgical factors, in particular surgical procedure groups. Reasons for inappropriateness varied according to the type of SAP, highlighting the need for targeted AMS interventions to address timing for procedural SAP and duration for postprocedural SAP. The Surgical NAPS data set is unique and extensive and continues to grow each year, with more and more Australian surgical centers participating. Ongoing analysis will continue to provide support and direction for AMS interventions, guideline development, and hospital policy.

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SUPPLEMENT.

eTable 1. Surgical NAPS Terminology and Definitions

eFigure 1. Surgical NAPS Data Collection Form

eTable 2. Summary of Australian Therapeutic Guidelines: Antibiotic Version 15 Recommendations

eFigure 2. Surgical NAPS Appropriateness Assessment Guide

eTable 3. Hospital, Patient and Surgical Factors and Adjusted Appropriateness of Procedural Prescriptions

eTable 4. Hospital, Patient and Surgical Factors and Adjusted Appropriateness of Post-procedural Prescriptions

Chapter 9: Identifying targets for improvement using a nationally standardised survey: Surgical antimicrobial prophylaxis in orthopaedic surgery

9.1 Introduction

This chapter illustrates the Surgical NAPS online auditing platforms ability to provide an in-depth description and analysis of SAP prescribing practices for surgical procedure groups across Australia. In **chapter 8**, orthopaedic procedures were identified as the most commonly audited procedure group with suboptimal rates of SAP appropriateness. The evidence and recommendations for SAP vary across different orthopaedic procedures, and this study further explored the variation in appropriateness within this surgical craft group.

The outcomes from this research project have highlighted the benefits of using SAP auditing data, such as identifying specific areas of action for AMS i.e., orthopaedic procedures. For example, SAP was commonly observed with clean procedures such as arthroscopy and hand surgeries that do not require SAP at all. Timing of procedural doses and prolonged duration of post-procedural SAP remain key targets for all orthopaedic procedure groups.

This project adopted an estimated marginal means statistical analysis (similar to **chapter 8**) to account for a range of patient, hospital and surgical factors. After adjusting for these factors, appropriateness of SAP was still low. An additional sub-

analysis examined SAP appropriateness for commonly audited orthopaedic sub-specialties. Appropriateness varied across these sub-specialties but was notably low.

There is much room for improvement of orthopaedic SAP prescribing in Australia. This chapter highlights the depth of data collected by the Surgical NAPS and its use to inform directions for AMS and quality improvement programs.

9.2 Submitted manuscript

The following manuscript was submitted and accepted with minor revisions to Infection Control and Hospital Epidemiology. This version was resubmitted on the 03/06/2020 and is pending final review.

The supplementary data submitted with this manuscript can be found in Appendix 4.

1 **Identifying targets for improvement using a nationally standardised survey: Surgical**
2 **Antimicrobial Prophylaxis in Orthopaedic Surgery**

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35 **Statement:**

36 An abstract of this manuscript was accepted as an oral presentation for the Society for
37 Healthcare Epidemiology of Americas'(SHEA) 6th Decennial International Conference on
38 Healthcare Associated Infections. However, this conference was cancelled due to the current
39 COVID19 pandemic. The abstract is pending publication in an ICHE supplement.

40 **Abbreviated title:** Antimicrobial Prophylaxis in Orthopaedics

41 **Word count:** 3000

42 **Abstract**

43 **Background:** Surgical antimicrobial prophylaxis (SAP) is commonly administered in
44 orthopaedic procedures. Research regarding SAP appropriateness for specific orthopaedic
45 procedures is limited and is required to facilitate targeted orthopaedic prescriber behaviour
46 change.

47 **Objectives:** To describe SAP prescribing and appropriateness for orthopaedic procedures in
48 Australian hospitals.

49 **Design, Setting, and Participants:** Multicentre, national, quality improvement study with
50 retrospective analysis of data collected from Australian hospitals via Surgical National
51 Antimicrobial Prescribing Survey audits from January 1, 2016, to April 15 2019 were
52 analysed.

53 **Methods:** Logistic regression identified hospital, patient and surgical factors associated with
54 appropriateness. Adjusted appropriateness (AA) was calculated from the multivariable
55 model. Additional sub-analyses were conducted on smaller subsets to calculate the AA for
56 specific orthopaedic procedures.

57 **Results:** 140 facilities contributed to orthopaedic audits in the Surgical NAPS, including
58 4,032 orthopaedic surgical episodes and 6,709 prescribed doses. Overall appropriateness was
59 low, 58.0% (n=3,894). This differed for prescribed procedural (n=3,978; 64.7%) and post-
60 procedural doses (n=2,731; 48.3%). The most common reasons for inappropriateness, when
61 prophylaxis was required, was timing for procedural doses (50.9%) and duration for post-
62 procedural prescriptions (49.8%). The AA of each orthopaedic procedure group was low for
63 procedural SAP (knee surgery, 54.1% to total knee joint replacement, 74.1%). Post-
64 procedural prescription AA was also low (hand surgery, 40.7% to closed reduction fractures,
65 68.7%).

66 **Conclusions** Orthopaedic surgical specialties demonstrated differences across procedural and
67 post-procedural appropriateness. The metric of appropriateness identifies targets for quality
68 improvement and is meaningful for clinicians. There is a need to develop targeted quality
69 improvement projects for orthopaedic specialties, to support optimisation of antimicrobial
70 use.

71 **Introduction**

72 Across Australian public and private facilities, hip, knee and shoulder arthroplasty accounted
73 for 122,500 surgical procedures in 2018.¹ As Australia's population ages, the need for joint
74 replacement procedures increase with recent epidemiological modelling of the Australian
75 Orthopaedic Association National Joint Replacement Registry (AOANJRR) dataset over 10
76 years (2003-2013) estimating the incidence of total knee joint replacement (TKJR) and total
77 hip joint replacement (THJR) for osteoarthritis to increase by 276% and 208%, respectively,
78 by 2030, with a total cost to the healthcare system estimated at \$AUD5.32 billion.² When
79 complications such as prosthetic joint infections arise, the cost of admission was calculated to
80 be 3.1 times greater than that of a primary arthroplasty.³ Thus, prevention of infection in high
81 volume orthopaedic procedures is warranted to improve patient care and costs to the health
82 care system.

83 Reflective of these high volumes, audits of surgical antimicrobial prophylaxis (SAP) usage
84 commonly target orthopaedic surgical procedures in Australia⁴⁻⁶ and internationally.⁷⁻⁹ The
85 Australian Surgical National Antimicrobial Prescribing Survey (Surgical NAPS) was
86 developed to facilitate and standardise SAP auditing via the collection of surgery details and
87 timing of antimicrobials for benchmarking and targeted feedback of SAP prescribing.^{4, 6}

88 The Surgical NAPS report demonstrated orthopaedics as the most commonly audited surgical
89 procedure group, accounting for 27.7% (1,294 of 4,674 doses) of all procedural doses and
90 41.8% (824 of 1,973 prescriptions) of all post-procedural SAP prescriptions.⁶ A recent
91 analysis of the Surgical NAPS data up until 30th June 2018 demonstrated high rates of SAP
92 prescribing inappropriateness for orthopaedic procedures.¹⁰ When taking into account a range
93 of hospital, patient and surgical factors, SAP appropriateness for orthopaedic procedures was
94 low across procedural (39.5%) and post-procedural prescriptions (53.0%).¹⁰

95 Current national guidelines (*Therapeutic Guidelines: Antibiotic*) recommend a pre-procedural
96 single-dose SAP for some procedures, (e.g. prosthetic large joint replacements), but not all
97 procedures require SAP (e.g. arthroscopy without implantation of prosthetic material).^{11, 12}
98 The guidelines acknowledge the lack of evidence regarding the optimal duration of
99 postoperative doses, particularly in TKJR surgery, recommending that, if post-operative
100 doses are administered, prophylaxis should not continue beyond 24 hours¹²(Table S1).

101 An in-depth analysis of the Surgical NAPS orthopaedic procedure data subset will provide
102 greater insight into potential variation across the subcategories and inform clinicians about
103 current SAP prescribing practices and areas for improvement.

104 **Aim**

105 The objective of this study was to describe SAP prescribing practices for orthopaedic surgical
106 procedures in Australian hospitals. Secondary aims include assessing SAP appropriateness
107 after accounting for a range of hospital, surgical and patient factors.

108 **Methods**

109 The key methods adopted for this research have been described previously.¹⁰ The Surgical
110 NAPS online auditing platform facilitates multicentre, national quality improvement research
111 by collecting a range of data across procedural and post-procedural settings.

112 **Survey metrics**

113 Three categories of antimicrobial prescriptions were defined for each surgical episode;
114 procedural, post-procedural and existing (definitions are outlined in Supplement Table S2).
115 Appropriateness was assessed by trained auditors (i.e., pharmacists, nurses and infectious
116 diseases physicians) at the surgical episode level and by each dose/prescription.
117 Appropriateness was assessed per dose/prescription and was a composite measure based on

118 antibiotic choice, timing of administration and duration applying the standardised
 119 Appropriateness Assessment Guide^{4, 10} (Supplement Figure S2).

120 The survey captures patient demographics (age, gender), clinical information (allergy status,
 121 antimicrobial choice, timing, duration) and procedure-related factors (surgical procedure).
 122 The list of surgical procedures and groups was developed from the Royal Australasian
 123 College of Surgeons' morbidity audit and logbook tool procedure list (Supplement Figure
 124 S2).

125 **Data collection**

126 Surgical NAPS was conducted as a voluntary survey in both public and private hospitals
 127 during any time in the year. Hospitals could participate multiple times over the three-year
 128 auditing period (2016 – 2019). The updated *Therapeutic Guidelines: Antibiotic* Version 16¹²
 129 were made available online on the 15th April 2019. All procedures from 18th April 2016 to the
 130 15th April 2019 were included to focus solely on assessments based on the previous Version
 131 15¹³ or locally endorsed guidelines.

132 Data were collected according to standardised methodology^{4, 10} and entered via the Surgical
 133 NAPS online portal.

134 **Inclusion and exclusion criteria**

135 Surgical episodes with an orthopaedic procedure documented as the main procedure were
 136 included. This study examines SAP quality, therefore existing antimicrobials and post-
 137 procedural prescriptions for treatment of infection or with a non-assessable indication were
 138 excluded. Procedural doses and post-procedural prescriptions that had a 'not-assessable'
 139 appropriateness were also excluded.

140 Surgical NAPS data collection and analysis were approved by Melbourne Health Human
 141 Research and Ethics Committee (approval number QA2013066).

142 **Statistical analysis**

143 An initial sub-group analysis compared the crude appropriateness of prescriptions when
144 antimicrobials were and were not prescribed for both procedural and post-procedural SAP.

145 Prescription data were stratified into ‘procedural’ and ‘post-procedural’ surgical prophylaxis.
146 Logistic regression models were used to identify hospital, patient and surgical factors
147 associated with appropriateness of prescribed doses. For univariate and multivariable analysis
148 exclusion of variables were required if data were missing, very low in number and/or
149 categorised as ‘unknown’ or ‘not assessable’. The top five prescribed antimicrobials
150 accounted for more than 90% of the data, and the remaining antimicrobials were classified as
151 ‘other.’

152 Model fitting was started with the maximal model, including all factors (peer group, gender,
153 age, allergies, ASA score, surgery number for admission, elective or emergency, trauma,
154 removal or insertion of prosthetic material, wound category, orthopaedic procedure group and
155 antimicrobial). Model selection was performed using likelihood ratio tests, and model fit
156 assessed by residual plots and goodness of fit measures (C-Statistic). Mixed-effects logistic
157 models fit with unique hospital identifiers as random intercepts, provided the best fit to the
158 data, and were selected. Two-tailed tests were conducted, and a *P* value of less than 0.05 was
159 considered statistically significant.

160 Estimated marginal means analyses calculated the mean (% appropriateness) for each
161 variable that was adjusted for the other model variables. This mean is reported as the adjusted
162 appropriateness (AA) with 95% confidence intervals.

163 Subgroup analyses were performed for three of the orthopaedic procedure groups (knees, hips
164 and open reduction and internal fixations); procedural and post-procedural data were
165 analysed separately for each group. The aforementioned best fit model was used to calculate

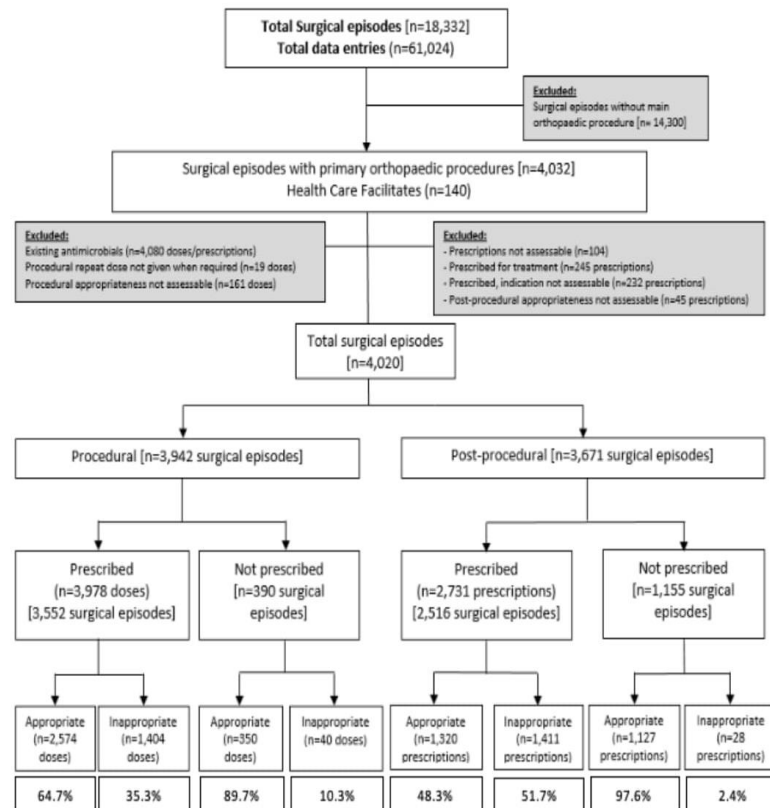
166 AA. Statistical analysis was conducted with Stata statistical software version 14.1 (StataCorp
167 LP).

168 **Results**

169 Overall, 140/156 (89.7%) hospitals participating in the surgical NAPS survey contributed
170 orthopaedic SAP data, representing 20.2% of Australian hospitals with the capacity to
171 perform elective procedures (256 public and 437 private hospitals).¹⁴⁻¹⁷ Figure 1 summarises
172 the studied dataset in terms of surgical episodes, procedural doses and post-procedural
173 prescriptions. Orthopaedic procedure groups accounted for 22.0% (n=4,032) of all surgical
174 episodes (inclusive of 8,254 antimicrobial doses and prescriptions) in the Surgical NAPS
175 dataset. The median age of patients across these orthopaedic surgical episodes was 65 years
176 (range 0-100). There were similar proportions of males and females (49.9% and 49.1%,
177 respectively).

178

179 **Figure 1 Audited surgical procedures: study inclusion and exclusion criteria**



180

181 Procedural antimicrobials were prescribed for the majority of episodes (n=3,978; 91.1%).

182 Comparatively, the post-procedural data subset (n=3,886) had a higher proportion of

183 antimicrobials not prescribed (n=1,155; 29.7%).

184 Overall appropriateness for prescribed procedural doses (n=3,978) was 64.7% and was lower

185 for prescribed post-procedural doses (n=2,731; 48.3%). When antimicrobials were not

186 prescribed, appropriateness was much higher for procedural and post-procedural prescriptions

187 (n= 350; 89.7% and n=1,127; 97.8% *respectively*) (Table 1).

188 **Table 1 Comparison of crude appropriateness for prescribed and non-prescribed surgical**
189 **antimicrobial prophylaxis**

	Total doses/ prescriptions	Appropriate N (%)	Inappropriate N (%)
TOTALS	8,254	5,371 (65.1)	2,883 (34.9)
Procedural	4,368	2924 (66.9)	1444 (33.1)
Prescribed	3,978	2,574 (64.7)	1,404 (35.3)
None prescribed	390	350 (89.7)	40 (10.3)
Post- Procedural	3,886	2447 (63.0)	1439 (37.0)
Prescribed	2,731	1,320 (48.3)	1,411 (51.7)
None prescribed	1,155	1,127 (97.6)	28 (2.4)

190 **Procedural Prescriptions**

191 Procedural prescriptions demonstrated a crude appropriateness of 64.7% (Table1). Table S3
192 in the Supplement describes the crude and adjusted appropriateness values for all the
193 variables included in the study.

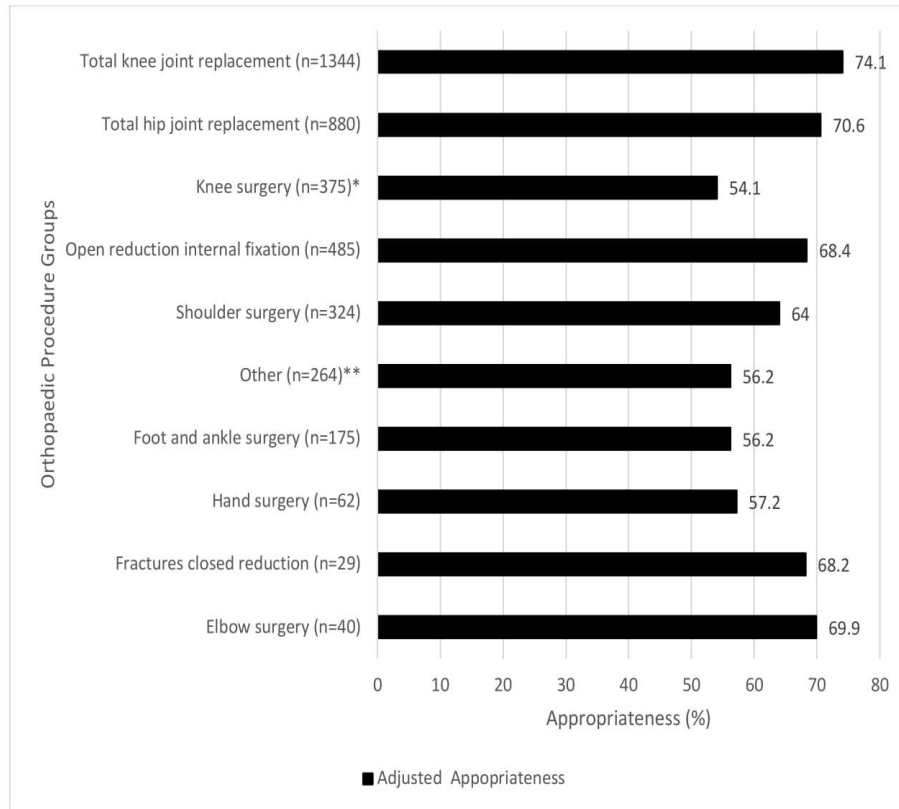
194 Multivariable analysis revealed the following variables to be significantly associated with
195 increased appropriateness of procedural SAP; peer group-private acute group C hospitals
196 (Odds Ratio [OR], 3.43; 95% CI, 1.27-9.26; $P=0.015$); 20-39 years old age group (OR, 1.55;
197 95%CI, 1.08-2.23; $P=0.016$) and; procedures involving removal or insertion of prosthetic
198 material. (OR, 2.09; 95%CI, 1.63-2.66; $P<0.005$) (Table S3).

199 The following orthopaedic procedure groups were significantly associated with a decrease in
200 procedural SAP appropriateness: knee (OR, 0.26; 95%CI, 0.17-0.41; $P<0.005$), shoulder
201 (OR, 0.49; 95%CI, 0.32-0.74; $P=0.001$), foot and ankle (OR, 0.30; 95%CI, 0.18-0.49,
202 $P<0.005$), hand (OR, 0.32; 95%CI, 0.15-0.69, $P=0.004$) and other (OR, 0.30; 95%CI, 0.19-
203 0.47, $P<0.005$) surgeries. Antimicrobial agents were also associated with a decreased
204 appropriateness including; gentamicin (OR, 0.02; 95%CI, 0.01-0.04; $P<0.005$), vancomycin
205 (OR, 0.09; 95%CI, 0.05-0.14; $P<0.005$) and clindamycin (OR, 0.05; 95%CI, 0.02-0.13,
206 $P<0.005$) (Table S3).

207 Figure 2 illustrates the crude and adjusted appropriateness for all assessable orthopaedic
208 procedural doses per orthopaedic procedure group. The AA for each orthopaedic procedure
209 group was low, ranging from 54.1% (knee surgery; 95%CI, 46.9-61.4) to 74.1% (TKJR;
210 74.1%; 95%CI, 69.5-78.7).

211 Cefazolin was the most commonly prescribed antimicrobial (86.3% of all procedural doses)
212 and was associated with the highest AA (73.6%; 95%CI, 69.2-78.1). Of the remaining
213 antimicrobials (13.7%), gentamicin was the next most commonly prescribed with 5.2% of
214 procedural doses. The AA for gentamicin was the lowest of the top 5 antimicrobials
215 prescribed (12.4%; 95%CI, 6.1-18.7) (Table S3).

216 **Figure 2 Appropriateness of orthopaedic procedural doses per orthopaedic procedure**
 217 **groups (%)**

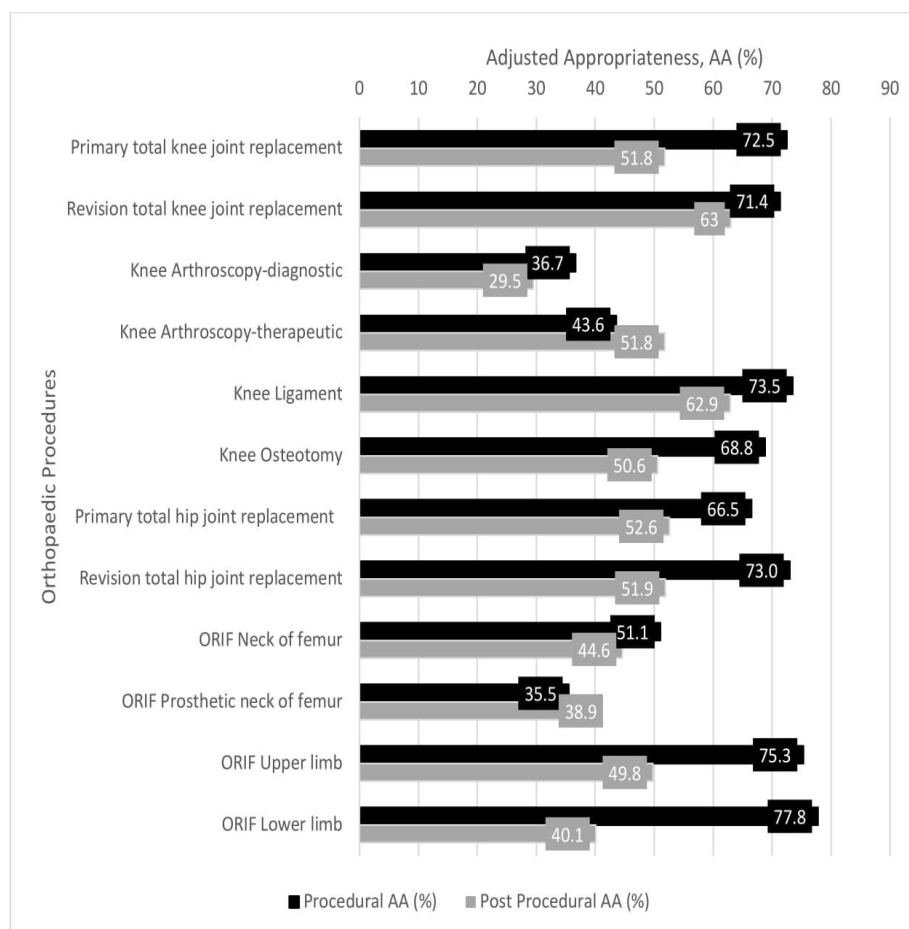


219 **Figure 2 Legend:**
 220 n=3,978 assessable orthopaedic procedural doses
 221 * Knee surgery excluding total knee joint replacements. e.g. knee arthroscopy
 222 ** Other surgical procedures included the following subcategories: 'Other', 'Soft tissue surgery',
 223 'Sacrococcygeal tumour excision' and 'Osteomyelitis (removal of implants/joint washout)'.
 224 Sub-group analyses of AA for specific orthopaedic procedures; knee, hip and open reduction
 225 internal fracture procedures were performed (Figure 3 and Tables S5, S7 and S9). For knee
 226 procedures, diagnostic and therapeutic knee arthroscopy, had the lowest rates of AA (36.7%
 227 and 43.6% respectively).
 228 Revision total hip replacements demonstrated a higher AA (73.0%), than primary hip
 229 replacements (66.5%) and ORIF procedures involving the neck of femur were lower (51.1%)
 230 than upper and lower limbs (75.3% and 77.8%, respectively). When prosthetic material was

231 present, inserted or removed, the AA was much lower (35.5%). This differs greatly to the
232 protective effect of appropriateness that was demonstrated by the presence of prosthetic
233 material on all orthopaedic procedures (Table S3).

234 Supplement Table S11 highlights the differing rates of appropriateness across the subset of
235 knee procedures where the evidence for SAP is limited and may be required on the basis of
236 the removal or insertion of prosthetic material. When prosthetic material was not present,
237 overall appropriateness was low (42.7%). Comparatively, when prosthetic material was
238 present, removed or inserted, appropriateness was higher (70.9% overall).

239 **Figure 3 Comparison of procedural and post-procedural adjusted appropriateness across**
 240 **orthopaedic surgical procedure sub-analyses**



241

242 **Figure 3 Legend:**

243 ^a Model adjusted for peer group, gender, age, allergies, ASA score, surgery admission number, elective or
 244 emergency classification, presence of trauma, presence, removal or insertion of prosthetic material, wound
 245 category, surgical procedure subcategories and top five antimicrobials prescribed per overall data.

246 ^b Procedural Knee Sub-Analysis Model C Statistic= 0.8765

247 ^c Post-Procedural Knee Sub-Analysis Model C Statistic= 0.9181

248 ^d Adjusted appropriateness not estimable due to low number of prescriptions and/or proportions

249 ^e Procedural Hip Sub-Analysis Model C Statistic= 0.8999

250 ^f Post-Procedural Hip Sub-Analysis Model C Statistic= 0.9252

251 ^g Procedural ORIF Sub-Analysis Model C Statistic= 0.8544

252 ^h Post-Procedural ORIF Sub-Analysis Model C Statistic= 0.8762

253 ⁱ Upper limb includes: carpus, clavicle, humerus, metacarpal, phalanx, olecranon, radius, scaphoid, ulna

254 ^j Lower limb includes: ankle, calcaneus, femur, patella, talus, tibia

255 *Reasons for inappropriateness*

256 Of the 1,404 inappropriate prescriptions, the leading reason for inappropriateness was the
257 administration of SAP when not required (27.2% of inappropriate prescriptions). Knee
258 surgery (excluding TKJR) was the procedure group with the highest rates of procedural SAP
259 prescribed when not indicated (72.6% of 168 inappropriate prescriptions).

260 When procedural SAP was indicated and deemed inappropriate (n=1,022 doses, n=1,042
261 documented reasons), the most common reason for inappropriateness was incorrect timing
262 (50.9%), consistent across all orthopaedic procedure groups (Table 2).

263 ***Table 2 Reasons for inappropriateness of Procedural doses per orthopaedic procedure***
264 ***group***

Orthopaedic procedure group - Orthopaedic Procedure	Total doses N, (% inappropriate)	Inappropriate N	Inappropriate and not indicated N (%)	Inappropriate and indicated N (%)	Total reasons for inappropriateness N	Reasons for inappropriateness ^a						
						Incorrect timing ^b N (%)	Incorrect dose/ frequency ^c N (%)	Incorrect route N (%)	Spectrum too broad N (%)	Spectrum too narrow N (%)	Allergy mismatch N (%)	Microbiology mismatch N (%)
Total N (%)	3,978 (35.3)	1,404 (100.0)	382 (27.2)	1,022 (72.8)	1,042 (100.0%)	530 (50.9)	278 (26.7)	20 (1.9)	152 (14.6)	41 (3.9)	18 (1.7)	3 (0.3)
Total knee joint replacement	1,344 (31.9)	429	69 (16.1)	360 (83.9)	378	180 (47.6)	100 (26.5)	6 (1.6)	69 (18.3)	14 (3.7)	8 (2.1)	1 (0.3)
- Primary	1249 (31.1)	388	68 (17.5)	320 (82.5)	326	153 (46.9)	86 (26.4)	6 (1.8)	61 (18.7)	11 (3.4)	8 (2.5)	1 (0.3)
- Revision	95 (43.2)	41	1 (2.4)	40 (97.6)	52	27 (51.9)	14 (26.9)	-	8 (15.4)	3 (5.8)	-	-
Total hip joint replacement	880 (35.1)	309	40 (12.9)	269 (87.1)	277	138 (49.8)	67 (24.2)	6 (2.2)	49 (17.7)	9 (3.2)	7 (2.5)	1 (0.4)
- Primary	793 (34.8)	276	36 (13.0)	240 (87.0)	245	124 (50.6)	56 (22.9)	5 (2.0)	44 (18.0)	8 (3.3)	7 (2.9)	1 (0.4)
- Revision	87 (37.9)	33	4 (12.1)	29 (87.9)	32	14 (43.8)	11 (34.4)	1 (3.1)	5 (15.6)	1 (3.1)	-	-

Knee surgery (excluding TKR)	375 (44.8)	168	122 (72.6)	46 (27.4)	46	15 (32.6)	19 (41.3)	3 (6.5)	5 (10.9)	3 (6.5)	-	1 (2.2)
Open reduction internal fixation of fracture (ORIF)	485 (28.9)	140	5 (3.6)	135 (96.4)	138	86 (62.3)	31 (22.5)	1 (0.7)	13 (9.4)	5 (3.6)	2 (1.4)	-
Shoulder surgery	324 (36.7)	119	54 (45.4)	65 (54.6)	57	30 (52.6)	14 (24.6)	2 (3.5)	8 (14.0)	3 (5.3)		-
Other	264 (42.4)	112	50 (44.6)	62 (55.4)	67	32 (47.8)	27 (40.3)	-	6 (9.0)	2 (3.0)	-	-
Foot and ankle surgery	175 (40.6)	71	17 (23.9)	54 (76.1)	51	37 (72.5)	11 (21.6)	-	-	2 (3.9)	1 (2.0)	-
Hand surgery	62 (41.9)	26	17 (65.4)	9 (34.6)	9	4 (44.4)	4 (44.4)	-	-	1 (11.1)	-	-
Fractures with closed reduction	29 (31.0)	9	2 (22.2)	7 (77.8)	8	4 (50.0)	3 (37.5)	-	-	1 (12.5)	-	-
Elbow surgery	40 (52.5)	21	6 (28.6)	15 (71.4)	11	4 (36.4)	2 (18.2)	2 (18.2)	2 (18.2)	1 (9.1)	-	-
a Rationale for the reasons for inappropriateness are described Surgical NAPS report ⁴ b Timing was only assessable for procedural prescriptions												

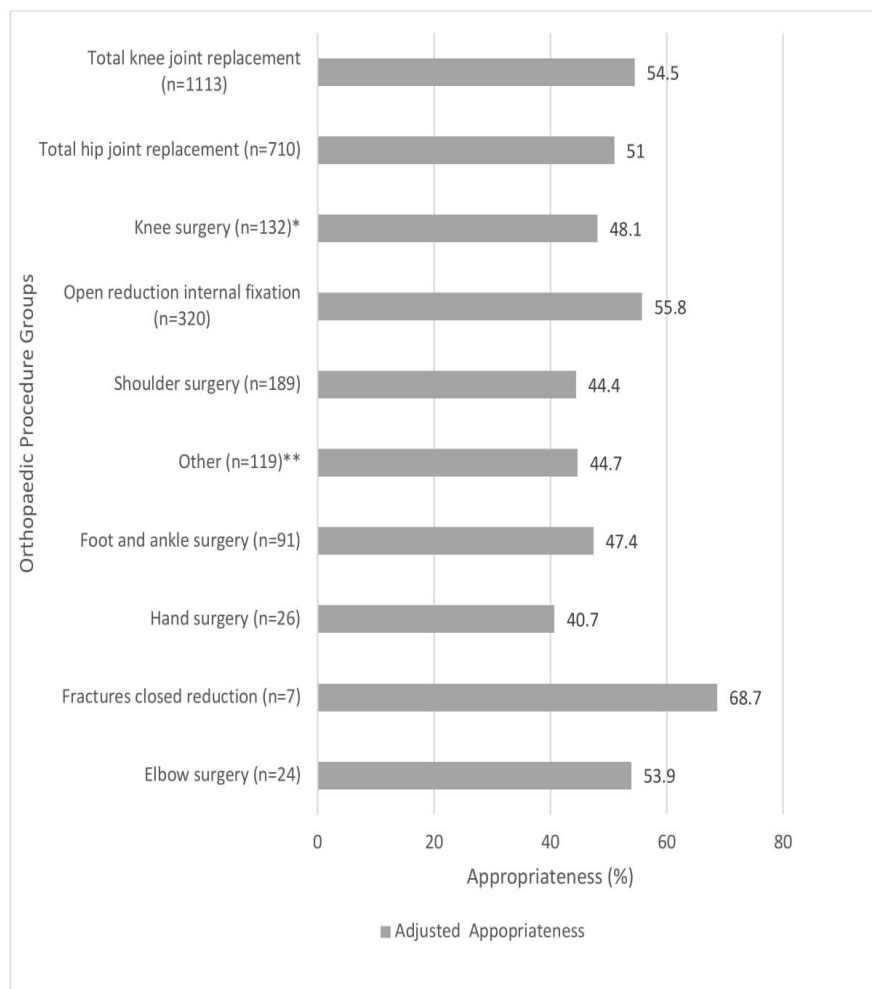
266 **Post-procedural prescriptions**

267 Post-procedural prescriptions demonstrated a crude appropriateness of 48.3%. Table S4
268 shows the crude and adjusted appropriateness values for all the hospital, patient, and surgical
269 variables included in the multivariable model.

270 On multivariable analysis (Table S4), the following were associated with appropriateness of
271 post-procedural antimicrobial prescriptions: peer group-private acute group D hospitals (OR,
272 14.49; 95%CI, 2.69-78.07; $P=0.002$); trauma (OR, 0.45; 95%CI, 0.24-0.83; $P=0.010$);
273 shoulder surgery (OR, 0.46; 95%CI, 0.26-0.81; $P=0.008$); other surgery (OR, 0.47; 95%CI,
274 0.25-0.90, $P<0.024$); prescriptions of cefalexin (OR, 0.04; 95%CI, 0.01-0.12; $P<0.005$),
275 vancomycin (OR, 0.19; 95%CI, 0.08-0.46; $P<0.005$) and gentamicin (OR, 0.10; 95%CI,
276 0.03-0.33; $P<0.005$).

277 Figure 4 illustrates the AA for all assessable post-procedural prescriptions for each
278 orthopaedic procedure group category. The AA for each procedure groups ranged from hand
279 surgery (40.7%; 95%CI, 24.3-57.0) to fractures closed reduction (68.7%; 95%CI, 38.9-95.6).

280 **Figure 4 Appropriateness of orthopaedic post-procedural prescriptions per orthopaedic**
 281 **procedure groups (%)**



282

283 **Figure 4 Legend:**

284 n= 2,731 assessable orthopaedic post-procedural prescriptions

285 * Knee surgery excluding total knee joint replacements e.g., knee arthroscopy

286 ** Other surgical procedures included the following subcategories: 'Other', 'Soft tissue surgery',

287 'Sacroccygeal tumour excision' and 'Osteomyelitis (removal of implants/joint washout)'.

288

289 Cefazolin represented the most commonly prescribed antimicrobial at 85.9% of all post-

290 procedural doses and demonstrated the highest rate of AA (55.2%; 95%CI, 48.4-61.9).

291 Cefalexin was the second most commonly prescribed antimicrobial (4.2%) and demonstrated

292 the lowest rate of AA (17.2%; 95%CI, 6.6-27.8) of the top five antimicrobials (Table S4).

293 Sub-group analyses of AA for knee, hip and open reduction internal fracture procedures were
294 performed (Figure 3 and Tables S6, S8 and S10). For knee procedures, osteotomy procedures
295 demonstrated the lowest rates of AA (50.6%). Primary TKJRs had a lower AA compared to
296 revisions (51.8% versus 63.0%).

297 Primary THJRs demonstrated a higher AA (52.6%) than revisions (51.9%). When prosthesis
298 was involved in neck of femur ORIFs, the AA was lower (40.1%) compared to no prosthesis
299 (44.6%).

300 *Reasons for inappropriateness*

301 Of the 1,411 inappropriate prescriptions, 47.6% were inappropriate because post-procedural
302 SAP was not indicated (Table 3). Procedure groups with the highest rates of post-procedural
303 SAP prescribed when not indicated were hand surgeries, (73.7% of 19 inappropriate
304 prescriptions) and foot and ankle surgery (63.5% of 52 inappropriate prescriptions) (Table 3).

305 When post-procedural SAP was indicated and deemed inappropriate (n=739 prescriptions, n=
306 836 documented reasons) the most common reason for inappropriateness was incorrect
307 duration (49.8%), followed by incorrect dose/frequency (42.3%); this finding was consistent
308 across all orthopaedic procedure groups (Table 3).

309 ***Table 3 Reasons for inappropriateness of Post-Procedural prescriptions per orthopaedic*** 310 ***procedure group***

Orthopaedic procedure group - Orthopaedic Procedure	Total doses N, (% inappropriate)	Inappropriate N	Inappropriate and not indicated N (%)	Inappropriate and indicated N (%)	Total reasons for inappropriateness N	Reasons for inappropriateness ^a						
						Incorrect dose/ frequency ^b N (%)	Incorrect duration ^c N (%)	Incorrect route N (%)	Spectrum too broad N (%)	Spectrum too narrow N (%)	Allergy mismatch N (%)	Microbiology mismatch N (%)
Total N (%)	2,731 (51.7)	1,411 (100.0)	672 (47.6)	739 (52.4)	836 (100.0%)	354 (42.3)	416 (49.8)	6 (0.7)	32 (9.0)	17 (2.0)	9 (1.1)	2 (0.2)
Total knee joint replacement	1,113 (50.2)	559	238 (42.6)	321 (57.4)	361	185 (51.2)	153 (42.4)	3 (0.8)	12 (3.3)	5 (1.4)	2 (0.6)	1 (0.3)
- Primary	1,045 (49.4)	516	227 (44.0)	289 (56.0)	324	167 (51.5)	140 (43.2)	3 (0.9)	9 (2.8)	3 (0.9)	1 (0.3)	1 (0.3)
- Revision	68 (63.4)	43	11 (25.6)	32 (74.4)	37	18 (48.6)	13 (35.1)	-	3 (8.1)	2 (5.4)	1 (2.7)	-
Total hip joint replacement	710 (46.8)	332	146 (44.0)	186 (56.0)	223	72 (32.3)	138 (61.9)	-	7 (3.1)	3 (1.3)	3 (1.3)	
- Primary	660 (46.1)	304	139 (45.7)	165 (54.3)	201	66 (32.8)	124 (61.7)	-	6 (3.0)	2 (1.0)	3 (1.5)	-
- Revision	50 (56.0)	28	7 (25.0)	21 (75.0)	22	6 (27.3)	14 (63.6)	-	1 (4.5)	1 (4.5)	-	-

Knee surgery (excluding TKR)	132 (57.6)	76	49 (64.5)	27 (35.5)	28	11 (39.3)	13 (46.4)		3 (10.7)			1 (3.6)
Open reduction internal fixation (ORIF)	320 (54.1)	173	91 (52.6)	82 (47.4)	93	36 (38.7)	46 (49.5)	1 (1.1)	4 (4.3)	3 (3.2)	3 (3.2)	
Shoulder surgery	189 (58.2)	110	57 (51.8)	53 (48.2)	57	23 (40.4)	28 (49.1)	1 (1.8)	3 (5.3)	2 (3.5)	-	-
Other	119 (58.0)	69	36 (52.2)	33 (47.8)	37	17 (45.9)	16 (43.2)	-	2 (5.4)	2 (5.4)	-	-
Foot and ankle surgery	91 (57.1)	52	33 (63.5)	19 (36.5)	22	7 (31.8)	13 (59.1)	-	-	1 (4.5)	1 (4.5)	-
Hand surgery	26 (73.1)	19	14 (73.7)	5 (26.3)	6	3 (50.0)	2 (33.3)			1 (16.7)		
Fractures closed reduction	7 (42.9)	3	2 (66.6)	1 (33.3)	0							
Elbow surgery	24 (75.0)	18	6 (33.3)	12 (66.6)	9	-	7 (77.8)	1 (11.1)	1 (11.1)	-	-	-
a Rationale for the reasons for inappropriateness are described Surgical NAPS report ⁴ b Duration and frequency were only assessable for post-procedural prescriptions												

311 **Discussion**

312 To our knowledge, our study is the first to examine appropriateness of procedural and post-
313 procedural SAP prescriptions across a range of orthopaedic procedures in Australian
314 hospitals. Our analysis has identified suboptimal rates of appropriate SAP prescriptions when
315 accounting for a range of hospital, patient and surgical factors. Detailed analysis and
316 comparison of SAP prescription appropriateness across speciality surgical procedures
317 subgroups facilitates meaningful assessment for targeted stakeholder groups, such as
318 orthopaedic surgeons.

319 Inappropriate and guideline non-compliant SAP for orthopaedic procedures been reported
320 consistently in Australian^{4, 6, 10, 18} and international literature.^{7-9, 19-21} Whilst orthopaedic
321 procedures are commonly audited for SAP, the current literature demonstrates a limited
322 number of studies that compare a subset of orthopaedic procedures,¹⁹ as opposed to
323 comparing orthopaedic procedures as a whole to other surgical specialties e.g. cardiac and
324 abdominal.^{7, 8, 10}

325 A posited driver for the identified variation in practice may be lack of awareness of SAP
326 guidelines, particularly for specific procedures. A questionnaire performed by the
327 Orthopaedic Trauma Association highlighted heterogeneity in opinions regarding guideline
328 value and evidence quality for single- versus- multiple dose SAP for closed long bone
329 fractures.²² The participating surgeons reported low awareness of SAP guidelines, however
330 they were receptive to changing their practice to single-dose SAP if supported by high-level
331 evidence.²² Similar Australian perceptions of the evidence may be reflective of our identified
332 suboptimal AA for SAP in closed bone fractures (68.2% procedurally and 68.7% post-
333 procedurally) (Figures 2 and 4).

334 There is limited and conflicting evidence to support SAP for diagnostic and therapeutic
335 shoulder and knee arthroscopy²³⁻²⁵ and hand surgery.²⁶ National and international guidelines
336 do not recommend use of SAP in routine arthroscopic procedures unless the procedure
337 involves insertion of prosthetic material or avascular tissue.^{12, 13, 27} Our study identified that
338 these procedures had the highest rates of procedural inappropriateness due to administration
339 when not required (shoulder 45.4%, knee 72.6% and hand surgery 65.4%, Table 3). We
340 therefore suggest greater dissemination of specific evidence and guideline recommendations
341 for these procedures, and that engagement with these niche specialties is required to
342 understand fully the motivating factors for continued prescribing of SAP for these procedures
343 (Figure 4).

344 Our analysis revealed post-procedural administration of SAP when not required accounted
345 for almost half (47.6%) of all inappropriate post-procedural prescriptions. Duration of post-
346 procedural SAP remains controversial, especially for hip and knee arthroplasty. Most
347 guidelines and professional bodies do not recommended SAP after wound closure.^{11-13, 27, 28}
348 However, the American Association of Hip and Knee Surgeons (AAHKS) argue that
349 recommendations for single-dose SAP are not supported by the available evidence.²⁹

350 In our surveyed population, incorrect duration and dose/frequency were the most common
351 reasons for inappropriateness for post-procedural prescriptions and highlights these
352 components of SAP prescribing as critical areas for quality improvement. The consequences
353 of antibiotic overuse such as prolonged SAP durations have been well described in the
354 literature and include lack of SSI reduction³⁰ and patient harms such as antibiotic side
355 effects³¹, *Clostridioides difficile* infections,^{30, 31} acute kidney injury,³⁰ and contribution to
356 antimicrobial resistance.³⁰

357 Qualitative research in Australia^{32, 33} and the UK³⁴ has highlighted potential influences on
358 SAP prescribing culture. The fear of causing patient harm, such as surgical site infections,^{32,}
359 ³³ and litigation claims for malpractice^{32, 33} have been identified as drivers for overuse of
360 SAP. Further education is required to highlight that antimicrobial overuse may also cause
361 significant patient harm.

