Developing an evidence-based intervention for surgical antibiotic prophylaxis use in women undergoing Caesarean delivery in Antigua and Barbuda

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Statement of contributions

I certify that the work in this thesis is my own. Where others have contributed, their initials have been used in the text.

Chapter 3 -Dr Denice Curtis (DC) contributed to duplicate data collection.

Chapter 4 – Dr Jong-Wook Ban (JWB) contributed to duplicate quality appraisal. Dr Wangari Waweru-Siika (WWS)- Contributed to duplicate title/abstract screening. Dr Helena Winston (HW) assisted with duplicate data extraction.

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List of abbreviations commonly used in this thesis

Abbreviations	Descriptions
AGREE	Appraisal of Guidelines for Research and Evaluation
AMC	Antimicrobial consumption
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
AMSTAR	Assessing the methodological quality of systematic reviews
APEASE	Affordability, practicability, effectiveness/cost-effectiveness, acceptability, side-effects/safety, equity
BCTTv1	Behaviour Change Techniques Taxonomy Version 1
BCW	Behaviour Change Wheel
BMI	Body mass index
BNF	British National Formulary
BPPL	Bacterial Priority Pathogens List
CARICOM	Caribbean Community
CDC	Center for Disease Control
CI	Confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COM-B	Capability, Opportunity, Motivation Behavioural
CPGs	Clinical practice guideline
CREDES	Conducting and Reporting Delphi Studies
C-section	Caesarean section
EBM	Evidence-Based Medicine
EMBASE	Excerpta Medica Database, Elsevier
EPOC	Effective Practice and Organisation of Care
GRADE	The Grading of Recommendations Assessment, Development and Evaluation
HCW	Healthcare worker
ICU	Intensive care unit
IOI	INEOS Oxford Institute for Antimicrobial Research
LILACS	Latin American and Caribbean Health Sciences Literature
LLMICs	Low and lower middle-income countries
MeSH	Medical Subject Heading

Abbreviations	Descriptions
MIC	Minimum inhibitory concentration
MMAT	Mixed Methods Appraisal Tool
MMSR	Mixed-methods systematic review
MRC	Medical Research Council
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
OXTREC	Oxford Tropical Research Ethics Committee
PAHO	Pan American Health Organization
PPS	Point prevalence survey
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
PROSPERO	International Prospective Register of Systematic Reviews
ROB	Risk of bias
ScR	Scoping review
SR	Systematic Review
SWiM	Synthesis without meta-analysis
TDF	Theoretical Domains Framework
WHO	World Health Organization

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Abstract

Antibiotic misuse in hospitals drives antimicrobial resistance (AMR) and threatens global health. An effective response requires locally generated evidence to inform the design of context-specific, evidence-based interventions. However, limited research on antibiotics in the Caribbean Community States constrains the region's efforts to address AMR.

The aim of this thesis was to develop an evidence-based intervention for standardising surgical antibiotic prophylaxis in women undergoing Caesarean deliveries (C-sections) in Antigua and Barbuda. A multi-phased approach comprising several study designs was guided by the Medical Research Council Framework for Complex Interventions. Three evidence syntheses defined the evidence base for antibiotic prescribing and use in CARICOM states, antimicrobial stewardship interventions targeting hospital workers across geographical locations, and global clinical practice recommendations for surgical antibiotic prophylaxis in C-sections. It was concluded that evidence on antibiotic use in CARICOM States is limited to two countries; AMS intervention components are poorly described and infrequently evaluated in low-income settings; and the quality of and recommendations for surgical antibiotic prophylaxis vary across countries. To understand antibiotic use in Antigua and Barbuda, a cross-sectional study on systemic antibiotic prescribing, a retrospective analysis of prophylactic antibiotic use in C-sections, and a COM-B informed qualitative study exploring factors influencing decision-making around surgical antibiotic prophylaxis in C-sections were conducted. The cross-sectional study showed that 37% (n=10,377) of all systemic antibiotic prescriptions were cephalosporins, while 24% (n=6709) were metronidazole. However, no clinical information was available, limiting interpretation of the

prescribing data. In the retrospective analysis, multivariable regression demonstrated significant temporal and consultant-based variation in the use of single-regimen preoperative surgical antibiotic prophylaxis and in the duration of postoperative prophylaxis ($p<0.001$). These findings were further supported by the qualitative investigation, which identified consultant preference as a key determinant of surgical antibiotic prophylaxis prescribing and insufficient physical resources and social opportunities as influences on prescribing behaviour.

Findings informed a Delphi study to establish formulary content consensus for surgical antibiotic prophylaxis. Expert consensus agreement was reached on 13 items to be included in a formulary. Using the Behaviour Change Wheel, cumulative findings from all investigations informed a context-specific intervention strategy to standardise surgical antibiotic prophylaxis during C-sections in Antigua and Barbuda.