362 A multicentre national retrospective cohort study of the US Veterans Affairs health care
363 system of 79,058 patients³⁰ demonstrated the adjusted odds ratio (aOR) for SSIs in
364 orthopaedic procedures increased when SAP was administered for longer than 24 hours (24-
365 <48 hours: aOR, 1.11; 95%CI, 0.82-1.51; 48-<72 hours: aOR, 2.04; 95%CI, 1.00-4.16; >72
366 hours: aOR, 1.63; 95%CI, 0.22-12.07).

367 A novel retrospective study of 20,382 primary TKJRs and THJRs compared single-dose
368 (n=4,523) SAP to multiple doses i.e., procedural and post-procedural SAP (n=16,159).³⁵
369 There was no difference in PJI rate at one year between single and multiple-dose SAP
370 (univariate aOR:0.674, $p=0.064$; multivariate aOR:0.755, $p=0.205$; propensity score matched
371 analysis aOR=0.746, $p=0.277$). Specifically, patients who received single-dose cefazolin,
372 were more likely to have a lower rate of PJI than those who received multiple doses (24
373 hours) ($p=0.054$).³⁵

374 Most recently, a systematic review with meta-analysis of 52 RCTs (19, 273 participants
375 across multiple surgical procedure types) demonstrated there was no significant benefit (SSI
376 reduction) from prolonging SAP (in comparison to no post-operative doses), with a pooled
377 RR of 0.89 (95%CI 0.79-1.00).³⁶

378 Multiple recent studies advocate for a well-powered, randomized, prospective trial comparing
379 infection outcomes using single- and multiple-dose SAP regimens for TKJR.^{30, 35, 37, 38} Of
380 importance, Duke University and the AAHKS are conducting a multicentre clinical trial

381 (estimated n=8,000) comparing single dose and prolonged duration (24 hours) of SAP for
382 elective primary TKJR and whether this significantly reduces the incidence of prosthetic joint
383 infections (ClinicalTrials.gov Identifier: NCT03283878; estimated completion date October
384 2020).

385 This research has a number of limitations. While the audit captured approximately 20% of
386 Australian hospitals performing elective procedures, reasons for non-participation are not
387 known. This may limit the generalizability of our results to other Australian and international
388 centres. A mixed-effects regression model accounted for the intra-hospital correlations;
389 however, the effects of an unbalanced survey design may persist. Variation of ‘Appropriate
390 Assessments’ is probable due to multiple auditors. A validation study⁴ comparing
391 assessments between local auditors and the NAPS clinical support team demonstrated a low
392 rate of disagreement (6.7%).

393 Our large, national audit demonstrated low rates of SAP appropriateness across orthopaedic
394 procedures. Our analysis identifies niche areas for orthopaedic SAP optimisation, including
395 procedures where procedural SAP is prescribed when not required and multiple post-
396 procedural doses are given when not indicated. These data provide meaningful metrics to
397 support the development of quality improvement programs in orthopaedic surgery.

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404 **Transparency and declarations**

405 No conflicts of interest to declare.

406 **Supplementary data**

407 Refer to Appendix 4 for Supplementary data.

408 Tables S1-S11 and Figures S1 and S2.

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Chapter 10: Factors associated with antimicrobial choice for surgical prophylaxis in Australia

10.1 Introduction

This chapter consists of a submitted manuscript that examines the appropriateness of antimicrobial choice for surgical antimicrobial prophylaxis (SAP). Cefazolin is the most commonly recommended antimicrobial in guidelines and the most commonly audited (**Chapters 8 and 9**). However, the Surgical National Antimicrobial Prescribing Survey (Surgical NAPS) reports (4, 8) and our analyses in **chapters 8 and 9**, reveal that there is a wide range of antimicrobials including broad-spectrum antimicrobials, prescribed for SAP. Inappropriate use of broad-spectrum antimicrobials is associated with increased patient harm and is a posited driver for antimicrobial resistance. Therefore, the identification of patient, hospital and surgical factors and their association with procedural SAP choice is warranted to provide targets for antimicrobial stewardship interventions to optimise selection of SAP antimicrobial choice.

To adjust for a range of patient, hospital and surgical factors, we adopted an estimated marginal means statistical analysis (similar to **chapters 8 and 9**). Both unadjusted and adjusted appropriateness of procedural SAP were low. We also conducted chi-squared analyses to compare appropriateness of the top five audited antimicrobials with clinically significant factors. Our research highlights that targeting SAP antimicrobial selection is an important area for AMS and quality improvement.

This research project has re-enforced the benefits of auditing SAP appropriateness. Appropriateness and guideline compliance are different measures and the Surgical NAPS adoption of appropriateness assessments in addition to guideline compliance is meaningful to clinicians. Both measures are useful and provide directions for surgical AMS interventions.

Various factors influence appropriateness of procedural SAP choice. Different surgical procedure groups have been identified as key targets for improving use of broad-spectrum antimicrobial/antimicrobial classes for procedural SAP. Examples of potentially inappropriate use include aminoglycoside use in urological surgery; glycopeptide use in orthopaedic and cardiac surgery, and broad-spectrum (third and fourth generation) cephalosporin use in abdominal surgery.

This body of work contributes to the increasing amount of antimicrobial auditing literature. There is a need to extend upon this work and provide feedback on SAP auditing data and engage with surgical teams to develop and implement high quality surgical antibiotic prescribing procedures.

10.2 Submitted manuscript

The following manuscript was accepted by the Journal of Antimicrobial Chemotherapy- Antimicrobial Resistance (JAC-AMR) on the 5/04/2020. The included manuscript is the final approved draft and is pending publication.

The supplementary data submitted with this manuscript can be found in Appendix 5.

Factors associated with antimicrobial choice for surgical prophylaxis in Australia[AQ7]

Ierano *et al.*

Factors associated with antibiotic choice in surgery

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ABSTRACT

Cefazolin is the most commonly recommended antimicrobial for surgical antimicrobial prophylaxis (SAP). However, the Australian Surgical National Antimicrobial Prescribing Survey revealed a wide range of antimicrobials prescribed for SAP. Inappropriate use of broad-spectrum antimicrobials is associated with increased patient harm and is a posited driver for antimicrobial resistance.

To describe patient, hospital and surgical factors that are associated with appropriateness of the top five prescribed antimicrobial/antimicrobial classes for procedural SAP.

All procedures audited from 18 April 2016 to 15 April 2019 in the Surgical National Antimicrobial Prescribing Survey were included in the analysis. Estimated marginal means analyses accounting for a range of variables and calculated a rate of adjusted appropriateness (AA). Subanalyses of the top five audited antimicrobials/antimicrobial classes identified associations between variables and appropriateness.

A total of 12 419 surgical episodes with 14 150 prescribed initial procedural doses were included for analysis. When procedural SAP was prescribed, appropriateness was low (57.7%). Allergy status, surgical procedure group and the presence of prosthetic material were positively associated with cefazolin and aminoglycoside appropriateness ($P < 0.05$). There were no significant positive associations with glycopeptides and third/fourth-generation cephalosporins. The use of broad-spectrum antimicrobials was the most common reason for inappropriate choice (67.9% of metronidazole to 83.3% of third/fourth generation cephalosporin prescriptions).

Various factors influence appropriateness of procedural SAP choice. Identification of these factors provides targets for antimicrobial stewardship interventions, e.g. procedures where surgeons are regularly prescribing broad-spectrum SAP. These can be tailored to address local hospital prescribing practices.

FUNDING

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Introduction

Surgical antimicrobial prophylaxis (SAP) is the most common indication for antimicrobial use in acute hospitals, accounting for 14.1% of 26 714 antimicrobial prescriptions audited in an Australian national point prevalence survey known as the Hospital National Antimicrobial Prescribing Survey (Hospital NAPS) in 2018.¹ Of these surgical prophylaxis prescriptions, 39.5% were identified as inappropriate.¹ Antimicrobial agent selection for SAP has been identified as an area with poor appropriateness and guideline compliance across national^{2–4} and international studies.^{5–11} Inappropriate antimicrobial use may be considered a potential driver for the emergence of antimicrobial resistance (AMR),¹² which poses a burden on both the patient and the community.

SAP prescribing is multifaceted and can occur across the pre- and intra-operative (or procedural) and post-procedural settings. The Surgical NAPS was developed to facilitate a more detailed assessment of SAP prescribing including the auditing and reporting of antimicrobial use across these surgical settings.^{2,13} The Surgical NAPS measures both appropriateness and guideline compliance of SAP prescriptions as these are both clinically meaningful to clinicians to facilitate prescribing behaviour change.

The Therapeutic Guideline: Antibiotic (TG: Antibiotic)^{14,15} is the recommended guideline for the prescribing of antimicrobials in Australia. Cefazolin is the most commonly recommended antimicrobial for surgical prophylaxis based on multiple factors including its narrow Gram-positive and Gram-negative spectrum coverage for common pathogens; i.e. *Staphylococcus aureus*, efficacy, safety profile and low cost.^{14,15}

Metronidazole is commonly recommended in addition to cefazolin to provide extended coverage of anaerobic pathogens. Surgical procedure groups where this may be warranted include abdominal, ear, nose and throat, gynaecological, oral/maxillofacial, head and neck and urological.^{14,15} Vancomycin is only recommended for SAP under defined circumstances. Examples include as an addition to cefazolin if the patient is, or is at risk of being, colonized or infected with MRSA, or as an alternative to cefazolin in patients with immediate or delayed hypersensitivity to penicillins.^{14,15}

Gentamicin is commonly recommended as an alternative SAP agent for patients with immediate severe or delayed severe penicillin hypersensitivity.^{14,15} Ceftriaxone is a broad-spectrum third-generation cephalosporin antimicrobial covering both Gram-positive and Gram-negative organisms and is not recommended for SAP in current Australian guidelines.^{14,15}

Metronidazole, gentamicin, vancomycin and ceftriaxone represented the second to fifth most commonly prescribed procedural antimicrobials for SAP (4.7%, 3.6%, 2.5% and 1.5%, respectively) as per the Surgical NAPS 2019 report.^{2,13} These antimicrobials are occasionally recommended; however, the report also demonstrated high rates of inappropriate use when they were prescribed (46.6%, 47.0%, 69.2% and 82.4%, respectively).²

This research aims to determine whether the drivers of appropriateness vary between the different antimicrobials prescribed. It is important, therefore, to try to understand why these antimicrobials are being prescribed and, specifically, which factors (patient, surgical and hospital-related) might be influencing prescribers to choose these broader-spectrum agents. This might include surgical-related factors such as use in emergency and trauma procedures and procedures involving prostheses, or patient-related factors such as allergies and age. Many of these factors are captured by the Surgical NAPS and further analysis may provide insight to inform future guidelines and to inform antimicrobial stewardship (AMS) interventions.

Aims

This study aimed to describe patient, hospital and surgical factors that are associated with appropriateness of antimicrobial choice for procedural SAP, with a focus on the top five antimicrobials/antimicrobial classes prescribed in the Surgical NAPS.

Methods

The Surgical NAPS is an Australian online auditing platform that has been described previously.^{2,13,16} We provide a summary of these methods here.

Survey design

The Surgical NAPS was co-designed through stakeholder consultation from a range of specialities. It collects data on patient demographics (age and gender) and clinical information [allergy status and American Society of Anesthesiologists (ASA) score].¹³

Data were collected across a patient's surgical episode. Three categories of antimicrobial prescriptions were defined for each surgical episode: procedural, post-procedural and existing (Table S1, available as [Supplementary data](#) at *JAC-AMR* Online). Elements of SAP prescribing that were collected include antimicrobial choice, dose, timing, duration and frequency.

Hospital demographics captured include: location (state or territory); funding type (public or private); Australian Institute of Health and Welfare (AIHW) peer groups;¹⁷ and Australian Bureau of Statistics (ABS) remoteness areas.¹⁸

Procedure-related factors include surgical procedure group, elective or emergency surgery status, wound class and presence of prosthesis (including removal or insertion). When multiple surgical 'procedure groups' were documented for a patient, only the main procedure system group was included.

Data collection and collation

Surgical NAPS was conducted as a voluntary annual survey during 2016–19 in both public and private hospitals at any timepoint throughout the year. Auditors had the flexibility to audit all procedures at a given timepoint or targeted surgical procedures. Hospitals could participate more than once over the 3 year auditing period. The updated 'TG: Antibiotics' version 16¹⁵ was made available online on 15 April 2019. All procedures from 18 April 2016 to 15 April 2019 were included in the analysis to focus solely on assessments based on the previous version 15.¹⁴

Data were collected by trained auditors (primarily pharmacists, nurses and infectious disease doctors) according to a standardized method and data collection form¹³ and were entered in the Surgical NAPS online auditing platform.

Appropriateness and guideline compliance are separate measures as they are not mutually exclusive. Appropriateness was a composite measure based on antimicrobial choice, timing of administration, duration and repeat dosing, applying the standardized Appropriateness Assessment Guide (Figure S1). Reasons for inappropriateness were based upon this guide. Guideline compliance of SAP prescribing was assessed against the national guidelines¹⁴ or local site-based guidelines available at the time of assessment.

This study focuses on initial antimicrobial choice for SAP, therefore the following exclusions were made: existing antimicrobial therapy and post-procedural antimicrobial prescription (definitions in Table S1); repeat procedural doses or where repeat doses were required but not given; and appropriateness assessments deemed 'not-assessable'. Data were excluded from univariable and multivariate analysis if prescriptions were categorized as 'not assessable' or if categories contained missing or small numbers.

Upon initial data inspection, it was decided *a priori* to group antimicrobials into their pharmacological classes, with the exception of cefazolin, due to its high volume and first-line recommendation for antimicrobial choice, and metronidazole and chloramphenicol, as no other antimicrobials of their same classes were prescribed. Cefepime was the only fourth-generation cephalosporin and was therefore grouped with third-generation cephalosporins due to sim-

ilar profiles. Antimicrobials prescribed with a frequency less than 10 were grouped together as ‘others’ and excluded from statistical analysis (Table S2).

The collection and analysis of data from Surgical NAPS has been approved by the Melbourne Health Human Research and Ethics Committee (approval number QA2013066).

Statistical analysis

An initial unadjusted subgroup analysis compared the appropriateness of prescriptions for surgical episodes when antimicrobials were and were not prescribed for both procedural and post-procedural SAP.

Logistic regression models were then used to identify hospital, patient and surgical factors associated with appropriateness. Model selection was performed using a likelihood ratio test and model fit assessed by residual plots. Clinically important variables were selected *a priori*, based on previous literature for inclusion in univariable and multivariable analysis. Mixed-effects logistic models with unique hospital identifiers as random intercepts provided the best fit to the data and were selected. Two-tailed χ^2 tests were conducted and a *P* value of less than 0.05 was considered statistically significant. ORs were calculated and values <1 were demonstrated to have a negative association of appropriateness i.e. promoted inappropriateness.

Crude estimates of appropriateness were adjusted for factors included in the model by calculating estimated marginal means (EMMs), presented as ‘adjusted appropriateness’ (AA) with 95% confidence intervals. The AA accounts for all factors included in the model by calculating an equal-weighted average across all subgroups. Therefore, the appropriateness is ‘adjusted’ for potential bias that may result from varying subgroup sizes in our sample.

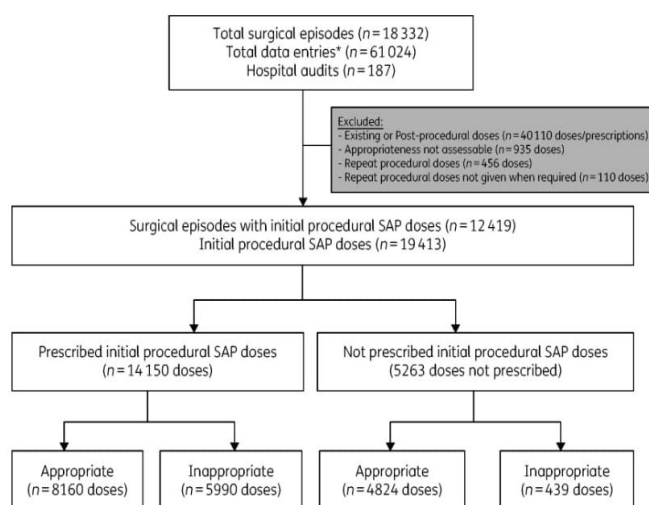
Subgroup analyses were performed for each of the top five prescribed antimicrobials/antimicrobial classes. Percentage of appropriateness was compared for clinically significant categorical variables with χ^2 tests.

Statistical analysis was conducted with Stata version 14.1 (StataCorp LP, College Station, TX, USA).

Results

A total of 18 332 surgical episodes across 185 hospital audits were included. Of all surgical episodes with initial procedural SAP prescribed (*n* = 12 419), 87.8% included at least one cefazolin prescription (*n* = 10 899). Figure 1 provides a summary of the categories of the included and excluded prescribed antimicrobial doses and prescriptions. Doses with an appropriateness assessment deemed ‘not assessable’ were excluded (*n* = 935), as were repeat doses (*n* = 456) and repeat doses not given when required (*n* = 110). A total of 12 419 surgical episodes with 14 150 prescribed initial procedural doses were included for analysis. The median age of patients was 58 years (range 0–100 years). Female patients accounted for 52.9% of the surgical episodes (*n* = 7488) and male patients for 46.7% (*n* = 6609).

Figure 1. Workflow summary diagram for data analysis. *Data entries pertain to all data collected within the surgical episode. Each surgical episode collects data on three antimicrobial categories: ‘procedural’, ‘post-procedural’ and ‘existing’, for which an antimicrobial could be ‘prescribed’, ‘not prescribed’ or ‘not assessable’.



Overall appropriateness was low (66.9%) (Table S3). When comparing SAP being prescribed and not being prescribed (regardless of indication), appropriateness was much higher for the latter (57.7% and 91.7%, respectively) (Table S3).

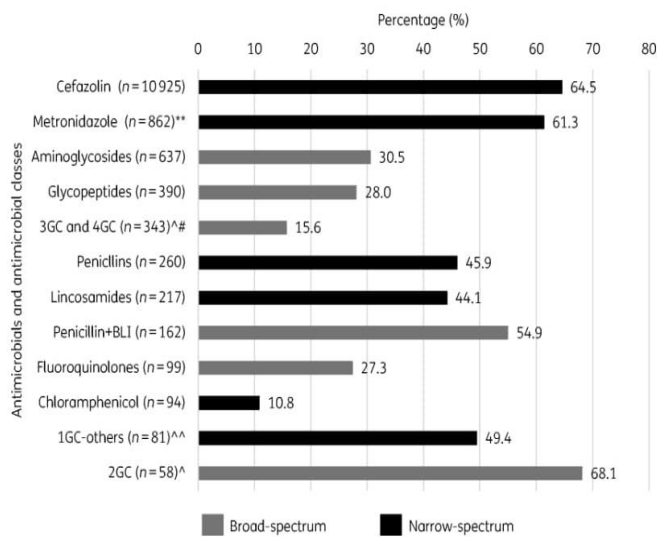
Participating hospitals and audited surgical procedure groups

Of the 187 participating hospitals, 98.4% ($n = 184$) undertook audits that utilized cefazolin. The remaining three hospitals audited very low numbers of procedures (range: 2–4) with alternative antimicrobials prescribed; cefalotin, chloramphenicol and gentamicin. All Australian states and territories contributed data to the Surgical NAPS (Table S4).

Surgical variables significantly associated with appropriateness of procedural SAP included presence of trauma (OR, 1.41; 95% CI, 1.13–1.77; $P = 0.002$); presence, removal or insertion of prosthetic material (OR, 1.68; 95% CI, 1.50–1.89; $P < 0.001$); clean-contaminated wound class (OR, 1.23; 95% CI, 1.08–1.41; $P = 0.002$); and surgical procedure groups: abdominal (OR, 0.84; 95% CI, 0.70–1.00; $P = 0.046$), dentoalveolar (OR, 0.25; 95% CI, 0.17–0.37; $P < 0.001$), gastrointestinal endoscopic (OR, 0.22; 95% CI, 0.09–0.54; $P = 0.001$), head and neck (OR, 0.46; 95% CI, 0.36–0.60; $P < 0.001$), neurosurgery (OR, 1.63; 95% CI, 1.23–2.16; $P = 0.001$), ophthalmology (OR, 2.09; 95% CI, 1.38–3.17; $P < 0.001$), plastic and reconstructive (OR, 0.59; 95% CI, 0.47–0.73; $P < 0.001$) and urological (OR, 0.59; 95% CI, 0.47–0.73; $P < 0.001$) (Table S4).

With regard to antimicrobial choice, AA was reported as low for all antimicrobials and classes, ranging from 10.8% for chloramphenicol to 68.1% for second-generation cephalosporins (Figure 2). Broad-spectrum antimicrobials and antimicrobial classes generally had lower rates of appropriateness, i.e. third/fourth-generation cephalosporins (15.5% AA), fluoroquinolones (27.3%), glycopeptides (28.0%) and aminoglycosides (30.5%).

Figure 2. AA (%) per antimicrobial/antimicrobial class ($n = 14\,128$). **Metronidazole was the only nitroimidazole reported and is therefore reported on its own, as opposed to class. ^First-, second-, third- and fourth-generation cephalosporins. ^^Other first-generation cephalosporins refers to all reported, excluding cefazolin. #Only one fourth-generation cephalosporin ($n = 5$) was reported and grouped with third-generation cephalosporins. ##BLI, β -lactamase inhibitor; 1GC, first-generation cephalosporins; 2GC, second-generation cephalosporins; 3GC, third-generation cephalosporins; 4GC, fourth-generation cephalosporins [AQ5].



Broad-spectrum antimicrobial use

A subgroup analysis of the top five prescribed antimicrobials/antimicrobial classes ($n = 13\ 157$) accounted for 93.0% of all procedural SAP doses ($n = 14\ 150$). Cefazolin ($n = 10\ 925$) and metronidazole ($n = 826$) are commonly recommended for SAP and accounted for 77.2% and 5.9% of all procedural SAP doses, respectively. The next three most frequently prescribed classes included broad-spectrum antimicrobials (aminoglycosides, glycopeptides and third/fourth-generation cephalosporins).

Table 1 illustrates a range of variables and their associations with appropriateness across the top five antimicrobials/antimicrobial classes. Allergy status ($P = 0.015$), surgical procedure group ($P = 0.000$) [AQ11] and the presence of prosthetic material ($P = 0.000$) were positively associated with cefazolin appropriateness. There were no significant positive associations between these variables and appropriateness of glycopeptides and third/fourth-generation cephalosporins.

Table 1. Appropriateness of the top five audited antimicrobials/antimicrobial classes by patient and surgical factors

Variables	Antimicrobial/antimicrobial class, n (%)									
	cefazolin		metronidazole		aminoglycosides		glycopeptides		3GC/4GC ^a	
	Total	appropriate	total	appropriate	total	appropriate	total	appropriate	total	appropriate
Total appropriateness, n (%)	10 925	6984 (63.9)	862	472 (54.8)	637	188 (29.5)	390	107 (27.4)	343	34 (9.9)
Allergy status χ^2 test [P value]	12.29 [0.015]		8.67 [0.070]		10.05 [0.040]		7.18 [0.127]		5.51 [0.239]	
nil known	9145	5889 (64.3)	721	392 (54.4)	498	148 (29.7)	277	69 (24.9)	303	29 (9.6)
not documented	194	118 (60.8)	9	6 (66.7)	13	7 (53.9)	5	3 (60.0)	4	0 (0.0)
β -lactam allergy	975	578 (59.3)	83	40 (48.2)	83	26 (31.3)	80	29 (36.3)	22	4 (18.2)
non- β -lactam allergy	380	253 (66.6)	39	27 (69.2)	28	6 (21.4)	14	3 (21.4)	11	1 (9.1)
non-antimicrobial allergy	221	145 (65.6)	10	7 (70.0)	15	1 (6.7)	14	3 (21.4)	3	0 (0.0)
Trauma χ^2 test [P value]	2.00 [0.157]		0.04 [0.851]		0.06 [0.800]		0.39 [0.533]		0.58 [0.447]	
no	10 191	6497 (63.8)	843	462 (54.8)	628	185 (29.5)	369	100 (27.1)	338	33 (9.8)
yes	734	487 (66.4)	19	10 (52.6)	9	3 (33.3)	21	7 (33.3)	5	1 (20.0)

Variables	Antimicrobial/antimicrobial class, <i>n</i> (%)									
	cefazolin		metronidazole		aminoglycosides		glycopeptides		3GC/4GC ^a	
	Total	appropriate	total	appropriate	total	appropriate	total	appropriate	total	appropriate
Prosthetic material χ^2 test [<i>P</i> value]	292.78 [0.000]		2.14 [0.144]		8.39 [0.004]		2.12 [0.145]		0.14 [0.712]	
no	6758	3903 (57.8)	791	439 (55.5)	323	112 (34.7)	131	42 (32.1)	261	25 (9.6)
yes	4167	3081 (73.9)	71	33 (46.7)	314	76 (24.2)	259	65 (25.1)	82	9 (11.0)
Surgical procedure group χ^2 test [<i>P</i> value]	661.71 [0.000]		33.7 [0.000]		153.83 [0.000]		6.39 [0.846]		17.61 [0.128]	
abdominal	1741	1097 (63.0)	493	297 (60.2)	32	5 (15.6)	5	2 (40.0)	121	17 (14.1)
breast	340	218 (64.1)	2	1 (50.0)	34	23 (67.7)	4	1 (25.0)	1	1 (100.0)
cardiac	581	385 (66.3)	0	—	57	7 (12.3)	118	35 (29.7)	8	0 (0.0)
dentoalveolar	157	34 (21.7)	5	4 (80.0)	0	—	0	—	0	—
gastrointestinal endoscopic	23	6 (26.1)	12	1 (8.3)	4	3 (75.0)	0	—	9	2 (22.2)
gynaecological	527	303 (57.5)	183	95 (51.9)	2	2 (100.0)	0	—	7	0 (0.0)
head and neck	411	186 (45.3)	7	3 (42.9)	2	0 (0.0)	3	0 (0.0)	3	0 (0.0)
neurosurgery	445	350 (78.7)	0	—	15	0 (0.0)	20	5 (25.0)	7	1 (14.3)
obstetrics	865	542 (62.7)	65	23 (35.4)	3	0 (0.0)	1	1 (100.0)	1	0 (0.0)
ophthalmology	426	393 (92.3)	0	—	15	1 (6.7)	13	3 (23.1)	2	0 (0.0)
orthopaedic	3374	2416 (71.6)	1	1 (100.0)	207	18 (8.7)	180	46 (25.6)	19	2 (10.5)
plastic and reconstructive	990	452 (45.7)	13	6 (46.2)	10	2 (20.0)	14	5 (35.7)	4	0 (0.0)
thoracic	93	70 (75.3)	2	2 (100.0)	1	0 (0.0)	2	0 (0.0)	1	0 (0.0)
urological	677	378 (55.8)	72	37 (51.4)	252	127 (50.4)	9	3 (33.3)	160	11 (6.9)
vascular	275	154 (56.0)	7	2 (28.6)	3	0 (0.0)	21	6 (28.6)	0	—

a Third- and fourth-generation cephalosporins.

Reasons for inappropriateness

Table 2 highlights the multiple reasons for inappropriateness of antimicrobial choice. The most common reason was the antimicrobial spectrum being too broad (55.7%) with the lowest rate of inappropriateness for cefazolin prescriptions (17.3%) and the highest rate for third/fourth-generation cephalosporins (83.3%).

Table 2. Common reasons for inappropriate antimicrobial choice for procedural SAP doses

Antimicrobial	Inappropriate doses (<i>n</i>)	SAP indicated and inappropriate, <i>n</i> (%)	Total reasons for inappropriate antimicrobial choice ^a (<i>n</i>)	Types of reasons for inappropriate antimicrobial choice, ^b <i>n</i> (%)			
				spectrum too broad	spectrum too narrow	allergy mismatch	microbiology mismatch
Total	5372	3966 (73.8)	1007	561 (55.7)	337 (33.5)	62 (6.2)	47 (4.7)
cefazolin	3941	2842	394	68 (17.3)	240 (60.9)	61 (15.5)	25 (6.3)
aminoglycosides	449	325	163	133 (81.6)	28 (17.2)	1 (0.6)	1 (0.6)
metronidazole	390	290	84	57 (67.9)	26 (31.0)	0 (0.0)	1 (1.2)
3GC/4GC ^c	309	260	240	200 (83.3)	23 (9.6)	0 (0.0)	17 (7.1)

Antimicrobial	Inappropriate doses (<i>n</i>)	SAP indicated and inappropriate, <i>n</i> (%)	Total reasons for inappropriate antimicrobial choice ^a (<i>n</i>)	Types of reasons for inappropriate antimicrobial choice, ^b <i>n</i> (%)			
				spectrum too broad	spectrum too narrow	allergy mismatch	microbiology mismatch
glycopeptides	283	249	126	103 (81.7)	20 (15.9)	0 (0.0)	3 (2.4)

a There was a total of 4826 reasons for inappropriateness of procedural SAP; only 1007 (23.5%) were in relation to the choice of antimicrobial agent.

b Rationale for the reasons for inappropriateness are described in [Figure S1](#). Surgical NAPS appropriateness assessment guide.

c Third- and fourth-generation cephalosporins.

Surgical procedure groups

Subgroup analysis of appropriate procedural prescriptions of the most common broad-spectrum antimicrobials (aminoglycosides, glycopeptides and third/fourth-generation cephalosporins) (*n* = 329 doses) identified procedure groups associated with their respective use (Table S5). For aminoglycosides, urological surgery (*n* = 127) was the most common procedure associated with appropriate use (67.6% of all procedural aminoglycoside doses). Orthopaedic surgery (*n* = 46, 43.0%) and cardiac surgery (*n* = 35, 32.7%) accounted for the common procedure groups associated with appropriate glycopeptides. Abdominal surgery accounted for 50% (*n* = 17) of all appropriate third/fourth-generation cephalosporin doses (Table S5).

Table S5 also illustrates the guideline compliance of these doses deemed appropriate and number of hospitals with local guidelines. For breast surgical procedures, the analysis identified that all appropriate aminoglycoside doses were from one hospital that endorses such use in their local guidelines. Local guidelines informed the appropriateness of broad-spectrum antimicrobial use in 28.3% (*n* = 93), compared with 52.9% for national guidelines (*n* = 174).

Discussion

Analysis of the Surgical NAPS data has continued to demonstrate poor rates of appropriateness across procedural SAP. Appropriateness varied across the choice of antimicrobial agent in our surveyed population but was low overall (57.7%). Lower rates of appropriateness were demonstrated where broad-spectrum antimicrobials such as glycopeptides, aminoglycosides and third/fourth-generation cephalosporins were used and these rates differed across a range of surgical procedure groups. Unsurprisingly, the different antimicrobial spectra covered by these antimicrobials reflected their use across different surgical procedures. Additionally, these antimicrobials are not routinely recommended, thus we would expect appropriateness to be low.

Our research contributes to the increasing adoption of appropriateness as a key measure for antimicrobial audits,^{1,2,16,19–26} as opposed to the sole use of guideline compliance. Standardized appropriateness measures aim to enable assessments to address issues of guideline implementability and recommendation flexibility to account for varying patient characteristics.²⁷

Glycopeptides such as vancomycin provide Gram-positive bacterial coverage and were frequently prescribed by surgeons inappropriately in orthopaedic, cardiac and vascular procedures. In these procedures, vancomycin is indicated as an addition to cefazolin if the patient is, or is at risk of being, colonized or infected with MRSA, or as an alternative to cefazolin in patients with immediate hypersensitivity to penicillins.¹⁴ However, neither scenario was reported in the included data. Directed therapy is considered an exception, but was rarely recorded and when it was, the microbiological data to support decision-making were absent. It is unclear whether these data were truly absent or not recorded by the auditor.

Ceftriaxone was the most commonly prescribed third-generation cephalosporin and provides broad Gram-negative bacteria coverage; it was commonly prescribed by surgeons as SAP for abdominal and urological procedures. The use of Gram-negative coverage is warranted in such procedures; however, *S. aureus* is a common pathogen^{28,29} and use

of broader-spectrum coverage (i.e. ceftriaxone instead of the first-line agent cefazolin) has not been clearly justified in our surveyed population.

The recently updated national guidelines recommend aminoglycosides such as gentamicin for urological procedures due to the emergence of cephalosporin resistance in Enterobacterales.^{15,29}

Whilst this recommendation was not included in the guidelines available for this analysis, we propose that this may have been a driving influence behind our observation of 67.6% of all appropriate gentamicin doses being prescribed for urological procedures.

Our research is novel and has demonstrated associations between risk factors (allergy status, presence of prosthetic material and surgical procedure groups) and appropriateness of antimicrobials for SAP. Surgical procedure groups remain the most common variable negatively associated with appropriateness in this study and in our previously published analysis of procedural and post-procedural SAP prescriptions.¹⁶ Surgical procedure groups vary in the terms of risks of infection and as such so do their requirements for SAP, particularly the antimicrobial agent of choice. Thus, surgeons must factor and mitigate these risks when making decisions regarding antimicrobial choice for SAP. Our research has demonstrated that whilst cefazolin is the most commonly recommended and prescribed antimicrobial in our surveyed population, there are still a range of antimicrobials being prescribed for SAP, particularly broad-spectrum antimicrobials that we propose as targets for tailored surgical AMS interventions. These targets include aminoglycoside use in urological, breast and orthopaedic surgery, glycopeptide use in cardiac and orthopaedic surgery and third/fourth-generation cephalosporin use in abdominal and urological surgery.

Reasons for inappropriate surgical prophylaxis prescriptions

Inappropriate SAP prescribing has been reported in both Australian^{3,16,30–32} and international literature.^{5,6,33–43} Common reasons for inappropriateness identified in this study are consistent with current literature regarding SAP. The timing of administration for procedural SAP remains the most commonly identified reason for inappropriateness in Australia^{16,31,32} and international research.^{34,36} Exploring factors influencing antimicrobial choice for SAP is limited and warranted to support targeted AMS interventions. Antimicrobial selection based on broader-spectrum coverage was also a common reason for inappropriateness in our surveyed population. Similarly, a small Iranian audit of 100 SAP cases identified that vancomycin and ceftriaxone accounted for one-fifth of all SAP doses (21%).⁵ An analysis of Qatar hospital SAP guidelines across 101 patients noted inappropriate antimicrobial selection as the second most common reason for non-compliance (31.5%). Whilst the commonly recommended antimicrobial cefazolin accounted for 44.6% of all antimicrobials, ceftriaxone was the third most common at 16.8%.⁴⁴

A Turkish point-prevalence study across 16 centres audited 161 SAP doses, with the type of antimicrobial agent most commonly chosen being inappropriate for 40.9%.³⁵ Antimicrobials commonly prescribed were of a broader spectrum and included ceftriaxone, glycopeptides and aminoglycosides.³⁵ Broad-spectrum antimicrobials such as third-generation cephalosporins were also the most commonly prescribed for all surgeries (80%) in an SAP audit of 100 patients in an Indian teaching hospital⁴⁴ and in a large multicentre prospective Chinese audit including 14 525 surgical procedures (20.5%, 3453 of 16 836 antimicrobial doses).⁶

Guideline compliance

Higher rates of guideline non-compliance were anticipated, given the second-line nature of aminoglycosides and glycopeptides. This was also anticipated for third/fourth-generation cephalosporins, which are not recommended at all in the Australian guidelines. The lack of guidelines (when assessing guideline compliance) as a means of potential justification for appropriate broad-spectrum SAP use was uncommon (1.5%) (Table S5). Further education of auditors and prescribers to ensure they are aware of what the guidelines cover may help address this issue. Additionally, greater transparency from guideline developers regarding which procedures are and are not covered under each recommendation may provide further decision support to optimize SAP prescriptions.

Compliance with local guidelines was low across the top five antimicrobials (Table S5). However, further analysis of appropriate broad-spectrum agents revealed that local guidelines were potentially endorsing use of broad-spectrum antimicrobials in 28.3% ($n = 93$) of appropriate doses ($n = 329$). We were unable to access content of all local hospital guidelines and therefore unable to critically analyse their content for discrepancies between local and national guide-

lines, and also for potential drivers of broad-spectrum antimicrobial use. This represents a novel area for ongoing research.

Guidelines from the Australian Orthopaedic Association and the American Academy of Orthopaedic Surgeons recommend addition of glycopeptides if the local rate of MRSA is high.^{45,46} Therefore, we advocate flexibility to adapt the national guidelines based on local epidemiology. We propose that hospitals conduct additional monitoring of antimicrobial adverse effects and surgical site infection microbiology to ensure no additional patient harm is associated with their use. This would support ongoing AMS activities and potentially illustrate further consequences of unwarranted broad-spectrum antimicrobial use.

Limitations

The limitations of the Surgical NAPS data have been described in previous publications.^{13,16} Key limitations include the voluntary nature of participation; data are not a random sample, which creates potential sampling and selection bias and survey flexibility, i.e. hospitals could audit any patients and/or surgical units. Thus, the data may include targeted audits reflecting higher volume or problematic units, which influences the interpretation of results.

Appropriateness assessments are not entirely objective and one auditor's interpretation may potentially differ from another. Whilst an assessment rubric (Figure S1) was available and support from the Surgical NAPS team was provided on request, assessment of inter-rater reliability is beyond the scope of this project and has also been discussed elsewhere.^{2,16}

A caveat to all antimicrobial audits is inadequate documentation, which is historically and universally completed poorly for antimicrobial prescriptions.^{1,19–23} However, we argue that the adoption of appropriateness measurements supports the standardization of these assessments, whilst allowing for some flexibility, as opposed to the measure of guideline compliance.

Our research does not account for a range of factors that the Surgical NAPS does not capture, including surgeon experience and perceptions of risk and their aversion. Qualitative research has highlighted that antimicrobial prescribing is influenced by surgical hierarchy and the fear and risk of causing infections and patient harm.⁴⁷ Ongoing research is required to explore decision-making of SAP choice and rationale for broad-spectrum use.

Conclusions

There are various factors that influence appropriateness of procedural SAP choice, including patient factors (ASA score and allergies), hospital factors (presence of local guidelines) and surgical factors (presence of trauma, prosthetic material and surgical procedure groups). Abdominal and urological surgery are key targeted areas to improve prescribing of third- and fourth-generation cephalosporins. Urological, breast and orthopaedic surgeries are targeted procedures to improve aminoglycoside prescribing, whilst orthopaedic and cardiac procedures should be targeted to improve the use of glycopeptides. Local guidelines endorsing routine broad-spectrum antimicrobials should consider additional monitoring of the unintentional consequences of their use, i.e. resistance patterns and adverse effects. Identification of these prescribing trends supports an ongoing examination of SAP prescribing practices in Australia and identification of potential targets for interventions across multiple health sectors such as AMS, guideline development and hospital policy.

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Transparency declarations

None to declare.

Supplementary data

Tables S1–S5, Figure S1 and the Reviewer report are available as [Supplementary data](#) at *JAC-AMR* Online.

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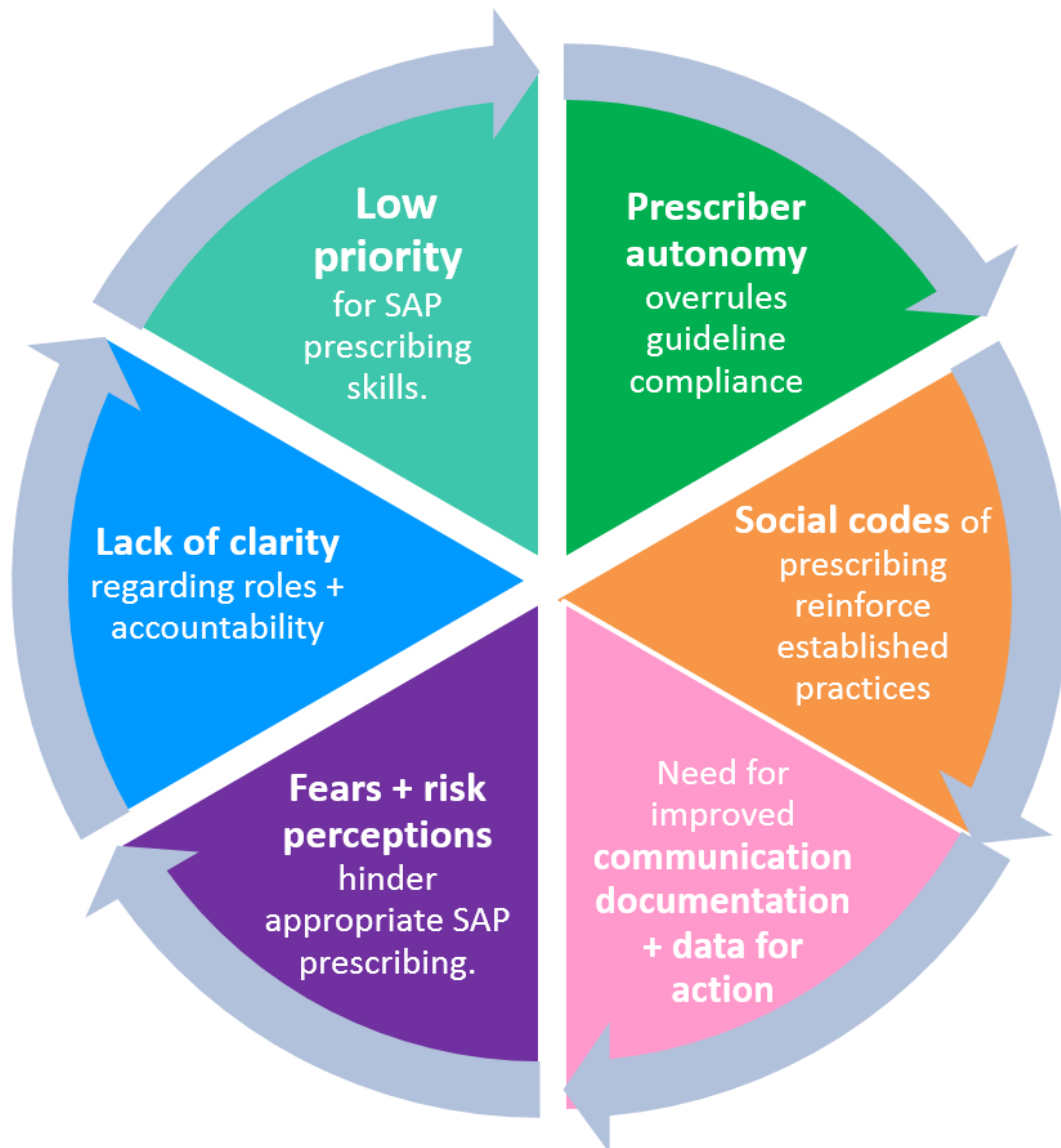
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Chapter 11: Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals

11.1 Introduction

This chapter details the large body of qualitative research that was undertaken to explore the phenomenon of SAP prescribing and decision-making (project 5). The publication examines the factors that shape SAP prescribing in surgical settings across public and private hospitals in Australia, with a focus on the barriers to and enablers of appropriate antimicrobial use and antimicrobial stewardship. Adoption of theoretical frameworks has facilitated a structurally sound analysis that has led to theoretically-informed recommendations to address barriers and support enablers, providing direction for quality improvement (i.e., surgical AMS) in surgical settings. This chapter builds upon the findings from previous chapters that identified various influences on SAP decision making; the context of the Australian healthcare system (**chapter 2**), the evidence behind guideline recommendations (**chapter 3**), other qualitative research examining antimicrobial prescribing behaviour (**chapter 5**) and guideline implementability (**chapter 7**). The key themes identified in this project are illustrated in Figure 1 and provide direction for the **chapter 12** and the proposal of a framework for surgical AMS (SAMS).

Figure 1 The six central themes to describe the influences on surgical antimicrobial prophylaxis prescribing and decision-making



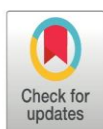
11.2 Publication

The supplementary data published with this manuscript can be found in Appendix 6.