CHAPTER ONE

Chapter 1: Overview and structure of thesis

1.1 Overview of thesis

This thesis investigated the evidence for the prescribing and use of antibiotics in the Caribbean Community (CARICOM) States. It culminates in the development of a complex, evidence-based intervention for surgical antibiotic prophylaxis in women undergoing caesarean delivery in Antigua and Barbuda. Several recent studies on antibiotic use originate in countries with relatively well-funded healthcare systems.[1-4] In settings such as the CARICOM States, evidence on how antibiotics are prescribed and used, and methods for monitoring and improving use, is inadequate.[5] With antibiotic resistance continuously emerging, the ramifications of this 'silent pandemic' on patient safety and global health would be most experienced in low-resource settings. This prompted an investigation into how antibiotics are prescribed in CARICOM states.

In line with the Medical Research Council's Framework for the development of complex interventions,[6, 7] two evidence syntheses were conducted to define the evidence base.

First, a mixed-methods systematic review (MMSR) on the prescribing and use of antibiotics and antimicrobial stewardship (AMS) interventions in CARICOM States showed limited research in a few CARICOM States.[5] Next, a scoping review of systematic reviews was conducted to investigate AMS interventions implemented in hospitals globally, particularly in low and lower-middle-income countries. The scoping review found a paucity of evidence on AMS interventions in low and lower-middle-income countries.[8] Based on the implications for additional research documented in Chapter 3, Chapter 5 presents a cross-sectional

review of systemic antibiotic prescriptions for hospitalised patients, which was conducted in a selected CARICOM State, Antigua and Barbuda. Further targeted investigations into antibiotic use in Antigua and Barbuda included a retrospective analysis of surgical antibiotic prophylaxis in women undergoing caesarean delivery (Chapter 6) and a qualitative inquiry into factors influencing decision-making around surgical antibiotic prophylaxis (Chapter 7). These studies identified several challenges in the setting, including unwarranted variation and a non-evidence-based approach to prescribing antibiotics. Based on the prescribing variations reported in Chapters 6 and 7, a systematic review of clinical practice guidelines (Chapter 8) was conducted to synthesise global practice recommendations on surgical antibiotic prophylaxis in C-sections. The findings of Chapter 8's evidence synthesis and relevant findings from Chapters 3, 4, 5, 6, and 7 were used to inform the criteria for Chapter 9's Delphi study on items to be included in a formulary on surgical antibiotic prophylaxis. Expert consensus was reached on several items presented in the Delphi study, and a simple formulary for surgical antibiotic prophylaxis was developed. In Chapter 10, the Behavioural Change Wheel [9] is applied to develop a complex, evidence-based intervention strategy to standardise the prescribing of surgical antibiotic prophylaxis for C-sections.

1.2 Aim of thesis

This thesis uses an evidence-based approach to develop an intervention to standardise the prescribing of surgical antibiotic prophylaxis for women undergoing Caesarean deliveries in Antigua and Barbuda.

1.3 Thesis objectives

a. Define the evidence base for the prescribing of antibiotics in hospitalised patients of the Caribbean Community (CARICOM) States.
b. Identify the global evidence base of evaluated healthcare worker-targeted antimicrobial stewardship interventions implemented in hospitals.
c. Investigate the prescribing patterns of systemic antibiotics for hospitalised patients at a tertiary care hospital in Antigua and Barbuda.
d. Evaluate the targeting of surgical antibiotic prophylaxis for women undergoing caesarean delivery at a tertiary care hospital in Antigua and Barbuda.
e. Identify drivers of surgical antibiotic prophylaxis use for women undergoing caesarean delivery at a tertiary care hospital in Antigua and Barbuda.
f. Investigate the global clinical practice recommendations for surgical antibiotic prophylaxis in caesarean sections and examine the underpinning evidence.
g. Generate consensus for items to be included in a formulary for surgical antibiotic prophylaxis in caesarean sections in Antigua and Barbuda.
h. Develop an evidence-based intervention for standardising surgical antibiotic prophylaxis in caesarean sections in Antigua and Barbuda.

1.4 Epistemological approach to thesis

The author does not align exclusively with a positivist/post-positivist or constructivist approach but adopts a pragmatic approach in this thesis, an orientation often associated with the use of mixed methods in research.[10, 11] Pragmatism is valuable in research because

it accommodates complex problems that require flexible research designs, diverse data sources, and iterative decision-making.[12] Since healthcare is dynamic and antibiotic prescribing is complex, a pragmatic approach allowed the author to select the most suitable research methods to address the specific research problems identified in this thesis.[10, 13] Moreover, this thesis aimed to develop a context-specific, evidence-based intervention to standardise surgical antibiotic prophylaxis in C-sections. This intervention development work aligns with the pragmatic philosophy, which supports practical innovation and outcome-oriented research inquiry methods.[14]

1.5 Structure of thesis

Table 1.1 shows the structure of this thesis, which was developed using the Medical Research Council's Framework for the Development of Complex Interventions.[6, 7]