RESEARCH ARTICLE

Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals

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Data Availability Statement: Public sharing of our de-identified transcripts was not included in our ethics and local governance applications, nor our

Abstract

Background

Surgical antimicrobial prophylaxis (SAP) is a leading indication for antibiotic use in the hospital setting, with demonstrated high rates of inappropriateness. Decision-making for SAP is complex and multifactorial. A greater understanding of these factors is needed to inform the design of targeted antimicrobial stewardship interventions and strategies to support the optimization of SAP and its impacts on patient care.

Methods

A qualitative case study exploring the phenomenon of SAP decision-making. Focus groups were conducted with surgeons, anaesthetists, theatre nurses and pharmacists across one private and two public hospitals in Australia. Thematic analysis was guided by the Theoretical Domains Framework (TDF) and the Capabilities, Opportunities, Motivators-Behaviour (COM-B) model.

Results

Fourteen focus groups and one paired interview were completed. Ten of the fourteen TDF domains were identified as relevant. Thematic analysis revealed six significant themes mapped to the COM-B model, and subthemes mapped to the relevant TDF domains in a combined framework. Key themes identified were: 1) Low priority for surgical antimicrobial prophylaxis prescribing skills; 2) Prescriber autonomy takes precedence over guideline

consent process. The content within transcripts includes the names of non-participants and workplaces and would allow identification of these non-participants but also may enable identification of participants and their workplaces. For these reasons we cannot share the de-identified transcripts. This research project was granted ethical approval following low-risk review from the Alfred Hospital Human Research Ethics Committee (HREC) on the 11/10/2017 and the Epworth HealthCare HREC on the 30/10/2017. Local governance approval was sought from both Alfred Health and Epworth. HealthCare in addition to Melbourne Health (Ethics approval inclusive of Alfred Health HREC approval). HREC Reference Number: HREC/17/Alfred/143. Alfred Health local project number: 469-17. Epworth HealthCare local project number: EH2017-270. Melbourne Health local project number: 2017.346. Ethics approval included consent for participation and potential publication. CONTACT DETAILS: 1. Alfred Health Office of Ethics & Research Governance, Email: research@alfred.org.au, Phone: +613 9076 3619. 2. Epworth HealthCare HREC Coordinator, Email: HREC@epworth.org.au, Phone: +613 9426 8806.

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Competing interests: The authors have declared that no competing interests exist.

compliance; 3) Social codes of prescribing reinforce established practices; 4) Need for improved communication, documentation and collection of data for action; 5) Fears and perceptions of risk hinder appropriate SAP prescribing; and 6) Lack of clarity regarding roles and accountability.

Conclusions

SAP prescribing is a complex process that involves multiple professions across the pre-, intra- and post-operative surgical settings. The utilisation of behaviour change frameworks to identify barriers and enablers to optimal SAP prescribing supports future development of theory-informed antimicrobial stewardship interventions. Interventions should aim to increase surgeon engagement, enhance the prioritisation of and accountability for SAP, and address the underlying social factors involved in SAP decision-making, such as professional hierarchy and varied perceptions or risks and fears.

Introduction

Surgical antibiotic prophylaxis (SAP) involves the administration of antibiotics for the purpose of preventing surgical site infections (SSIs), and is a well-established infection prevention measure. As such, SAP is a leading indication for antibiotic use in the hospital setting [1, 2].

Australian and international studies have observed high rates of inappropriate SAP prescribing [1–9], which may consequently contribute to sub-optimal patient care and outcomes, and is also considered a driver of the emergence of antimicrobial resistance (AMR) [10]. Thus, appropriate use of SAP is desired to improve patient care and reduce the burden of inappropriate prescribing on both the patient and health care system.

Antimicrobial stewardship (AMS) has been identified in global policy initiatives [11, 12] as a key clinical strategy for the containment of AMR. It responds to the emergence of AMR by aiming to reduce inappropriate use of antimicrobial medications and thus conserve the effectiveness of these medications; its primary aim is the enhancement of patient care through improved management of antimicrobial therapy [13]. AMS programs and interventions vary immensely. The development and tailoring of AMS interventions to target areas of high concern, such as surgical prophylaxis, is warranted to further optimise antimicrobial usage and patient health.

This study examines clinicians' perceptions across public and private hospitals as research demonstrates a difference in SAP guideline compliance between the two settings [14]. Public hospitals generally deal with more complicated and acute cases, while private hospitals have higher rates of elective and day procedures [14, 15]. This difference may contribute to observed variations in SAP practices.

This qualitative study utilises the Theoretical Domains Framework (TDF) [16] and COM-B model [17, 18] to explore and describe decision-making processes for SAP prescribing. It is important to understand the underlying factors that drive SAP prescribing. AMS interventions aimed at enhancing the appropriateness of SAP prescribing need to consider the contextual and environmental factors that influence SAP prescribing. The utilisation of theoretical frameworks for the identification of barriers and enablers to prescribing can assist in the development of AMS interventions that may successfully be implemented and sustained [19].

Methods

Aim

The primary aim of this study was to identify barriers and enablers of appropriate SAP prescribing and evidence-based guideline compliance. The secondary aim was to compare the perceptions of health professionals in surgical specialties across both public and private hospital settings regarding these barriers and enablers.

Project type and design

Exploratory, multi-site, collective qualitative case study. Exploring the phenomenon of decision-making processes related to SAP prescribing and guideline compliance across three tertiary public and private hospitals in Australia.

Participant recruitment

Recruitment was iterative and aimed at achieving adequate representation from key stakeholders and qualitative data saturation. Surgeons, anaesthetists, pharmacists and theatre nurses were identified via purposive sampling, which was complemented with a snowball sampling strategy.

Conducting sixteen focus group discussions, with a minimum of four participants in each, was proposed to gain knowledge of decision-making for SAP prescribing from multiple perspectives across a range of surgical specialties. Surgical specialties including orthopaedics, general surgery and cardiac surgery were targeted as they represent the most commonly performed procedures in Australia [15]. Additional specialties such as vascular, and plastic and reconstructive surgery were targeted to ensure representation of surgical specialties with demonstrated high rates of inappropriate SAP, as informed by the Australian Surgical National Antimicrobial Prescribing Survey (Surgical NAPS)[4]. Focus groups targeted these specialty groups separately.

In circumstances where four participants were recruited, but fewer than four attended, the focus group still proceeded. In circumstances where four participants could not be recruited, a semi-structured paired interview was conducted instead.

Project Information Statement letters were sent to the key informant and/or organiser of the focus group and distributed to potential participants via email. Additional copies of the Project Information Statement letter were available at the focus group meeting, to ensure all participants were aware of the details of the project and to facilitate provision of consent. Implied consent was provided when participants attended the focus group.

This research project was granted ethical approval following low-risk review the Alfred Hospital Human Research Ethics Committee (HREC) on the 11/10/2017 and the Epworth HealthCare HREC on the 30/10/2017. Local governance approval was sought from both Alfred Health and Epworth HealthCare in addition to Melbourne Health (Ethics approval inclusive of Alfred Health HREC approval). Ethics approval included consent for participation and potential publication.

Data collection

Focus group guides based upon the TDF[16] and COM-B [18] were developed, and adapted for the speciality staff participating. Questions pertained to roles and responsibilities for SAP prescribing, factors that influence SAP decision-making, and strategies and resources to facilitate change (Tables A and B in [S1 Appendix](#)). Focus groups were audio-recorded and transcribed.

Data analysis

The phases of thematic analysis[20] were adapted to reflect the utilisation of the TDF (a behaviour change framework) for the codebook structure and deductive coding. Theme codes were developed for each of the 14 domains within the TDF. Deductive and inductive coding was based upon these theme codes.

Focus group transcripts were the primary data source and were imported into the data management software NVivo11®. Coding for thematic analysis was undertaken by researcher CI. Approximately 20% of transcripts was double-coded by researcher AR. The coding strategy was reviewed iteratively by CI, AR and DA to promote rigour.

Deductive coding identified key TDF domains[16], which were mapped to the COM-B model [18, 21]. Concurrent inductive coding enabled identification of emerging themes; where possible, inductive codes were matched to, or sub categorised within the fourteen TDF theme nodes as sub-codes. Relevant and dominant themes were identified through consensus between two researchers (CI and AR).

Results

Fourteen focus groups and one paired interview were completed. Table 1 summarises the characteristics of the focus groups/interview and their participants. The average number of participants was five and the average duration 47 minutes.

The analysis of SAP prescribing behaviour revealed six significant themes with additional sub-themes. These themes were mapped to the relevant TDF and COM-B domains (Table C in S2 Appendix) and are described in detail below.

Theme 1. Low priority for surgical antimicrobial prophylaxis prescribing skills

Most participants, across the specialties, deemed SAP prescribing skills to be a low priority, and characterised surgical site infections and post-operative complications as “complex issues”

Table 1. Focus group participant details.

Focus group code	Site Funding	Health Profession	Participants (n)	Duration^ (mins)
F1.1TN	Public	Theatre Nurses	8	32
F2.1A	Public	Anaesthetists	3*	56
F3.2A	Private	Anaesthetists	3*	64
F4.3CS	Public	Surgeons- colorectal	9	54
F5.3PS	Public	Surgeons- plastic and reconstructive	4	56
F6.3NS	Public	Surgeons- neurological	4	58
F7.2VS	Private	Surgeons- vascular	2	28
F8.3US	Public	Surgeons- urological	3*	39
F9.1CTS	Public	Surgeons- cardiothoracic	13	22
F10.3A	Public	Anaesthetists	4	64
F11.2TN	Private	Theatre Nurses	5	49
F12.1P	Public	Pharmacists	4	42
F13.2P	Private	Pharmacists	4	55
F14.3SR	Public	Surgical registrars and residents	6	46
F15.3OS	Public	Surgeons- orthopaedics	5	42

^ Seconds rounded off to the nearest minute

* One of the four participants became unavailable at the last minute.

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(F9, public cardiothoracic surgeon) that can't be solely prevented by the administration of SAP. Participants noted that multiple factors contribute to the risk of infection, and that *"you can't just draw it down to antibiotics, hand washing, or whether there are cobwebs in the ceiling in the operating theatre"* (F9, public cardiothoracic surgeon).

1.1: Surgical technique is of greater importance. Participating surgeons highlighted that, in terms of infection prevention and control, greater importance was placed on surgical technique than on how antibiotics are prescribed in the surgical setting (Table 2). This was, therefore, considered a barrier to the optimisation of SAP prescribing.

1.2: Deskillling surgeons. The need to improve SAP prescribing was identified, but not at the expense of surgical technique. When asked about the inclusion of other professionals' involvement in SAP prescribing (i.e., AMS, infectious diseases [ID] and anaesthetists), surgical participants expressed apprehensions about the potential deskillling of surgeons (Table 2) and reinforced the importance of surgeons maintaining their prescribing skills and autonomy.

Theme 2. Prescriber autonomy takes precedence over guideline compliance

Prescriber autonomy and discretion were considered to be paramount when participants described how SAP decisions were made. Participants were notably aware of guidelines; however, the need to comply with them did not perceivably drive or regulate current practices.

Autonomy was perceived to be greater in the private hospital setting than in the public hospital setting. Nursing staff noted that private surgeons had the capacity to *"dictate their own practice"* (F11, private theatre nurse), which was not necessarily driven by guidelines or hospital policy, as they were *"doing their own thing and renting the space"* (F11, private theatre nurse).

Surgical registrars also felt they had less prescribing autonomy compared to their medical registrar colleagues, as noted by an orthopaedic registrar when they compared their level of autonomy to that of their partner, a general medicine trainee:

"Just the level of autonomy that physicians are granted from, like, two to three years out of [university], in terms of writing a patient up. . . If you refer to a surgical unit, you get the opinion of a consultant. Everything that we do goes to the consultants." (F15, public orthopaedic surgeon)

2.1: Guideline knowledge and awareness of limitations. Guidelines were considered to be useful, particularly to junior health professionals (Table 3), and their accessibility was considered an enabler for appropriate SAP prescribing. However, guidelines were also perceived as broad and insufficiently detailed to account for the expansive range of surgical procedures and any confounding environmental and patient-specific factors, and thus are a barrier to optimal SAP decision-making in complex scenarios (Table 3).

Table 2. Representative quotations from Theme 1 reflecting 'Physical Capability' of the COM-B model.

Theme 1: Low priority for surgical antimicrobial prophylaxis prescribing skills.			
Subtheme	TDF Domain	Illustrative quotes	Barrier or Enabler?
Surgical technique of greater importance	Skills	<i>"The thing that's going to reduce the infection rates is technique."</i> (F6, public neurosurgeon)	Barrier
		<i>"I don't think that giving them more antibiotics makes the infections less likely. . . a lot of it has to do with my technique. . . I don't feel that I can overcome my failings that much with antibiotics."</i> (F4, public colorectal surgeon)	
Deskillling surgeons		<i>"We were discouraged from [prescribing antibiotics] and discouraged from doing the fluids because we were taking it away from the residents. Yeah, de-skilling the residents."</i> (F10, public anaesthetist)	Barrier

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Table 3. Representative quotations from Theme 2 reflecting 'Psychological Capability' of the COM-B model.

Theme 2: Prescriber autonomy overrules guideline compliance.			
Subtheme	TDF Domains	Illustrative quotes	Barrier or enabler?
Guideline knowledge and awareness of limitations	• Knowledge • Memory, attention and decision processes • Behavioural regulation	"No, because every patient is different. So, guidelines are guidelines. They're not rules. So, they can be helpful, and they may, you know, stop you from giving them for five days. But, it's not going to stop you from worrying. Especially, contamination. It's not going to stop me." (F4, public colorectal surgeon)	Barrier
		"I think this generation are very quick to refer to guidelines and look things up. I think they're very good at accessing them. The sort of stuff that we used to carry around in our heads, it's just not necessary anymore because you just have a look at the antibiotic guidelines and it's there for you." (F4, public colorectal surgeon)	Enabler
		"Even though there might be recognised guidelines, many surgeons have their own preferences; which they will override, and they might say, 'Yeah, I know there's no evidence for antibiotics, but I want them anyway.' Or, 'I know the guideline says use cefazolin or whatever, but I like ceftriaxone.'" (F3, private anaesthetist)	Barrier
		"I think the assumption for most of the surgeons would be that their practice that is deviating from these guidelines, does not deviate because they're unaware of the guidelines. And us (pharmacists), just letting them know that they exist isn't going to solve the problem. . . . The education of the surgeon is not necessarily the gap." (F3, private pharmacist)	
Competition as a means to regulate behaviour	• Behavioural regulation	"So, where you feed that (audit data). . . I mean, people in medicine, particularly doctors, are very competitive. So, you know, people don't like to be down at the bottom of the pack. . . And, they want to do what's best overall. So, if you show that they're not meeting the guidelines, then they will work to get the results." (F3, private anaesthetist)	Enabler
		"Neurosurgeons are very competitive. If you can show a unit that their infection rate is crap, they'll try and do something about it". (F6, public neurosurgeon)	
		"If you can benchmark and compare them (surgeons) to other people, that's another way (to change practice)." (F12, public pharmacist)	

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There was awareness of national and local guidelines, but participants commonly highlighted the perceived existence of many gaps in the current evidence and how these warranted deviation from guideline recommendations. However, participants also noted that the rationale for deviation was not always documented. Common issues identified by participants could be mapped to specific targets for future educational stewardship strategies. These include timing of SAP administration (in relation to incision time), intra-operative re-doing, post-operative durations, the use of topical SAP, and SAP in relation to concurrent antimicrobial therapy and complex patients (Table 4).

Guideline implementation was not standardised across the three hospitals. Education around guidelines, or lack thereof, was not a concern, as there was an assumption that most surgeons were aware of their guideline non-compliance (Table 3). Insufficient motivation to address this, or to intervene to promote guideline compliance, served as a barrier to optimisation of SAP prescribing. Inconsistent guideline implementation was seen as an accepted part of current practice.

2.2: Competition as a means to regulate behaviour. It was noted by participants that surgeons are highly driven and competitive. Capitalising on these behavioural traits may be an enabler of improved SAP prescribing. Peer-to-peer and unit-to-unit comparisons of SAP prescribing may induce professional competitiveness and, as such, facilitate quality improvement initiatives (Table 3).

Theme 3. Social codes of prescribing reinforce established practices

3.1: Intra-specialty hierarchy rules. Surgical registrars, residents and interns were not comfortable modifying and ceasing SAP prescriptions without confirming the acceptability of

Table 4. Commonly referenced gaps in current guidelines and evidence as per participants.

Examples	Quote (Focus group reference)
Timing	"How late can you give it? It's probably more relevant to the anaesthetist. . . Does it matter if it's two minutes before the operation or twenty minutes before?" (F2, public anaesthetist)
Re-dosing	"There's a lot of debate about whether it should be three or four hours." (F10, public anaesthetist)
Weight-based dosing	"I had an orthopod who was very concerned that . . . this was like a very serious operation. And, so gave the 3 grams for this not morbidly obese patient because they really wanted to give a good serious dose." (F10, public anaesthetist)
Post-operative durations	"The guidelines say only one dose, but all surgeons that I work with want three doses for joints." (F3, private anaesthetist) "We just continue antibiotics, you know, till the drains are out. We just do our own thing. It's a case-by-case thing. It's not particularly evidence-based. . . I wasn't even really aware of those guidelines." (F5, public plastic surgeon)
Oral antibiotics	"If you've had them on IV cefazolin, and you're then going to prescribe them an [oral course of antibiotics]. . . If the wound's dry and it's not infected, why're you giving someone antibiotics? I try and avoid that. But, it'll usually be the boss to say, 'five days of orals'." (F15, public orthopaedic surgeon)
Complex patients	"Being hit on the head in a car is different to being kicked in the face by a horse, for instance. So, they both might have similar fracture patterns but would have vastly different organisms and contamination. So, we're naturally suspicious of protocol-driven care because I don't think it's nuanced enough currently to actually give us a meaningful answer." (F5, public plastic surgeon)
Topical antibiotics	"There was a neurosurgeon I worked with in Adelaide who used to open the flucloxacillin, and put the powder into a pack, and sprinkle it on the wound. I was like, 'gosh, 'Mr. [surgeon], is there any evidence for that?' He goes, 'No, absolutely none, but I like to do it anyway. Makes me feel better'." (F3, private anaesthetist)
Concurrent antimicrobial therapy	"If they're on the ward, like ICU, and they're on some mega, you know, fancy pants drug you've never heard of. . . what do we do then? Do we just give them some cefazolin? You know, is that the wrong thing to do or, you know, because. . . We certainly don't have mega penicillin that they give. . . and even though they're not due for a next dose of meropenem, say, for another four hours, what do we do? I don't know." (F2, public anaesthetist)

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such decisions with their consultants, indicating the influence of intra-speciality hierarchy on decision-making. Continuation of SAP orders in the absence of documentation, infection or evidence for use was perceived as a default practice, reinforced by preferences that have been passed down the hierarchy.

Prescribing behaviour was defined and regulated at a senior level, dependent on the surgical consultant's preference as opposed to guideline recommendations. Participants noted, to generate changes in SAP prescribing practices, acceptance of interventions from the most senior medical level was required. Targeting SAP stewardship interventions at junior surgeons was not perceived as helpful, as their prescribing was heavily regulated by their seniors' preferences, as opposed to externally-received advice advocating guideline compliance (Table 5).

Orthopaedic registrars and residents noted that pointing out deviations from the guidelines when "the boss wants to do something else" was a form of "challenging" their boss (F15, public orthopaedic surgeon). Despite collegial support, they did not feel they were truly empowered to challenge the status quo and were expected to continue current SAP prescribing practices regardless of the deviation from evidence-based recommendations:

"I think, the reality of the relationship with surgeons is that they don't want to be challenged by their junior staff. People often encourage us to do things, like the College of Surgeons has got this escalation of stuff [framework]. It's all BS [bullshit]." (F15, public orthopaedic surgeon)

Participants noted that, with time, the social codes are changing, with the new generation of younger surgical consultants demonstrating greater awareness of evidence-based recommendations. However, these surgeons still have to overcome established default practices such as the perceived standard practice of prescribing antibiotics for 24 hours post-operation.

"I think, some of the younger consultants are up-to-date with [the evidence]. . . And, I think that's what is going to change it—it's just the next generation. But, the problem is, things get handed down, and, you know, because your boss did 24 hours [of post-operative SAP], I have to do 24 hours." (F14, public surgical resident/registrar)

3.2: Cross-specialty prescriber etiquette shapes decision-making. Surgeons, regarded as being at the top of the hierarchy, expressed reluctance to receive advice and feedback from those not at a similar level of seniority (i.e., a trained nurse practitioner), or stewardship recommendations (Table 5).

The way feedback is given to surgeons was perceived as constituting prescriber etiquette. AMS and ID specialties were not considered to be part of the surgical team, and, as such, their recommendations were to be considered but not mandatorily enforced. Participants noted AMS and ID physicians were less likely to actively modify or cease prescriptions out of professional etiquette and only provide a recommendation. The final decision remained with the surgeon (Table 5).

Theme 4. Need for improved communication, documentation and data for action

4.1: Poor documentation and communication. Communication at both inter- and intra-specialty levels was perceived to be lacking and a barrier to appropriate SAP prescribing and decision-making. In the peri-operative setting, the theatre environment was considered to be time-poor, hindering access to patient information and guidelines for antimicrobial clinical decisions. Participants noted an increasing availability of digital guidelines, which facilitates greater use among trainees, and may result in more guideline-compliant prescribing practices.

"Most theatres have computers. Otherwise, we've got them (electronic guidelines) in our pockets at all times." (F14, public surgical resident/registrar)

Table 5. Representative quotations from Theme 3, reflecting 'Social Opportunity' of the COM-B model.

Theme 3: Social codes of prescribing reinforce established practices			
Subtheme	TDF Domains	Quotes (source)	Barrier or enabler?
Intra-specialty hierarchy rules	Social Influences	<i>"It's (up to) the consultants, you can't (change practice to single dose SAP). . . They've got to be on board with it. Because, at the end of the day, you stop the antibiotics based on evidence, and something goes wrong—it will be your fault. It'll reflect badly on you because the consultant will say, 'That's not what I do.' And, the guidelines are not enough to stand against a consultant who's got very set ways, in terms of their antibiotic prescribing. . . Often, I'll just go with what my seniors have told me because, you know, that's what we do."</i> (F14, public surgical resident/ registrar)	Barrier
Cross-specialty prescriber etiquette		<i>"We would resist, or not embrace, a nurse practitioner type approach to antibiotic use in theatre. We would welcome some input, but we wouldn't necessarily agree or follow those instructions. It is. . . I know that it sounds somewhat snobby, but, if that was advice given to me by an ID physician, I would follow it because, I think, they come from a more informed position. . . If someone had just done a one-year course on a weekend to become a nurse practitioner to give advice on antibiotics, it just doesn't sit well with me. I would back myself."</i> (F5, public plastic surgeon)	Barrier
		<i>"(Prescriber) etiquette also extends to a surgeon (who) gets a formal ID consult on one of their patients. . . They'll (ID) just recommend that the surgeon stops antibiotics. . . Some of the ID guys won't cross off the antibiotics. They'll just say, 'If they surgeon's happy, I think, you could stop the IV [antibiotics]. I'm still going to leave it in your hands.' I mean, it's all very polite."</i> (F13, private pharmacist)	Barrier

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Additionally, it was noted that documentation of timing for surgical incision and SAP administration was completed poorly, thus making it difficult for anaesthetists and surgeons to receive accurate feedback (Table 6).

4.2: ‘Time-out’ supports pre-operative communication; post-operative management is less standardised. The ‘time-out’ process is part of the ‘universal protocol’ [22] and ‘World Health Organization Surgical Safety Checklist’ [23]. The ‘time-out’ process has been adopted globally to provide reassurance of “*accurate patient identity, surgical site and the planned procedure*” [24, 25]. ‘Time-out’ was perceived to be an enabler for optimal procedural SAP prescribing and a successful workflow process that has been embedded into current practice and supports communication between the team. It also includes questions regarding “*allergies and what antibiotics patients are getting*” (F5, public plastic surgeon).

Participants noted the absence of a similar process in the post-operative setting and observed that post-operative plans “*won’t say anything about antibiotics*” (F11, private theatre nurse). If antibiotics were wanted by the surgeon, the plan was communicated poorly and usually handed over passively and verbally by the anaesthetist; for example, “*This surgeon wants three more doses*” (F11, private theatre nurse). Similarly, the discharge workflow and communications regarding the management of post-operative complications and/or infections between GPs, pharmacists and surgeons were perceived as being sub-optimal.

Participants agreed that inclusion of a discussion about SAP duration as part of the pre-operative time-out, or the addition of a post-operative ‘time-out’ or checklist, would serve as a potentially useful intervention that would enhance the clarity of the documentation and planning of SAP duration.

“I would think the best place to do it is in the time-out in the theatre, and then trying to change the paperwork to that. . . So, then you can say, ‘Right, this can be written for 24 hours or this can be a one-off.’ You get clear on that.” (F11, public theatre nurse)

Table 6. Representative quotations from Theme 4, reflecting ‘Physical Opportunity’ of the COM-B model.

Theme 4. Need for improved communication, documentation and data for action			
Subtheme	TDF Domains	Quotes (source)	Barrier or enabler?
Poor documentation and communication	Environmental context and resources	<i>“Probably the biggest caveat to any anaesthetic record is that it’s a record rather than a prescription. So, it’s often done in retrospect. So, they’ll give it and then they record it. So, if they’ve forgotten actually what they’ve given at what time. . . Sometimes, it might not happen.”</i> (F12, public pharmacist)	Barrier
‘Time-Out’ supports pre-operative communication; post-operative management is less standardised		<i>“They (surgeons, anaesthetists and scrub nurses) definitely use the time-out. Everyone uses the time-out. But, I’m not sure about the guidelines.”</i> (F11, private theatre nurse)	Enabler
		<i>“Orthopaedics will put in the operation notes–‘IV cefazolin 24hours.’ Which usually means intra-op and three doses. And that’s very clear. And that’s easy to denote on the med charts. And, other units, not necessarily–not as clear.”</i> (F14, public surgical resident/ registrar)	Barrier and enabler
		<i>“The number of times patients come back post-operatively for a check, and all they’ve had is a minor little dehiscence and the GP has just given them two-weeks of antibiotics. . . It’s completely inappropriate.”</i> (F7, private vascular surgeon)	Barrier
Data for action		<i>“Audit it [antibiotic use] and compare it to previous use where there has been prescription of antibiotics and there was no change. That would be the outcome required to convince surgeons to change their practice.”</i> (F15, public orthopaedic surgeon)	Enabler

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4.3: Data for action. Many participants stated that local data on appropriateness of antimicrobial prescribing and outcome data such as surgical site infections, was of greater interest to surgeons, and an enabler of SAP optimisation. It was perceived that the use of local data was more likely to generate behaviour change and improve SAP prescribing (Table 6). Many participants expressed the view that the guidelines and the underlying evidence base weren't tailored to their unique patients and setting; they wanted local data to inform their practice. However, it was also noted that there was limited funding for localised data collection and dissemination of feedback.

Theme 5. Fears and perceptions of risk hinder appropriate SAP prescribing

5.1: Fear of infections. Participants expressed many concerns and fears in relation to SAP prescribing, and how this impacted upon both the patient and themselves. Overall, all fears illustrated in Table 7 were barriers to appropriate SAP prescribing. There was awareness of how inappropriate prescribing may contribute to patient harm and the development of multi-

Table 7. Representative quotations from Theme 5 reflecting 'Automatic Motivation' of the COM-B model.

Theme 5: Fears and perceptions of risk hinder appropriate SAP prescribing.			
Subtheme	TDF Domains	Quotes (source)	Barrier or enabler?
Fear of infections	Emotion	"I think the problem is that an infection is a nightmare. An infected joint is a catastrophe... It could end up with the whole joint being removed. The patient having amputation... I can completely understand why a surgeon would want more than one dose." (F3, private anaesthetist)	Barrier
		"They don't care about the multidrug resistant bugs... They care about what looks bad on their [statistics]... What looks bad on their [statistics] is when they get a post-op wound infection. But, these patients with multidrug resistant bugs. The problem is down the track, it's not (an issue)." (F15, public orthopaedic surgeon)	Barrier
Varied risk perceptions across specialties		"I think, as colorectal surgeons, most of us... if we had a localised surgical site infection, antibiotics are not the first thing we would use. We would open up the wound or drain any pus that's around. And, most of the time... if I had a post-operative wound infection which was superficial on the abdomen, I probably won't use antibiotics. So, I think, we don't usually use antibiotics. Whereas, plastics on the other hand... you know, if you went and rubbed a bit of faeces on to one of their skin grafts (laughing), it'll be horrifying. We do flaps in the anus, and we don't use long, extended antibiotics for that." (F4, public colorectal surgeon)	Barrier and enabler
		"I think, 21 days of [piperacillin/tazobactam] is the longest. We've had some head and neck patients on maybe like three or four weeks of IV cefazolin because everyone chickened out of taking it off. We've had patients started back on IV cefazolin because they looked a little bit red with no objective evidence of any infection." (F14, public surgical resident/registrar)	Barrier
Fear of litigation		"I think, a lot of the surgeons are really, genuinely scared about being sued. I'm sure that drives practice... I think it makes surgeons very reluctant to undertreat infections because they're the ones who're going to cop it if the patient has a complication." (F8, public urological surgeon)	Barrier
		"I think (that's) what's a major contaminant in the space... is the behaviour of Medibank Private, who are looking to not fund readmissions and problems for post-operative infections, etc. I think that is a significant pressure that some surgeons will feel, and will mitigate against. So, someone will say, 'Yeah, I want to give more antibiotics. I'm worried about (infections)'." (F4, public colorectal surgeon)	Barrier
Risking career progression and job security		"We're working in an environment now where making criticisms of your colleague's practices is extremely troublesome. And, I think, my experience, as someone who gets frustrated and tends to make comments, is being told to shut up." (F15, public orthopaedic surgeon)	Barrier
		"I think, if you made a pattern of behaviour, where even if you're advocating for a patient but you're asking some questions that were seen to be undermining the authority of the surgeon, depending on personality, or just creating a headache for them, in that, 'Who's this registrar? Always asking me these tough questions that I don't know the answer to.' I think you could get into a position where, you know, it affects your relationship with that surgeon... If you're annoying and ask stupid questions, that slowly will affect their view. They're not going to respect you necessarily, for asking the tough questions. They just will consider you a hassle." (F15, public orthopaedic surgeon)	Barrier

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drug resistant organisms (MDROs), but the risk of development of MDROs and adverse consequences from antibiotic overuse was perceived as being outweighed by the risk of perceived underuse causing direct patient harm, particularly in the form of not preventing surgical site infections (Table 7).

Surgeons reported attributing blame for MRDOs to other health professionals, such as GPs, with little reported acknowledgement of their own contributions and prescribing behaviour. Other health professionals were perceived as having greater responsibility for the problem.

"I've heard (other) surgeons say, 'Oh, it's not our fault. It's the bloody GPs, you know, prescribing [antibiotics] in the community.' No one wants to take blame for that problem." (F15, public orthopaedic surgeon)

To facilitate prescribing behaviour change, it was suggested that the discussion around SAP appropriateness needs to shift from highlighting the lack of evidence for prolonged duration of SAP to focusing on the potential harms of inappropriate antibiotic use, emphasising the importance of appropriate use and responsibility for enhancing patient care.

"Our message up till now has been there's no great evidence of benefit of continuing the [antibiotics]. We haven't really sold the message of what's the risk of harm. Because, if there's none, then it's, '3 days of cefazolin, who cares?'" (F13, private pharmacist)

5.2: Varied risk perceptions across specialties. Risk perception varied across the surgical specialties and was both a barrier and an enabler to appropriate antibiotic use. Colorectal surgeons were less likely to use antibiotics for a post-operative infection, whereas plastics surgeons were considered to be overcautious, prescribing prolonged durations (Table 7).

Surgeons were less likely to be aware of antibiotic-related adverse events such as *Clostridioides difficile* infections, and less likely to factor the risk of adverse events into their prescribing decisions.

"Clostridium [Clostridioides] difficile is not an orthopaedic problem area. Clostridium [Clostridioides] difficile does not stand in an orthopaedic bed cart [not an orthopaedic admission] and it's not a headache for us". (F15, public orthopaedic surgeon)

5.3: Fears of litigation. The fear of litigation from patients for post-operative complications drives antibiotic overuse as a preventative measure, and this perception emerged across all participating cohorts. Negative experiences such as previous complications and litigations also appeared to encourage the over-prescribing of SAP (Table 7).

Surgeons perceived that there was a 'backlash' for post-operative complications and SSIs from many sources: the hospital, surgical colleagues, other medical professionals and health insurance companies. Avoidance of this outcome appeared to be a justification for overuse of SAP in the post-operative setting.

Health/medical insurance companies influence how risk is perceived and managed in the private setting. Clinicians perceive insurers as being resistant to funding readmissions prompted by post-operative SSI occurrence. This may drive an overcautious approach to SAP prescribing (Table 7).

5.4 Risking career progression and job security. Challenging senior consultants about antibiotic prescriptions was not considered to be worth the perceived associated risk of jeopardising their career and relationship with that surgeon, and therefore serves as a barrier to optimal SAP prescribing (Table 7). Junior surgeons were less willing to dispute their seniors' sub-optimal SAP decision-making, out of fear of appearing "difficult", "annoying" and

“troublesome” (F15, public orthopaedic surgeon), which they believed would consequently affect their career prospects.

Theme 6. Lack of clarity regarding roles and accountability

6.1. The buck stops with the surgeon; ownership required. Ultimately, the responsibility for SAP lies with the surgeon as “*the buck stops with them*” (F13, private pharmacist). Post-operative complications were viewed as a serious issue and addressing these was considered, by default, to be the surgeon’s responsibility.

Participants reported that responsibility for SAP prescribing in general was transferred to the most senior professional (surgeon or anaesthetist) in the theatre at a given point in time. However, the multiple roles required for clear decision-making around SAP prescribing pre-, intra- and post-operatively are less clearly defined, with adverse implications for accountability for these decisions.

When other professionals were involved in SAP prescribing, the responsibility associated with each role varies, creating further confusion amongst the team; and was considered as a barrier to appropriate SAP prescribing. Ideally, clarification and ownership of these roles and responsibilities is required for all professionals in the surgical setting. This may enhance both prescriber accountability and correct and timely referral to the appropriate decision-maker for queries pertaining to SAP. Participants noted that such clarity would support optimisation of antimicrobial use in the surgical setting (Table 8).

6.2: Passive prescribing hinders accountability and SAP cessation. Prescribing for SAP appeared to be undertaken passively by anaesthetists in the peri-operative setting, and by surgical residents/registrar and interns in the post-operative setting.

Decisions regarding SAP depend upon the surgeon; however, anaesthetists, who have an established role in SAP administration, are expected to have SAP prepared prior to surgery, where decisions may have not been finalised. This places them in an unclear position of responsibility; and serves as a barrier to appropriate SAP prescribing.

Discussion regarding the initiation of procedural SAP appeared to be part of the current workflow and ‘time-out’ process, with anaesthetists noting that they would commonly prescribe and administer SAP on behalf of the surgical consultant. This routine would be based upon previous discussions regarding the surgeon’s preference, as opposed to guidelines. Some surgeons deferred SAP decision-making to the anaesthetist, which was considered successful in improving guideline compliance (Table 8).

While surgeons were identified as being responsible for SAP, they were also perceived to be abrogating responsibility to junior registrars without clearly communicating their expectations (Table 8).

There did not appear to be a regular process or pathway for prompting discussion about cessation and/or continuation of post-procedural SAP. Consequently, junior surgeons passively prescribed SAP on behalf of their consultants without further discussion of a plan.

Cessation of SAP requires active intervention, and, by default, SAP was commonly and passively continued in the post-operative setting until someone confirmed cessation with the consultant. Junior surgeons were reluctant to question their senior’s decisions and consequently reluctant to change or cease post-operative SAP.

“As a resident... they (nurses and pharmacists) do ask you, ‘Should we be stopping this?’ or, ‘How long are we giving this for?’ Like, it’s not within my power to say, ‘Just stop it.’ I have to ask someone else.” (F15, public orthopaedic surgeon)

Table 8. Representative quotations from Theme 6 reflecting 'Reflective Motivation' of the COM-B model.

Theme 6. Lack of clarity regarding the roles and accountability			
Subtheme	TDF Domains	Quotes (source)	Barrier or enabler?
The buck stops with the surgeon, ownership required	• Social/ professional role and identity • Beliefs about Capabilities • Beliefs about Consequences	"Well, they (surgeons) are (responsible). And, part of the reason for that is because the buck stops with them when it all turns horrid. . . It's ultimately theirs. . . There's a reason why they get to make the call." (F13, private pharmacist)	Barrier
		"We've got a good thing in place at the moment where the anaesthetists are owning it intraoperatively, and, I think, postoperatively, it's put back on to the teams, which is then where we see the major variance in practice." (F12, public pharmacist)	Enabler
		"I think someone needs to own it. So, I would say most hospitals. . . whether it's the anaesthetist or surgeon, someone has to own it. If you give it to too many people, no one's going to own it, and no one will do it. So, they need to have a champion. So, whether it's anaesthetists in theatre. . . for us, here, it's quite anaesthetic-driven. Which has been good." (F12, public pharmacist)	Enabler
Passive prescribing hinders accountability and SAP cessation		"Most of the time, they're (surgical consultants) not really aware of what their residents and registrars are charting." (F10, public anaesthetist)	Barrier
		"But, most of the teams here, because they work together for so long, it is, you know, practice of what they've always done. So, I guess, it's a conversation that they've (anaesthetists and surgeons) had previously, and it is assumed that that's what they just keep going with." (F11, private theatre nurse)	Barrier and enabler
		"The default for the resident is to continue with the status quo until someone tells them it's okay to stop. So, again, the pharmacist will often only get access to the resident, who won't know what to do necessarily, and they'll continue it as a default. It's access to the senior decision-makers that is often the gap." (F10, public anaesthetist)	Barrier
Capacity for role expansion of pharmacists and nurses.		"There is orthopaedic prophylaxis that is charted by the PAC pharmacists in pre-admission clinic, which is again very protocol driven. . . And, that includes any post-operative prophylaxis. I think, it's a very collaborative model. (F12, public pharmacist)	Enabler
		We do rounds with the pharmacists. . . They question us about everything. . . They (pharmacists) are very helpful. (F9, public cardiothoracic surgeon)	Enabler
		"A lot of the antibiotic decisions go over the pharmacists' heads because they don't have that real clinical insights as to the decisions that were made. I quite often have discussions with the pharmacists about why we've chosen antibiotics for plastics, for head and neck patients, and they just don't have any understanding of, like the intraoral communication and what difference that makes. . ." (F14, public surgical resident/ registrar)	Barrier
		"I think, nurses are much better at following guidelines. . . And, ward pharmacists. If there was a very clear statement around these (antibiotics) in the surgeries, that they should or shouldn't (be prescribed), then they will flag that up" (F10, public anaesthetist)	Enabler

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This perceived lack of leadership for SAP cessation was noted by participants across all professions.

6.3: Capacity for role expansion of pharmacists and nurses. Participants reported that pharmacists were not regularly present in the operating theatres across all sites included in our study, and therefore were perceived to have minimal influence of SAP decision making. One site described the novel expansion of the pre-admission clinic pharmacists' role in response to poor adherence of their guidelines. The procedural SAP was charted and administered via the anaesthetic record and pharmacists undertook an active role in the charting of post-operative doses (two additional doses of cefazolin 2 grams every eight hours, for a total of 24 hours) for orthopaedic hip and knee arthroplasty as per their local protocol (Table 8). Ultimately, changes could be made by the orthopaedic unit. The capacity building undertaken for this pharmacy role expansion was perceived to be beneficial, as it ensured correct weight-based dosing and SAP duration. This intervention supported local protocol compliance which had been endorsed by the hospital and orthopaedic unit, thus serving as an enabler to SAP optimisation and standardisation.

Pharmacists were noted for their active role in reviewing post-operative SAP when patients returned from theatre. This was generally perceived as helpful by other professions (Table 8). However, as previously discussed, the final decision was dependent upon the junior doctors following up on the pharmacists concerns and querying these with their surgical consultant.

The pharmacists' scope of practice and knowledge of antibiotics decision-making was queried by surgical residents, in which one stated that pharmacists lacked "real clinical insight" (F14, public surgical resident/ registrar) into their decision-making and were frustrated by their constant need to justify their decision-making to pharmacists. This served as a barrier to expanding the pharmacist roles and capacity for SAP optimisation.

The role of the pharmacist varied across the included hospital sites. One of the public hospitals noted the pharmacy departments' strong clinical presence on the wards had led to an embedded practice where all prescriptions must be reviewed by a pharmacist prior to discharge (F9, public pharmacist). Another site, a private hospital, highlighted the difficulties of timely access to surgeons and subsequent reduced ability to providing accurate post-prescription review and feedback (F13, private pharmacist).

Theatre nurses were noted to have multiple roles in the operating room. Their role regarding SAP was perceived to be highly protocolised. Experienced nurses were perceived to be more confident in their ability to prompt anaesthetists and surgeons regarding pre-operative SAP administration. Nurses did not feel empowered to have an active role in improving SAP as they were not in charge of administration and documentation;

"I don't think we're in charge of documenting when it can be given, to be honest with you. . . That power is taken out of our hands as to when it can actually be administered" (F11, private theatre nurse)

SAP decision-making in the post-procedural setting was unanimously perceived as beyond a theatre nurses' scope of practice (F11, private theatre nurse). However, they did acknowledge the importance of their role as key communicators between theatres, recovery and ward nurses to ensure that the surgeons plan for antibiotics was followed up on.

Whilst decision-making was beyond their scope of practice, nurses believed they could become more actively engaged in the process if an intervention was of similar format to the 'time-out' process, in which they felt comfortable in following the prompts of a check-list and/or protocol, as it had been endorsed as hospital policy and their questioning of the surgical team appeared justified (Table 6, Subtheme 4.2).

Discussion

Results from this study have highlighted the complexity of SAP prescribing behaviour and the need to understand these influences to inform the development of targeted AMS interventions. Our study has identified six themes that reflect key issues relating to the complex nature of decision-making around SAP prescribing. These themes were developed using the TDF[16] and COM-B[18] models, with the majority of themes identifying barriers to appropriate SAP prescribing.

SAP is a low priority for surgeons

The notion that SAP is a low priority for surgeons was also highlighted by Broom *et al*[26] in their qualitative study involving Australian surgeons and anaesthetists. In this study, the authors' focus was largely on the lack of priority for re-dosing intra-operative SAP, which was also illustrated in our analysis. Antibiotic management was perceived as a peripheral role by

surgeons in a UK ethnographic study[27], whilst a lack of motivation and time to develop non-technical skills was also highlighted in a Sri Lankan qualitative study involving fifteen surgeons[28].

This lower prioritisation notably reflects the current poor uptake of SAP guidelines. The Therapeutic Guidelines[29] are the nationally endorsed and recommended guidelines in the AMS Clinical Care Standards[13]. They have also recently been updated since the completion of this research[29]. Guidelines were commonly identified as a reference point for SAP decision-making, with junior surgeons perceived to be more likely to access them. However, their limitations were widely acknowledged (Table 3), and prescriber preferences and autonomy were commonly seen as justifying non-compliance.

Broom *et al* [26] proposed that ‘improvisation’, and social and professional ‘norms’ work against guideline compliance. Similarly, we found there was a perceived need among prescribers to exercise their autonomy, and to improvise and deviate from recommendations. We believe that engagement with surgeons to address their perceptions about guidelines, and to gain consensus regarding recommendations, at both a national (specialty boards) and local (local guideline committees) level, is critical for the improvement of SAP prescribing. These findings also highlight that lack of knowledge about SAP is not necessarily a key barrier that drives inappropriate SAP prescribing. Education regarding the evidence that underpins guidelines is important but does not appear to be solely effective. An effective AMS intervention should be multifaceted and consider the multiple additional factors that influence prescribing behaviour. Table 9 provides a summary of recommendations, mapped to the TDF and COM-B frameworks, for the optimisation of SAP decision-making and prescribing based upon our findings.

Hierarchy influences prescribing behaviour

Our findings about hierarchy heavily influencing prescribing reinforce the existing literature [26, 28, 30–35]. Charani *et al*[35] proposed that medical hierarchy necessitates ‘prescriber etiquette’, whereby “unwritten but widely accepted cultural rules”[34] influence how health professionals prescribe and interact with other health professionals regarding SAP prescription, administration, monitoring and cessation. The preference for ‘non-interference’ is demonstrated in our study, where participants reported perceiving AMS/ID physicians as being reluctant to actively cease antimicrobials and alternatively provide recommendations that may not be implemented as this is dependent on the surgeons final decision.

Surgical hierarchy also influences how receptive surgeons are to feedback. Feedback was considered to have higher impact if delivered by health professionals of ‘similar status’, i.e., anaesthetists and ID consultants, as opposed to pharmacists and nurses. Thus, we recommend that future AMS interventions and strategies are tailored to suit the targeted audience and their level of hierarchy (Table 9).

Need for greater standardisation, documentation and communication

Our study highlighted a need for greater clarity of roles and responsibilities for SAP prescribing and identified many gaps in communication and documentation across the patient’s surgical journey. The quality of the information on SAP prescribing that is recorded in the medical notes can vary between different specialities.

The standardisation of the SAP workflow and documentation practices supports accountability for all professionals in the surgical setting. Standardising communication regarding and documentation of the specifications of both procedural and post-procedural SAP prescribing would help rectify the routinely observed absence of this information in the medical notes, and help facilitate better auditing, education and feedback strategies.

Table 9. Recommendations for change to optimise appropriate SAP decision-making and prescribing.

COM-B	Theme	Subtheme	Recommendations for change
Physical Capability	Low priority for surgical antimicrobial prophylaxis prescribing skills.	Surgical technique of greater importance Deskilling surgeons	• Provide targeted education and training on principles for SAP and AMS as part of orientation training. • Increase surgeon engagement in SAP decision-making and prescribing.
Psychological Capability	Prescriber autonomy overrules guideline compliance.	Guideline knowledge and awareness of limitations Competition as a means to regulate behaviour	• Continue to increase accessibility of guidelines in the operative setting. • Increase engagement of surgeons and anaesthetists in guideline development. • Mandate documentation for rationale of guideline deviation. • Conduct and feedback SAP prescribing audit data to departmental heads to facilitate benchmarking at multiple levels—consultant, surgical unit, hospital, state.
Social Opportunity	Social codes of prescribing reinforce established practices	Intra-specialty Hierarchy Rules Cross-specialty prescriber etiquette	• Target AMS interventions at senior surgical consultants. • Engage with senior surgical consultants for the development and implementation of quality improvement initiatives such as AMS.
Physical Opportunity	Need for improved communication, documentation and data for action	Poor documentation and communication ‘Time-Out’ supports pre-operative communication; post-operative management is less standardised Data for action	• Promote standardisation of SAP workflow and documentation, specifically; - Indication for procedural and post-procedural SAP; - Duration of post-procedural SAP, and differentiation between SAP and antibiotics for treatment of actual infection; and - Details regarding antibiotic management in the hospital discharge summary for GPs and plans for re-referral. • Modify the ‘time-out’ process to include discussion of post-operative SAP. • Develop tailored clinical decision support systems and prompts for SAP. • Engage with surgeons to identify relevant quality indicators. • Support ongoing SAP prescribing audits. • Increase capacity for auditing of outcomes in relation to quality of SAP prescribing.
Automatic Motivation	Fears and perceptions of risk hinder appropriate SAP prescribing.	Fear of infections Varied risk perceptions across specialties Fear of litigation Risking career progression and job security	• Collect local outcome data that supports evidence-based SAP, rather than prolonging SAP out of fear of infections. • Highlight the potential harms to the patient from inappropriate antibiotic use to promote AMS initiatives. • Tailor AMS interventions that are reflective of the surgical specialties’ niche risk perceptions, e.g., recommend alternative non-antibiotic creams and ointments post-plastic surgical procedures. • Gather support from hospitals at an executive/policy level to enable surgeons to prescribe evidence-based SAP. • Undertake further research into the impacts and influence of private health insurers on antimicrobial prescribing. • Increase awareness of current fears and issues facing junior surgeons. • Collaborate with existing programs such as the RACS action plan to build a ‘culture of respect’.
Reflective Motivation –	Lack of clarity regarding the roles and accountability	The buck stops with the surgeon, ownership required Passive prescribing hinders accountability and SAP cessation Capacity for role expansion of pharmacists and nurses.	• Promote collaboration between surgeons and anaesthetists for the development of a SAP pathway or workflow that defines both professionals’ roles pre-, intra- and post-operatively to increase role clarity and accountability for SAP. • Promote electronic prescribing and AMS workflow to support greater prescriber accountability. • Development and training for emerging roles of nurse and pharmacist prescribers. • Development of Enhanced Recovery After Surgery (ERAS) pathways that include both pre and post-procedural SAP and AMS principles across the operative setting. • Partnered/collaborative SAP prescribing models

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The uptake of electronic medical records (EMR) and prescribing has the potential to support prescriber accountability as the prescriber's name is more visible as opposed to an uninterpretable signature on the current paper medical charts and documentation. The Rawson *et al* [36] systematic review suggests adoption of clinical decision support systems (CDSS) may improve evidence-based antimicrobial use. We advocate for the development of CDSS and prompts that are tailored to SAP management for the optimisation of SAP prescribing (Table 9). The increasing uptake of EMR also facilitates the standardisation of documentation for SAP, in particular defining duration, thus potentially minimising inappropriate passive prescribing practices. The role of EMR was not a focus of our study as none of the hospitals included had adopted EMR and computerised physician order entry (CPOE) at the time of the focus groups.

Clinical pathways such as enhanced recovery after surgery (ERAS) protocols are well-established multi-disciplinary approaches that have been successfully implemented across hospital services worldwide [37, 38]. SAP administration is a common component of ERAS Society recommendations for peri-operative care [37, 39, 40]. However, clarification of post-operative antibiotic management is omitted. Expansion of existing pathways to include this would facilitate further standardisation of post-operative antibiotics, which as per recommendations [29] would be infrequent and for a defined set of surgical procedures (e.g. laryngectomy, total knee arthroplasty and orthognathic surgery). A review of ERAS in relation to antibiotic use by Mofat-Bruce *et al* [38] proposed that the application of surgical guidelines within ERAS protocols and its expansion into the EMR environment would improve clinical workflow and reduce errors. Specific examples include: the development of order sets and dynamic orders for specific antimicrobial courses with procedure specific durations and stop times to be entered prior to surgery.

Modifying the time-out process, which was unanimously regarded by prescribers as a successful intervention, to better incorporate discussion of and planning around SAP prescribing would further enhance prescribing practices by addressing and rectifying some of the communication and information gaps in current practice that were highlighted by participants. Facilitating inclusion of SAP discussion within the surgical workflow through a check list or other prompt within the time-out process, and improved documentation, supports prescriber accountability, and increases role clarification for the rest of the team regarding the initiation, continuation and cessation of SAP (Table 9). Greater prescriber accountability will also reduce passive prescribing and delegation of SAP management to junior staff, which was also noted by the Charani *et al* [27] ethnographic study of a surgical ward round in a 1300-bed multisite healthcare organisation in the UK.

Engaging with surgeons and the operative team to identify important quality indicators will facilitate data collection that supports meaningful feedback and action for change and quality improvement (Table 9).

The efficacy of clinical pathway structures and systematic approaches to managing SAP dosing and duration could be supported by new and emerging roles of nurse and pharmacist practitioners. Evidence demonstrates that non-medical prescribing by nurses and pharmacists in the UK is as safe and effective as doctor prescribing [41]. A recent systematic review of fifteen studies demonstrated low to moderate evidence that pharmacists can prescribe to the same standards as doctors [42]. In Australia, non-medical prescribing has been adopted with various prescribing models across multiple specialties: dentists, nurse practitioners, midwives, podiatrists and optometrists [43].

Nurse practitioners are an established profession in Australia, with approximately 1,800 registered in 2019 [44]. Nurse practitioners are legally qualified to prescribe antimicrobials, which account for approximately one-third of their prescriptions [45]. Nurse practitioners are

more experienced in advanced practice frameworks, demonstrate leadership skills[46], and are familiar with antimicrobial stewardship and the operative environment[47–49], thus we would consider them to have a positive impact in the development and implementation of an SAP optimisation intervention. Barriers that prevent the success of such initiatives exist and largely reflect the identified issues regarding hierarchical influences of SAP prescribing. Engagement and collaboration with surgical specialties is essential for the development and implementation of such initiatives.

Pharmacists currently do not have prescribing privileges in Australia. There is currently no research in Australia comparing the role of peri-operative pharmacists or nurses charting SAP in comparison to their surgical and anaesthetic colleagues. However, there are many examples in the current literature where clinical pharmacists have been involved in the charting of medications in Australian hospital settings[50–54]. One Australian hospital adopted a partnered-pharmacist charting model in their general medical and emergency chart stay units as an alternative to medical prescribing. The study identified that partnered charting between medical staff and pharmacists significantly reduced inpatient medication errors (standard medical charting: 78.7% vs partnered pharmacist charting: 3.7%, $p < 0.001$)[50].

Another Australian hospital demonstrated a statistically significant reduction in medication errors when they compared their intervention of introducing a 'Pre-Operative and Prescribing' (PREP) pharmacist to join an elective surgery multidisciplinary team to improve accuracy of medication history, inpatient prescribing and discharge prescriptions[54]. The small study ($n = 104$) demonstrated significant benefits in medication history (9% [$n = 53$] vs. 96% [$n = 51$]; $P < .001$) and inpatient prescribing in the intervention arm, with fewer errors than the control group (0.64 vs. 1.31 errors per patient; $P = 0.047$)[54].

Many barriers to pharmacist prescribing exist. A scoping review of these barriers by Zhou *et al* [55] revealed three key themes that should be factored in to the current debate: (1) the socio-political context; (2) resourcing issues; and (3) prescriber competence. We advocate for the ongoing exploration of the expansion of the peri-operative pharmacists and nurses' role in prescribing and collaborative partnered charting models. An intervention of this nature would require extensive research into capacity for training and development of such roles and addressing the barriers Zhou *et al* [55] described; in particular implementation issues such as policy development, engagement with stakeholders, especially surgeons and anaesthetists.

Fear of consequences to patient

The fear of causing direct harm to the patient by not preventing infections was a driving factor for the prolongation of SAP. Similar to our study, a US qualitative study of thirty inpatient physicians[32] highlighted that the potential adverse effects of antimicrobial use and concerns about AMR were not prominent considerations in SAP decision-making. Prevention of SSIs was considered a more important and tangible outcome.

Perceptions regarding risk notably varied between the health professions and at the surgical craft group level. Comparisons have been reported between medical and surgical antibiotic decision-making[56], but not across the surgical craft groups. Further analysis of our qualitative data is warranted and may reveal specialised targets for AMS initiatives that specifically respond to niche surgical craft groups concerns.

The perceived influence of private health insurers on a surgeon's autonomy was considered a barrier to optimal SAP prescribing and promoted prolonged SAP as a measure to prevent infection and avert blame for causing infection. Medical overtreatment such as prolonged antibiotic use is considered common practice, and fear of being reported for malpractice was identified as the most common reason for this (84.7%) in a US survey of 2,106 physicians[57].

Further research into the impact of health insurance companies and their influence on SAP decision-making will be beneficial for informing AMS interventions at a national health policy level.

Of noted concern, many participating surgeons felt that they could not speak up against their colleagues or seniors regarding antibiotic management due to fear of a negative impact on their career progression. In 2015, the Royal Australasian College of Surgeons (RACS) published an Action Plan[58], as an initiative to build a 'culture of respect' in order to improve patient safety; however, some participants questioned the success of such initiatives. Collaboration with stakeholders across RACS, other surgical craft group specialties, junior surgical fellows and trainees with AMS and ID specialties is required for the development of effective AMS initiatives that will address ongoing issues of hierarchy and fear of career regression, thus supporting prescriber accountability for SAP decision-making.

Strengths

The use of qualitative methodologies to develop a greater understanding of complex prescribing behaviours is well established in the current infectious diseases and AMS literature [26, 27, 32, 34, 56, 59, 60]. Over time, health care services have shifted to a multi-disciplinary collaborative model. Therefore, we included surgeons, anaesthetists, theatre nurses and pharmacists across the public and private hospital sectors to better understand the broader context of SAP decision-making. Our study is the first to explore observations and perceptions regarding SAP decision-making across a range of health professionals and surgical specialties. Previously, a qualitative study focusing on antibiotic decision-making in surgery was undertaken in the UK [27]. Following on from this, Australian qualitative research including twenty in-depth semi-structured interviews with surgeons and anaesthetists has been published[26, 59].

Our findings have been developed through the application of theoretical frameworks. The adoption of theoretical frameworks provides structure to the design and analysis of qualitative research and is well-described in the current literature [61–64]. McIsaac *et al* (37) proposed that the combination of the TDF and BCW delivered a stronger theoretical approach to implementation research. However, the literature suggests there are limited published interventions targeting antimicrobial use that use behavioural theory[65, 66]. Michie *et al*[67] suggested the consideration of human behaviour theories may improve an intervention's efficacy.

The application of social and behavioural sciences assists in improving understanding of current behaviours and problems relating to AMS[68] and supports the adoption of a theory-driven approach to AMS intervention design. We propose our findings provide direction for theory-informed AMS interventions that account for the complexities of the surgical setting. Table 9 provides a summary of our recommendations to improve practice in relation to the barriers and enablers identified in our analysis. Further exploration of the current qualitative dataset using the BCW will support greater translation of findings on barriers and enablers of SAP decision-making in the form of targeted interventions and policy initiatives [17].

Proposed triangulation with existing quantitative data, such as the Australian Surgical NAPS[4], will validate our findings and further illuminate the current state of SAP prescribing in Australia. Such methodologies could be adapted by others to support their research on SAP prescribing.

Limitations

Our study was conducted across only three hospitals within the Australian state of Victoria, and, therefore, the opinions represented may not be truly representative of all surgeons, anaesthetists, pharmacists and theatre nurses in Australia. The recruitment of surgeons for focus groups was time consuming. Focus groups with a minimum of four participants were

organised and, in few cases, when a participant could no longer attend at the last minute, we proceeded with those present. Whilst we have been able to include numerous surgical specialties, not all have been represented in this research. Engagement with surgeons in AMS research has been identified as suboptimal. We found that engaging with surgical consultants in the private hospital setting to be challenging. The reasons for non-participation were not collected and deemed beyond the scope of this study. We believe these findings were not unique to our study, as other Australian[59] and UK[27] qualitative studies have also demonstrated poor engagement of surgeons in SAP prescribing, guideline compliance and AMS research.

A limitation of utilising focus group methodology is the inability to guarantee equal representation of all participants within the group. We acknowledge that some participants are more vociferous than others and therefore their own personal views may project across the focus group. In an attempt to minimise this, the sampling and recruitment of the focus groups was designed to ensure that participants felt comfortable to voice their opinions. If junior staff did not voice their thoughts in the focus group, follow up interviews were planned to be conducted if necessary. An additional focus group solely for surgical registrars and residents was also included to promote participant comfortability.

Conclusions

Our study identified six key themes that complement and build upon the existing literature and can be applied to enhance understanding of the enablers and address barriers of SAP optimisation, and support development of theory-informed AMS interventions. Many challenges remain for the optimisation of SAP across multiple surgical settings. We advocate for the development of initiatives that aim to enhance the prioritisation of and accountability for SAP, via the standardisation of workflow, roles and documentation across the peri-, intra- and post-operative settings. Interventions should address the underlying social issues that influence SAP decision-making, such as professional hierarchy, varied risk perceptions and fears about patient harm, litigation and career regression. Increased engagement of surgeons and the operative team in the development of data collection practices, local policies and guidelines will likely enhance the uptake of quality improvement actions and minimise the gap between evidence-based and current practices. Future research across different national and international hospital settings and additional surgical specialties will further build upon this exploration of SAP decision-making and strengthen the need for theory-driven AMS interventions.

Supporting information

S1 Appendix. Focus group question and discussion guides. - Tables A and B.
(PDF)

S2 Appendix. Themes and subthemes mapped to the COM-B Model and Theoretical Domains Framework. - Table C.
(PDF)

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Chapter 12: Discussions and conclusions: A framework for surgical antimicrobial stewardship

12.1 Introduction

Chapter 12 forms the discussion of this thesis and triangulates the key quantitative and qualitative findings of this doctoral research program. Recommendations for a framework for surgical Antimicrobial Stewardship (SAMS) are proposed for future research to improve prescribing of antimicrobials in the surgical setting.

12.2 Importance of surgical antimicrobial stewardship

Administration of surgical antimicrobial prophylaxis is a key and effective measure for the prevention of surgical site infections (SSI) (56, 81, 82, 85, 118, 349). SSIs are the most commonly reported healthcare-associated infection (HAI) in the United States. In Australia, approximately 160,000 HAIs develop each year (350), with SSIs occurring in approximately 3% of surgical procedures (351, 352). A HAI point prevalence survey (n= 2,767 patients) conducted in 2018, the first Australian survey in 34 years, demonstrated SSIs were the most common type of HAI (prevalence 3.6%; 95%CI: 2.9–4.4) (353). Thus, rationalisation of SAP represents a critical target for hospital antimicrobial stewardship (AMS) and infection prevention services nationally.

AMS programs are embedded into Australian hospitals, largely due to the fact that they are now required for national hospital accreditation (11, 45). The Hospital NAPS (1-3, 5-7) and Surgical NAPS (4, 8) continue to demonstrate high rates of inappropriate use of SAP. In 2018, the requirement to specifically implement SAP auditing as a key outcome measure of AMS services was introduced (64). However, limited guidance and few resources have been developed to support this. Thus, a tailored AMS framework for SAP is required, to support the optimisation of antimicrobial prescribing in the surgical setting and assist hospitals to meet national accreditation standards.

As of September 2019, there were approximately 42 new antibiotics in clinical development (354). However, the rate of success for clinical drug development is low; approximately 1 in 5 infectious diseases products (e.g., antibiotics) that begin phase 1 clinical trials are approved for patients (355). Therefore, AMS remains a key strategy for the conservation of antimicrobials and minimisation of the burden of antimicrobial resistance on patients and the healthcare system at national and international levels.

12.3 Summary: Addressing research questions

This body of work has fulfilled the aims and objectives of this thesis as outlined in the introductory chapter 1. The aim of this PhD was explore challenges in SAP prescribing and strategies for the optimisation of SAP prescribing in Australia. To achieve this aim, the following objectives were addressed.

Objective1: Describe current SAP prescribing in Australian hospitals.

Quantitative analyses of the Surgical NAPS database led to multiple projects across **chapters 8, 9 and 10**. Project two of **chapter 8** explored the dataset broadly from its implementation in January 2016 up until June 2018. Novel application of logistic regression with estimated marginal means (EMM) analysis facilitated identification of key patient, hospital and surgical factors that influence appropriateness of SAP. SAP was prescribed poorly overall but differences in adjusted appropriateness across surgical procedure groups were noted. Thus, our findings demonstrate a need to target surgical AMS at each surgical specialty individually and engage with the surgical teams to highlight the issues and develop appropriate interventions collaboratively.

Project three of **chapter 9** illustrated the depth and quality of data the Surgical NAPS online auditing platform collects; the platform facilitated a deep-dive analysis of orthopaedic surgical procedures. Building upon the use of EMM analyses from **chapter 8**, this project demonstrated that the appropriateness of SAP varied by surgical procedure group, i.e., differences in appropriateness were observed at the specific orthopaedic procedure level. Therefore, surgical AMS interventions should be adaptable to support rational antimicrobial use at both broad and specific surgical procedure levels. This adaptability may also further facilitate engagement of surgeons, as surgeons would be able to examine national rates of SAP appropriateness for their own subspecialty (e.g., elbow arthroplasty) and thus note the implications for their practice. Specific target areas identified in our analysis include orthopaedic procedures where procedural SAP is prescribed when not

required (e.g., knee and shoulder arthroscopy, and clean hand surgeries); and procedures where SAP is continued beyond a single dose (e.g., all procedures except total knee arthroplasty).

Project four of **chapter 10** explores the variables that may influence procedural SAP choice. While cefazolin remains the most common choice, per national and international recommendations, we continue to observe administration of broad-spectrum antimicrobials for procedural SAP. Analysis of assessments of appropriateness of antimicrobial choice and spectrum within the Surgical NAPS facilitated identification of specific targets to address concerns regarding unnecessary broad-spectrum antimicrobial use. The analysis identified a number of surgical specialties as priority target areas. For example, abdominal and urological surgery for third- and fourth-generation cephalosporins; urological, breast and orthopaedic surgeries for aminoglycosides; and, orthopaedic and cardiac procedures for use of glycopeptides.

Objective 2: Describe current strategies for the optimisation of SAP prescribing in hospitals.

Chapter 4 reviews the current body of evidence in support of surgical AMS and highlights the efficacy of key successful components, including guideline implementation, audit and feedback, bundles of care and the adoption of behaviour change techniques. In summary, we identified that successful and sustainable surgical AMS requires a multi-faceted and multi-collaborative approach that is built upon an understanding of prescribing behaviour.

Objective 3: Identify and explore the underlying facilitators and barriers to appropriate SAP prescribing.

Chapter 2 contains an analysis of how the Australian healthcare system operates and highlights the current policy infrastructure to support surgical AMS in Australian hospitals, i.e., government mandating of SAP auditing and AMS programs in hospitals as part of hospital accreditation. However, a barrier to this is the lack of support and resources to facilitate the implementation of such services.

The evidence for SAP was critiqued in **chapter 3**, which highlighted the need for expert consensus-based guidelines to bridge the gap between ageing level-1 evidence, new lower-level evidence, and the Australian microbiological landscape (349). While high-quality evidence may not be found for each specific surgical procedure, surgical AMS programs can engage with surgical teams to address such concerns to advocate for appropriate SAP prescribing that minimises the risk of patient harm.

Expert consensus review of SAP evidence is presented in the nationally endorsed guidelines. However, **chapter 7** highlights that guideline implementability is as important as guideline quality and proposes potential solutions to address gaps in current guideline implementation (356).

Examination of the phenomenon of SAP prescribing and decision-making through a qualitative case study facilitated the identification of a range of barriers and facilitators of appropriate SAP prescribing. The adoption of theoretical frameworks in

chapter 11 facilitated the development of theoretically-informed recommendations to address barriers and support facilitators, providing direction for quality improvement in surgical settings (357).

Objective 4: Propose a theoretically-informed framework for solutions to support sustainable AMS for SAP.

As discussed in **chapter 6**, this doctoral study adopts a mixed-methods design, focusing on the triangulation of quantitative and qualitative research to gain a deeper understanding of SAP prescribing practices and culture, and the factors that influence prescribing behaviours. The integration of both quantitative and qualitative methods for an overarching analysis facilitated the achievement of objective 3. Triangulation of the vast range of data collected and analysed throughout this doctoral study facilitated the development of a theoretically-informed framework for surgical AMS. This forms the premise for this chapter and is discussed in greater detail below. Additionally, we recently published a manuscript in the *Infection, Disease and Health* journal discussing our integration of quantitative and qualitative research across this thesis to advocate for the development of a national surgical AMS framework (Appendix 7)(358).

12.4 Development of a framework for surgical antimicrobial stewardship

Analysis of the current literature and data collected across this doctoral study led to the identification of key issues that need to be addressed for optimisation of SAP prescribing. There is a need for:

- resources, infrastructure and a framework to establish surgical AMS programs and interventions;
- multidisciplinary collaboration, particularly with surgeons;
- meaningful data (such as data linking surgical outcomes to SAP quality) to promote action; and
- a multifaceted surgical AMS program that can be adapted and scaled to different surgical settings across Australia.

These key requirements have been addressed in the proposed theoretically-informed framework for surgical AMS (SAMS). The framework was developed through the triangulation of quantitative and qualitative data, and is underpinned by the Behaviour Change Wheel (BCW) (28, 29). The BCW facilitates behaviour change intervention mapping, and uses both the Theoretical Domains Framework (TDF) (27) (for the identification of barriers and enablers) and the Capabilities, Opportunities and Motivators of Behaviour (COM-B) model (28, 29). The framework is structured around three key themes: ***the need for multidisciplinary collaboration and engagement, meaningful data for action, and a multi-faceted, quality improvement intervention program*** that includes a suite of theoretically-informed and evidence-based interventions.

Table 1 illustrates how the themes generated through the qualitative analysis conducted in **chapter 11** were then mapped to the BCW's 'intervention' and 'policy' domains (28, 29). The interventions proposed in project five, **chapter 11** (357), were then mapped to the relevant themes of the proposed SAMS framework.

Table 1: Summary of themes developed from project 5, mapped to Behaviour Change Wheel interventions and policies, and the proposed surgical AMS (SAMS) framework.

Themes from Project 5 (COM-B) (357)	BCW Interventions (28, 29)	BCW Policies (28, 29)		Proposed interventions based on theoretical frameworks and models from Project 5 (357)	Themes of SAMS Framework
Low priority for SAP prescribing skills (Physical capability)	Enablement Training	Guidelines	Regulation	- Develop and implement targeted education and training on principles for SAP and AMS as part of hospital orientation training. - Support surgeon engagement in SAP decision-making/ prescribing and interventions.	Collaboration/ engagement
		Fiscal measures	Legislation		Multi-faceted quality improvement program
		Environmental/ Social planning	Service provision		
Prescriber autonomy overrules guideline compliance (Psychological capability)	Enablement Education Training	Guidelines	Regulation	- Continue to increase accessibility of guidelines in the operative setting. - Increase engagement of surgeons and anaesthetists in guideline development and site implementation. - Regulate documentation for rationale of guideline deviation.	Collaboration/ engagement
		Fiscal measures	Legislation		Multi-faceted quality improvement program
		Environmental/ Social planning	Service provision		
		Communication/ Marketing			
Social codes of prescribing reinforce	Enablement	Guidelines	Regulation	- Target AMS interventions at senior surgical consultants. - Engage with senior surgical consultants for	Collaboration/ engagement
	Restriction Environmental	Fiscal measures	Legislation		Multi-faceted quality

established practices (Social opportunity)	restructuring	Environmental/ Social planning	Service provision	the development and implementation of quality improvement initiatives such as AMS. - Engage with hospital executives and surgical colleges to commit to SAP stewardship	improvement program
Need for improved communication, documentation and data for action (Physical opportunity)	Enablement	Guidelines	Regulation	- Promote standardisation of SAP workflow and documentation, specifically; indication, duration, discharge management plans. - Modification of existing successful interventions to address SAP; ‘time-out’ and Enhanced recovery After Surgery (ERAS) protocols. - Develop tailored clinical decision support systems and prompts for SAP. - Engage with surgeons and other stakeholders to identify relevant quality indicators. - Support/conduct ongoing SAP prescribing audits. Feedback audit data to facilitate benchmarking at multiple levels; national, state, hospital, surgical unit and consultant. - Increase capacity for auditing of outcomes in relation to quality of SAP prescribing.	Data for action
	Restriction	Fiscal measures	Legislation		Multi-faceted quality improvement program
	Environmental restructuring	Environmental/ Social planning	Service provision		

Fears and perceptions of risk hinder appropriate SAP prescribing (Automatic motivation)	Enablement	Guidelines	Regulation	- Collect data on surgical outcomes in relation to SAP appropriateness to highlight benefits of appropriate and harms of inappropriate SAP prescribing - Develop tailored AMS interventions that are reflective of the surgical specialties’ niche risk perceptions, e.g., recommend alternative non-antibiotic creams and ointments post-procedures. - Collaborate and facilitate support from hospitals at an executive/policy level to advocate for evidence-based SAP. - Promote awareness of current fears and issues facing junior surgeons - Collaborate RACS and their existing action plan to build a ‘culture of respect’.	Collaboration/ engagement
	Persuasion	Fiscal measures	Legislation		Multi-faceted quality improvement program
	Incentivisation	Environmental/ Social planning	Service provision		
	Coercion	Communication/ Marketing			
	Environmental restructuring				
Modelling					
Unclear roles, responsibilities and accountability (Reflective motivation)	Education	Guidelines	Regulation	- Develop a SAP pathway or workflow that defines both professionals’ roles pre-, intra- and post-operatively to increase role clarity and accountability for SAP. - Develop a pathway to include electronic prescribing and AMS workflow to support	Data for action
	Persuasion	Fiscal measures	Legislation		Multi-faceted quality improvement program
	Incentivisation	Environmental/ Social planning	Service provision		
	Coercion	Communication/ Marketing			

			greater prescriber accountability; training for emerging roles of nurse and pharmacist prescribers; and modified 'time-out' and ERAS protocols to adopt SAP stewardship across the operative setting.	
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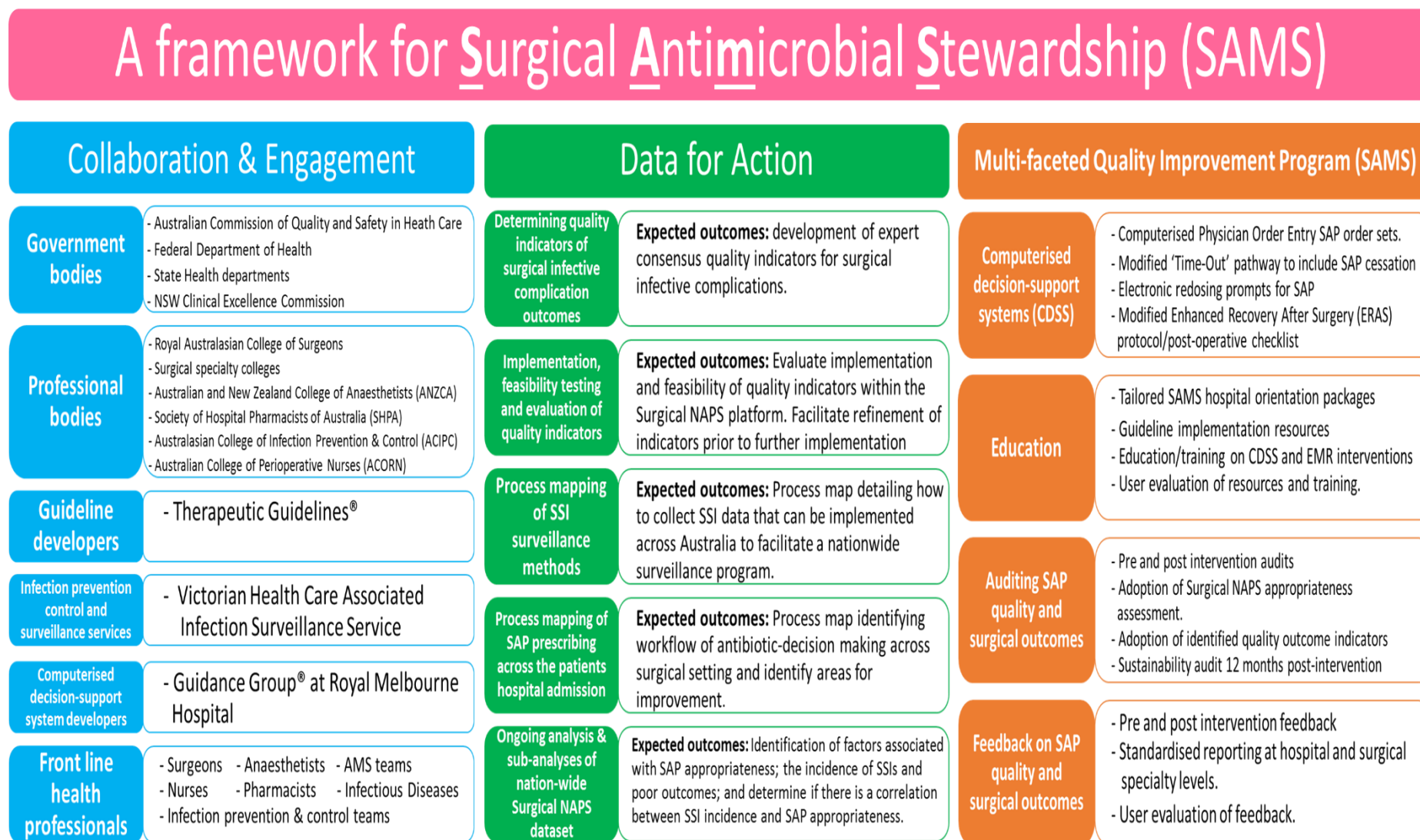
Figure 1 provides an overview of the SAMS framework and its three key themes, with examples of important collaborations required, data needed for action and proposed interventions that have demonstrated success in optimisation of SAP across the surgical setting.

Theme 1: Multidisciplinary collaboration and engagement

Effective AMS requires a multidisciplinary approach (11, 160, 359, 360), this is also applicable to SAMS. However, it has been identified that surgeons are less engaged in AMS activities (21, 23-25, 357, 361). The need for multi-disciplinary engagement and collaboration is a critical theme that has emerged across all projects in this doctoral study; therefore, it forms a core part of the SAMS framework. Figure 1 highlights the key collaborators who are required to support the development, refinement and implementation of a SAMS framework at a local hospital level and ensure the national scalability of this framework.

The need for surgical AMS support from government bodies was highlighted in **chapter 2**. Findings in **chapter 11** suggest this ideally would be supplemented by advocacy from professional bodies such as the Royal Australasian College of Surgeons. Development of guidelines and implementation resources was proposed in **chapters 3 and 7** (project 1). There is a need for active engagement and collaboration between guideline developers, AMS experts and, most importantly, prescribers (surgeons and anaesthetists). **Chapter 4** includes discussion of a range of interventions that have been shown to improve SAP prescribing, many involving the use of electronic medical records and

Figure 1 Framework for Surgical Antimicrobial Stewardship (SAMS)



computerised decision-support (156, 195-199). Engaging with key information technology stakeholders is essential to ensuring the sustainability and adaptability of surgical AMS interventions.

Project 5 in **chapter 11** highlighted various levels of engagement in SAP decision-making across multiple health-professionals, with many gaps in communication between them. Standardising workflow and communication across the surgical setting may support clarification of professional roles and SAP decision-making (357).

Professional hierarchy in the surgical setting was identified as a significant barrier to SAP prescribing behaviour change in **chapter 11**. Engagement at all levels of the hierarchy across these health disciplines is critical to supporting behaviour change in antimicrobial prescribing across the surgical setting (357). However, we note that senior consultants should be considered the primary target given their strong influence on their junior staff. Surgical AMS requires champions and leaders; surgeons should and should want to be involved in such programs. Current AMS programs need to focus on extending their networks to support surgeon collaboration, while also gaining support from various levels, i.e., departmental, hospital and national.

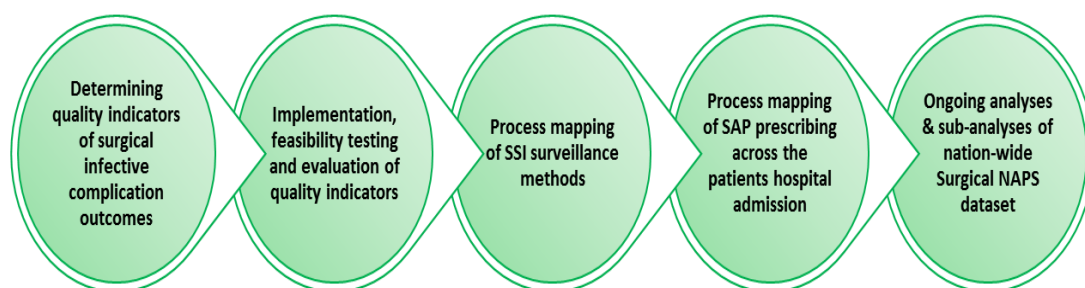
Theme 2: Meaningful data for action

Our qualitative research in **chapter 11** highlighted many barriers to appropriate SAP prescribing but also some enablers. The key enabler identified in the analysis was that there is a need to collect and disseminate meaningful local data to generate

prescribing behaviour change. Surgeons were interested in gaining a better understanding of how their prescribing impacted on their patients. Another enabler was competitiveness among surgeons and surgical settings. Capitalising on this trait may support behaviour change; the use of performance metrics to induce competition among surgeons may prompt improvements in prescribing behaviour.

This theme within the SAMS framework addresses issues and opportunities with current data, and the need to support the development and collection of surgical outcome data (Figure 2). A gap in Australian data noted across **chapters 8, 9 and 10** is the lack of information about surgical outcomes. This component of the Surgical NAPS is not mandatory due to the additional resources and time required to accurately collect the data.

Figure 3 Theme 2: Developing and collecting meaningful data for action



In addition to this, there is no national platform for surveillance of surgical complications such as surgical site infections in Australia. Many other countries, including the US (362), UK (363) and New Zealand (208), have adopted national surveillance programs for a broad range of surgical procedures. In Australia, various state-based services do exist, such as the Victorian Health Care-Associated Infection Surveillance Service (VICNISS), which have adopted the US National Surgical Infection

Prevention Project guidelines (364, 365). Engaging and collaborating with these stakeholders is critical for the development of a national surveillance service.

To facilitate the development of such a service, the required quality indicators for surgical infective complication outcomes should be identified through consensus among stakeholders nationally. These quality indicators should then undergo implementability and feasibility evaluations to promote effective implementation of surveillance, as discussed in **chapter 5**.

Our qualitative research, in **chapter 11**, has generated a deeper understanding of SAP prescribing and behaviour. Additional qualitative research such as ongoing case studies and ethnographic observational studies may provide further insight into antimicrobial decision-making and prescribing workflow across surgical settings and further facilitate the identification of target areas for improvement. This proposed framework also suggests that similar research on surgical outcome data collection processes is conducted to provide a greater understanding of the feasibility and implementability of surveillance activities. This future research has the potential to identify opportunities for improvement of surgical outcome data collection and facilitate the standardisation of surveillance workflow to be adopted and implemented as part of a national surveillance program.

Developing a national surgical outcome surveillance program would complement the existing Surgical NAPS platform and facilitate the linking of surgical outcome data to SAP prescribing quality. Our qualitative research in **chapter 11** highlighted that

health professionals want data that either validates or provides support for discontinuation of current prescribing behaviours and practices.

Additionally, **chapter 11** highlights the fear of missing the treatment of infections as a significant driver for antimicrobial overuse in the surgical setting. We identified that clinicians require meaningful data as described above to reassure them that their patients will not be adversely impacted if they changed their prescribing practice to single-dose SAP.

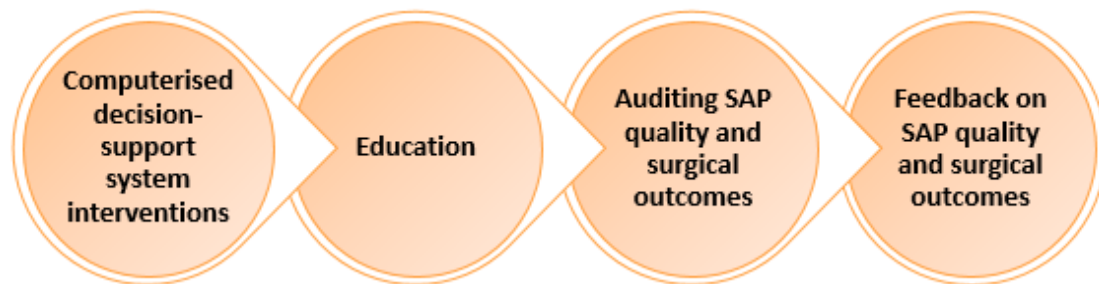
Data collection and analysis that has the potential to determine association between appropriateness of prescribing and patient harm is of great interest to surgeons and anaesthetists and has been identified in our research as a strong influence on fear and risk mitigation, prescribing behaviour, and, therefore, behaviour change.

Theme 3: Multi-faceted quality improvement program (SAMS)

Various AMS interventions have been adopted in hospitals and in surgical settings specifically, as identified in **chapter 4**. No intervention type has been demonstrated to be superior due to the heterogeneity of AMS research. Additionally, in some cases, many interventions have been combined into one research project, and, therefore, the individual effects cannot be determined. This thesis has highlighted that both hospital AMS and surgical AMS programs require multi-disciplinary teams (theme 1), and meaningful data and quality indicators (theme 2). Building upon these themes and the literature supporting bundled interventions, theme 3 proposes

a range of surgical AMS interventions as part of a multi-disciplinary and multi-faceted approach to improving antimicrobial prescribing across the surgical setting.

Figure 3 Theme 3: A multi-faceted quality improvement program - surgical AMS (SAMS)



Computerised decision-support systems (CDSS) can be adopted across the pre- (156, 192, 196, 197, 199), intra- (197, 198) and post-operative (192-194, 196, 199) settings to support surgical AMS programs. Electronic medical record implementation across Australian hospitals is increasing and represents a novel opportunity for the development and implementation of CDSS for surgical AMS. Education has been identified in the literature as a common surgical AMS intervention (149-155, 158, 159); however, this framework proposes that it should be implemented to complement other interventions such as use of CDSS, i.e., development of educational and training materials regarding CDSS and auditing interventions to support multidisciplinary participation.

The updated advisory in 2018 requiring SAP audits to be part of the national hospital accreditation standard for AMS (45, 64) has had a positive influence on the use of auditing as a common surgical AMS intervention in Australia. However, additional resources are required to support standardisation of data collection (such as through

use of the Surgical NAPS), and to support end users to collect data and close the loop of such an intervention by then providing timely feedback.

We identified a gap in the literature on AMS interventions that many intervention programs discuss the auditing process and results, but do not detail how this information was fed back and the impacts of the feedback provided on antimicrobial prescribing (174, 178, 186-188). Providing feedback is a method of engaging with all stakeholders, particularly prescribers such as surgeons, and is, therefore, a key intervention component of this proposed SAMS framework.

The Surgical NAPS online platform currently generates reports to assist end users in providing feedback and is currently undergoing an upgrade for 2020. We propose developers engage with end users for their feedback on current reporting processes to ensure that what is produced is relevant and meaningful for end uses, enabling them to succinctly provide feedback to their local prescribers and hospital executives.

12.5 Future directions and conclusions

With antimicrobial resistance increasing in prevalence globally, there is a sense of urgency about the need to rationalise the use of antimicrobials. Antimicrobial use in surgery has been identified as an area requiring critical action due to data highlighting high volume use and high rates of inappropriateness. Surgical AMS provides a theoretical and evidence-based approach to improving patient quality of care and outcomes at a local level while also addressing the pressing issue of AMR at a national and global level.

Key recommendations from this research program include;

- ongoing data collection of SAP prescribing and appropriateness with support from policy makers and healthcare organisations (for the collection of outcome data that can be mapped to SAP appropriateness);
- engagement and collaboration with key stakeholders (surgeons, anaesthetists, perioperative nurses, pharmacists, antimicrobial stewardship, infection prevention and infectious diseases, guideline developers, healthcare organisations and state and federal policy makers);
- further exploration of barriers and enablers of SAP prescribing behaviour across Australia; and
- policy makers to support the development and implementation of a scalable surgical AMS framework.

In summary, this research program has achieved the following meaningful contributions to the field of antimicrobial stewardship:

1. Identification of current SAP prescribing practices across Australian public and private hospitals, and, therefore, identification of areas of concern requiring targeted SAMS interventions:

- procedural dose timing;
- post-procedural prescription duration;
- broad-spectrum antibiotic usage across targeted surgical procedure groups, e.g., third- and fourth-generation cephalosporins in urological procedures;

- surgical procedure groups performed and audited in high volumes, e.g., orthopaedic procedures;
- surgical procedure groups with high rates of inappropriateness, e.g., plastic and reconstructive, breast, dentoalveolar and head and neck surgery; and
- surgical procedures where SAP is not indicated but still administered, e.g., arthroscopy and other clean procedures with no insertion or removal of prosthetic procedures.

2. Examination of current SAP guideline implementability and proposal of solutions such as implementation resource development, stakeholder engagement, integration with electronic medical record systems and ongoing evaluation of guideline implementability.

3. Novel exploration of underlying behavioural barriers and enablers of SAP prescribing and decision-making among Australian surgeons, anaesthetists, pharmacists and theatre nurses from both public and private hospitals. This research facilitated the development of key themes that were mapped to proposed interventions to support surgical AMS and optimise SAP use.

4. Proposal of a theoretically-informed framework for surgical AMS with solutions to address the barriers and enablers described throughout this thesis. The refinement, development, implementation and ongoing evaluation of this framework, in particular the multifaceted quality improvement SAMS program, could support a scalable national SAMS program.

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Appendices

1. Relevant appendices of the Surgical National Antimicrobial Prescribing Survey public report – 2017 and 2018.

Supplementary data includes the following:

- Appendix 1: Procedure groups
- Appendix 4: Surgical NAPS data collection form
- Appendix 5: Surgical NAPS appropriateness assessment guide



Appendix 1: Procedure groups

The procedures listed in the Surgical NAPS database are text-searchable for ease of navigation. These have been adopted from The Royal Australasian College of Surgeons Morbidity Audit and Logbook tools.¹⁵

The surgical procedure groups listed were:

- Abdominal surgery
 - anorectal
 - bariatric and other
 - biliary
 - colorectal
 - gastro-oesophageal
 - hepatic
 - pancreas and duodenum
- Breast surgery
- Cardiac surgery
- Dentoalveolar surgery
- Gastrointestinal endoscopic procedures
- Gynaecological surgery
- Head and neck surgery; including ear, nose and throat surgery
 - laryngology
 - otology
 - rhinology
- Neurosurgery
 - cerebrovascular
 - peripheral nerve
 - spinal
 - other
- Obstetrics
- Ophthalmology
- Orthopaedic surgery
- Plastic and reconstructive surgery
- Thoracic surgery
- Urological surgery
 - endoscopic procedures
 - laparoscopic procedures
 - open procedures
 - other
- Vascular surgery
 - dialysis access

Appendix 4: Surgical NAPS data collection form

Patient identification Number	Date of birth / age	Gender	Date of admission	Date of discharge	Specialty	Height cm	Weight kg	eGFR / CrCl ml/min																				
	/ /	M / F / O	/ /	/ /																								
Surgical details Surgery date / / Surgery this admission ☐ Initial ☐ subsequent Procedures ☐ emergency ☐ elective ☐ not assessable ☐ trauma ☐ removal/insertion of prosthetic material ☐ excessive blood loss Surgeon code Anaesthetist code Time of first incision : ☐ not documented ☐ not applicable If not documented or not applicable; surgery start time (or estimated) : End time (or estimated) : Wound classification ☐ clean ☐ clean-contaminated ☐ contaminated ☐ dirty ☐ unknown ☐ not applicable ASA score ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ unknown																												
Risk factors ☐ none identified All procedures ☐ current smoker ☐ diabetes ☐ peritoneal or haemodialysis ☐ obesity (BMI>30) ☐ pregnancy ☐ rheumatoid arthritis ☐ current malignancy ☐ previous radiation therapy ☐ immunocompromised ☐ systemic corticosteroids ☐ other immunosuppressive treatments ☐ presence of prostheses ☐ MRSA colonisation ☐ MDR Gram negative colonisation ☐ one or more of: • prosthetic cardiac valve • previous infective endocarditis • congenital heart disease with defects • rheumatic heart disease in Aboriginal/Torres Strait Islanders Transrectal prostatic biopsy ☐ quinolone therapy in preceding 3 months ☐ recent travel to Asia or Southern Europe in preceding 6 months Gastroduodenal or oesophageal procedures ☐ reduced gastric acidity or motility ☐ gastrointestinal bleeding ☐ gastric outlet obstruction ☐ perforation Biliary surgery ☐ acute cholecystitis ☐ obstructive jaundice ☐ common bile duct stones ☐ non-functioning gallbladder																												
Allergies and adverse drug reactions to antimicrobials ☐ nil known ☐ not documented ☐ present; specify drug and nature																												
Surgical or clinical notes, microbiology, radiology 																												
Existing antimicrobial therapy Any antimicrobial for treatment or medical prophylaxis or another condition. Prescribed in the 24 hours prior (72 hours if on dialysis) to the procedure ☐ none prescribed ☐ not assessable <table border="1"> <thead> <tr> <th>Antimicrobial</th> <th>Route</th> <th>Dose</th> <th>Date and time of last dose</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td>/ / : :</td> </tr> <tr> <td></td> <td></td> <td></td> <td>/ / : :</td> </tr> <tr> <td></td> <td></td> <td></td> <td>/ / : :</td> </tr> <tr> <td></td> <td></td> <td></td> <td>/ / : :</td> </tr> </tbody> </table>									Antimicrobial	Route	Dose	Date and time of last dose				/ / : :				/ / : :				/ / : :				/ / : :
Antimicrobial	Route	Dose	Date and time of last dose																									
			/ / : :																									
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Doc: SurgicalNAPS-DGFv7, 20160413

Peri-operative doses			Documented administration time					Was this a repeat dose?	Guideline compliance (1-6)	Appropriateness (1-5)								
Antimicrobial	Route	Dose	Not assessable	Nearest 15 minutes	Exact time	Start time	End time			Allergy mismatch	Microbiology mismatch	Incorrect dose	Incorrect route	Incorrect timing	Spectrum too broad	Spectrum too narrow	Peri-operative antimicrobials not required	Procedure requires antimicrobials
						:	:											
						:	:											
						:	:											
☐ Repeat dose required, but not given									4									4
☐ No antimicrobial prescribed																		

Post-operative antimicrobials							Indication			Guideline compliance (1-6)	Appropriateness (1-5)							
Start date and time*	End date and time*	Antimicrobial	Route	Dose	Freq		For prophylaxis only	For treatment of infection related to the procedure	Not assessable		Allergy mismatch	Microbiology mismatch	Incorrect dose / frequency	Incorrect route	Incorrect duration	Spectrum too broad	Spectrum too narrow	Post-operative antimicrobials not required
/ / :	/ / :																	
/ / :	/ / :																	
/ / :	/ / :																	
/ / :	/ / :																	
*If time unknown, write unknown		☐ None prescribed																

30 Day follow up		Guideline compliance			Appropriateness	
Surgical site infection ☐ none identified ☐ not assessable ☐ identified; select one type and list any relevant microbiology ☐ superficial ☐ Microbiology ☐ deep incisional ☐ organ space ☐ prosthesis		Clostridium difficile infection MDR organism Unplanned ICU admission Unplanned hospital readmission Death Other morbidity (if yes, specify)	☐ yes ☐ no ☐ unknown ☐ yes ☐ no ☐ unknown ☐ yes ☐ no ☐ unknown ☐ yes ☐ no ☐ unknown ☐ yes ☐ no ☐ unknown ☐ yes ☐ no ☐ unknown	1. Compliant with Therapeutic Guidelines 2. Compliant with locally endorsed guidelines 3. Directed therapy 4. Non-compliant with guidelines 5. No guidelines available 6. Not assessable	1. Optimal 2. Adequate 3. Sub-optimal 4. Inadequate 5. Not assessable	

Doc:SurgicalNAPS-DCFv7;20160413

Appendix 5: Surgical NAPS appropriateness assessment guide

	Appropriate		Inappropriate		5 - Not assessable
	1 - Optimal	2 - Adequate	3 - Suboptimal	4 - Inadequate	
Allergy mismatch	Where antimicrobials are prescribed exactly according to Therapeutic Guidelines or local guidelines – antimicrobial choice, dose, route, timing and duration; or where there is an appropriate reason for deviation from guidelines		Mild or non-life threatening allergy mismatch	Life threatening allergy mismatch	Where there is insufficient information available or the case is too complex for assessment.
Microbiology mismatch				Antimicrobial used is too narrow (where sensitivity results available)	
Incorrect dose or frequency			Dose or frequency too high (with exception of gentamicin)	Dose or frequency too low Gentamicin dose too high or too frequent	
Incorrect route			An intravenous antimicrobial has been prescribed when the patient is able to safely take it orally	The prescribed route does not reach the site of infection or surgery	
Incorrect timing	If any reason is selected for incorrect prescribing, the prescription will no longer be optimal.	Repeat dose given too soon (including patients who were already on existing antimicrobial therapy) <i>taking into consideration patients with renal impairment</i>	Antimicrobial prophylaxis given less than 15 minutes before surgical incision (with exception of vancomycin) Vancomycin started less than 30 minutes before surgical incision	Antimicrobial prophylaxis given greater than 60 minutes before surgical incision (with exception of vancomycin) Vancomycin started greater than 120 minutes before surgical incision Repeat dose given too late (including patients already on existing antimicrobial therapy) <i>taking into account renal impairment</i>	
Incorrect duration				Surgical prophylaxis greater than 24 hours (except where guidelines endorse this)	
Spectrum too broad		Choice of antimicrobial is too broad Additional antimicrobial added unnecessarily			
Spectrum too narrow			Choice of antimicrobial does not cover likely organisms		
Procedure does not require any antimicrobials	Procedure does not require any antimicrobials, but antimicrobials were still prescribed				
Procedure requires antimicrobials	Procedure requires antimicrobials but no antimicrobials were prescribed AND there were no existing antimicrobials				
Repeat dose required, but not given	This will automatically be selected for auditors				
No antimicrobial prescribed	No antimicrobial required		Procedure requires antimicrobials but no antimicrobials were prescribed and there were no pre-existing antimicrobials		

2. Supplementary data for published manuscript “Surgical antibiotic prophylaxis – The evidence and understanding its impact on consensus guidelines”.

Supplementary data includes the following:

- Appendix 1: Characteristics of systematic reviews and meta-analyses included in review

1 Surgical antibiotic prophylaxis – the evidence and 2 understanding its impact on consensus guidelines

3 Appendix 1

4 *Appendix 1 Characteristics of systematic reviews and meta-analyses included in review.*

Surgical Procedure Class	Frequency of SR/MA (n)	Author	Year	Number of studies included	Date range of included studies	Number of participants
Cataract	3	Kessel et al (9)	2015	1 RCT and 17 Non-RCTs	2005-2014	>2.3million procedures**
		Huang et al (10)	2016	24 studies (RCTs and Non-RCTs)	2002-2016	1,264,797 eyes***
		Gower et al (11)	2017	5 RCTs	1979-2013	101,005
Orthopaedic	7	Voigt et al(12)	2015	30 RCTs	1973-2014	17738
		Morrison (13)	2012	4 RCTs	1987-2006	921
		Gillespie et al(14)	2010	23 RCTs	1973-2000	8447
		Al Buhairan et al(15)	2008	26 RCTs	1979-2002	11 343
		Slobogean et al (16)	2008	7 RCTs	1987-2006	3808
		Southwell-Keely et al (17)	2004	15 RCTs	1973-2000	5193
		Barker et al (18)	2002	6 RCTs	1974-1994	843
Cardiac	5	Salch et al(19)	2015	14 RCTs	1991-2010	8952
		Lador et al (20)	2012	59 RCTs	1968-2010	N/A
		Mertz et al (21)	2011	12 RCTs	1972-2008	7893
		Kreter et al (22)	1992	28 RCTs	1972-1988	6759
		Darouiche et al (23)	2012	15 RCTs	1978-2009	3970
Abdominal	20	Daskalakis et al (24)	2014	12 RCTs plus Cochrane SR(25)	1994-2011	N/A
		Andersen et al (25)	2005	45 RCTs	1965-1995	9576
		Nelson et al (26)	2014	260 RCTs	1967-2011	43,451
		Liang et al (27)	2016	21 RCTs	1997-2014	5207
		Pasquali et al (60)	2016	19 RCTs	1997-2015	5259
		Yan et al (61)	2011	12 RCTs	1999-2009	N/A
		Sanabria et al (62)	2010	11 RCTs	1995-2010	1664
		Zhou et al (63)	2009	15 RCTs	1997-2007	2961
		Choudhary et al (64)	2008	9 RCTs	1997-2007	1437
		Catarci et al (65)	2004	6 RCTs	1997-2001	974
		Al-Ghnaniem et al(66)	2003	5 RCTs	1997-2001	899
		Meijer et al (28)	1990	42 RCTs	1965-1988	4129
		Boonchan et al (29)	2017	15 RCTs	2001-2014	5159
		Eradas et al (67)	2016	16 RCTs	2000-2014	5519
		Miserez et al (68)	2014	12 RCTs	2000-2011	N/A
		Mazaki et al (30)	2013	12 RCTs	2000-2013	1902
		Sanchez-Manuel et al(69)	2012	17 RCTs	1973-2011	7843
		Yin et al (31)	2012	9 RCTs	2000-2011	3317
		Sanabria et al (32)	2007	6 RCTs	2000-2005	2507
		Aufenacker et al (70)	2006	6 RCTs	2000-2005	2499
Obstetric and gynaecological	13	Low et al(33)	2012	19 RCTs	1981-2008	9715
		Achilles et al(34)	2011	13 RCTs	1980-1994	8687
		Sawaya et al (35)	1996	12 RCTs	1981-1993	5188
		Smaill et al (36)	2014	95 RCTs	1971-2005	>15000
		Gyte et al (37)	2014	35 RCTs	1980-2014	7697

		Mackeen et al (38)	2014	10 RCTs	1990-2013	5041
		Baaqeel et al (39)	2013	6 RCTs	1997-2011	2313
		Tita et al (40)	2009	15 RCTs	1979-2008	>23000
		Costantine et al (41)	2008	5 RCTs	1983-2007	1826
		Tanos et al (42)	1994	17 RCTs	1978-1991	2572
		Mittendorf et al (43)	1993	25 RCTs	1972-1989	3604
		Wttewaall-Evelaar et al (44)	1990	17 RCTs	1972-1986	2095
		Aycleke et al (45)	2017	37 RCTs	1973-2002	6079
Vascular* and Plastic	2	Stewart et al(46)	2009	34 RCTs	1978-2000	N/A
		Ariyan et al(47)	2015	67 studies (Both RCTs and non-RCTs)	1962-2011	N/A
Key: *(Peripheral arterial reconstruction) ** Number of Procedures reported instead of number of participants ***Number of eyes operated on instead of number of participants. N/A= Data not available.						

5

3. Supplementary data for published manuscript “Appropriateness of surgical antimicrobial prophylaxis in Australia”.

Supplementary data includes the following:

- eTable 1. Surgical NAPS Terminology and Definitions
- eFigure 1. Surgical NAPS Data Collection Form
- eTable 2. Summary of Australian Therapeutic Guidelines: Antibiotic Version 15 Recommendations
- eFigure 2. Surgical NAPS Appropriateness Assessment Guide
- eTable 3. Hospital, Patient and Surgical Factors and Adjusted Appropriateness of Procedural Prescriptions
- eTable 4. Hospital, Patient and Surgical Factors and Adjusted Appropriateness of Post-procedural Prescriptions

eTable1. Surgical NAPS Terminology and Definitions

Procedural antimicrobial prophylaxis	All antimicrobials administered either immediately prior to or during the surgical procedure for the purpose of prophylaxis; each dose/prescription of the antimicrobial administered is recorded and reported individually.
Post-procedural antimicrobial prophylaxis	All antimicrobials prescribed following, but directly relating to, the procedure for the purposes of prophylaxis; each prescription course of the antimicrobial is recorded and reported, including any inpatient or discharge scripts.
Existing antimicrobial therapy	Any antimicrobial prescribed for treatment or prophylaxis in the 24 hours prior (72 hours if on dialysis) to the procedure; these are not analyzed individually but are able to be taken into account when assessing the appropriateness of whether procedural antimicrobials were given or not given.
Surgical episodes	Any individual procedure or set of multiple procedures performed together during the one session and the subsequent post-procedural care associated with the procedure(s).
Appropriateness	As per the Surgical NAPS Appropriate Assessment Guide (eFigure 2). Data assessed as 'optimal' and 'adequate'.
Inappropriateness	As per the Surgical NAPS Appropriate Assessment Guide (eFigure 2). Data assessed as 'suboptimal' and 'inadequate'.
Overall Appropriateness /Inappropriateness	Assessment per entire surgical episode as opposed to the individual antimicrobial doses/prescriptions. e.g. A surgical episode may be deemed to be overall inappropriate if any part of the prescription (procedural or post-procedural prophylaxis) was deemed inappropriate, including allergy or microbiology mismatch, timing, dose, route, frequency, duration, spectrum too broad, spectrum too narrow or if the procedure did not require any antimicrobials.

eFigure 1. Surgical NAPS Data Collection Form



SURGICAL NAPS
 National Antimicrobial Prescribing Survey




Patient identification Number	Date of birth / age	Gender	Date of admission	Date of discharge	Specialty	Height cm	Weight kg	eGFR / CrCl ml/min
	/ /	M / F / O	/ /	/ /				

Surgical details

Surgery date / / Surgery this admission ☐ Initial ☐ subsequent

Procedures ☐ emergency ☐ elective ☐ not assessable

☐ trauma ☐ removal/insertion of prosthetic material ☐ excessive blood loss

Surgeon code

Anaesthetist code

Time of first incision : ☐ not documented ☐ not applicable
 If not documented or not applicable; surgery start time (or estimated) :

End time (or estimated) :

Wound classification
☐ clean ☐ clean-contaminated ☐ contaminated ☐ dirty ☐ unknown ☐ not applicable

ASA score ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ unknown

Risk factors ☐ none identified

All procedures

- ☐ current smoker
- ☐ diabetes
- ☐ peritoneal or haemodialysis
- ☐ obesity (BMI>30)
- ☐ pregnancy
- ☐ rheumatoid arthritis
- ☐ current malignancy
- ☐ previous radiation therapy
- ☐ immunocompromised
- ☐ systemic corticosteroids
- ☐ other immunosuppressive treatments
- ☐ presence of prostheses
- ☐ MRSA colonisation
- ☐ MDR Gram negative colonisation
- ☐ one or more of:
 - prosthetic cardiac valve
 - previous infective endocarditis
 - congenital heart disease with defects
 - rheumatic heart disease in Aboriginal/Torres Strait Islanders

Transrectal prostatic biopsy

- ☐ quinolone therapy in preceding 3 months
- ☐ recent travel to Asia or Southern Europe in preceding 6 months

Gastroduodenal or oesophageal procedures

- ☐ reduced gastric acidity or motility
- ☐ gastrointestinal bleeding
- ☐ gastric outlet obstruction
- ☐ perforation

Biliary surgery

- ☐ acute cholecystitis
- ☐ obstructive jaundice
- ☐ common bile duct stones
- ☐ non-functioning gallbladder

Allergies and adverse drug reactions to antimicrobials

☐ nil known ☐ not documented ☐ present; specify drug and nature

Existing antimicrobial therapy

Any antimicrobial for treatment or medical prophylaxis or another condition. Prescribed in the 24 hours prior (72 hours if on dialysis) to the procedure

☐ none prescribed ☐ not assessable

Antimicrobial	Route	Dose	Date and time of last dose
			/ / : :
			/ / : :
			/ / : :
			/ / : :

Surgical or clinical notes, microbiology, radiology

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Peri-operative doses			Documented administration time						Was this a repeat dose?	Guideline compliance (1-6)	Guideline compliance (1-6)								Appropriateness (1-5)
Antimicrobial	Route	Dose	Not assessable	Nearest 15 minutes	Exact time	Start time	End time	Allergy mismatch			Microbiology mismatch	Incorrect dose	Incorrect route	Incorrect timing	Spectrum too broad	Spectrum too narrow	Post-operative antimicrobials not required	Procedure requires antimicrobials	
☐ Repeat dose required, but not given										4									4
☐ No antimicrobial prescribed																			

Post-operative antimicrobials							Indication			Guideline compliance (1-6)	Guideline compliance (1-6)								Appropriateness (1-5)
Start date and time*	End date and time*	Antimicrobial	Route	Dose	Freq		For prophylaxis only	For treatment of infection related to the procedure	Not assessable		Allergy mismatch	Microbiology mismatch	Incorrect dose / frequency	Incorrect route	Incorrect duration	Spectrum too broad	Spectrum too narrow	Post-operative antimicrobials not required	
/ / : : :	/ / : : :																		
/ / : : :	/ / : : :																		
/ / : : :	/ / : : :																		
/ / : : :	/ / : : :																		
*If time unknown, write unknown		☐ None prescribed																	

30 Day follow up		Guideline compliance		Appropriateness	
Surgical site infection ☐ identified; select one type and list any relevant microbiology ☐ superficial ☐ deep incisional ☐ organ space ☐ prosthesis	☐ none identified ☐ not assessable Microbiology	Clostridium difficile infection ☐ yes ☐ no ☐ unknown MDR organism ☐ yes ☐ no ☐ unknown Unplanned ICU admission ☐ yes ☐ no ☐ unknown Unplanned hospital readmission ☐ yes ☐ no ☐ unknown Death ☐ yes ☐ no ☐ unknown Other morbidity (if yes, specify) ☐ yes ☐ no ☐ unknown	1. Compliant with Therapeutic Guidelines 2. Compliant with locally endorsed guidelines 3. Directed therapy 4. Non-compliant with guidelines 5. No guidelines available 6. Not assessable	1. Optimal 2. Adequate 3. Sub-optimal 4. Inadequate 5. Not assessable	

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eTable 2. Summary of Australian Therapeutic Guidelines: Antibiotic Version 15 Recommendations

eTable 2 was developed as a resource for those who do not have access to the Australian Therapeutic Guidelines version 15, in which the Surgical NAPS Appropriateness Assessments were in relation too. This serves as a brief summary of the guideline's recommendations in relation to the general principles of SAP prescribing.

Antibiotic Prescribing Principles	Summary of recommendations from the Australian Therapeutic Guidelines: Antibiotic Version 15
Indication	Do not use SAP unless there is a clear indication for its use i.e. when there is a significant risk of infection or if post-operative infection would have serious consequences.
Antimicrobial choice	The prophylactic antibiotic regimen should be directed against the organism(s) most likely to cause postoperative infection.
	Cefazolin is the preferred drug for the majority of procedures that require prophylaxis.
	Modification may be necessary in relation to patient clinical factors (e.g., pre-existing infections, recent antimicrobial use, potential for colonisation of multidrug-resistant organisms, prolonged hospitalisation., presence of prostheses and antibiotic allergy) and environmental factors (e.g., organisms causing infection within the institution and the patterns of antibiotic susceptibility, the potential selection pressure of antibiotic use).
	Strong recommendation to avoid use of broad-spectrum antibiotics for SAP.
Dose/ Frequency	Common dosing for cefazolin is 2 grams.
	Dosage adjustment in obesity may be necessary.
	Vancomycin dosing: 15 to 20mg/kg (actual body weight).
	A repeat intraoperative dose is required if the procedure is prolonged or the drug has a short half-life. The interval between pre- and intra-operative doses should be equal to approximately two half-lives of the drug e.g., cefazolin should be administered every four hours.
Route	Usually parenteral, intravenous (IV) or intramuscular (IM) are the first line recommendation.
	In some circumstance rectal or oral route may be appropriate.
	Topical antimicrobials for SAP are not recommended.
Timing	Timing of SAP should ensure adequate plasma and tissue concentrations are achieved at the time of surgical incision and for the duration of the procedure.
	The optimal time for pre-operative IV SAP administration is within the 60 minutes before surgical incision. Administration 15 to 30 minutes before surgical incision may be optimal.
	Vancomycin infusions should ideally be started 30 to 120 minutes before surgical incision, due to its long infusion time.
Duration	A single dose is sufficient for the significant majority of procedures.
	Post-operative doses of IV antibiotics (up to 24 hours) are only required in defined circumstances (e.g. some cardiac and vascular surgeries and lower limb amputation).
	Prophylaxis (IV and oral) should not extend beyond 24 hours, regardless of surgical procedure.
	Urinary or intravascular catheters or indwelling surgical drains are note a justification for the extension of SAP duration.

eFigure 2. Surgical NAPS Appropriateness assessment guide



Surgical NAPS appropriateness definitions



	Appropriate		Inappropriate			
	1 - Optimal	2 - Adequate	3 - Suboptimal	4 - Inadequate	5 - Not assessable	
Allergy mismatch	Where antimicrobials are prescribed exactly according to Therapeutic Guidelines or local guidelines – antimicrobial choice, dose, route, timing and duration; or where there is an appropriate reason for deviation from guidelines <i>If any reason is selected for incorrect prescribing, the prescription will no longer be optimal.</i>		Mild or non-life threatening allergy mismatch	Life threatening allergy mismatch	Where there is insufficient information available or the case is too complex for assessment.	
Microbiology mismatch				Antimicrobial used is too narrow (where sensitivity results available)		
Incorrect dose or frequency			Dose or frequency too high (with exception of gentamicin)	Dose or frequency too low		
Incorrect route			An intravenous antimicrobial has been prescribed when the patient is able to safely take it orally	Gentamicin dose too high or too frequent		
Incorrect timing		Repeat dose given too soon (including patients who were already on existing antimicrobial therapy) <i>taking into consideration patients with renal impairment</i>	Antimicrobial prophylaxis given less than 15 minutes before surgical incision (with exception of vancomycin)	Antimicrobial prophylaxis given greater than 60 minutes before surgical incision (with exception of vancomycin)		
			Vancomycin started less than 30 minutes before surgical incision	Vancomycin started greater than 120 minutes before surgical incision		
Incorrect duration		Patient already on existing antimicrobials where last dose would have provided sufficient prophylaxis for the duration of the procedure		Repeat dose given too late (including patients already on existing antimicrobial therapy) <i>taking into account renal impairment</i>		
Spectrum too broad			Choice of antimicrobial is too broad Additional antimicrobial added unnecessarily	Surgical prophylaxis greater than 24 hours (except where guidelines endorse this)		
Spectrum too narrow						
Procedure does not require any antimicrobials				Choice of antimicrobial does not cover likely organisms		
Procedure requires antimicrobials				Procedure does not require any antimicrobials, but antimicrobials were still prescribed		
Repeat dose required, but not given				Procedure requires antimicrobials but no antimicrobials were prescribed AND there were no existing antimicrobials		
No antimicrobial prescribed	No antimicrobial required			This will automatically be selected for auditors		
				Procedure requires antimicrobials but no antimicrobials were prescribed and there were no pre-existing antimicrobials		

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eTable 3. Hospital, patient and surgical factors and adjusted appropriateness of procedural prescriptions

FACTORS	PROCEDURAL PRESCRIPTIONS				
	TOTAL PRESCRIPTIONS	APPROPRIATE (No.) (%)	INAPPROPRIATE (No.) (%)	NOT ASSESSABLE (No.) (%)	MIXED EFFECTS MODEL: ADJUSTED APPROPRIATENESS (%) [95% CI]
TOTAL	10,740	5,770 (53.7)	4,355 (40.5)	615 (5.7)	-
HOSPITAL FACTORS					
STATE/TERRITORY					
Australian Capital Territory	28	12 (42.9)	16 (57.1)	-	48.5 [11.6-85.3]
New South Wales	2,586	1,553 (60.1)	837 (32.4)	196 (7.6)	70.9 [65.3-76.5]
Northern Territory	50	36 (72.0)	10 (20.0)	4 (8.0)	Not estimable ^d
Queensland	1,962	805 (41.0)	1,053 (53.7)	104 (5.3)	50.1 [41.8-58.4]
South Australia	1,089	636 (58.4)	402 (36.9)	51 (4.7)	61.4 [49.9-72.8]
Tasmania ^a	63	62 (98.4)	1 (1.6)	-	-
Victoria	3,089	1,628 (52.7)	1,249 (40.4)	212 (6.9)	57.1 [50.1-64.1]
Western Australia	1,873	1,038 (55.4)	787 (42.0)	48 (2.6)	55.0 [45.6-64.4]
ABS REMOTENESS AREA					
Major cities	8,528	4,681 (54.9)	3,356 (39.4)	491 (5.8)	60.0 [55.7-64.2]
Inner regional	1,716	851 (49.6)	760 (44.3)	105 (6.1)	54.3 [45.7-62.9]
Outer regional	415	217 (52.3)	179 (43.1)	19 (4.6)	63.9 [51.7-76.1]
Remote	80	20 (25.0)	60 (75.0)	-	45.7 [19.6-71.8]
Very remote ^a	1	1 (100.0)	-	-	-
HOSPITAL FUNDING					
Public	6,222	3,417 (54.9)	2,441 (39.2)	364 (5.9)	-
Private	4,518	2,353 (52.1)	1,914 (42.3)	251 (5.6)	-
HOSPITAL PEER GROUP					
Principal referral	1,985	1,224 (61.7)	662 (33.4)	99 (5.0)	61.5 [52.0-71.1]
Public acute group A	2,217	1,141 (51.5)	989 (44.6)	87 (3.9)	56.6 [48.9-64.3]
Public acute group B	786	466 (59.3)	301 (38.3)	19 (2.4)	62.1 [51.4-72.9]
Public acute group C	600	265 (44.2)	308 (51.3)	27 (4.5)	56.9 [44.5-69.3]
Public acute group D	7	3 (42.9)	2 (28.6)	2 (28.6)	Not estimable ^d
Mixed sub- & non-acute	69	27 (39.1)	21 (3.0)	21 (3.0)	Not estimable ^d
Mixed day procedure	235	117 (49.8)	86 (36.6)	32 (13.6)	72.3 [51.9-92.7]
Other acute specialised	337	264 (78.3)	69 (20.5)	4 (1.2)	78.0 [63.5-92.6]
Other day procedure	119	3 (2.5)	8 (6.7)	108 (90.8)	43.9 [5.8-82.1]
Women's hospital	176	91 (51.7)	67 (38.1)	18 (10.2)	56.5 [30.0-83.0]
Children's hospital	123	63 (51.2)	59 (48.0)	1 (0.8)	63.2 [37.6-88.8]
Unpeered hospitals	17	14 (82.4)	2 (11.8)	1 (5.9)	Not estimable ^d
Private acute group A	517	230 (44.5)	251 (48.5)	36 (7.0)	53.1 [37.9-68.3]
Private acute group B	1,456	602 (41.3)	780 (53.6)	74 (5.1)	46.4 [35.9-56.9]
Private acute group C	593	387 (65.3)	194 (32.7)	12 (2.0)	64.1 [53.1-75.1]
Private acute group D	1,503	873 (58.1)	556 (37.0)	74 (4.9)	64.8 [55.0-74.5]
PATIENT FACTORS					
GENDER					
Male	4,962	2,627 (52.9)	2,043 (41.2)	292 (5.9)	59.1 [55.4-62.7]
Female	5,727	3,108 (54.3)	2,308 (40.3)	323 (5.6)	59.2 [55.7-62.8]
Unknown ^a	51	35 (68.6)	16 (31.4)	-	-
AGE (n=10,733)^b					
0-19	539	259 (48.1)	267 (49.5)	13 (2.4)	55.0 [49.6-60.4]
20-39	2,349	1,264 (53.8)	976 (41.5)	109 (4.6)	58.1 [54.2-62.0]
40-59	2,701	1,456 (53.9)	1,119 (41.4)	126 (4.7)	58.9 [55.1-62.7]

60-79	4,170	2,292 (55.0)	1,583 (38.0)	295 (7.1)	61.4 [57.8-65.0]
<80	974	494 (50.7)	408(41.9)	72 (7.4)	55.5 [51.1-60.0]
SURGICAL FACTORS					
SURGERY NUMBER FOR ADMISSION					
Initial	10,302	5,526 (53.6)	4,193 (40.7)	583 (5.7)	59.0 [55.5-62.5]
Subsequent	438	244 (55.7)	162 (37.0)	32 (7.3)	63.0 [57.8-68.2]
SURGERY CLASSIFICATION					
Elective	8,670	4,610 (53.2)	3,527 (40.7)	533 (6.1)	58.7 [55.1-62.2]
Emergency	1,893	1,072 (56.6)	759 (40.1)	63 (3.3)	60.3 [56.3-64.3]
Not Assessable	177	89 (50.3)	69 (39.0)	19 (10.7)	69.8 [62.4-77.2]
TRAUMA					
Yes	582	371 (63.7)	197 (33.8)	14 (2.4)	66.0 [61.1-71.0]
No	10,158	5,399 (53.2)	4,158 (40.9)	601 (5.9)	58.7 [55.2-62.2]
PROSTHESIS REMOVAL/INSERTION					
Yes	3,850	2,308 (59.9)	1,331 (34.6)	211 (5.5)	65.4 [61.8-69.0]
No	6,890	3,462 (50.2)	3,024 (43.9)	404 (5.9)	55.7 [52.0-59.4]
EXCESSIVE BLOOD LOSS					
Yes	150	101 (67.3)	46 (30.7)	3 (2.0)	65.9 [58.5-73.4]
No	10,590	5,669 (53.5)	4,309 (40.7)	612 (5.8)	59.0 [55.6-62.5]
SURGICAL PROCEDURE GROUP					
Orthopedic surgery	2,953	1,824 (70.3)	1,013 (34.3)	116 (4.5)	60.5 [56.6-64.5]
Abdominal surgery	2,049	1,137 (55.5)	860 (42.0)	52 (2.5)	60.4 [56.4-64.4]
Breast surgery	326	172 (52.8)	117 (35.9)	37 (11.3)	57.8 [51.8-63.8]
Cardiac surgery	681	379 (55.7)	226 (33.2)	76 (11.2)	63.8 [58.4-69.1]
Dentoalveolar surgery	187	45 (24.1)	140 (74.9)	2 (1.1)	33.7 [26.3-41.2]
Gynecological surgery	612	331 (54.1)	245 (40.0)	36 (5.9)	62.0 [57.0-66.9]
Head and Neck surgery	397	172 (43.3)	205 (51.6)	20 (5.0)	54.7 [49.1-60.4]
Neurosurgery	389	260 (66.8)	104 (26.7)	25 (6.4)	68.9 [63.2-74.5]
Obstetrics	740	448 (60.5)	270 (36.5)	22 (3.0)	63.3 [58.2-68.3]
Ophthalmology	301	111 (36.9)	70 (23.3)	120 (39.9)	68.0 [60.1-75.9]
Plastic and reconstructive surgery	818	331 (40.5)	449 (54.9)	38 (4.6)	47.0 [42.3-51.8]
Thoracic surgery	78	49 (62.8)	20 (25.6)	9 (11.5)	61.9 [50.5-73.3]
Urological surgery	1016	407 (40.1)	554 (54.5)	55 (5.4)	56.7 [52.0-61.5]
Vascular surgery	193	104 (53.9)	82 (42.5)	7 (3.6)	59.2 [52.2-66.1]
ANTIMICROBIAL					
1.Cefazolin	7,991	4,839 (60.6)	2,827 (35.4)	325 (4.1)	64.7 [61.1-68.3]
2.Metronidazole	692	378 (54.6)	277 (40.0)	37 (5.3)	64.3 [59.5-69.2]
3.Gentamicin	544	120 (22.1)	331 (60.8)	93 (17.1)	28.6 [23.5-33.7]
4. Vancomycin	295	65 (22.0)	192 (65.1)	38 (12.9)	26.3 [20.5-32.1]
5. Ceftriaxone	267	26 (9.7)	236 (88.4)	5 (1.9)	13.3 [8.4-18.2]
6.Piperacillin-tazobactam	131	64 (48.9)	63 (48.1)	4 (3.1)	49.6 [40.7-58.5]
7. Ciprofloxacin	106	13 (12.3)	87 (82.1)	6 (5.7)	21.8 [12.4-31.2]
8. Chloramphenicol	98	6 (6.1)	33 (33.7)	59 (60.2)	18.1 [3.4-32.9]
9. Clindamycin	93	40 (43.0)	50 (53.8)	3 (3.2)	44.5 [35.0-54.0]
10. Cefoxitin	77	55 (71.4)	21 (27.3)	1 (1.3)	68.3 [58.0-78.5]
11. Other (11-31) ^c	446	164 (36.8)	238 (53.4)	44 (9.9)	48.4 [42.5-54.3]
Footnotes:					
^a Excluded due to low/disproportionate numbers					
^b Age data missing for 7 prescriptions and therefore excluded					
^c Other antimicrobials, outside of the top ten most frequently prescribed					
^d AA Not estimable due to low number of prescriptions					

eTable 4. Hospital, patient and surgical factors and adjusted appropriateness of post-procedural prescriptions

FACTORS	POST-PROCEDURAL PRESCRIPTIONS				
	TOTAL PRESCRIPTIONS	APPROPRIATE (No.) (%)	INAPPROPRIATE (No.) (%)	NOT ASSESSABLE (No.) (%)	MIXED EFFECTS MODEL: ADJUSTED APPROPRIATENESS (%) [95% CI]
TOTAL	4655	1722 (36.9)	2801 (60.2)	132 (2.8)	-
HOSPITAL FACTORS					
STATE/TERRITORY					
Australian Capital Territory	16	1 (6.3)	15 (93.8)	-	Not estimable ^d
New South Wales	1,232	363 (29.5)	849 (68.9)	20 (1.6)	47.4 [37.4-57.3]
Northern Territory	10	7 (70)	3 (30)	-	Not estimable ^d
Queensland	804	220 (27.4)	564 (70.1)	20 (2.5)	30.4 [18.9-41.9]
South Australia	516	298 (57.8)	215 (41.7)	3 (0.6)	54.6 [37.8-71.4]
Tasmania ^a	64	64 (100.0)	-	-	-
Victoria	1,122	323 (28.8)	724 (64.5)	75 (6.7)	34.2 [24.1-44.3]
Western Australia	891	446 (50.1)	431 (48.4)	14 (1.6)	50.3 [35.7-64.9]
ABS REMOTENESS AREA					
Major cities	3,830	1,405 (36.7)	2,310 (60.3)	115 (3.0)	42.2 [36.1-48.4]
Inner regional	711	286 (40.2)	413 (58.1)	12 (1.7)	46.9 [34.4-59.5]
Outer regional	98	27 (27.6)	68 (69.4)	3 (3.1)	52.5 [31.8-73.2]
Remote	14	4 (28.6)	8 (57.1)	2 (14.3)	Not estimable ^d
Very remote ^a	2	-	2 (100.0)	-	-
HOSPITAL FUNDING					
Public	2,625	971 (37.0)	1,544 (58.8)	110 (4.2)	-
Private	2,030	751 (37.0)	1,257 (61.9)	22 (1.1)	-
HOSPITAL PEER GROUP					
Principal referral	952	366 (38.4)	573 (60.2)	13 (1.4)	39.2 [25.7-52.7]
Public acute group A	1,037	393 (37.9)	629 (60.7)	15 (1.4)	42.0 [30.3-53.7]
Public acute group B	205	49 (23.9)	153 (74.6)	3 (1.5)	37.3 [20.6-54.1]
Public acute group C	144	34 (23.6)	97 (67.4)	13 (9.0)	37.1 [17.3-56.8]
Public acute group D	3	-	2 (66.6)	1 (33.3)	-
Mixed sub- & non-acute ^a	0	-	-	-	-
Mixed day procedure	68	30 (44.1)	38 (55.9)	-	Not estimable ^d
Other acute specialised	91	68 (74.7)	20 (22.0)	3 (3.3)	51.3 [21.0-81.5]
Other day procedure	72	-	15 (20.8)	57 (79.2)	-
Women's hospital	21	11 (52.4)	3 (14.3)	7 (33.3)	Not estimable ^d
Children's hospital	88	32 (36.4)	56 (63.6)	-	53.6 [15.8-91.4]
Unpeered hospitals	93	86 (92.5)	6 (6.5)	1 (1.1)	Not estimable ^d
Private acute group A	250	79 (31.6)	163 (65.2)	8 (3.2)	35.5 [13.8-57.2]
Private acute group B	703	178 (25.3)	522 (74.3)	3 (0.4)	33.0 [19.2-46.8]
Private acute group C	377	134 (35.5)	239 (63.4)	4 (1.1)	42.8 [26.6-59.0]
Private acute group D	551	262 (47.5)	285 (51.7)	4 (0.8)	60.4 [46.4-74.4]
PATIENT FACTORS					
GENDER					
Male	2,255	882 (39.1)	1,312 (58.2)	61 (2.7)	43.6 [38.1-49.0]
Female	2,366	816 (34.5)	1,479 (62.5)	71 (3.0)	42.5 [37.0-48.0]
Unknown ^a	34	24 (70.6)	10 (29.4)	-	-
AGE (n4,651)^b					
0-19	286	94 (32.3)	186 (65)	6 (2.1)	46.7 [39.3-54.1]
20-39	751	214 (28.5)	516 (68.7)	21 (2.8)	42.8 [36.8-48.7]
40-59	955	343 (35.9)	593 (62.1)	19 (2.0)	44.1 [38.4-49.9]
60-79	2,104	869 (41.3)	1,164 (55.3)	71 (3.4)	42.9 [37.4-48.4]

>80	555	201 (36.2)	339 (61.1)	15 (2.7)	40.2 [34.1-46.2]
SURGERY NUMBER FOR ADMISSION					
Initial	4,512	1,690 (37.5)	2,695 (59.7)	127 (2.8)	43.3 [37.9-48.7]
Subsequent	143	32 (22.4)	106 (74.1)	5 (3.5)	36.1 [28.3-43.9]
SURGERY CLASSIFICATION					
Elective	3,763	1,379 (36.6)	2,275 (60.5)	109 (2.9)	41.1 [35.7-46.5]
Emergency	847	332 (39.2)	495 (58.4)	20 (2.4)	50.8 [44.8-56.8]
Not Assessable	45	11 (24.4)	31 (68.9)	3 (6.7)	47.7 [32.2-63.2]
TRAUMA					
Yes	381	153 (40.2)	221 (58.0)	7 (1.8)	42.5 [35.7-49.2]
No	4,274	1,569 (36.7)	2,580 (60.4)	125 (2.9)	43.1 [37.7-48.5]
PROSTHESIS REMOVAL/INSERTION					
Yes	2,307	1,017 (44.1)	1,271 (55.1)	19 (0.8)	44.0 [38.4-49.6]
No	2,348	705 (30.0)	1,530 (65.2)	113 (4.8)	42.0 [36.4-47.5]
EXCESSIVE BLOOD LOSS					
Yes	70	39 (55.7)	28 (40.0)	3 (4.3)	52.9 [43.4-62.4]
No	4,585	1,683 (36.7)	2,773 (60.5)	129 (2.8)	42.9 [37.5-48.2]
SURGICAL PROCEDURE GROUP					
Orthopedic surgery	1,954	981 (50.2)	958 (49.0)	15 (0.8)	47.0 [41.0-53.1]
Abdominal surgery	295	90 (30.5)	203 (68.8)	2 (0.7)	41.5 [34.0-48.9]
Breast surgery	132	17 (12.9)	115 (87.1)	-	21.5 [13.4-29.7]
Cardiac surgery	529	217 (41.0)	308 (58.2)	4 (0.8)	55.1 [47.5-62.6]
Dentoalveolar surgery	84	12 (14.3)	72 (85.7)	-	24.1 [13.2-34.9]
Gynecological surgery	81	12 (14.8)	67 (77.0)	2 (2.5)	23.6 [13.3-33.8]
Head and Neck surgery	229	27 (11.8)	192 (83.8)	10 (4.4)	29.4 [21.7-37.2]
Neurosurgery	165	57 (34.5)	105 (63.6)	3 (1.8)	44.4 [36.6-52.3]
Obstetrics	173	31 (17.9)	127 (73.4)	15 (8.7)	31.1 [22.2-40.1]
Ophthalmology	265	134 (50.6)	70 (26.4)	61 (23.0)	58.7 [47.9-69.4]
Plastic and reconstructive surgery	423	85 (20.1)	330 (78.0)	8 (1.9)	32.3 [25.7-38.9]
Thoracic surgery	58	13 (22.4)	44 (75.9)	1 (1.7)	34.2 [22.8-45.7]
Urological surgery	236	34 (14.4)	191 (80.96)	11 (4.7)	29.4 [21.9-36.8]
Vascular surgery	31	12 (38.7)	19 (61.3)	-	40.7 [28.4-53.0]
ANTIMICROBIAL					
1. Cefazolin	2,752	1,331 (48.4)	1,395 (50.7)	26 (0.9)	49.3 [43.6-55.0]
2. Cefalexin	520	72 (13.8)	441 (84.8)	7 (1.3)	29.1 [22.7-35.5]
3. Chloramphenicol	245	68 (27.8)	115 (46.9)	62 (25.3)	38.6 [29.5-47.7]
4. Metronidazole	190	37 (19.5)	147 (77.4)	6 (3.2)	35.0 [26.7-43.3]
5. Amoxicillin/Clavulanic Acid	148	31 (20.9)	110 (74.3)	7 (4.7)	43.1 [34.2-51.9]
6. Mupirocin	105	45 (42.9)	57 (54.3)	3 (2.9)	37.3 [29.1-45.5]
7. Vancomycin	89	23 (25.8)	64 (71.9)	2 (2.2)	28.0 [19.6-36.3]
8. Ceftriaxone	79	14 (17.7)	63* (79.7)	2 (2.5)	32.7 [22.8-46.7]
9. Amoxycillin	79	9 (11.4)	68 (86.1)	2 (2.5)	26.8 [15.8-37.7]
10. Gentamicin	67	10 (14.9)	54 (80.6)	3 (4.5)	35.5 [23.8-47.2]
11. Other (11-38) ^c	381	82 (21.5)	287 (75.3)	12 (3.1)	30.1 [23.6-36.6]
Footnotes:					
^a Excluded from multivariate analysis due to low/disproportionate numbers					
^b Age data missing for 4 prescriptions and therefore excluded					
^c Other antimicrobials, outside of the top ten most frequently prescribed					
^d AA Not estimable due to low number of prescriptions					

4. Supplementary data for submitted manuscript “Identifying targets for improvement using a nationally standardised survey: Surgical Antimicrobial Prophylaxis in Orthopaedic Surgery”.

Supplementary data includes the following:

- Table S1 Summary of Australian Therapeutic Guidelines: Antibiotic Version 15 Recommendations in orthopaedic procedures
- Table S2 Surgical NAPS Terminology and Definitions
- Figure S1 Surgical NAPS Appropriateness assessment guide
- Figure S2 Royal Australian College of Surgeons Morbidity Audit and Logbook Tool: Orthopaedic Procedure
- Table S3 Appropriateness and Adjusted Appropriateness of assessable procedural doses
- Table S4 Appropriateness and Adjusted Appropriateness of assessable post-procedural prescriptions
- Table S5 Sub analysis 1: Appropriateness and adjusted appropriateness of assessable procedural doses for knee surgical procedures
- Table S6 Sub analysis 2: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for knee surgical procedures
- Table S7 Sub analysis 3: Appropriateness and adjusted appropriateness of assessable procedural doses for hip surgical procedures
- Table S8 Sub analysis 4: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for hip surgical procedures
- Table S9 Sub analysis 5: Appropriateness and adjusted appropriateness of assessable procedural doses for open reduction internal fixation (ORIF) surgical procedures
- Table S10 Sub analysis 6: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for open reduction internal fixation (ORIF) surgical procedures
- Table S11: Subgroup analysis: Appropriateness of orthopaedic knee procedures per presence, insertion or removal of prosthetic material

Table S1 Summary of Australian Therapeutic Guidelines: Antibiotic Version 15 Recommendations in orthopaedic procedures

Table S1 was developed as a resource for those who do not have access to the Australian Therapeutic Guidelines version 15, in which the Surgical NAPS Appropriateness Assessments were in relation too. This serves as a brief summary of the guideline's recommendations in relation to the general principles of SAP prescribing for orthopaedic procedures.

Antibiotic Prescribing Principles	Summary of recommendations from the Australian Therapeutic Guidelines: Antibiotic Version 15	
Indication	Do not use SAP unless there is a clear indication for its use i.e. when there is a significant risk of infection or if post-operative infection would have serious consequences.	
	Procedure	Is SAP indicated?
	<i>routine arthroscopy procedures not involving insertion of prosthetic material or avascular tissue</i>	<i>No</i>
	<i>prosthetic large joint replacement*</i>	<i>Yes</i>
	<i>procedures involving insertion of prosthetic or allograft material</i>	<i>Yes</i>
	<i>internal fixation of fractures of large bones</i>	<i>Yes</i>
Antimicrobial choice	Directed against the organism(s) most likely to cause post-operative infection.	
	Cefazolin is the preferred drug for the majority of procedures that require prophylaxis.	
	For patients colonised or infected with methicillin-resistant <i>S. aureus</i> (MRSA), or at increased risk of being colonised or infected with MRSA (e.g. patients undergoing a joint arthroplasty procedure that is a reoperation [return to theatre or early revision]; add vancomycin to the cefazolin regimen.	
	Modification may be necessary in relation to: - <u>Patient clinical factors</u>: e.g., pre-existing infections, recent antimicrobial use, potential for colonisation of multi-drug resistant organisms, prolonged hospitalisation, presence of prostheses and antibiotic allergy and; - <u>Environmental factors</u>: e.g., organisms causing infection within the institution and the patterns of antibiotic susceptibility, the potential selection pressure of antibiotic use.	
	Strong recommendation to avoid use of broad-spectrum antibiotics for SAP	
Dose/Frequency	Common dosing for cefazolin is 2 grams.	
	Dosage adjustment in obesity may be necessary i.e. Cefazolin 3g if weight >120 kg.	
	Vancomycin dosing: 15 to 20mg/kg (actual body weight).	
	A repeat intraoperative dose is required if the procedure is prolonged or the drug has a short half-life.	
	The interval between pre- and intra-operative doses should be equal to approximately two half-lives of the drug e.g., cefazolin should be administered every four hours	
Route	Parenteral, intravenous (IV) is the first line recommendation.	
	Topical antimicrobials for SAP are not recommended	
Timing	Timing of SAP should ensure adequate plasma and tissue concentrations are achieved at the time of surgical incision and for the duration of the procedure.	
	The optimal time for pre-operative IV SAP administration is within the 60	

	minutes before surgical incision.
	Administration 15 to 30 minutes before surgical incision may be optimal.
	Vancomycin infusions should ideally be started 30 to 120 minutes before surgical incision, due to its long infusion time.
Duration	A single dose is sufficient for the significant majority of procedures.
	Post-operative doses of IV antibiotics (up to 24 hours) are only required in defined circumstances (e.g. lower limb amputations*).
	Prophylaxis (IV and oral) should not extend beyond 24 hours, regardless of surgical procedure.
	Urinary or intravascular catheters or indwelling surgical drains are not a justification for the extension of SAP duration.
* Although a single preoperative dose of surgical antibiotic prophylaxis is expected to be sufficient to prevent post-operative infection following total knee arthroplasty, there is insufficient evidence to show that a single dose of prophylaxis is as effective as 24 hours of prophylaxis. Studies are ongoing. Post-operative doses can be considered but prophylaxis (intravenous or oral) should not continue beyond 24 hours.	

Table S2 Surgical NAPS Terminology and Definitions

Procedural antimicrobial prophylaxis	All antimicrobials administered either immediately prior to or during the surgical procedure for the purpose of prophylaxis; each dose/prescription of the antimicrobial administered is recorded and reported individually.
Post-procedural antimicrobial prophylaxis	All antimicrobials prescribed following, but directly relating to, the procedure for the purposes of prophylaxis; each prescription course of the antimicrobial is recorded and reported, including any inpatient or discharge scripts.
Existing antimicrobial therapy	Any antimicrobial prescribed for treatment or prophylaxis in the 24 hours prior (72 hours if on dialysis) to the procedure; these are not analyzed individually but are able to be taken into account when assessing the appropriateness of whether procedural antimicrobials were given or not given.
Surgical episodes	Any individual procedure or set of multiple procedures performed together during the one session and the subsequent post-procedural care associated with the procedure(s).
Appropriateness	As per the Surgical NAPS Appropriate Assessment Guide (4, 366). Data assessed as 'optimal' and 'adequate'.
Inappropriateness	As per the Surgical NAPS Appropriate Assessment Guide (4, 357). Data assessed as 'suboptimal' and 'inadequate'.
Overall Appropriateness /Inappropriateness	Assessment per entire surgical episode as opposed to the individual antimicrobial doses/prescriptions. e.g., A surgical episode may be deemed to be overall inappropriate if any part of the prescription (procedural or post-procedural prophylaxis) was deemed inappropriate, including allergy or microbiology mismatch, timing, dose, route, frequency, duration, spectrum too broad, spectrum too narrow or if the procedure did not require any antimicrobials.

References

1. Australian Commission on Safety and Quality in Health Care. Surgical national antimicrobial prescribing in Australia: Results of the 2016 pilot. In: ACSQHC, editor. Sydney: Australian Commission for Safety and Quality in Health Care; 2017.
2. Ierano C, Thursky K, Marshall C, et al. Appropriateness of surgical antimicrobial prophylaxis practices in Australia. JAMA Network Open. 2019;2(11):e1915003.

Figure S1 Surgical NAPS Appropriateness assessment guide

		Surgical NAPS appropriateness definitions			 
	Appropriate		Inappropriate		5 - Not assessable
	1 - Optimal	2 - Adequate	3 - Suboptimal	4 - Inadequate	
Allergy mismatch	Where antimicrobials are prescribed exactly according to Therapeutic Guidelines or local guidelines – antimicrobial choice, dose, route, timing and duration; or where there is an appropriate reason for deviation from guidelines <i>If any reason is selected for incorrect prescribing, the prescription will no longer be optimal.</i>		Mild or non-life threatening allergy mismatch	Life threatening allergy mismatch	Where there is insufficient information available or the case is too complex for assessment.
Microbiology mismatch				Antimicrobial used is too narrow (where sensitivity results available) Dose or frequency too low	
Incorrect dose or frequency			Dose or frequency too high (with exception of gentamicin)	Gentamicin dose too high or too frequent	
Incorrect route		Repeat dose given too soon (including patients who were already on existing antimicrobial therapy) <i>taking into consideration patients with renal impairment</i>	An intravenous antimicrobial has been prescribed when the patient is able to safely take it orally	The prescribed route does not reach the site of infection or surgery	
Incorrect timing			Antimicrobial prophylaxis given less than 15 minutes before surgical incision (with exception of vancomycin) Vancomycin started less than 30 minutes before surgical incision	Antimicrobial prophylaxis given greater than 60 minutes before surgical incision (with exception of vancomycin) Vancomycin started greater than 120 minutes before surgical incision Repeat dose given too late (including patients already on existing antimicrobial therapy) <i>taking into account renal impairment</i> Surgical prophylaxis greater than 24 hours (except where guidelines endorse this)	
Incorrect duration					
Spectrum too broad		Patient already on existing antimicrobials where last dose would have provided sufficient prophylaxis for the duration of the procedure	Choice of antimicrobial is too broad Additional antimicrobial added unnecessarily		
Spectrum too narrow				Choice of antimicrobial does not cover likely organisms	
Procedure does not require any antimicrobials				Procedure does not require any antimicrobials, but antimicrobials were still prescribed	
Procedure requires antimicrobials				Procedure requires antimicrobials but no antimicrobials were prescribed AND there were no existing antimicrobials	
Repeat dose required, but not given				This will automatically be selected for auditors	
No antimicrobial prescribed	No antimicrobial required			Procedure requires antimicrobials but no antimicrobials were prescribed and there were no pre-existing antimicrobials	

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Figure S2 Royal Australian College of Surgeons Morbidity Audit and Logbook Tool: Orthopaedic Procedure Lists

ROYAL AUSTRALASIAN COLLEGE OF SURGEONS

Morbidity Audit and Logbook Tool

Procedure list for SET and IMG - Orthopaedic Surgery



ELBOW SURGERY

Procedure	Alternative search terms
Arthroplasty	elbow
Ligament	elbow

FOOT & ANKLE SURGERY

Procedure	Alternative search terms
Major many digits	osteotomy foot
Minor	osteotomy foot

FRACTURES CLOSED REDUCTION

Procedure	Alternative search terms
Lower limb	fractures closed reduction
Upper limb	fractures closed reduction

HAND SURGERY

Procedure	Alternative search terms
Elective Major >1 Digit	hand
Elective Minor	hand
Traumatic Major >1 Digit	hand
Traumatic Minor	hand

KNEE SURGERY

Procedure	Alternative search terms
Arthroscopy diagnostic	arthroscop knee arthroscopic
Arthroscopy therapeutic	arthroscop knee
Ligament acute	knee osteotomy
Ligament chronic	hip osteotomy knee
Osteotomy	knee

ORIF LOWER LIMB

Procedure	Alternative search terms
Ankle	orif lower limb
Femur	orif lower limb
ORIF NOF	orif lower limb
Other	orif lower limb
Prosthesis NOF	orif lower limb
Tibia	orif lower limb



ROYAL AUSTRALASIAN COLLEGE OF SURGEONS

Morbidity Audit and Logbook Tool

Procedure list for SET and IMG - Orthopaedic Surgery



ORIF UPPER LIMB

Procedure	Alternative search terms
Carpus	orif upper limb
Clavicle	orif upper limb
Humerus	orif upper limb
Other	orif upper limb
Radius	orif upper limb
Ulna	orif upper limb

OSTEOMYELITIS & JOINT WASHOUT

Procedure	Alternative search terms
Removal of implants	osteomyelitis joint joints

PAEDIATRIC SURGERY

Procedure	Alternative search terms
Feet Major	Paediatrics
Feet Minor	Paediatrics
Hips CDH	Paediatrics
Osteotomy	Paediatrics
Other Major	Paediatrics
Other Minor	Paediatrics
Spine	Paediatrics

SHOULDER SURGERY

Procedure	Alternative search terms
Arthroplasty	shoulder
Arthroscopy & decompression	shoulder decompression
Other	shoulder
Rotator Cuff	shoulder
Stabilisation	shoulder

SOFT TISSUE SURGERY

Procedure	Alternative search terms
Major wounds	soft tissue
Minor wounds	soft tissue
Tendons (exc hands)	soft tissue



ROYAL AUSTRALASIAN COLLEGE OF SURGEONS

Morbidity Audit and Logbook Tool

Procedure list for SET and IMG - Orthopaedic Surgery



SPINAL SURGERY

Procedure	Alternative search terms
Adult scoliosis	spine spinal
Decompression laminectomy	spine spinal
Discectomy lumbar	spine spinal
Lumbar	spine spinal
Spinal Fusion Cervical	
Trauma	spine spinal

TOTAL JOINT REPLACEMENT

Procedure	Alternative search terms
Hips Primary	total Joint Replacement
Hips Revision	total Joint Replacement
Knees Primary	total Joint Replacement
Knees Revision	total Joint Replacement

TUMOUR SURGERY

Procedure	Alternative search terms
Amputations not digits	tumour
Biopsy & local resect	tumour
Major resection	tumour

ALL OTHER SURGERY

Procedure	Alternative search terms
All other surgery	



Table S3 Appropriateness and Adjusted Appropriateness of assessable procedural doses

PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^b		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS		3,978	2,574 (64.7)	1,404 (35.3)	-	-	-	-	-
HOSPITAL FACTORS									
Funding	Public	1,828	1,192 (65.2)	636 (34.8)	Ref	Ref	Excluded (Exc) ^a	Exc ^a	Exc ^a
	Private	2,150	1,382 (64.3)	768 (35.7)	0.96 [0.84-1.09]	0.541	Exc ^a	Exc ^a	Exc ^a
Peer group	Principal referral	504	338 (67.1)	166 (32.9)	1.15 [0.92-1.43]	0.227	1.16 [0.48-2.84]	0.739	66.4 [55.8-76.9]
	Public acute group A	1,082	692 (64.0)	390 (36.0)	Ref	Ref	Ref	Ref	64.1 [55.8-72.4]
	Public acute group B	118	88 (74.6)	30 (25.4)	1.65 [1.07-2.55]	0.023	1.14 [0.33-3.91]	0.838	66.0 [49.4-82.6]
	Public acute group C	107	67 (62.6)	40 (37.4)	0.94 [0.63-1.42]	0.783	1.32 [0.42-4.09]	0.636	68.1 [53.8-82.5]
	Private acute group A	190	123 (64.7)	67 (35.3)	1.03 [0.75-1.43]	0.836	1.15 [0.38-3.44]	0.804	66.2 [52.0-80.3]
	Private acute group B	787	424 (53.9)	363 (46.1)	0.66 [0.55-0.79]	<0.005	0.76 [0.30-1.93]	0.561	59.7 [47.6-71.9]
	Private acute group C	269	191 (71.0)	78 (29.0)	1.38 [1.03-1.85]	0.030	3.43 [1.27-9.26]	0.015	80.2 [71.4-88.9]
	Private acute group D	777	525 (67.6)	252 (32.4)	1.17 [0.97-1.43]	0.106	2.08 [0.79-5.48]	0.139	74.3 [64.2-84.5]
	Mixed day procedure	2	1 (50.0)	1 (50.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
	Other acute specialised	125	118 (94.4)	7 (5.6)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
	Childrens'	17	7 (41.2)	10 (58.8)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PATIENT FACTORS									
Gender	Male	1,959	1,293 (66.0)	666 (34.0)	Ref	Ref	Ref	Ref	68.3 [63.8-72.8]
	Female	1,968	1,247 (63.4)	721 (36.6)	0.89 [0.78-1.02]	0.084	0.89 [0.74-1.09]	0.262	66.7 [62.1-71.3]
	Unknown	51	34 (66.7)	17 (33.3)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Age	0-19	175	106 (60.6)	69 (39.4)	0.83 [0.60-1.13]	0.234	0.91 [0.54-1.52]	0.720	65.1 [56.8-73.3]
	20-39	489	328 (67.1)	161 (32.9)	1.09 [0.89-1.35]	0.399	1.55 [1.08-2.23]	0.016	72.6 [67.2-78.0]
	40-59	807	526 (65.2)	281 (34.8)	1.01 [0.85-1.19]	0.951	1.16 [0.89-1.51]	0.263	68.6 [63.6-73.7]
	60-79	2,029	1,320 (65.1)	709 (34.9)	Ref	Ref	Ref	Ref	66.5 [61.8-71.2]
	<80	475	292 (61.5)	183 (38.5)	0.86 [0.70-1.05]	0.142	0.86 [0.62-1.18]	0.349	64.2 [57.9-70.4]
	Unknown	3	2 (66.7)	1 (33.3)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Allergies	Nil Known	3,207	2,127 (66.3)	1,080 (33.7)	Ref	Ref	Ref	Ref	67.7 [63.3-72.2]
	Not Documented	82	57 (69.5)	25 (30.5)	1.16 [0.72-1.86]	0.546	1.26 [0.55-2.87]	0.584	71.0 [59.2-82.7]
	Present (beta-lactam antibiotic)	448	242 (54.0)	206 (56.0)	0.60 [0.49-0.73]	<0.005	0.81 [0.59-1.11]	0.184	64.6 [58.5-70.8]
	Present (non beta-	140	86 (61.4)	54 (38.6)	0.81 [0.57-1.15]	0.232	1.01 [0.61-1.64]	0.983	67.8 [59.8-75.9]

	lactam antibiotic)								
	Present (non antibiotic)	101	62(61.4)	39 (38.6)	0.81 [0.54-1.21]	0.303	1.12 [0.62-2.01]	0.707	69.3 [60.3-78.4]
ASA score	1	759	482 (63.5)	277 (36.5)	Ref	Ref	Ref	Ref	67.2 [61.8-72.5]
	2	1,510	969 (64.2)	541 (35.8)	1.03 [0.86-1.23]	0.755	0.94 [0.71-1.24]	0.651	66.2 [61.5-70.9]
	3	1,043	674 (64.6)	369 (35.4)	1.05 [0.86-1.28]	0.626	1.16 [0.84-1.62]	0.368	69.3 [64.5-74.2]
	4	78	48 (61.5)	30 (38.5)	0.92 [0.57-1.49]	0.732	1.37 [0.66-2.85]	0.393	71.6 [61.8-81.4]
	Unknown/ Not applicable	588	401 (68.2)	187 (31.8)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	3,813	2,483 (65.1)	1,330 (34.9)	Ref	Ref	Ref	Ref	67.7 [63.4-72.1]
	Subsequent	165	91 (55.2)	74 (44.9)	0.66 [0.48-0.90]	0.009	0.67 [0.41-1.11]	0.120	61.7 [52.8-70.7]
Elective or Emergency	Elective	3,380	2,185 (64.6)	1,195 (35.4)	Ref	Ref	Ref	Ref	67.7 [63.3-72.2]
	Emergency	556	363 (65.3)	193 (34.7)	1.03 [0.85-1.24]	0.769	0.91 [0.58-1.43]	0.674	66.3 [59.1-73.5]
	Not Assessable	42	26 (61.9)	16 (38.1)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Trauma	No	3,469	2,230 (64.3)	1,239 (35.72)	Ref	Ref	Ref	Ref	67.0 [62.6-71.5]
	Yes	509	344 (67.6)	165 (32.4)	1.16 [0.95-1.41]	0.146	1.28 [0.81-2.00]	0.288	70.5 [63.7-77.3]
Removal or insertion of prosthetic material	No	1,198	702 (58.6)	496 (41.4)	Ref	Ref	Ref	Ref	59.9 [54.5-65.3]
	Yes	2,780	1,872 (67.3)	908 (32.7)	1.46 [1.27-1.67]	<0.005	2.09 [1.63-2.66]	<0.005	70.9 [66.6-75.3]
Wound category	Clean	3,624	2,336 (64.5)	1,288 (35.6)	Ref	Ref	Ref	Ref	67.6 [63.3-72.0]
	Clean-contaminated	57	28 (49.1)	29 (50.9)	0.53 [0.32-0.90]	0.018	0.53 [0.25-1.01]	0.098	57.9 [45.2-70.7]
	Contaminated /Dirty	57	38 (66.7)	19 (33.3)	1.10 [0.63-1.92]	0.730	1.26 [0.55-2.91]	0.584	70.9 [59.1-82.7]
	Unknown/Not Applicable	240	172 (71.7)	68 (28.3)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Orthopaedic procedure	Total knee joint replacement	1344	915 (68.1)	429 (31.9)	Ref	Ref	Ref	Ref	74.1 [69.5-78.7]
	Total hip joint replacement	880	571 (64.9)	309 (35.1)	0.87 [0.72-1.04]	0.118	0.76 [0.58-1.01]	0.059	70.6 [65.5-75.7]
	Knee surgery ^d	375	207 (55.2)	168 (44.8)	0.58 [0.46-0.73]	<0.005	0.26 [0.17-0.41]	<0.005	54.1 [46.9-61.4]
	Open reduction internal fixation (ORIF)	485	345 (71.1)	140 (28.9)	1.16 [0.92-1.45]	0.213	0.66 [0.41-1.05]	0.082	68.4 [61.8-75.1]
	Shoulder surgery	324	205 (63.3)	119 (36.7)	0.81 [0.63-1.04]	0.098	0.49 [0.32-0.74]	0.001	64.0 [57.1-70.8]
	Other ^e	264	152 (57.6)	112 (42.4)	0.64 [0.49-0.83]	0.001	0.30 [0.19-0.47]	<0.005	56.2 [48.5-63.8]
	Foot and ankle surgery	175	104 (59.4)	71 (40.6)	0.69 [0.50-0.95]	0.023	0.30 [0.18-0.49]	<0.005	56.2 [47.8-64.6]

	Hand surgery	62	36 (58.1)	26 (41.9)	0.65 [0.39-1.09]	0.102	0.32 [0.15-0.69]	0.004	57.2 [44.5-70.0]
	Fractures closed reduction	29	20 (69.0)	9 (31.0)	1.04 [0.47-2.31]	0.919	0.64 [0.19-2.13]	0.471	68.2 [51.0-85.3]
	Elbow surgery	40	19 (47.5)	21 (52.5)	0.42 [0.23-0.80]	0.008	0.73 [0.27-1.94]	0.525	69.9 [56.1-83.4]
Antimicrobial	Cefazolin	3,435	2,442 (71.1)	993 (28.9)	Ref	Ref	Ref	Ref	73.6 [69.2-78.1]
	Gentamicin	207	18 (8.7)	189 (91.3)	0.04 [0.02-0.06]	<0.005	0.02 [0.01-0.04]	<0.005	12.4 [6.1-18.7]
	Vancomycin	177	44 (24.9)	133 (75.1)	0.13 [0.09-0.19]	<0.005	0.09 [0.05-0.14]	<0.005	31.4 [22.4-40.4]
	Cefalothin	34	27 (79.4)	7 (20.6)	1.57 [0.68-3.61]	0.291	0.34 [0.08-1.39]	0.133	55.6 [30.0-81.3]
	Clindamycin	36	7 (19.4)	29 (80.6)	0.10 [0.04-0.22]	<0.005	0.05 [0.02-0.13]	<0.005	22.8 [8.4-37.3]
	Other (6-18) ^f	89	36 (40.4)	53 (59.6)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Ref= Reference group Exc= Excluded ^a Excluded from multivariate analysis due to collinearity. ^b Excluded from analysis due to low number of prescriptions and/or proportions ^c Excluded from analysis due to unknown/ not applicable status ^d Knee surgery excluding total knee joint replacements. ^e Other surgical procedures included the following subcategories: 'Other', 'Soft tissue surgery', 'Sacroccygeal tumour excision' and 'Osteomyelitis (removal of implants/joint washout)'. ^f Other antimicrobials= outside of the top five most frequently prescribed. ^g Model C Statistic= 0.8420									

Table S4 Appropriateness and Adjusted Appropriateness of assessable post-procedural prescriptions

POST-PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^g		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS		2,731	1,320 (48.3)	1,411 (51.7)					
HOSPITAL FACTORS									
Funding	Public	1,242	627 (50.5)	615 (49.5)	Ref	Ref	Excluded (Exc) ^a	Exc ^a	Exc ^a
	Private	1,489	693 (46.5)	796 (53.5)	0.85 [0.73-0.99]	0.040	Exc ^a	Exc ^a	Exc ^a
Peer group	Principal referral	326	145 (44.5)	181 (55.5)	0.66 [0.51-0.86]	0.002	0.65 [0.15-2.82]	0.565	43.5 [27.2-59.9]
	Public acute group A	783	429 (54.8)	354 (45.2)	Ref	Ref	Ref	Ref	49.6 [36.9-62.3]
	Public acute group B	62	28 (45.2)	34 (54.8)	0.68 [0.40-1.14]	0.145	1.17 [0.13-10.69]	0.889	51.8 [23.5-80.2]
	Public acute group C	66	23 (34.9)	43 (65.2)	0.44 [0.26-0.75]	0.002	0.17 [0.02-1.61]	0.122	26.3 [3.2-49.5]
	Private acute group A	123	52 (42.3)	71 (57.7)	0.60 [0.41-0.89]	0.010	0.37 [0.06-2.28]	0.285	35.9 [15.2-56.7]
	Private acute group B	625	162 (25.9)	463 (74.1)	0.29 [0.23-0.36]	<0.005	0.74 [0.16-3.49]	0.704	45.3 [27.6-63.1]
	Private acute group C	229	111 (48.5)	118 (51.5)	0.78 [0.58-1.04]	0.092	0.73 [0.15-3.746]	0.689	45.1 [27.2-63.0]
	Private acute group D	440	303 (68.9)	137 (31.1)	1.83 [1.43-2.33]	<0.005	14.49 [2.69-78.07]	0.002	81.6 [69.3-93.9]
	Other acute specialised	72	65 (90.3)	7 (9.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
	Childrens'	5	2 (40.0)	3 (60.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PATIENT FACTORS									
Gender	Male	1,275	634 (49.7)	641 (50.3)	Ref	Ref	Ref	Ref	52.3 [45.5-59.1]
	Female	1,421	662 (46.6)	759 (53.4)	0.88 [0.76-1.03]	0.103	0.97 [0.76-1.25]	0.844	51.9 [45.2-58.7]
	Unknown	35	24 (68.6)	11 (31.4)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Age	0-19	84	45 (53.6)	39 (46.4)	1.20 [0.77-1.86]	0.427	2.05 [0.94-4.46]	0.070	59.9 [48.8-71.0]
	20-39	242	110 (46.5)	132 (54.6)	0.86 [0.66-1.13]	0.290	1.41 [0.85-2.36]	0.187	55.1 [46.4-63.8]
	40-59	515	246 (47.8)	269 (52.2)	0.95 [0.78-1.16]	0.596	1.29 [0.92-1.80]	0.146	53.9 [46.5-61.2]
	60-79	1,529	751 (49.1)	778 (50.9)	Ref	Ref	Ref	Ref	50.6 [43.8-57.4]
	<80	359	167 (46.5)	192 (53.5)	0.90 [0.72-1.13]	0.375	1.12 [0.74-1.70]	0.587	52.1 [44.1-60.1]
	Unknown	2	1 (50.0)	1 (50.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Allergies	Nil Known	2,187	1,071 (49.0)	1,116 (51.0)	Ref	Ref	Ref	Ref	52.5 [45.8-59.1]
	Not Documented	47	24 (51.1)	23 (48.9)	1.09 [0.61-1.94]	0.777	1.33 [0.43-4.15]	0.625	56.2 [40.2-72.1]
	Present (beta-lactam antibiotic)	317	147 (46.4)	170 (53.6)	0.90 [0.71-1.14]	0.387	0.81 [0.54-1.23]	0.331	49.8 [41.5-58.0]
	Present (other antibiotics)	107	42 (39.3)	65 (60.7)	0.67 [0.45-1.00]	0.051	0.63 [0.35-1.15]	0.134	46.5 [36.6-56.3]

	Present (non-antibiotic)	73	36 (49.3)	37 (50.7)	1.01 [0.64-1.62]	0.954	1.30 [0.59-2.87]	0.508	52.5 [45.8-59.1]
ASA score	1	428	197 (46.0)	231 (54.0)	Ref	Ref	Ref	Ref	49.9 [42.1-57.6]
	2	1,077	546 (50.7)	531 (49.3)	1.21 [0.96-1.51]	0.102	1.22 [0.83-1.80]	0.310	52.5 [45.7-59.3]
	3	774	359 (46.4)	415 (53.6)	1.01 [0.80-1.29]	0.906	1.20 [0.78-1.86]	0.407	52.3 [45.3-59.3]
	4	55	26 (47.3)	29 (52.7)	1.05 [0.60-1.84]	0.862	1.81 [0.69-4.75]	0.226	57.6 [44.7-70.5]
	Unknown/ Not applicable	397	192 (48.4)	205 (51.6)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
PROCEDURAL FACTORS									
Surgery number for admission	Initial	2,641	1,299 (49.2)	1,342 (50.8)	Ref	Ref	Ref	Ref	52.3 [45.7-58.8]
	Subsequent	90	21 (23.3)	69 (76.7)	0.31 [0.19-0.52]	<0.005	0.57 [0.26-1.25]	0.161	44.9 [32.9-56.8]
Elective or emergency	Elective	2,317	1,139 (49.2)	1,178 (50.8)	Ref	Ref	Ref	Ref	51.2 [44.6-57.9]
	Emergency	384	169 (44.0)	215 (56.0)	0.81 [0.65-1.01]	0.062	1.52 [0.82-2.82]	0.179	56.7 [47.4-66.0]
	Not Assessable	30	12 (40.0)	18 (60.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Trauma	No	2,396	1,189 (49.6)	1,207 (50.4)	Ref	Ref	Ref	Ref	53.4 [46.8-60.1]
	Yes	335	131 (39.1)	204 (60.9)	0.65 [0.52-0.82]	<0.005	0.45 [0.24-0.83]	0.010	43.0 [33.6-52.4]
Removal or insertion of prosthetic material	No	684	341 (49.9)	343 (50.2)	Ref	Ref	Ref	Ref	50.3 [43.0 -57.6]
	Yes	2,047	979 (47.8)	1,068 (52.2)	0.92 [0.78-1.10]	0.358	1.20 [0.86-1.68]	0.284	52.7 [46.0-59.4]
Wound category	Clean	2,490	1,195 (48.0)	1,295 (52.0)	Ref	Ref	Ref	Ref	51.9 [45.4-58.5]
	Clean-contaminated	30	17 (56.74)	13 (43.3)	1.42 [0.69-2.93]	0.3470	1.57 [0.52-4.76]	0.429	57.8 [42.5-73.0]
	Contaminated/ Dirty	32	16 (50.0)	16 (50.0)	1.08 [0.54-2.18]	0.821	1.67 [0.40-6.93]	0.482	58.6 [39.6-77.5]
	Unknown/Not Applicable	179	92 (51.4)	87 (48.6)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
Surgical procedure group	Total knee joint replacement	1113	554 (49.8)	559 (50.2)	Ref	Ref	Ref	Ref	54.5 [47.4-61.6]
	Total hip joint replacement	710	378 (53.4)	332 (46.6)	1.15 [0.95-1.39]	0.149	0.77 [0.55-1.08]	0.125	51.0 [43.7-58.3]
	Knee surgery ^d	132	56 (42.4)	76 (57.6)	0.74 [0.52-1.07]	0.111	0.61 [0.31-1.21]	0.160	48.1 [38.1-58.1]
	Open reduction internal fixation	320	147 (45.9)	173 (54.1)	0.86 [0.67-1.10]	0.226	1.10 [0.60-2.03]	0.752	55.8 [46.9-64.7]
	Shoulder surgery	189	79 (41.8)	110 (58.2)	0.72 [0.53-0.99]	0.043	0.46 [0.26-0.81]	0.008	44.4 [35.3-53.4]
	Other ^e	119	50 (42.0)	69 (58.0)	0.73 [0.50-1.07]	0.109	0.47 [0.25-0.90]	0.024	44.7 [35.2-54.3]
	Foot and ankle surgery	91	39 (42.9)	52 (57.1)	0.76 [0.49-1.17]	0.206	0.58 [0.28-1.22]	0.153	47.4 [36.5-58.4]

	Hand surgery	26	7 (26.9)	19 (73.1)	0.37 [0.16-0.89]	0.027	0.34 [0.10-1.20]	0.095	40.7 [24.3-57.0]
	Fractures closed reduction	7	4 (57.1)	3 (42.9)	1.35 [0.30-6.04]	0.699	3.17 [0.23-43.78]	0.390	68.7 [38.9-95.6]
	Elbow surgery	24	6 (25.0)	18 (75.0)	0.34 [0.13-0.85]	0.022	0.95 [0.23-3.92]	0.947	53.9 [34.6-73.1]
Anti-microbials	1. Cefazolin	2,347	1,246 (53.1)	1,101 (46.9)	Ref	Ref	Ref	Ref	55.2 [48.4-61.9]
	2. Cefalexin	114	7 (6.1)	107 (93.9)	0.06 [0.03-0.12]	<0.005	0.04 [0.01-0.12]	<0.005	17.2 [6.6-27.8]
	3. Vancomycin	65	15 (23.1)	50 (76.9)	0.27 [0.15-0.47]	<0.005	0.19 [0.08-0.46]	<0.005	33.6 [21.6-45.65]
	4. Gentamicin	60	4 (6.7)	56 (93.3)	0.06 [0.02-0.17]	<0.005	0.10 [0.03-0.33]	<0.005	27.4 [13.0-41.7]
	5. Cefalothin	37	21 (56.8)	16 (43.2)	1.16 [0.60-2.23]	0.658	0.82 [0.17-3.87]	0.801	55.2 [33.7-76.6]
	Others (6-24) ^f	108	27 (25.0)	81 (75.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Ref= Reference group Exc= Excluded ^a Excluded from multivariate analysis due to collinearity. ^b Excluded from analysis due to low number of prescriptions and/or proportions ^c Excluded from analysis due to unknown/ not applicable status ^d Knee surgery excluding total knee joint replacements. ^e Other surgical procedures included the following subcategories: 'Other', 'Soft tissue surgery', 'Sacroccygeal tumour excision' and 'Osteomyelitis (removal of implants/joint washout)'. ^f Other antimicrobials= outside of the top five most frequently prescribed. ^g Model C Statistic= 0.8933									

Table S5 Sub analysis 1: Appropriateness and adjusted appropriateness of assessable procedural doses for knee surgical procedures

PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^e		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTAL (n)		1719	1122 (65.3)	597 (34.7)	1292		1292		1292
HOSPITAL FACTORS									
Peer group	Principal referral	153	86 (56.2)	67 (43.8)	0.62 [0.42-0.91]	0.016	0.60 [0.20-1.83]	0.374	59.9 [46.8-72.9]
	Public acute group A	371	250 (67.4)	121 (32.6)	Ref	Ref	Ref	Ref	67.0 [57.9-76.2]
	Public acute group B	33	29 (87.9)	4 (12.1)	3.51 [1.21-10.21]	0.021	2.78 [0.36-21.20]	0.324	79.3 [59.7-98.9]
	Public acute group C	51	31 (60.8)	20 (39.2)	0.75 [0.41-1.37]	0.350	1.01 [0.25-4.08]	0.986	67.2 [50.5-83.9]
	Private acute group A	63	49 (77.8)	14 (22.2)	1.69 [0.90-3.19]	0.102	2.30 [0.49-10.85]	0.293	77.3 [62.0-92.5]
	Private acute group B	484	280 (57.9)	204 (42.1)	0.66 [0.51-0.88]	0.005	0.62 [0.21-1.80]	0.378	60.2 [47.9-72.4]
	Private acute group C	137	98 (71.5)	39 (28.5)	1.22 [0.79-1.87]	0.372	2.07 [0.62-6.89]	0.237	76.1 [65.0-87.2]
	Private acute group D	378	256 (67.7)	122 (32.3)	1.02 [0.75-1.38]	0.921	1.96 [0.64-5.96]	0.236	75.5 [65.4-85.6]
	Other acute specialised	45	43 (95.6)	2 (4.4)	Excluded (exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
	Childrens'	4	0 (0.0)	4 (100.0)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	827	542 (65.5)	285 (34.5)	Ref	Ref	Ref	Ref	69.1 [63.7-74.4]
	Female	877	566 (64.5)	311 (35.5)	0.96 [0.78-1.17]	0.665	0.85 [0.62-1.16]	0.306	66.7 [61.4-72.4]
	Unknown	15	14 (93.3)	1 (6.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	62	39 (62.9)	23 (37.1)	0.84 [0.50-1.44]	0.532	1.48 [0.52-4.23]	0.464	71.5 [58.9-84.2]
	20-39	163	109 (66.9)	54 (33.1)	1.00 [0.71-1.43]	0.978	2.42 [1.14-5.13]	0.021	77.2 [69.4-85.0]
	40-59	305	186 (61.0)	119 (39.0)	0.78 [0.60-1.01]	0.063	1.17 [0.75-1.83]	0.476	68.6 [62.1-75.1]
	60-79	1026	685 (66.8)	341 (33.2)	Ref	Ref	Ref	Ref	66.5 [60.9-72.1]
	<80	161	102(63.4)	59 (36.6)	0.86 [0.61-1.22]	0.395	0.77 [0.45-1.32]	0.340	62.9 [54.2-71.6]
	Unknown	2	1 (50.0)	1 (50.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Allergies	Nil Known	1404	938 (66.8)	466 (33.2)	Ref	Ref	Ref	Ref	68.2 [63.1-73.3]
	Not Documented	35	27 (77.1)	8 (22.9)	1.68 [0.76-3.72]	0.204	3.72 [0.87-15.90]	0.076	82.7 [69.6-95.9]
	Present (beta-lactam antibiotic)	185	100 (54.1)	85 (45.9)	0.58 [0.43-0.80]	0.001	0.72 [0.44-1.17]	0.179	63.6 [55.6-71.7]
	Present (non beta-lactam antibiotic)	41	25 (61.0)	16 (39.0)	0.78 [0.41-1.47]	0.436	1.28 [0.50-3.29]	0.608	71.4 [59.2- 83.5]
	Present (non antibiotic)	54	32 (59.3)	22 (40.7)	0.72 [0.42-1.26]	0.250	0.86 [0.40-1.87]	0.711	66.2 [54.9-77.6]
ASA score	1	270	162 (23.0)	108 (76.0)	Ref	Ref	Ref	Ref	66.3 [58.6-73.9]

	2	688	460 (66.9)	228 (33.1)	1.35 [1.01-1.80]	0.046	1.15 [0.69-1.93]	0.591	68.2 [62.8-73.6]
	3	465	309 (66.5)	156 (33.5)	1.32 [0.97-1.80]	0.079	1.21 [0.69-2.14]	0.511	68.8 [62.9-74.7]
	4	16	10 (62.5)	6 (37.5)	1.11 [0.39-3.15]	0.843	0.80 [0.18-3.55]	0.769	63.2 [42.8-83.6]
	Unknown/ Not applicable	280	181 (64.6)	99 (35.4)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	1667	1092 (65.5)	575 (34.5)	Ref	Ref	Ref	Ref	67.9 [62.9-72.9]
	Subsequent	52	30 (57.7)	22 (42.3)	0.72 [0.41-1.26]	0.246	1.13 [0.40-3.22]	0.816	69.5 [55.5-83.5]
Elective or Emergency	Elective	1664	1094 (65.7)	570 (34.3)	Ref	Ref	Ref	Ref	67.9 [62.9-72.9]
	Emergency	35	19 (54.3)	16 (45.7)	0.62 [0.32-1.21]	0.162	1.39 [0.31-6.14]	0.665	72.1 [53.6-90.5]
	Not Assessable	20	9 (45.0)	11 (55.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	1692	1109 (65.5)	583 (34.5)	Ref	Ref	Ref	Ref	68.1 [63.1-73.1]
	Yes	27	13 (48.1)	14 (51.9)	0.49 [0.23-1.05]	0.065	0.49 [0.13-1.88]	0.297	57.9 [37.0-78.8]
Removal or insertion of prosthetic material	No	479	261 (54.5)	218 (45.5)	Ref	Ref	Ref	Ref	61.5 [54.5-68.5]
	Yes	1240	861 (69.4)	379 (30.6)	1.90 [1.53-2.36]	<0.001	1.96 [1.26-3.06]	0.003	70.8 [65.5-76.0]
Wound category	Clean	1605	1041 (64.9)	564 (35.1)	Ref	Ref	Ref	Ref	68.1 [63.1-73.1]
	Clean-contaminated	12	5 (41.7)	7 (58.2)	0.39 [0.12-1.22]	0.106	0.30 [0.04-2.09]	0.222	50.3 [19.6-80.9]
	Contaminated /Dirty	8	3 (37.5)	5 (62.5)	0.33 [0.08-1.37]	0.125	0.64 [0.07-5.95]	0.698	62.0 [30.0-94.0]
	Unknown/Not Applicable	94	73 (77.7)	21 (22.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic knee surgical procedure	Primary total knee joint replacement	1249	861 (68.9)	388 (31.1)	Ref	Ref	Ref	Ref	72.5 [67.3-77.8]
	Revision total knee joint replacement	95	54 (56.8)	41 (43.2)	0.59 [0.39-0.91]	0.016	0.92 [0.41-2.06]	0.832	71.4 [60.5-82.4]
	Knee arthroscopy - diagnostic	52	20 (38.5)	32 (61.5)	0.28 [0.16-0.50]	<0.001	0.10 [0.03-0.27]	<0.001	36.7 [21.1-52.3]
	Knee arthroscopy-therapeutic	191	83 (43.5)	108 (56.5)	0.35 [0.25-0.47]	<0.001	0.15 [0.07-0.30]	<0.001	43.6 [32.6-54.6]
	Knee - ligament	119	94 (79.0)	25 (21.0)	1.69 [1.07-2.68]	0.024	1.08 [0.42-2.78]	0.867	73.5 [62.5-84.6]
	Knee - osteotomy	13	10 (76.9)	3 (23.1)	1.50 [0.41-5.49]	0.538	0.75 [0.11-4.99]	0.767	68.8 [43.6-94.1]
Antimicrobial	Cefazolin	1449	1053 (72.7)	396 (26.3)	Ref	Ref	Ref	Ref	75.2 [70.0-80.4]
	Gentamicin	120	13 (10.8)	107 (89.2)	0.05 [0.03-0.08]	<0.001	0.02 [0.01-0.05]	<0.001	16.5 [7.4-25.5]
	Vancomycin	93	25 (26.9)	68 (74.1)	0.14 [0.09-0.22]	<0.001	0.09 [0.04-0.17]	<0.001	35.6 [23.3-47.9]
	Cefalothin	28	26 (92.9)	2 (7.1)	4.89 [1.16-20.69]	0.031	1.23 [0.10-15.25]	0.871	77.8 [Not estimable ^c]

Clindamycin	11	1 (9.1)	10 (90.9)	0.04 [0.004-0.29]	0.002	0.02 [0.002-0.19]	0.001	15.7 [Not estimable ^c]
Other (7) ^d	18	4 (22.2)	14 (77.8)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from analysis due to unknown/ not applicable status

^c Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions

^d Other antimicrobials= seven other antimicrobials prescribed (n=<5)

^e Model C Statistic= 0.8765

Table S6 Sub analysis 2: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for knee surgical procedures

POST-PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^f		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS		1245	610 (49.0)	635 (51.0)	877		877		877
HOSPITAL FACTORS									
Peer group	Principal referral	96	42 (43.8)	54 (56.2)	0.49 [0.31-0.79]	0.003	0.61 [0.09-4.16]	0.615	48.8 [27.9-69.7]
	Public acute group A	288	176 (61.1)	112 (38.9)	Ref	Ref	Ref	Ref	55.3 [40.8-69.8]
	Public acute group B	16	10 (62.5)	6 (37.5)	1.06 [0.38-3.00]	0.912	0.68 [0.03-16.90]	0.813	50.2 [10.0-90.3]
	Public acute group C	29	7 (24.1)	22 (75.9)	0.20 [0.08-0.49]	<0.001	0.10 [0.01-1.46]	0.093	27.0 [1.9-52.1]
	Private acute group A	42	21 (50.0)	21 (50.0)	0.63 [0.33-1.22]	0.173	0.50 [0.05-4.72]	0.548	46.2 [20.3-72.1]
	Private acute group B	405	95 (23.5)	310 (76.5)	0.20 [0.14-0.27]	<0.001	0.29 [0.05-1.83]	0.188	38.9 [20.2-57.7]
	Private acute group C	129	75 (58.1)	54 (41.9)	0.88 [0.58-1.35]	0.567	0.68 [0.10-4.67]	0.697	50.3 [29.5-71.0]
	Private acute group D	201	151 (75.1)	50 (24.9)	1.92 [1.29-2.86]	0.001	16.82 [2.04-139.05]	0.009	84.6 [71.9-97.3]
	Other acute specialised	37	33 (89.2)	4 (10.8)	Excluded (Exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
	Childrens'	2	0 (0.0) (89.2)	2 (100.0)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	574	280 (48.8)	294 (51.2)	Ref	Ref	Ref	Ref	54.5 [46.0-62.9]
	Female	662	322 (48.6)	340 (51.4)	0.99 [0.80-1.24]	0.961	0.78 [0.52-1.19]	0.253	51.5 [43.3-59.8]
	Unknown	9	8 (88.9)	1 (11.1)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	31	15 (48.4)	16 (51.6)	0.95 [0.46-1.94]	0.881	0.88 [0.17-4.56]	0.880	50.8 [30.5-71.1]
	20-39	71	30 (42.3)	41 (57.7)	0.74 [0.45-1.21]	0.226	0.81 [0.21-3.07]	0.758	49.8 [33.4-66.2]
	40-59	203	96 (47.3)	107 (52.7)	0.91 [0.67-1.23]	0.529	1.19 [0.68-2.07]	0.548	54.4 [44.8-64.0]
	60-79	824	410 (49.8)	414 (50.2)	Ref	Ref	Ref	Ref	52.3 [44.1-60.6]
	<80	115	58 (50.4)	57 (49.6)	1.03 [0.70-1.52]	0.892	1.36 [0.68-2.74]	0.383	56.1 [45.1-67.0]
	Unknown	1	1 (100.0)	0 (0.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Allergies	Nil Known	1003	494 (49.3)	509 (50.7)	Ref	Ref	Ref	Ref	52.7 [44.6-60.7]
	Not Documented	24	13 (54.2)	11 (45.8)	1.22 [0.54-2.74]	0.635	1.07 [0.19-6.00]	0.935	53.5 [31.5-75.6]
	Present (beta-lactam antibiotic)	142	71 (50.0)	71 (50.0)	1.03 [0.73-1.46]	0.868	1.00 [0.52-1.93]	0.995	52.7 [42.2-63.2]
	Present (non beta-lactam antibiotic)	34	14 (41.2)	20 (58.8)	0.72 [0.36-1.44]	0.356	1.03 [0.37-2.89]	0.958	53.0 [38.7-67.3]
	Present (non antibiotic)	42	18 (42.9)	24 (57.1)	0.77 [0.41-1.44]	0.418	1.37 [0.51-3.72]	0.536	56.5 [42.4-70.5]
ASA score	1	152	63 (41.4)	89 (58.6)	Ref	Ref	Ref	Ref	44.9 [34.0-55.8]

	2	521	273 (52.4)	248 (47.6)	1.56 [1.08-2.24]	0.018	2.38 [1.10-5.16]	0.027	55.3 [47.0-63.7]
	3	357	170 (47.6)	187 (52.4)	1.28 [0.87-1.89]	0.201	1.78 [0.78-4.07]	0.173	51.8 [43.1-60.5]
	4	12	9 (75.0)	3 (25.0)	4.24 [1.1-16.28]	0.035	7.22 [0.78-67.03]	0.082	68.0 [44.6-91.4]
	Unknown/ Not applicable	203	95 (46.8)	108 (53.2)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	1203	605 (50.3)	598 (49.7)	Ref	Ref	Ref	Ref	53.4 [45.4-61.4]
	Subsequent	42	5 (11.9)	37 (88.1)	0.13 [0.05-0.34]	<0.001	0.16 [0.03-0-.85]	0.032	32.5 [4.1-50.9]
Elective or Emergency	Elective	1207	597 (49.5)	610 (50.5)	Ref	Ref	Ref	Ref	52.9 [44.9-60.8]
	Emergency	24	11 (45.8)	13 (54.2)	0.86 [0.38-1.95]	0.725	0.90 [0.11-7.33]	0.923	51.6 [25.5-77.8]
	Not Assessable	14	2 (14.3)	12 (85.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	1227	605 (49.3)	622 (50.7)	Ref	Ref	Ref	Ref	53.1 [45.1-61.1]
	Yes	18	5 (27.8)	13 (72.2)	0.40 [0.14-1.12]	0.080	0.22 [0.03-1.63]	0.140	35.6 [13.4-57.9]
Removal or insertion of prosthetic material	No	264	130 (49.2)	134 (50.8)	Ref	Ref	Ref	Ref	51.6 [41.9-61.3]
	Yes	981	480 (48.9)	501 (51.1)	0.99 [0.75-1.30]	0.928	1.15 [0.62-2.11]	0.662	53.2 [45.1-61.4]
Wound category	Clean	1157	567 (49.0)	590 (51.0)	Ref	Ref	Ref	Ref	52.8 [44.8-60.8]
	Clean-contaminated	6	4 (66.7)	2 (33.3)	2.08 [0.38-11.41]	0.398	1.76 [0.07-43.95]	0.731	59.5 [21.7-97.3]
	Contaminated /Dirty	2	1 (50.0)	1 (50.0)	1.04 [0.06-16.68]	0.978	Exc ^c	Exc ^c	Exc ^c
	Unknown/Not Applicable	80	38 (47.5)	42 (52.5)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic knee surgical procedure	Primary total knee joint replacement	1045	529 (50.6)	516 (49.4)	Ref	Ref	Ref	Ref	51.8 [43.6-60.0]
	Revision total knee joint replacement	68	25 (36.8)	43 (63.2)	0.57 [0.34-0.94]	0.029	2.58 [0.75-8.84]	0.133	63.0 [47.6-78.4]
	Knee arthroscopy-diagnostic	5	1 (20.0)	4 (80.0)	0.24 [0.03-2.19]	0.208	0.14 [<0.01-4.37]	0.261	29.5 [Not estimable ^d]
	Knee arthroscopy-therapeutic	48	19 (39.6)	29 (60.4)	0.64 [0.35-1.15]	0.138	1.00 [0.25-4.02]	0.997	51.8 [34.6-69.1]
	Knee- ligament	69	29 (42.0)	40 (58.0)	0.71 [0.43-1.16]	0.169	2.55 [0.55-11.78]	0.231	62.9 [45.5-80.2]
	Knee - osteotomy	10	7 (70.0)	3 (30.0)	2.28 [0.59-8.85]	0.235	0.90 [0.11-7.14]	0.922	50.6 [25.5-75.6]
Antimicrobial	Cefazolin	1090	578 (57.3)	512 (42.6)	Ref	Ref	Ref	Ref	55.5 [47.4-63.7]
	Cefalexin	25	0 (0.0)	25 (100.0)	0.07 [0.02-0.28]	<0.001	0.02 [<0.01-0.27]	0.004	13.6 [Not estimable ^d]
	Vancomycin	34	5 (14.7)	29 (85.3)	0.15 [0.06-0.40]	<0.001	0.06 [0.01-0.30]	0.001	23.9 [7.6-40.2]
	Gentamicin	29	2 (6.9)	27 (93.1)	1.59 [0.73-3.49]	0.242	1.16 [0.14-9.56]	0.889	57.3 [31.0-83.7]

	Cefalothin	28	18 (64.3)	10 (35.7)	0.09 [0.01-0.69]	0.021	0.05 [<0.01-0.66]	0.023	22.3 [Not estimable ^d]
	Other (12) ^e	39	7 (17.9)	32 (82.1)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group
 Exc= Excluded
^a Excluded from analysis due to low number of prescriptions and/or proportions
^b Excluded from analysis due to unknown/ not applicable status
^c Removed from model due to successful predictions for perfect or failure
^d Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions
^e Other antimicrobials= twelve other antimicrobials prescribed (n=<11)
^f Model C Statistic= 0.9181

Table S7 Sub analysis 3: Appropriateness and adjusted appropriateness of assessable procedural doses for hip surgical procedures

PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^f		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS		880	571 (64.9)	309 (35.1)	673		673		673
HOSPITAL FACTORS									
Peer group	Principal referral	91	70 (76.9)	21 (23.1)	1.73 [1.00-2.99]	0.049	2.69 [0.62-11.6]	0.186	61.6 [49.8-73.3]
	Public acute group A	278	183 (65.8)	95 (34.2)	Ref	Ref	Ref	Ref	73.8 [60.9-86.7]
	Public acute group B	21	16 (76.2)	5 (23.8)	1.66 [0.59-4.67]	0.336	1.02 [0.13-8.05]	0.986	61.8 [35.6-88.0]
	Public acute group C	36	27 (75.0)	9 (25.0)	1.56 [0.70-3.45]	0.274	2.48 [0.28-21.76]	0.413	72.9 [51.0-94.8]
	Private acute group A	56	33 (58.9)	23 (41.1)	0.75 [0.41-1.34]	0.325	2.32 [0.36-14.84]	0.375	72.2 [53.4-90.9]
	Private acute group B	168	85 (50.6)	83 (49.4)	0.53 [0.36-0.79]	0.002	0.78 [0.19-3.30]	0.737	58.1 [41.1-75.0]
	Private acute group C	40	25 (62.5)	15 (37.5)	0.87 [0.44-1.72]	0.679	2.25 [0.37-13.50]	0.376	71.8 [54.2-89.4]
	Private acute group D	182	124 (68.1)	58 (31.9)	1.11 [0.75-1.65]	0.608	3.48 [0.71-16.92]	0.123	76.4 [63.6-89.3]
	Other acute specialised	8	8 (100.0)	0 (0.0)	Excluded (Exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	356	248 (69.7)	108 (30.7)	Ref	Ref	Ref	Ref	69.7 [63.0-76.3]
	Female	494	307 (62.1)	187 (37.9)	0.71 [0.53-0.96]	0.023	0.70 [0.44-1.12]	0.142	65.4 [58.8-71.9]
	Unknown	30	16 (53.3)	14 (46.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	6	5 (83.3)	1 (16.7)	2.73 [0.32-23.56]	0.360	2.96 [0.18-49.18]	0.449	78.5 [Not estimable ^d]
	20-39	11	9 (81.8)	2 (18.2)	2.46 [0.53-11.50]	0.252	4.23 [0.31-57.18]	0.277	81.6 [Not estimable ^d]
	40-59	133	94 (70.7)	39 (29.3)	1.32 [0.87-1.99]	0.189	1.35 [0.69-2.64]	0.374	70.4 [61.6-79.3]
	60-79	563	364 (64.7)	199 (35.3)	Ref	Ref	Ref	Ref	66.8 [60.4-73.1]
	<80	167	99 (59.3)	68 (40.7)	0.80 [0.56-1.13]	0.206	0.82 [0.45-1.50]	0.511	64.2 [55.3-73.0]
Allergies	Nil Known	678	458 (67.6)	220 (32.4)	Ref	Ref	Ref	Ref	68.1 [62.0-74.3]
	Not Documented	14	9 (64.3)	5 (35.7)	0.86 [0.29-2.61]	0.796	0.74 [0.08-6.59]	0.793	64.4 [36.0-92.9]
	Present (beta-lactam antibiotic)	112	59 (52.7)	53 (46.3)	0.53 [0.36-0.80]	0.002	0.69 [0.33-1.45]	0.330	63.4 [53.0-73.9]
	Present (non beta-lactam antibiotic)	52	31 (59.6)	21 (40.4)	0.71 [0.40-1.26]	0.243	0.72 [0.31-1.69]	0.449	63.9 [51.8-76.1]
	Present (non antibiotic)	24	14 (58.3)	10 (41.7)	0.67 [0.29-1.54]	0.347	0.84 [0.24-2.98]	0.792	66.0 [49.4-82.6]
ASA score	1	71	47 (66.2)	24 (33.8)	Ref	Ref	Ref	Ref	67.9 [56.6-79.1]
	2	355	228 (64.2)	127 (35.8)	0.92 [0.54-1.57]	0.751	0.82 [0.34-1.96]	0.652	65.4 [58.6-72.2]
	3	305	197 (64.6)	108 (35.4)	0.93 [0.54-1.61]	0.798	1.07 [0.43-2.65]	0.892	68.6 [61.9-75.4]

	4	24	15 (62.5)	9 (37.5)	0.85 [0.33-2.23]	0.742	1.49 [0.26-8.37]	0.653	72.5 [55.6-89.3]
	Unknown/Not applicable	125	84 (67.2)	41 (32.8)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	844	552 (65.4)	292 (34.6)	Ref	Ref	Ref	Ref	67.2 [61.3-73.2]
	Subsequent	36	19 (52.8)	17 (47.2)	0.59 [0.30-1.15]	0.124	0.80 [0.18-3.59]	0.766	64.3 [44.3-84.4]
Elective or Emergency	Elective	791	509 (64.3)	282 (35.7)	Ref	Ref	Ref	Ref	67.6 [61.5-73.8]
	Emergency	82	56 (68.3)	26 (31.7)	1.19 [0.73-1.94]	0.477	0.69 [0.19-2.49]	0.575	62.9 [46.5-79.3]
	Not Assessable	7	6 (85.7)	1 (14.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	821	529 (64.4)	292 (35.6)	Ref	Ref	Ref	Ref	66.7 [60.6-72.9]
	Yes	59	42 (71.2)	17 (28.8)	1.36 [0.76-2.44]	0.296	1.51 [0.38-6.04]	0.563	71.6 [56.2-86.9]
Removal or insertion of prosthetic material	No	158	116 (73.4)	43 (26.4)	ref	Ref	Ref	Ref	69.8 [61.0-78.6]
	Yes	722	456 (63.2)	266 (36.8)	0.64 [0.44-0.94]	0.022	0.77 [0.38-1.53]	0.449	66.6 [60.4-72.8]
Wound category	Clean	828	532 (64.3)	296 (35.7)	Ref	Ref	Ref	Ref	67.1 [61.2-73.1]
	Clean-contaminated	3	3 (100.0)	0 (0.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Contaminated /Dirty	1	0 (0.0)	1 (100.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Unknown/Not Applicable	48	36 (75.0)	12 (25.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic hip surgical procedure	Primary total hip joint replacement	793	517 (65.2)	276 (34.8)	Ref	Ref	Ref	Ref	66.5 [60.4-72.6]
	Revision total hip joint replacement	87	54 (62.1)	33 (37.9)	0.87 [0.55-1.38]	0.562	1.76 [0.61-5.08]	0.298	73.0 [61.6-84.5]
Antimicrobial	Cefazolin	727	550 (75.7)	177 (24.3)	Ref	Ref	Ref	Ref	76.3 [69.9-82.8]
	Gentamicin	75	3 (4.0)	72 (96.0)	0.13 [<0.01-0.04]	<0.001	0.01 [<0.01-0.03]	<0.001	8.5 [Not estimable ^d]
	Vancomycin	51	9 (17.6)	42 (82.4)	0.07 [0.03-0.14]	<0.001	0.05 [0.01-0.14]	<0.001	27.7 [10.5-44.9]
	Cefalothin	1	0 (0.0)	1 (100.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Clindamycin	7	4 (57.1)	3 (42.9)	0.43 [0.10-1.93]	0.271	0.39 [0.04-4.21]	0.434	62.3 [Not estimable ^d]
	Other (6) ^e	19	5 (26.3)	14 (74.7)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from analysis due to unknown/ not applicable status

^c Removed from model due to successful predictions for perfect or failure

^d Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions

^e Other antimicrobials= six other antimicrobials prescribed (n=<9).

^f Model C Statistic= 0.8999

Table S8 Sub analysis 4: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for hip surgical procedures

POST-PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS		710	378 (53.2)	332 (46.8)	528		528		528
HOSPITAL FACTORS									
Peer group	Principal referral	73	34 (46.6)	39 (55.4)	0.43 [0.25-0.74]	0.002	1.05 [0.16-7.01]	0.957	57.5 [42.0-73.0]
	Public acute group A	224	150 (67.0)	74 (33.0)	Ref	Ref	Ref	Ref	58.2 [37.1-79.3]
	Public acute group B	17	10 (58.8)	7 (41.2)	0.70 [0.26-1.93]	0.495	0.74 [0.05-11.81]	0.832	53.3 [17.4-89.2]
	Public acute group C	35	16 (45.7)	19 (54.3)	0.42 [0.20-0.85]	0.017	0.13 [0.01-2.01]	0.144	29.6 [Not estimable ^d]
	Private acute group A	40	15 (37.5)	25 (62.5)	0.30 [0.15-0.59]	0.001	0.01 [<0.001-0.36]	0.010	9.3 [Not estimable ^d]
	Private acute group B	131	39 (29.8)	92 (70.2)	0.21 [0.13-0.33]	<0.001	0.28 [0.04-1.90]	0.192	39.5 [18.0-60.9]
	Private acute group C	42	21 (50.0)	21 (50.0)	0.49 [0.25-0.96]	0.038	0.22 [0.02-2.21]	0.198	36.3 [10.0-62.6]
	Private acute group D	141	86 (61.0)	55 (39.0)	0.77 [0.50-1.20]	0.246	3.26 [0.42-25.32]	0.258	72.6 [53.5-91.6]
	Other acute specialised	7	7 (100.0)	0 (0.0)	Excluded (Exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	285	172 (60.4)	113 (39.6)	Ref	Ref	Ref	Ref	51.8 [42.5-61.1]
	Female	402	191 (47.5)	211 (52.5)	0.59 [0.44-0.81]	0.001	1.11 [0.64-1.92]	0.722	53.1 [44.4-61.8]
	Unknown	23	15 (65.2)	8 (34.8)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	7	7 (100.0)	0 (0.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	20-39	8	4 (50.0)	4 (50.0)	0.94 [0.23-3.80]	0.930	0.56 [0.06-5.21]	0.610	44.7 [15.0-74.4]
	40-59	112	65 (58.0)	47 (42.0)	1.30 [0.85-1.98]	0.221	1.25 [0.60-2.62]	0.548	55.2 [43.7-66.6]
	60-79	446	230 (51.6)	216 (48.4)	Ref	Ref	Ref	Ref	52.2 [43.6-60.9]
	<80	137	72 (52.6)	65 (47.4)	1.04 [0.71-1.53]	0.840	0.97 [0.47-2.02]	0.938	51.9 [40.8-63.0]
Allergies	Nil Known	545	293 (53.8)	252 (46.4)	Ref	Ref	Ref	Ref	51.7 [43.3-60.2]
	Not Documented	11	5 (45.5)	6 (54.5)	0.72 [0.22-2.38]	0.586	1.27 [0.09-18.6]	0.861	54.9 [19.6-90.2]
	Present (beta-lactam antibiotic)	96	51 (53.1)	45 (46.9)	0.97 [0.63-1.51]	0.908	1.75 [0.72-4.25]	0.215	59.0 [46.5-71.4]
	Present (non beta-lactam antibiotic)	43	18 (41.9)	25 (58.1)	0.62 [0.33-1.16]	0.135	0.58 [0.21-1.60]	0.289	44.5 [29.7-59.3]
	Present (non antibiotic)	15	11 (73.3)	4 (26.7)	2.37 [0.74-7.52]	0.145	3.47 [0.41-28.97]	0.251	67.2 [42.6-91.9]
ASA score	1	58	33 (56.9)	25 (43.1)	Ref	Ref	Ref	Ref	52.3 [0.38-66.6]
	2	290	157 (54.1)	133 (45.9)	0.89 [0.51-1.58]	0.700	0.92 [0.33-2.54]	0.867	51.1 [42.1-60.1]
	3	245	126 (51.4)	119 (48.6)	0.80 [0.45-1.43]	0.454	1.13 [0.39-3.29]	0.829	53.8 [44.4-63.2]

	4	18	9 (50.0)	9 (50.0)	0.76 [0.26-2.19]	0.608	2.09 [0.25-17.66]	0.498	61.7 [37.3-86.1]
	Unknown/Not applicable	99	53 (53.5)	46 (46.5)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	691	371 (53.7)	320 (46.3)	Ref	Ref	Ref	Ref	52.4 [44.2-60.7]
	Subsequent	19	7 (36.8)	12 (63.2)	0.50 [0.20-1.29]	0.154	1.72 [0.18-16.42]	0.637	59.4 [30.4-88.5]
Elective or Emergency	Elective	644	343 (53.3)	301 (46.7)	Ref	Ref	Ref	Ref	52.7 [44.2-61.3]
	Emergency	59	30 (50.8)	29 (49.2)	0.91 [0.53-1.55]	0.722	0.89 [0.15-5.32]	0.902	51.3 [28.8-73.7]
	Not Assessable	7	5 (71.4)	2 (28.6)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	668	358 (53.6)	310 (46.4)	Ref	Ref	Ref	Ref	53.1 [44.8-61.4]
	Yes	42	20 (47.6)	22 (52.4)	0.79 [0.42-1.47]	0.453	0.57 [0.08-3.90]	0.568	45.8 [20.8-70.8]
Removal or insertion of prosthetic material	No	132	92 (69.7)	40 (30.0)	Ref	Ref	Ref	Ref	60.1 [49.0-71.3]
	Yes	578	286 (49.5)	292 (50.5)	0.43 [0.28-0.64]	<0.001	0.48 [0.23-1.04]	0.063	50.8 [42.2-59.3]
Wound category	Clean	661	348 (52.6)	313 (47.4)	Ref	Ref	Ref	Ref	52.6 [44.4-60.8]
	Clean-contaminated	1	1 (100.0)	0 (0.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Contaminated /Dirty	1	1 (100.0)	0 (0.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Unknown/Not Applicable	47	28 (59.6)	19 (40.4)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic hip surgical procedure	Primary total hip joint replacement	660	356 (53.9)	304 (46.1)	Ref	Ref	Ref	Ref	52.6 [44.3-60.9]
	Revision total hip joint replacement	50	22 (44.0)	28 (56.0)	0.67 [0.38-1.20]	0.177	0.94 [0.24-3.63]	0.932	51.9 [33.4-70.3]
Antimicrobial	Cefazolin	634	364 (57.4)	270 (42.6)	Ref	Ref	Ref	Ref	55.4 [47.1-63.7]
	Cefalexin	3	1 (33.3)	2 (66.7)	0.05 [0.01-0.22]	<0.001	0.10 [0.02-0.52]	0.006	26.4 [6.6-46.2]
	Vancomycin	17	3 (17.6)	14 (82.4)	0.16 [0.05-0.56]	0.004	0.06 [0.01-0.45]	0.006	21.2 [1.1-41.4]
	Gentamicin	30	2 (6.7)	28 (93.3)	0.49 [0.08-2.98]	0.442	1.12 [0.05-25.72]	0.944	56.9 [15.7-98.1]
	Cefalothin	5	2 (40.0)	3 (60.0)	0.19 [0.02-1.67]	0.21	0.03 [<0.01-0.55]	0.019	13.9 [Not estimable ^d]
	Other (8) ^e	21	6 (28.6)	15 (71.4)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from analysis due to unknown/ not applicable status.

^c Removed from model due to successful predictions for perfect or failure

^d Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions

^e Other antimicrobials= eight other antimicrobials prescribed (n=<5)

^f Model C Statistic= 0.9252

Table S9 Sub analysis 5: Appropriateness and adjusted appropriateness of assessable procedural doses for open reduction internal fixation (ORIF) surgical procedures

PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^h		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTAL (n)		485	345 (71.1)	140 (28.9)	351		351		351
HOSPITAL FACTORS									
Peer group	Principal referral	146	110 (75.3)	36 (24.7)	1.46 [0.91-2.33]	0.116	1.91 [0.69-5.30]	0.216	69.0 [58.4-79.6]
	Public acute group A	223	151 (67.7)	72 (32.3)	Ref	Ref	Ref	Ref	78.2 [68.6-87.9]
	Public acute group B	31	20 (64.5)	11 (35.5)	0.87 [0.39-1.91]	0.722	0.50 [0.10-4.47]	0.395	57.0 [30.9-83.0]
	Public acute group C	1	0	1 (100.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Private acute group A	16	13 (81.3)	3 (18.8)	2.07 [0.57-7.48]	0.269	2.94 [0.21-40.41]	0.420	83.2 [Not estimable ^d]
	Private acute group B	11	2 (18.2)	9 (81.8)	0.11 [0.02-0.50]	0.005	0.06 [0.01-0.59]	0.016	20.5 [Not estimable ^d]
	Private acute group C	10	8 (80.0)	2 (20.0)	1.91 [0.39-9.21]	0.422	1.64 [0.15-17.70]	0.683	76.3 [Not estimable ^d]
	Private acute group D	27	23 (85.2)	4 (14.8)	2.74 [0.91-8.22]	0.072	8.3 [0.77-90.42]	0.082	94.3 [Not estimable ^d]
	Other acute specialised	16	15 (93.8)	1 (6.2)	Excluded (Exc ^a)	Exc ^a	Exc ^a	Exc ^a	Exc ^a
	Childrens'	4	3 (75.0)	1 (25.0)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	260	192 (73.8)	68 (26.2)	Ref	Ref	Ref	Ref	73.6 [66.7-80.5]
	Female	220	149 (67.7)	71 (32.3)	0.74 [0.50-1.10]	0.141	0.79 [0.42-1.48]	0.466	70.2 [62.1-78.4]
	Unknown	5	4 (80.0)	1 (20.0)	exc ^c	exc ^c	exc ^c	exc ^c	exc ^c
Age	0-19	46	30 (65.2)	16 (34.8)	0.80 [0.39-1.65]	0.541	0.69 [0.20-2.40]	0.555	65.8 [50.1-81.5]
	20-39	137	99 (72.3)	38 (27.7)	1.11 [0.64-1.92]	0.716	0.83 [0.30-2.29]	0.726	68.8 [58.4-79.2]
	40-59	98	79 (80.6)	19 (19.4)	1.77 [0.93-3.36]	0.082	1.45 [0.50-4.21]	0.494	76.5 [66.0-86.9]
	60-79	114	80 (70.2)	34 (29.8)	Ref	Ref	Ref	Ref	71.5 [60.6-82.3]
	<80	89	56 (62.9)	33 (37.1)	0.72 [0.40-1.30]	0.276	1.49 [0.45-4.94]	0.516	76.8 [63.5-90.1]
	Unknown	1	1 (100.0)	0	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Allergies	Nil Known	391	284 (72.6)	107 (27.4)	Ref	Ref	Ref	Ref	70.8 [64.3-77.4]
	Not Documented	18	13 (72.2)	5 (27.8)	0.98 [0.34-2.81]	0.969	1.33 [0.18-10.02]	0.784	74.8 [Not estimable ^d]
	Present (beta-lactam antibiotic)	58	37 (63.8)	21 (36.2)	0.66 [0.37-1.19]	0.166	1.73 [0.61-4.94]	0.305	78.1 [65.9-90.3]
	Present (non beta-lactam antibiotic)	14	9 (64.3)	5 (35.7)	0.68 [0.22-2.07]	0.495	1.68 [0.22-12.95]	0.619	77.7 [Not estimable ^d]
	Present (non antibiotic)	4	2 (50.0)	2 (50.0)	0.38 [0.05-2.71]	0.332	Exc ^c	Exc ^c	Exc ^c
ASA score	1	142	102 (71.8)	40 (28.2)	Ref	Ref	Ref	Ref	69.7 [59.7-79.6]

	2	158	113 (71.5)	45 (28.50)	0.98 [0.60-1.63]	0.952	1.06 [0.50-2.23]	0.885	70.5 [61.8-79.1]
	3	87	55 (63.2)	32 (36.8)	0.67 [0.38-1.19]	0.174	1.33 [0.41-4.24]	0.634	73.6 [62.1-85.2]
	4	26	16 (61.5)	10 (38.5)	0.63 [0.26-1.50]	0.294	5.63 [0.71-44.58]	0.102	88.4 [Not estimable ^d]
	Unknown/Not applicable	72	59 (81.9)	13 (18.1)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	460	326 (70.9)	134 (29.1)	Ref	Ref	Ref	Ref	72.1 [66.0-78.2]
	Subsequent	25	19 (76.0)	6 (24.0)	1.30 [0.51-3.33]	0.582	1.04 [0.24-4.52]	0.956	72.7 [52.4-93.0]
Elective or Emergency	Elective	151	114 (75.5)	37 (24.5)	Ref	Ref	Ref	Ref	75.6 [64.7-86.5]
	Emergency	327	226 (69.1)	101 (30.9)	0.73 [0.47-1.13]	0.153	0.71 [0.27-1.85]	0.482	70.9 [63.8-77.9]
	Not Assessable	7	5 (71.4)	2 (28.6)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	167	118 (70.7)	49 (29.3)	Ref	Ref	Ref	Ref	66.0 [54.6-77.5]
	Yes	318	227 (71.4)	91 (28.6)	1.04 [0.69-1.56]	0.867	1.75 [0.75-4.09]	0.196	74.2 [67.6-80.9]
Removal or insertion of prosthetic material	No	110	88 (80.0)	22 (20.0)	Ref	Ref	Ref	Ref	77.8 [67.8-87.9]
	Yes	375	257 (68.5)	118 (31.5)	0.54 [0.33-0.91]	0.021	0.58 [0.24-1.44]	0.242	70.6 [63.7-77.4]
Wound category	Clean	399	292 (73.2)	107 (26.8)	Ref	Ref	Ref	Ref	72.8 [66.7-78.9]
	Clean-contaminated	21	12 (57.1)	9 (42.9)	0.49 [0.20-1.19]	0.116	0.47 [0.13-1.70]	0.250	61.0 [39.4-82.6]
	Contaminated /Dirty	19	14 (73.7)	5 (26.3)	1.03 [0.36-2.92]	0.962	0.91 [0.21-3.95]	0.898	71.4 [50.3-92.6]
	Unknown/Not Applicable	46	27 (58.7)	19 (41.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic ORIF surgical procedure	Neck of femur (NOF)	79	50 (63.3)	29 (36.7)	Ref	Ref	Ref	Ref	51.1 [33.2-69.0]
	Prosthetic NOF	21	9 (42.9)	12 (57.1)	0.43 [0.16-1.16]	0.095	0.42 [0.07-2.54]	0.341	35.5 [5.6-65.4]
	Upper limb ^e	211	156 (73.9)	55 (26.1)	1.65 [0.95-2.85]	0.077	4.43 [1.37-14.36]	0.013	75.3 [67.8-82.7]
	Lower limb ^f	174	130 (74.7)	44 (25.3)	1.71 [0.97-3.03]	0.065	5.39 [1.67-17.41]	0.005	77.8 [70.5-85.1]
Antimicrobial	Cefazolin	447	333 (74.5)	114 (25.6)	Ref	Ref	Ref	Ref	74.9 [68.8-81.1]
	Gentamicin	4	1 (25.0)	3 (75.0)	0.11 [0.01-1.11]	0.061	0.36 [0.01-9.99]	0.550	58.4 [Not estimable ^d]
	Vancomycin	13	4 (30.8)	9 (69.2)	0.15 [0.05-0.50]	0.002	0.02 [<0.01-0.19]	0.001	11.7 [Not estimable ^d]
	Cefalothin	1	0	1 (100.0)	Exc ^c	Exc ^c	Exc ^c	Exc ^c	Exc ^c
	Clindamycin	8	1 (12.5)	7 (87.5)	0.05 [0.01-0.40]	0.005	0.01 [<0.01-0.23]	0.004	7.9 [Not estimable ^d]
	Other (4) ^g	12	6 (50.0)	6 (50.0)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from analysis due to unknown/ not applicable status.

^c Removed from model due to successful predictions for perfect or failure

^d Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions

^e Upper limb includes: carpus, clavicle, humerus, metacarpal, phalanx, olecranon, radius, scaphoid, ulna

^f Lower limb includes: ankle, calcaneus, femur, patella, talus, tibia

^g Other antimicrobials= four other antimicrobials prescribed (n=<5).

^h Model C Statistic= 0.8544

Table S10 Sub analysis 6: Appropriateness and adjusted appropriateness of assessable post-procedural prescriptions for open reduction internal fixation (ORIF) surgical procedures

POST-PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness ^h		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio [95% CI]	P-Value	Odds Ratio [95% CI]	P-Value	
TOTALS (n)		320	147 (45.9)	173 (54.1)	239	-	239	-	239
HOSPITAL FACTORS									
Peer group	Principal referral	100	53 (53.0)	47 (47.0)	1.24 [0.75-2.04]	0.402	1.04 [0.31-3.51]	0.950	43.4 [28.0-58.7]
	Public acute group A	163	95 (58.3)	68 (41.7)	Ref	Ref	Ref	Ref	42.7 [29.8-55.6]
	Public acute group B	16	9 (56.3)	7 (43.7)	1.09 [0.39-3.06]	0.875	1.80 [0.13-24.51]	0.657	52.6 [11.8-93.4]
	Private acute group A	9	4 (44.4)	5 (55.6)	1.75 [0.45-6.74]	0.419	5.77 [0.23-143.48]	0.285	70.5 [Not estimable ^d]
	Private acute group B	7	2 (28.6)	5 (71.4)	3.49 [0.66-18.54]	0.142	2.65 [0.16-45.25]	0.501	58.9 [Not estimable ^d]
	Private acute group C	8	6 (75.0)	2 (25.0)	0.47 [0.09-2.38]	0.358	0.14 [0.01-2.69]	0.190	15.1 [Not estimable ^d]
	Private acute group D	11	4 (14.3)	7 (85.7)	2.44 [0.69-8.68]	0.167	6.89 [0.46-102.15]	0.161	72.8 [Not estimable ^d]
	Other acute specialised	5	5 (100.0)	0 (0.0)	Excluded (exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
	Childrens'	1	1 (100.0)	0	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	167	79 (47.3)	88 (52.7)	Ref	Ref	Ref	Ref	46.5 [36.3-56.7]
	Female	150	67 (44.7)	83 (55.3)	0.90 [0.58-1.40]	0.638	0.78 [0.37-1.65]	0.517	42.4 [31.5-53.3]
	Unknown	3	1 (33.3)	2 (66.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	27	13 (48.1)	14 (51.9)	0.85 [0.35-2.07]	0.723	1.18 [0.23-6.00]	0.844	50.7 [27.2-74.2]
	20-39	88	44 (50.0)	44 (50.0)	0.92 [0.49-1.72]	0.787	0.87 [0.28-2.69]	0.807	45.7 [31.6-59.7]
	40-59	66	33 (50.0)	33 (50.0)	0.92 [0.47-1.80]	0.801	1.25 [0.39-3.98]	0.707	51.7 [37.0-66.4]
	60-79	69	36 (52.2)	33 (47.8)	Ref	Ref	Ref	Ref	48.0 [33.0-63.1]
	<80	69	21 (30.4)	48 (69.6)	0.40 [0.20-0.81]	0.010	0.34 [0.08-1.41]	0.138	30.7 [12.8-48.6]
	Unknown	1	0	1 (100.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Allergies	Nil Known	265	125 (47.2)	140 (52.8)	Ref	Ref	Ref	Ref	45.3 [36.3-54.3]
	Not Documented	6	3 (50.0)	3 (50.0)	1.12 [0.22-5.65]	0.891	1.59 [0.09-26.84]	0.748	53.0 [7.1-98.8]
	Present (beta-lactam antibiotic)	39	13 (33.3)	26 (66.7)	0.56 [0.28-1.14]	0.109	0.61 [0.18-2.07]	0.428	37.3 [18.1-56.5]
	Present (non beta-lactam antibiotic)	8	4 (50.0)	4 (50.0)	1.12 [0.27-4.57]	0.875	1.02 [0.09-11.39]	0.988	45.6 [5.6-85.6]
	Present (non antibiotic)	2	2 (100.0)	0	Exc ^d	Exc ^d	Exc ^d	Exc ^d	Exc ^d
ASA score	1	86	44 (51.2)	42 (48.8)	Ref	Ref	Ref	Ref	41.1 [28.6-53.6]

	2	100	45 (45.0)	55 (55.0)	0.78 [0.44-1.39]	0.402	0.92 [0.37-2.24]	0.845	39.7 [28.3-51.0]
	3	72	32 (44.4)	40 (55.6)	0.76 [0.41-1.43]	0.400	2.38 [0.69-8.25]	0.171	55.0 [40.2-69.7]
	4	18	3 (16.7)	15 (83.3)	0.19 [0.05-0.71]	0.013	1.71 [0.22-13.17]	0.609	49.6 [20.2-79.0]
	Unknown/Not applicable	44	23 (52.3)	21 (47.7)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	310	143 (46.1)	167 (53.9)	Ref	Ref	Ref	Ref	45.1 [36.3-53.8]
	Subsequent	10	4 (40.0)	6 (60.0)	0.78 [0.22-2.81]	0.703	0.43 [0.06-3.05]	0.402	31.9 [3.1-60.6]
Elective or Emergency	Elective	76	36 (47.4)	40 (52.6)	Ref	Ref	Ref	Ref	33.3 [18.1-48.8]
	Emergency	236	107 (45.4)	129 (54.6)	0.92 [0.55-1.55]	0.757	2.46 [0.81-7.49]	0.113	47.8 [38.3-57.3]
	Not Assessable	8	4 (50.0)	4 (50.0)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	107	58 (54.2)	49 (45.8)	Ref	Ref	Ref	Ref	49.0 [34.9-63.1]
	Yes	213	89 (41.8)	124 (58.2)	0.61 [0.38-0.97]	0.036	0.68 [0.25-1.80]	0.435	42.6 [32.6-52.6]
Removal or insertion of prosthetic material	No	72	48 (66.7)	24 (33.3)	Ref	Ref	Ref	Ref	59.6 [44.8-74.4]
	Yes	248	99 (39.9)	149 (60.1)	0.33 [0.19-0.58]	<0.001	0.32 [0.12-0.87]	0.025	40.7 [31.2-50.2]
Wound category	Clean	260	117 (45.0)	143 (55.0)	Ref	Ref	Ref	Ref	44.4 [35.6-53.3]
	Clean-contaminated	15	9 (60.0)	6 (40.0)	1.83 [0.63-5.30]	0.263	0.88 [0.19-3.99]	0.869	42.4 [18.0-66.7]
	Contaminated /Dirty	14	7 (50.0)	7 (50.0)	1.22 [0.42-3.59]	0.715	1.61 [0.21-12.23]	0.647	52.2 [19.2-85.2]
	Unknown/Not Applicable	31	14 (45.2)	17 (54.8)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Orthopaedic ORIF procedure	Neck of femur (NOF)	55	21 (38.2)	34 (61.8)	Ref	Ref	Ref	Ref	44.6 [25.6-63.7]
	Prosthetic NOF	18	5 (27.8)	13 (72.2)	0.62 [0.19-2.00]	0.426	0.70 [0.07-6.72]	0.759	38.9 [4.5-73.3]
	Upper limb ^e	122	65 (53.3)	57 (46.7)	1.85 [0.96-3.54]	0.064	1.36 [0.35-5.31]	0.656	49.8 [37.6-62.0]
	Lower limb ^f	125	56 (44.8)	69 (55.2)	1.31 [0.69-2.51]	0.409	0.76 [0.20-2.85]	0.680	40.1 [28.9-51.3]
Antimicrobial	Cefazolin	271	139 (51.3)	132 (48.7)	Ref	Ref	Ref	Ref	49.5 [40.0-58.9]
	Cefalexin	30	2 (6.7)	28 (93.3)	0.07 [0.02-0.29]	<0.001	0.03 [0.01-0.19]	<0.001	7.1 [Not estimable ^d]
	Vancomycin	8	4 (50.0)	4 (50.0)	0.95 [0.23-3.88]	0.943	0.94 [0.11-8.50]	0.960	48.5 [9.4-87.6]
	Other (5) ^g	11	9 (81.8)	2 (18.2)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a

Ref= Reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from analysis due to unknown/ not applicable status.

^c Removed from model due to successful predictions for perfect or failure

^d Adjusted appropriateness 95% CI not estimable due to low number of prescriptions and/or proportions

^e Upper limb includes: carpus, clavicle, humerus, metacarpal, phalanx, olecranon, radius, scaphoid, ulna

^f Lower limb includes: ankle, calcaneus, femur, patella, talus, tibia

^g Other antimicrobials= five other antimicrobials prescribed (n=<4).

^h Model C Statistic= 0.8762

Table S11: Subgroup analysis: Appropriateness of orthopaedic knee procedures per presence, insertion or removal of prosthetic material

Orthopaedic Knee Procedures (n=507)	No presence, insertion or removal of prosthetic material n=342 (67.5%)		Presence, insertion or removal of prosthetic material n=165 (32.5%)	
	Appropriate n=146 (42.7)	Inappropriate n=196 (57.3)	Appropriate n=117 (70.9)	Inappropriate n=48 (29.1)
Diagnostic Arthroscopy (n=57)	19 (37.3)	32 (62.8)	2 (33.3)	4 (66.7)
Therapeutic arthroscopy (n=239)	61 (33.7)	120 (66.3)	41 (70.7)	17 (29.3)
Ligament (n=188)	59 (59.6)	40 (40.4)	64 (71.9)	25 (28.1)
Osteotomy (n=23)	7 (63.6)	4 (36.4)	10 (83.3)	2 (16.7)

5. Supplementary data for published manuscript “Factors associated with antimicrobial choice for surgical prophylaxis in Australia”.

Supplementary data includes the following:

- Table S1: Surgical NAPS Terminology and Definitions
- Figure S1: Surgical NAPS Appropriateness assessment guide
- Table S2: List of antimicrobial and antimicrobial class categories
- Table S3: Initial subgroup analysis of appropriateness of prescribed and non-prescribed procedural SAP doses
- Table S4: Unadjusted Appropriateness, univariate and multivariable analyses and adjusted appropriateness of procedural doses
- Table S5: Broad-spectrum procedural doses deemed appropriate per surgical procedure group with rates of guideline compliance

Table S1 Surgical NAPS Terminology and Definitions

Procedural antimicrobial prophylaxis	All antimicrobials administered either immediately prior to or during the surgical procedure for the purpose of prophylaxis; each dose/prescription of the antimicrobial administered is recorded and reported individually.
Post-procedural antimicrobial prophylaxis	All antimicrobials prescribed following, but directly relating to, the procedure for the purposes of prophylaxis; each prescription course of the antimicrobial is recorded and reported, including any inpatient or discharge scripts.
Existing antimicrobial therapy	Any antimicrobial prescribed for treatment or prophylaxis in the 24 hours prior (72 hours if on dialysis) to the procedure; these are not analyzed individually but are able to be taken into account when assessing the appropriateness of whether procedural antimicrobials were given or not given.
Surgical episodes	Any individual procedure or set of multiple procedures performed together during the one session and the subsequent post-procedural care associated with the procedure(s).
Appropriateness	As per the Surgical NAPS Appropriate Assessment Guide (4, 366). Data assessed as 'optimal' and 'adequate'.
Inappropriateness	As per the Surgical NAPS Appropriate Assessment Guide (4, 366). Data assessed as 'suboptimal' and 'inadequate'.
Overall Appropriateness /Inappropriateness	Assessment per entire surgical episode as opposed to the individual antimicrobial doses/prescriptions. e.g., A surgical episode may be deemed to be overall inappropriate if any part of the prescription (procedural or post-procedural prophylaxis) was deemed inappropriate, including allergy or microbiology mismatch, timing, dose, route, frequency, duration, spectrum too broad, spectrum too narrow or if the procedure did not require any antimicrobials.

References

1. Australian Commission on Safety and Quality in Health Care. Surgical national antimicrobial prescribing in australia: Results of the 2016 pilot. In: ACSQHC, editor. Sydney: Australian Commission for Safety and Quality in Health Care; 2017.
2. Ierano C, Thursky K, Marshall C, et al. Appropriateness of surgical antimicrobial prophylaxis practices in australia. JAMA Network Open. 2019;2(11):e1915003.

Figure S1 Surgical NAPS Appropriateness assessment guide

SURGICAL NAPS National Antimicrobial Prescribing Survey

Surgical NAPS appropriateness definitions

GUIDANCE | NCAS

	Appropriate		Inappropriate		
	1 - Optimal	2 - Adequate	3 - Suboptimal	4 - Inadequate	5 - Not assessable
Allergy mismatch	Where antimicrobials are prescribed exactly according to Therapeutic Guidelines or local guidelines – antimicrobial choice, dose, route, timing and duration; or where there is an appropriate reason for deviation from guidelines		Mild or non-life threatening allergy mismatch	Life threatening allergy mismatch	Where there is insufficient information available or the case is too complex for assessment.
Microbiology mismatch				Antimicrobial used is too narrow (where sensitivity results available)	
Incorrect dose or frequency			Dose or frequency too high (with exception of gentamicin)	Dose or frequency too low	
Incorrect route			An intravenous antimicrobial has been prescribed when the patient is able to safely take it orally	Gentamicin dose too high or too frequent	
Incorrect timing	If any reason is selected for incorrect prescribing, the prescription will no longer be optimal.	Repeat dose given too soon (including patients who were already on existing antimicrobial therapy) <i>taking into consideration patients with renal impairment</i>	Antimicrobial prophylaxis given less than 15 minutes before surgical incision (with exception of vancomycin) Vancomycin started less than 30 minutes before surgical incision	Antimicrobial prophylaxis given greater than 60 minutes before surgical incision (with exception of vancomycin) Vancomycin started greater than 120 minutes before surgical incision Repeat dose given too late (including patients already on existing antimicrobial therapy) <i>taking into account renal impairment</i>	
Incorrect duration		Patient already on existing antimicrobials where last dose would have provided sufficient prophylaxis for the duration of the procedure		Surgical prophylaxis greater than 24 hours (except where guidelines endorse this)	
Spectrum too broad			Choice of antimicrobial is too broad Additional antimicrobial added unnecessarily		
Spectrum too narrow				Choice of antimicrobial does not cover likely organisms	
Procedure does not require any antimicrobials	No antimicrobial required			Procedure does not require any antimicrobials, but antimicrobials were still prescribed	
Procedure requires antimicrobials				Procedure requires antimicrobials but no antimicrobials were prescribed AND there were no existing antimicrobials	
Repeat dose required, but not given				This will automatically be selected for auditors	
No antimicrobial prescribed				Procedure requires antimicrobials but no antimicrobials were prescribed and there were no pre-existing antimicrobials	

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Table S2 List of antimicrobial and antimicrobial class categories

Antimicrobial Class/ Antimicrobial list for research project (n)	Antimicrobial as per Surgical NAPS dataset	Total (n)
1GC*- Cefazolin (n=10,925)	Cefazolin	10,925
Nitroimidazoles-Metronidazole (n=862)	Metronidazole	862
Aminoglycosides (n=637)	Amikacin	1
	Gentamicin	628
	Tobramycin	8
Glycopeptides (n=390)	Teicoplanin	36
	Vancomycin	354
3GC* & 4GC* (n=343)	Cefepime	5
	Cefotaxime	10
	Ceftazidime	3
	Ceftriaxone	325
Penicillins (n=260)	Amoxicillin	65
	Ampicillin	76
	Benzylpenicillin	29
	Flucloxacillin	90
Lincosamides (n=217)	Clindamycin	137
	Lincomycin	80
Penicillin and Beta-lactamase Inhibitors (n=162)	Piperacillin-tazobactam (Tazocin®)	150
	Amoxicillin-clavulanic acid (Augmentin® or Augmentin Duo Forte®)	12
Fluoroquinolones (n=99)	Ciprofloxacin	93
	Ofloxacin	6
Chloramphenicol (n=94)	Chloramphenicol	94
1GC*-Others (n=81)	Cefalexin	8
	Cefalothin	73
2GC* (n=58)	Cefaclor	1
	Cefoxitin	57
Carbapenem-Meropenem (n=11)	Meropenem	11
Others (n=11)	Erythromycin	3
	Azithromycin	2
	Daptomycin	2
	Mupirocin	2
	Fluconazole	1
	Rifampicin	1
*1GC/2GC/3GC/4GC= First, second, third and fourth generation cephalosporins		

Table S3 Initial subgroup analysis of appropriateness of prescribed and non-prescribed procedural SAP doses

TOTALS	Total doses/ prescriptions N	Appropriate N (%)	Inappropriate N (%)
Procedural	19413	12984 (66.9)	6429 (33.1)
Prescribed	14150	8160 (57.7)	5990 (42.3)
None prescribed	5263	4824 (91.7)	439 (8.3)

Table S4 Unadjusted Appropriateness, univariate and multivariable analyses and adjusted appropriateness of procedural doses

PROCEDURAL FACTORS		Total doses	Appropriate (no.) (%)	Inappropriate (no.) (%)	Univariate Appropriateness		Multivariable Appropriateness [^]		Mixed Effects Model: Adjusted Appropriateness (%) [95% CI]
					Odds Ratio* [95% CI]	P-Value	Odds Ratio* [95% CI]	P-Value	
TOTAL (n)		14,150	8,160 (57.7)	5,990 (42.3)					
HOSPITAL FACTORS									
State	ACT	363	240 (66.1)	123 (33.9)	1.43 [1.14-1.80]	0.002	1.72 [0.49-6.08]	0.399	66.0 [46.3-85.8]
	NSW	3,636	2,312 (63.6)	1,324 (36.4)	1.28 [1.17-1.41]	<0.001	2.13 [1.31-3.46]	0.002	69.4 [63.9-74.9]
	NT	69	48 (69.6)	21 (30.4)	1.68 [1.00-2.81]	0.049	2.69 [0.45-16.07]	0.278	73.0 [47.6-98.4]
	QLD	2,282	948 (41.5)	1,334 (59.5)	0.52 [0.47-0.58]	<0.001	0.64 [0.36-1.14]	0.132	48.6 [39.9-57.3]
	SA	1,388	840 (60.5)	548 (39.5)	1.13 [0.99-1.28]	0.064	1.32 [0.64-2.74]	0.450	61.6 [51.2-72.1]
	TAS	63	62 (98.4)	1 (1.6)	45.54 [6.31-328.74]	<0.001	23.17 [1.23-437.19]	0.036	93.4 [Exc [†]]
	VIC	3,828	2,207 (57.7)	1,621 (42.4)	Ref	Ref	Ref	Ref	56.7 [50.3-63.0]
	WA	2,521	1,503 (59.6)	1,018 (40.4)	1.08 [0.98-1.20]	0.120	0.98 [0.56-1.71]	0.932	56.2 [48.1-64.3]
Remoteness	Major cities	11,079	6,441 (58.1)	4,638 (21.9)	Ref	Ref	Ref	Ref	59.0 [55.0-63.1]
	Inner regional	2,480	1,413 (57.0)	1,067 (43.0)	0.95 [0.87-1.04]	0.290	1.04 [0.63-1.72]	0.875	59.8 [52.5-67.0]
	Outer regional	459	261 (56.9)	198 (43.1)	0.95 [0.79-1.15]	0.588	1.54 [0.71-3.34]	0.276	66.3 [54.7-77.9]
	Remote	131	44 (33.6)	87 (66.4)	0.36 [0.25-0.52]	<0.001	0.55 [0.16-1.94]	0.357	48.5 [26.7-70.3]
	Very remote	1	1 (100.0)	0 (0.0)	Excluded (Exc) ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
Peer group	Principal referral	3,038	1,843 (60.7)	1,195 (39.3)	1.38 [1.24-1.53]	<0.001	1.31 [0.69-2.48]	0.410	60.5 [52.0-68.9]
	Public acute group A	2,873	1,518 (52.8)	1,355 (47.2)	Ref	Ref	Ref	Ref	55.7 [48.5-62.8]
	Public acute group B	780	474 (60.8)	306 (39.2)	1.38 [1.18-1.62]	<0.001	1.56 [0.74-3.31]	0.243	63.5 [52.8-74.2]
	Public acute group C	904	418 (46.2)	486 (53.8)	0.77 [0.66-0.89]	0.001	1.18 [0.60-2.31]	0.633	58.6 [47.6-69.6]
	Public acute group D	30	10 (33.3)	20 (66.7)	0.45 [0.21-0.96]	0.038	0.18 [0.03-1.05]	0.056	25.8 [Exc [†]]
	Private acute group A	589	313 (53.1)	276 (46.9)	1.01 [0.85-1.21]	0.893	1.51 [0.65-3.52]	0.337	63.0 [50.5-75.4]
	Private acute group B	1,957	949 (48.5)	1,008 (51.1)	0.84 [0.75-0.94]	0.003	0.58 [0.30-1.14]	0.114	45.8 [35.8-55.7]
	Private acute group C	912	577 (63.3)	335 (36.7)	1.54 [1.32-1.79]	<0.001	1.55 [0.79-3.02]	0.202	63.3 [54.1-72.6]
	Private acute group D	1,794	1,118 (62.3)	676 (37.7)	1.48 [1.31-1.67]	<0.001	1.74 [0.87-3.47]	0.115	65.3 [55.9-74.7]
	Other acute specialised	456	349 (76.5)	107 (23.5)	2.91 [2.32-3.66]	<0.001	4.84 [1.64-14.25]	0.004	80.1 [68.1-92.0]
	Other day procedure	11	3 (27.3)	8 (72.7)	0.33 [0.09-1.26]	0.107	0.10 [<0.01-2.07]	0.136	17.9 [Exc [†]]
	Mixed day procedure	360	300 (83.3)	60 (16.7)	4.46 [3.35-5.94]	<0.001	1.94 [0.41-9.15]	0.405	67.1 [42.6-91.5]

	Mixed sub- & non-acute	48	27 (56.3)	21 (43.8)	1.15 [0.65-2.04]	0.639	0.44 [0.05-4.09]	0.470	40.7 [1.6-79.9]
	Womens hospitals	177	102 (57.6)	75 (42.4)	1.21 [0.89-1.65]	0.216	0.98 [0.22-4.40]	0.974	55.2 [29.2-81.2]
	Childrens'	121	61 (50.4)	60 (49.6)	0.91 [0.63-1.31]	0.601	2.18 [0.47-10.06]	0.320	68.9 [45.8-92.0]
	Unpeered	16	14 (87.5)	12 (12.5)	6.25 [1.42-27.54]	0.015	19.87 [1.35-293.01]	0.029	92.4 [Exc ^c]
	Eye surgery centres	84	84 (100.0)	0 (0.0)	Exc ^a	Exc ^a	Exc ^a	Exc ^a	Exc ^a
PATIENT FACTORS									
Gender	Male	6,609	3,797 (57.5)	2,812 (42.6)	Ref	Ref	Ref	Ref	59.4 [55.9-62.8]
	Female	7,488	4,327 (57.8)	3,161 (42.2)	1.01 [0.95-1.08]	0.689	0.99 [0.90 -1.10]	0.889	59.3 [55.8-62.7]
	Unknown	53	36 (67.9)	17 (42.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Age	0-19	695	326 (46.9)	369 (53.1)	0.58 [0.49-0.68]	<0.001	0.56 [0.44-0.72]	<0.001	50.5 [45.2-55.8]
	20-39	3080	1742 (56.6)	1338 (43.4)	0.85 [0.78-0.93]	0.001	0.95 [0.82-1.11]	0.523	59.8 [56.1-63.6]
	40-59	3511	2009 (57.2)	1502 (42.8)	0.88 [0.81-0.96]	0.003	0.96 [0.85-1.09]	0.532	60.0 [56.4-63.6]
	60-79	5483	3310 (60.4)	2173 (39.6)	Ref	Ref	Ref	Ref	60.7 [57.2-64.2]
	<80	1372	767 (55.9)	605 (44.1)	0.83 [0.74-0.94]	0.003	0.74 [0.63-0.87]	<0.001	55.4 [51.1-59.7]
	Unknown	9	6 (66.7)	3 (33.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Allergies	Nil Known	11673	6802 (58.3)	4871 (41.7)	Ref	Ref	Ref	Ref	57.7 [54.0-61.4]
	Not Documented	235	136 (57.9)	99 (42.1)	0.98 [0.76-1.28]	0.902	1.19 [0.80-1.7]	0.393	58.6 [55.2-62.1]
	Present (beta-lactam antimicrobial)	1,478	773 (52.3)	705 (47.7)	0.79 [0.70-0.88]	<0.001	0.90 [0.77-1.05]	0.188	61.1 [57.5-64.7]
	Present (non beta-lactam antimicrobial)	497	293 (59.0)	204 (41.0)	1.03 [0.86-1.23]	0.762	1.07 [0.84-1.37]	0.565	64.1 [59.0-69.2]
	Present (non antimicrobial)	267	156 (58.4)	111 (41.6)	1.01 [0.79-1.29]	0.959	0.90 [0.64-1.27]	0.561	58.9 [35.8-81.9]
ASA score	1	3,043	1,708 (56.1)	1,335 (43.9)	Ref	Ref	Ref	Ref	59.4 [56.1-62.8]
	2	5,329	2,986 (56.0)	2,343 (44.0)	1.00 [0.91-1.09]	0.932	1.05 [0.93-1.19]	0.397	62.4 [55.0-69.8]
	3	3,197	1,905 (60.0)	1,292 (40.4)	1.15 [1.04-1.27]	0.006	1.22 [1.04-1.42]	0.012	57.6 [53.5-61.8]
	4	665	421 (63.3)	244 (36.7)	1.35 [1.13-1.60]	0.001	1.45 [1.10-1.92]	0.009	60.7 [55.5-65.9]
	5	15	10 (66.7)	5 (33.3)	1.56 [0.53-4.58]	0.416	1.07 [0.29-3.96]	0.923	57.7 [50.9-64.5]
	Unknown/ Not applicable	1,901	1,130 (59.4)	771 (40.6)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b

PROCEDURAL FACTORS									
Surgery Number for Admission	Initial	13,586	7,837 (57.7)	5,749 (42.3)	Ref	Ref	Ref	Ref	59.2 [55.9-62.5]
	Subsequent	564	323 (57.3)	241 (42.7)	0.98 [0.83-1.17]	0.845	1.21 [0.95-1.53]	0.129	62.4 [57.3-67.5]
Elective or Emergency	Elective	11,369	6,631 (58.3)	4,738 (41.7)	Ref	Ref	Ref	Ref	59.5 [56.1-62.8]
	Emergency	2,526	1,428 (56.5)	1,098 (43.5)	0.93 [0.85-1.01]	0.099	0.95 [0.82-1.10]	0.468	58.6 [54.7-62.5]
	Not Assessable	255	101 (39.6)	154 (60.4)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Trauma	No	13,302	7,620 (57.3)	5,682 (42.7)	Ref	Ref	Ref	Ref	58.9 [55.6-62.3]
	Yes	848	540 (63.7)	308 (36.3)	1.31 [1.13-1.51]	<0.001	1.41 [1.13-1.77]	0.002	64.8 [60.1-69.5]
Removal or insertion of prosthetic material	No	8,986	4,789 (53.3)	4,197 (46.7)	Ref	Ref	Ref	Ref	56.1 [52.6-59.5]
	Yes	5,164	3,371 (65.3)	1,793 (34.7)	1.65 [1.54-1.77]	<0.001	1.68 [1.50-1.89]	<0.001	65.1 [61.6-68.6]
Wound category	Clean	9,112	5,557 (61.0)	3,555 (39.0)	Ref	Ref	Ref	Ref	58.1 [54.8-61.5]
	Clean-contaminated	3,308	1,645 (49.7)	1,663 (50.3)	0.63 [0.58-0.69]	<0.001	1.23 [1.08-1.41]	0.002	61.8 [58.1-65.4]
	Contaminated	444	251 (56.5)	193 (43.5)	0.83 [0.69-1.01]	0.061	1.20 [0.92-1.56]	0.184	61.2 [55.9-66.5]
	Dirty	262	126 (48.1)	136 (51.9)	0.59 [0.46-0.76]	<0.001	1.33 [0.96-1.86]	0.091	63.1 [56.8-69.3]
	Unknown/Not Applicable	1,024	581 (56.7)	443 (43.3)	Exc ^b	Exc ^b	Exc ^b	Exc ^b	Exc ^b
Surgical procedure group	Abdominal surgery	2,595	1,508 (58.1)	1,087 (41.9)	0.74 [0.67-0.82]	<0.001	0.84 [0.70-1.00]	0.046	59.4 [55.5-63.3]
	Breast surgery	409	254 (62.1)	155 (37.9)	0.88 [0.71-1.09]	0.231	0.98 [0.73-1.30]	0.880	62.2 [56.6-67.8]
	Cardiac surgery	783	436 (55.7)	347 (44.3)	0.67 [0.58-0.79]	<0.001	1.13 [0.84-1.52]	0.424	64.6 [58.9-70.4]
	Dentoalveolar surgery	222	62 (27.9)	160 (72.1)	0.21 [0.15-0.28]	<0.001	0.25 [0.17-0.37]	<0.001	37.3 [29.8-44.8]
	Gastrointestinal endoscopic procedures	59	19 (32.2)	40 (67.8)	0.25 [0.15-0.44]	<0.001	0.22 [0.09-0.54]	0.001	35.1 [19.4-50.7]
	Gynaecological surgery	744	413 (55.5)	331 (44.5)	0.67 [0.57-0.78]	<0.001	0.88 [0.69-1.12]	0.307	60.3 [55.4-65.3]
	Head and neck surgery	503	216 (42.9)	287 (57.1)	0.40 [0.33-0.49]	<0.001	0.46 [0.36-0.60]	<0.001	48.6 [43.0-54.1]
	Neurosurgery	511	369 (72.2)	142 (27.8)	1.39 [1.14-1.71]	0.001	1.63 [1.23-2.16]	0.001	70.6 [65.5-75.7]
	Obstetrics	960	579 (60.3)	381 (39.7)	0.82 [0.71-0.94]	0.006	1.08 [0.83-1.40]	0.556	63.9 [59.0-68.8]
	Ophthalmology	525	416 (79.2)	109 (20.8)	2.05 [1.64-22.55]	<0.001	2.09 [1.38-3.17]	<0.001	74.4 [68.0-80.7]

	Orthopaedic surgery	3,914	2,547 (65.1)	1,367 (34.9)	Ref	Ref	Ref	Ref	62.6 [58.8-66.3]
	Plastic and reconstructive surgery	1,169	517 (44.2)	652 (55.8)	0.43 [0.37-0.49]	<0.001	0.42 [0.35-0.51]	<0.001	46.8 [42.3-51.3]
	Thoracic surgery	106	73 (68.9)	33 (31.1)	1.19 [0.78-1.80]	0.419	1.26 [0.72-2.22]	0.413	66.5 [56.9-76.1]
	Urological surgery	1,323	582 (44.0)	741 (56.0)	0.42 [0.37-0.48]	<0.001	0.59 [0.47-0.73]	<0.001	53.0 [48.3-57.6]
	Vascular surgery	327	169 (51.7)	158 (48.3)	0.57 [0.46-0.72]	<0.001	0.80 [0.58-1.11]	0.183	58.7 [52.3-65.1]
Anti-microbial	Cefazolin	10,925	6,984 (63.9)	3,941 (36.1)	Ref	Ref	Ref	Ref	64.5 [61.1-67.9]
	Metronidazole	862	472 (54.8)	390 (45.2)	0.69 [0.59-78.5]	<0.001	0.84 [0.69-1.02]	0.081	61.3 [56.5-66.2]
	Aminoglycosides	637	188 (29.5)	449 (70.5)	0.24 [0.20-0.28]	<0.001	0.15 [0.12-0.20]	<0.001	30.5 [25.6-35.4]
	Glycopeptides	390	107 (27.4)	283 (72.6)	0.21 [0.17-0.27]	<0.001	0.13 [0.10-0.18]	<0.001	28.0 [22.5-33.4]
	3 rd and 4 th Generation Cephalosporins (GC)	343	34 (9.9)	309 (90.1)	0.06 [0.04-0.09]	<0.001	0.05 [0.03-0.08]	<0.001	15.6 [110.6-20.7]
	Penicillins	260	78 (30.0)	182 (70.0)	0.24 [0.18-0.32]	<0.001	0.37 [0.26-0.52]	<0.001	45.9 [38.5-53.3]
	Lincosamides	217	86 (39.6)	131 (60.4)	0.37 [0.28-0.49]	<0.001	0.33 [0.24-0.48]	<0.001	44.1 [36.8-51.5]
	Penicillin + Beta-lactamase inhibitor (BLI)	162	83 (51.2)	79 (48.8)	0.59 [0.43-0.81]	0.001	0.59 [0.39-0.90]	<0.001	54.9 [46.3-63.5]
	Fluoroquinolones	99	18 (18.2)	81 (81.8)	0.13 [0.08-0.21]	<0.001	0.13 [0.07-0.25]	0.015	27.3 [16.7-37.9]
	Chloramphenicol	94	21 (22.3)	73 (77.7)	0.16 [0.10-0.26]	<0.001	0.03 [0.01-0.07]	<0.001	10.8 [4.3-17.3]
	Other 1 st GC	81	42 (51.9)	39 (48.2)	0.61 [0.39-0.94]	0.026	0.44 [0.22-0.88]	<0.001	49.4 [35.9-62.9]
	2 nd GC	58	36 (62.1)	22 (37.9)	0.92 [0.54-1.57]	0.769	1.23 [0.61-2.48]	0.020	68.1 [55.8-80.3]
	Others	22	11 (50.0)	11 (50.0)	Exc ^d	Exc ^d	Exc ^d	Exc ^d	Exc ^d

^a Model C Statistic= 0.8100

* Odds Ratio (OR) <1 = negative association of appropriateness i.e., promote inappropriateness.

Ref= reference group

Exc= Excluded

^a Excluded from analysis due to low number of prescriptions and/or proportions

^b Excluded from multivariate analysis due to unknown/ not applicable status

^c Adjusted appropriateness 95%CI not estimable due to low number of prescriptions and/or proportions

^d Other antimicrobials= frequency less than 10: erythromycin, azithromycin, daptomycin, mupirocin, fluconazole, rifampicin (n=<11)

Table S5 Broad-spectrum procedural doses deemed appropriate per surgical procedure group with rates of guideline compliance

Surgical procedure groups	Total Appropriate doses (n=329)	Antimicrobial/Class, n (% of surgical procedure group)			Guideline compliance of appropriate broad-spectrum antimicrobials n (% of surgical procedure group)						Hospitals with local guide lines (n=32)
		Aminoglycosides, n=188 (57.1%)	Glycopeptides, n=107 (32.5%)	3GC + 4GC*, n=34 (10.3%)	Non-compliant with guidelines (10.3%)	Compliant with national guidelines, n=174 (52.9%)	Compliant with local guidelines, n=93 (28.3%)	Directed therapy n=20 (6.1%)	No guidelines available n= 5 (1.5%)	Not assessable n=3 (0.9%)	
Abdominal	24	5 (2.7)	2 (1.9)	17 (50.0)	5 (20.8)	11 (45.8)	3 (12.5)	2 (8.3)	3 (12.5)	-	2
Breast	25	23 (12.2)	1 (0.9)	1 (2.9)	-	2 (8.0)	23 (92.0)	-	-	-	1
Cardiac	42	7 (3.7)	35 (32.7)	-	4 (9.5)	20 (47.6)	16 (38.1)	1 (2.4)	1 (2.4)	-	6
Gastrointestinal endoscopic procedures	5	3 (1.6)	-	2 (5.9)	2 (40.0)	3 (60.0)	-	-	-	-	-
Gynaecological	2	2 (1.1)	-	-	1 (50.0)	1 (50.0)	-	-	-	-	-
Neurosurgery	6	-	5 (4.7)	1 (2.9)	1 (16.7)	4 (67.0)	-	1 (16.7)	-	-	-
Obstetrics	1	-	1 (0.9)	-	-	1 (100.0)	-	-	-	-	-
Ophthalmology	4	1 (0.5)	3 (2.8)	-	-	2 (50.0)	-	-	-	2 (50.0)	-
Orthopaedic	66	18 (9.6)	46 (43.0)	2 (5.9)	6 (9.1)	31 (47.0)	19 (28.8%)	9 (13.6)	-	1 (1.5)	10
Plastic and reconstructive	7	2 (1.1)	5 (4.7)	-	-	2 (28.6)	2 (28.6%)	3 (42.9)	-	-	2
Urological	141	127 (67.6)	3 (2.8)	11 (32.4)	15 (10.6)	92 (65.3)	29 (20.6)	4 (2.8)	1 (0.7)	-	10
Vascular	6	-	6 (5.6)	-	-	5 (83.3)	1 (16.7)	-	-	-	1

*3GC/4GC= Third and fourth generation cephalosporins

6. Supplementary data for published manuscript “Influences on surgical antimicrobial prophylaxis decision making by surgical craft groups, anaesthetists, pharmacists and nurses in public and private hospitals”.

6.1. Project Information Statement



NCAS
National Centre for
Antimicrobial Stewardship



MONASH
University



theAlfred



Epworth



MELBOURNE HEALTH

INVITATION TO PARTICIPATE IN A RESEARCH PROJECT

PROJECT INFORMATION STATEMENT

Project Title: Barriers and enablers of surgical antimicrobial prophylaxis prescribing

Co-ordinating Investigator: Dr. Trisha Peel: trisha.peel@monash.edu

Site Principal Investigators: RMH- Prof Karin Thursky: karin.thursky@mh.org.au

: Alfred Health & Epworth HealthCare- Dr. Trisha Peel

Associate Investigators:

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- A/Prof Caroline Marshall: caroline.marshall@mh.org.au
- Dr. Arjun Rajkhowa: arjun.rajkhowa@unimelb.edu.au

Dear <insert name>

You are invited to participate in a research project being conducted by the National Centre for Antimicrobial Stewardship (NCAS) and University of Melbourne (UoM) in affiliation with Monash University, Alfred Health, Epworth HealthCare and Melbourne Health.

Please read this sheet carefully. If you have any questions about the project, please ask the Dr Trisha Peel (Co-ordinating Investigator) or Ms Courtney Ierano (Associate Investigator).

Who is involved in this research project? Why is it being conducted?

Ms Courtney Ierano is conducting this research as part of her PhD studies and Dr Trisha Peel and Prof Karin Thursky are her co-primary supervisors. Ethics has been approved for this research project by Alfred Health HREC. The aim of this research is to identify barriers and enablers of surgical antimicrobial prescribing and guideline compliance.

Why have you been approached?

To gain further insight into the decision making processes surrounding surgical antimicrobial prophylaxis (SAP) prescribing, we have purposively sought participants from a range of experts from multiple disciplines within this field. Your participation is voluntary and your consent is implied by your presence at the focus group and response to emails confirming focus group details.

What is the project about? What are the questions being addressed?

This project aims to identify barriers and enablers of surgical antimicrobial prescribing, including guideline concordance and implementability. Identification of these factors may highlight reasons for the currently observed poor compliance with SAP prescribing recommendations and may inform future guideline development, antimicrobial stewardship (AMS) programs.

If I agree to participate, what will I be required to do?

Participation will require attendance of a focus group. Focus groups will be purposively targeted to different health professionals (surgeons, anaesthetists and theatre nurses)

Page 1 of 2

across both public and private hospitals to explore the decision making process behind SAP prescribing and potential barriers and enablers of appropriate prescribing. Focus groups will be organised at a time convenient to your professional cohort and should run for up to an hour. Refreshments will be provided and you will receive a Certificate of Participation to contribute to your Continuing Professional Development (CPD) record.

What will happen to the information I provide?

All focus group participants are advised and encouraged to maintain confidentiality of other participants, although this cannot be guaranteed. Recordings of focus groups will be transcribed and transcriptions will be non-identifiable to maintain confidentiality. Data collected will be kept confidential at the University of Melbourne for 7 years before being destroyed. Only the listed investigators will have access to this information for research purposes. Non-identifiable results may be published in relevant journal and made available to conferences and various other sources.

What are my rights as a participant?

- You have the right to withdraw from the focus group
- You have the right to have any unprocessed data withdrawn and destroyed, provided it can be reliably identified.
- You have the right to have any questions answered at any time.

Whom should I contact if I have any questions?

For further information regarding this project, please contact Ms Courtney Ierano on 0424 989 744.

For any complaints relating to this project please contact:

Alfred Health Complaints Officer, Office of Ethics & Research Governance

Email: research@alfred.org.au

Phone: 03 90763619

FOCUS GROUP TIME: _____

FOCUS GROUP LOCATION: _____

Yours sincerely



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Page 2 of 2

6.2. *S1 Appendix and S2 Appendix*

S1 Appendix. Focus group question and discussion guides

Table A Question and discussion guide for focus groups with surgeons, anaesthetists and pharmacists

Number	Question	Approximate time allocation (mins)
Q1	Can you tell us who decides what prophylaxis is given and who administers it? Who is ultimately responsible for this decision?	5
Q2	How is this decision for SAP made?	5
Q3	Do you routinely check if antibiotics have been given at the right time? Do you check if they are stopped at 24 hours?	5
Q4	Current recommendations suggest SAP should be administered within 60 minutes of knife-to-skin. Does this fit in with the general workflow in the theatre?	5
Q5	Recent WHO and CDC guidelines now recommend a single dose of SAP for all clean-contaminated procedures. What are your thoughts on this? Will this change practice?	5
Q6	Finally, how can SAP prescribing be improved?	5
Q7	Any other comments you wish to make?	5

Table B Question and discussion guide for focus groups with nurses

Number	Question	Approximate time allocation (mins)
Q1	Can you tell us who decides what prophylaxis is given and who administers it? Who is ultimately responsible for this decision?	5
Q2	How is this decision for SAP made?	5
Q3	Is there a role for nurses in relation to SAP?	5
Q4	Do you routinely check if antibiotics have been given at the right time? Do you check if they are stopped at 24 hours?	5
Q5	Current recommendations suggest SAP should be administered within 60 minutes of knife-to-skin. Does this fit in with the general workflow in the theatre?	5
Q6	Recent WHO and CDC guidelines now recommend a single dose of SAP for all clean-contaminated procedures. What are your thoughts on this? Will this change practice?	5
Q7	Finally, how can SAP prescribing be improved? Should nurses be involved? How can nurses be involved?	5
Q8	Any other comments you wish to make?	5

1 S2 Appendix. Themes and subthemes mapped to the COM-B Model
2 and Theoretical Domains Framework

3

4 **Table C Themes and subthemes mapped to the COM-B Model and Theoretical Domains Framework**

Themes	Sub Themes	COM-B Model Components	Relevant Domains (Theoretical Domains Framework)
Low priority for surgical antimicrobial prophylaxis prescribing skills.	Surgical technique of greater importance	Physical Capability	Skills
	Deskilling surgeons		
Prescriber autonomy overrules guideline compliance	Guideline knowledge and awareness of limitations	Psychological Capability	Knowledge
	Competition as a means to regulate behaviour		Memory, attention and decision processes
Social codes of prescribing reinforce established practices	Hierarchy Rules	Social Opportunity	Social Influences
	Cross-specialty prescriber etiquette		
Need for improved communication, documentation and data for action	Poor documentation and communication	Physical Opportunity	Environmental context and resources
	'Time-Out' supports pre-operative communication; post-operative management is less standardised		
Fears and perceptions of risk hinder appropriate SAP prescribing.	Data for action	Automatic Motivation	Emotion
	Fear of infections		
	Varied risk perceptions across specialties		
	Fear of litigation		
Unclear roles, responsibilities and accountability	Risking career progression and job security	Reflective Motivation	Social/ professional role and identity
	The buck stops with the surgeon		
	Passive prescribing hinders accountability and SAP cessation		
	Capacity for role expansion of pharmacists and nurses		Beliefs about Capabilities
			Beliefs about Consequences

5

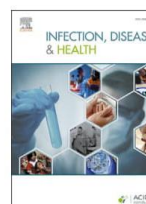
6

7. Published manuscript: *“Antibiotic prescribing in surgery: a clinically and socially complex problem in Australia”*

The manuscript entitled: “Antibiotic prescribing in surgery: a clinically and socially complex problem in Australia” was published with the journal Infection, Disease and Health (20/05/2020). It builds upon the work across this thesis, providing a commentary on the identified clinical and social factors influencing antimicrobial prescribing in surgery.

Available online at www.sciencedirect.com

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journal homepage: <http://www.journals.elsevier.com/infection-disease-and-health/>

Discussion paper

Antibiotic prescribing in surgery: A clinically and socially complex problem in Australia

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KEYWORDS

Antimicrobial;
Surgical antimicrobial
prophylaxis;
Behaviour change;
Antimicrobial
stewardship;
Infection prevention;
Infection control

Abstract Surgical prophylaxis is a common indication for antimicrobial use in Australian hospitals with demonstrated poor rates of appropriateness. Ongoing analysis of the Surgical National Antimicrobial Prescribing Survey and exploration of influences on antimicrobial prescribing decisions can help identify clinical and behavioural issues that contribute to problematic antimicrobial use. Triangulation of quantitative and qualitative data supports the development of surgical antimicrobial stewardship, i.e., quality improvement initiatives for the optimisation of surgical antimicrobial prophylaxis. Such initiatives should be developed and implemented at both local and national levels to ensure that they remain effective and sustainable.

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Highlights

- Antimicrobials for surgical prophylaxis are poorly prescribed in Australian hospitals.
- Quantitative research has identified clinical issues associated with problematic antimicrobial use in surgery.

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- Qualitative research has identified barriers and enablers to appropriate antimicrobial prescribing.
- Australia lacks a national surveillance program for surgical site complications to support prescriber behaviour change.

Introduction

When a patient is admitted to hospital, antimicrobials are commonly prescribed as a part of their care. An Australian point-prevalence survey, the Hospital National Antimicrobial Prescribing Survey (NAPS) [1–6], has, over the last six years, consistently identified that surgical antimicrobial prophylaxis (SAP) is the most common reason for antimicrobials to be prescribed in hospitals (14.1% of all antimicrobial prescriptions in 2018) [6]. Antimicrobials are commonly administered before surgery to prevent surgical site infections. However, not all surgical procedures require antimicrobials, and, when they are required, usually only a single dose before (and no doses after) surgery is recommended [7].

The Hospital NAPS has also consistently highlighted that antimicrobial prescribing for SAP is assessed as having the one of the highest rates of inappropriateness (39.5%) [6]. To further explore the quality of SAP prescribing across Australia, the Surgical NAPS online auditing platform was developed in 2015 [8]. The Surgical NAPS supported more detailed auditing of antimicrobial use in surgery, facilitating a review of antimicrobial use across the surgical admission, including for existing therapy, procedural SAP (doses administered before and during surgery) and post-procedural SAP (doses administered after surgery). Differences in inappropriateness between procedural and post-procedural SAP (36.6% and 63.7% respectively) were noted in the most recent public report [9]. Ongoing data collection and analysis of the Surgical NAPS will facilitate benchmarking of SAP prescribing quality, support hospitals with their antimicrobial stewardship (AMS) and accreditation activities, and inform local and national guideline development. Most importantly, the Surgical NAPS can identify antimicrobial prescribing quality improvement targets, and, as such, inform the development of targeted AMS and infection prevention interventions.

Discussion

Our recent study analysing the Surgical NAPS (2016–18) data showed a low rate of appropriateness of SAP prescribing (48.7% appropriate across 15,395 prescriptions for 9,351 surgical episodes) [10]. Both procedural (40.5%) and post-procedural SAP (60.2%) had high rates of inappropriateness; however, antimicrobial use for post-procedural SAP appears to be of greater concern. After accounting for a range of hospital, patient and surgical factors, appropriateness of SAP prescribing – both procedural (range: 33.7%–68.9%) and post-procedural (range: 21.5%–58.7%) – was low across a range of surgical procedure groups [10].

When procedural SAP was clinically indicated but considered inappropriate, the most common reason for inappropriateness was timing (49.5%). A caveat to this is that of all surgical episodes, the incision time was documented only 65.6% of the time, thus making it difficult to truly assess the appropriateness of SAP timing. In comparison, for clinically indicated post-procedural SAP that was deemed inappropriate, the most common reason for inappropriateness was prolonged duration (54.3%) [10]. Prolonged duration was also the most common reason for inappropriateness for all surgical procedure groups (from 43.8% for ophthalmology to 86.3% for breast surgery).

Antimicrobial use in surgery is complex, and includes more than procedural and post-procedural use. Patients may already be prescribed antimicrobial therapy for pre-existing infection (e.g., appendicitis, cholecystitis and trauma debridement of contaminated wounds). We excluded such data from our statistical analysis as this is not considered surgical prophylaxis. However, the administration of this therapy prior to surgery may void the use of additional procedural SAP. How SAP should be distinguished from existing and post-operative treatment is not clearly outlined in current guidelines and deserves greater attention in surgical training. Other concerns regarding SAP include uncertainty about routes of administration; there is limited evidence for topical and intra-operative powders, washes and solutions, and these are generally not recommended. Auditing these elements of prescribing will provide greater insight into current practices and identify targeted areas for improvement.

Overall, this research highlights much room for improvement of SAP prescribing in general. It demonstrates that SAP is prescribed poorly across all surgical specialties, and there is a need to improve documentation of incision time, and appropriateness of SAP administration timing and duration in the post-procedural setting.

Decision-making about surgical antimicrobial prescribing can be complex, and can involve multiple clinicians across the pre-, intra- and post-operative surgical settings. There is a need to explore the underlying drivers of behaviour to support the development of meaningful and sustainable behaviour change interventions [11,12].

We undertook a qualitative study involving focus groups with surgeons, anaesthetists, peri-operative nurses and clinical pharmacists across both public and private hospitals [13]. We analysed our qualitative data using validated theoretical frameworks, and identified six themes in clinicians' perceptions about decision-making for antimicrobial use across surgical settings: 1) SAP prescribing skills are considered a low priority; 2) prescriber autonomy takes precedence over guideline compliance; 3) the social codes of prescribing reinforce established practices; 4) there is a need for improved communication, documentation and

collection of data for action; 5) fears and perceptions about risk hinder appropriate SAP prescribing; and 6) there is a lack of clarity regarding roles and accountability for SAP prescribing.

Our findings highlight multiple factors that influence SAP prescribing and decision-making, as well as barriers to and enablers of appropriate prescribing. For example, poor documentation and communication regarding SAP prescriptions was considered a barrier, and noted across pre-, intra- and postoperative settings. One successful tool for communication regarding procedural SAP that was identified by participants was the 'time-out' process [14]:

"They (surgeons, anaesthetists and scrub nurses) definitely use the time-out. Everyone uses the time-out. But I'm not sure about the guidelines." (FG11, private theatre nurse.)

However, this does not address the issue of excessive post-procedural duration as identified in the Surgical NAPS. A potential solution would be to expand upon the success of this existing standardised workflow process and link it to other clinical pathways such as the Enhanced Recovery After Surgery (ERAS) protocol [15] to support greater clarity regarding a surgeon's SAP prescribing decisions, and advocate for standardised and guideline-compliant practices. This would minimise antimicrobial use in the post-operative setting and the subsequent burden on the patient in terms of side effects and antimicrobial resistance. Peri-operative nurses noted a high level of engagement in and uptake of protocols such as the 'time out' process [14,15]. We advocate for a multidisciplinary approach to surgical AMS that capitalises on existing skills but also supports capacity building for peri-operative nursing staff for implementation of interventions to improve antimicrobial use in the surgical setting.

The influence of medical and surgical hierarchy on SAP prescribing is well discussed in the literature [11,16]. We identified that Australian junior surgeons were reluctant to challenge the decisions of their consultants as this would disrupt surgical hierarchical culture.

"I think, the reality of the relationship with surgeons is that they don't want to be challenged by their junior staff." (FG15, public orthopaedic surgeon.)

"As a resident ... it's not within my power to say, 'Just stop it [the antibiotics]'. I have to ask someone else." (FG15, public orthopaedic surgeon.)

Participants observed that responsibility for the patient ultimately lay with the surgical consultant, and junior surgeons' actions should reflect the preferences of their superiors rather than their own clinical decision-making, competence, and awareness of guidelines and evidence-based practice.

"It's (up to) the consultants, you can't (change practice to single-dose SAP) ... They've got to be on board with it. Because, at the end of the day, you stop the antibiotics based on evidence, and something goes wrong – it will be your fault. It'll reflect badly on you because the consultant will say, 'That's not what I do.' And, the

guidelines are not enough to stand against a consultant who's got very set ways, in terms of their antibiotic prescribing ... Often, I'll just go with what my seniors have told me because, you know, that's what we do." (FG14, public surgical resident/registrar.)

Potential solutions to address the issues raised regarding surgical hierarchy include targeting AMS interventions at senior surgical consultants (as opposed to junior surgeons), and engaging with senior surgical consultants for the development and implementation of these quality improvement initiatives.

Fear of causing patient harm in the form of surgical site infections (SSI) was also identified as a driver of prolonged durations of SAP [13].

"I think the problem is that an infection is a nightmare. An infected joint is a catastrophe ... It could end up with the whole joint being removed. The patient having amputation ... I can completely understand why a surgeon would want more than one dose." (FG3, private anaesthetist.)

"I think, a lot of the surgeons are really, genuinely scared about being sued. I'm sure that drives practice ... I think it makes surgeons very reluctant to under treat infections because they're the ones who're going to cop it if the patient has a complication." (FG8, public urologist.)

Clinicians require meaningful data to provide reassurance regarding patient safety, and need evidence that their patients will not be adversely impacted if they change their prescribing practice to single-dose SAP. However, Australia does not have a nationally standardised approach to SSI surveillance. A recent health care-associated infection (HAI) point-prevalence study involving 19 Australian hospitals was conducted in 2018 [17]. This was the first in Australia in 34 years, and included 2,767 acute adult inpatients; it found 363 HAIs were present in 273 patients. The most common HAIs identified were SSIs (prevalence 3.6% [95%CI: 2.9–4.4]) [17].

Regular auditing of HAIs in conjunction with auditing of SAP prescribing quality is critical for surgical prescribing behaviour change [13,17]. The increasing uptake of electronic medication records further enables SAP and outcome auditing whilst supporting prescriber accountability and responsibility.

We advocate for the development of a national surgical AMS framework that enables the collection of meaningful data at a national level (SSI surveillance and prescribing quality), while engaging key stakeholders and prescribers, and designing and implementing targeted interventions to optimise antimicrobial use across the surgical setting.

Surgeons have acknowledged that, as part of their commitment to enhancing patient care, they have a role to play in addressing national and global concerns regarding the over-prescribing of antimicrobials in surgery. Health care in Australia operates within a multi-disciplinary and collaborative framework; thus, surgical AMS is not solely a surgeon's responsibility, and requires extensive collaboration among surgeons; anaesthetists; infectious diseases,

infection control and AMS clinicians; pharmacists; nurses; guideline developers; hospital management; representative bodies such as the Royal Australasian College of Surgeons (RACS), Australian and New Zealand College of Anaesthetists (ANZCA), Australian College of Perioperative Nurses (ACORN), Australian Private Hospitals Association (APHA), National Centre for Antimicrobial Stewardship (NCAS) and national hospital accreditation bodies such as the Australian Commission on Safety and Quality in Health Care (ACSQHC).

In 2018, the ACSQHC convened a 'Surgical Antimicrobial Prophylaxis Working Group' with representatives from the RACS, ANZCA, ACORN, APHA, NCAS, and state and territory health department representatives. The working group was established to support the development of resources to improve SAP prescribing. To date, two resources have been developed, a PowerPoint presentation and a poster [18]. No statements, progress reports or development of a national framework have been published.

Whilst a multi-disciplinary approach is essential, we also argue that as surgeons are the primary prescribers and carers of surgical patients, ownership and leadership from surgeons is required to support surgical AMS. Development and implementation of a national surgical AMS framework requires engagement with surgeons at both national and local levels to facilitate scaling and ensure that the framework is adaptable and will suit a range of surgical services. We advocate for RACS to have a greater role in this emerging field of quality improvement by engaging with the aforementioned potential collaborators and providing support for the development of further surgical education and training in this domain. Ongoing research is required to support the development of targeted and theoretically-informed interventions to support surgeons to optimise SAP prescribing.

Authorship statement

CI- conducted data analysis, developed analysis plan, wrote analysis, drafted and revised paper.
AR-conducted data analysis, developed analysis plan, wrote analysis, drafted and revised paper.
TP- revised paper.
CM-revised paper.
DA-revised paper.
KT-wrote analysis, revised paper.

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Ethics approval not required as this is a discussion (or review) paper.

Declaration of Competing Interest

Nil conflicts of interest to declare.

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