Table 1.1 Outline of thesis using the Medical Research Council Framework

MRC Framework		Thesis aims	Study design
Developing complex intervention	Identify the evidence base	1. Define the evidence base for the prescribing of antibiotics in hospitalised patients of the Caribbean Community (CARICOM) States.	**Chapter 3:** Mixed methods systematic review
		2. Identify the global evidence base of evaluated healthcare worker-targeted antimicrobial stewardship interventions implemented in hospitals.	**Chapter 4**: Scoping review of systematic reviews
	Identify/ develop appropriate theory	3. Investigate the prescribing patterns of systemic antibiotics for hospitalised patients at a tertiary care hospital in Antigua and Barbuda.	**Chapter 5:** Cross-sectional study
		4. Evaluate the targeting of surgical antibiotic prophylaxis for women undergoing caesarean sections at a tertiary care hospital in Antigua and Barbuda.	**Chapter 6**: Retrospective analysis
		5. Identify drivers of surgical antibiotic prophylaxis use for women undergoing caesarean delivery at a tertiary care hospital in Antigua and Barbuda.	**Chapter 7**: Qualitative investigation
		6. Investigate the global clinical practice recommendations for surgical antibiotic prophylaxis in caesarean sections and examine the underpinning evidence.	**Chapter 8**: Systematic review
	Modelling process and outcomes	7. Generate consensus for items to be included in a formulary for surgical antibiotic prophylaxis in caesarean sections in Antigua and Barbuda.	**Chapter 9:** Delphi study

MRC- Medical Research Council, CARICOM-Caribbean Community, HCW- healthcare worker, AMS-antimicrobial stewardship,

Chapter 2: Thesis background

Chapter 2 provides a historical perspective on antibiotics, their usefulness in human medicine, the principles of use, and the consequences of misuse for global health. It provides a comprehensive overview of the literature on antibiotic use and antibiotic resistance, with a focus on the CARICOM States. This chapter highlights the limited research on antibiotics in the CARICOM States and discusses the need to establish a robust evidence base for this region. The use of the Medical Research Council's Framework for Complex Intervention Development[6] and the Behaviour Change Wheel[9] are presented as they can be used in tandem to develop an intervention to improve antibiotic prescribing.

Chapter 3 The prescribing of antibiotics in Caribbean Community (CARICOM) States

In Chapter 3, a mixed-methods systematic review (MMSR) synthesises the evidence base on prescribing antibiotics to hospitalised patients across the Caribbean Community (CARICOM) States. Eight studies published more than 5 years before this MMSR were conducted met the review's inclusion criteria and were therefore included. It was determined that evidence on antibiotic prescribing and the implementation of AMS interventions in CARICOM States is limited to a few CARICOM States. This MMSR was presented at the Hilary Term 2021 Doctoral Research Seminar and the 2022 EBM Live Conference in Oxford. The findings were published in the Journal of Hospital Infection.[5]

Chapter 4: Global evidence base of healthcare worker-targeted antimicrobial stewardship interventions used in hospitals.

A descriptive summary of the evidence for antimicrobial stewardship (AMS) interventions targeting healthcare workers in hospitals was reported in Chapter 4. A scoping review of systematic reviews combined global evidence on AMS intervention components and the methods used to conduct these studies. Intervention components were classified according to the Effective Practice and Organisation of Care (EPOC) Taxonomy of Health Systems interventions.[15] Audit and feedback and clinical practice guidelines were the most evaluated intervention components. However, there was insufficient evidence from AMS interventions implemented in LLMICs, as 18 systematic reviews, comprising 547 primary studies, included only 12 publications from low- and lower-middle-income countries. The findings of this review were published in the Journal of Hospital Infection.[8]

Chapter 5: Prescribing of antibiotics for systemic use in general wards at a tertiary care hospital in Antigua and Barbuda.

Chapter 5 outlines the prescribing of antibiotics for systemic use in hospitalised patients at a tertiary care hospital in Antigua and Barbuda. A cross-sectional review of systemic antibiotic prescriptions for hospitalised patients was conducted using the pharmacy drug dispensing dataset spanning January 1, 2014, to September 30, 2021. Evidence shows that cephalosporins were the most commonly prescribed antibiotic class; antibiotic prescriptions are often empirical and administered intravenously for extended periods. The findings of this study were presented in poster format at the INEOS Oxford Institute for Antimicrobial

Research (IOI) Early Career Researcher Conference 2026. This study is currently under preparation for publication in Antimicrobial Stewardship & Healthcare Epidemiology.

Chapter 6: Use of surgical antibiotic prophylaxis for women undergoing caesarean sections at a tertiary care public hospital in Antigua and Barbuda.

For Chapter 6, the author conducted a retrospective analysis of medical records of women who delivered via Caesarean sections (C-sections) from January 1, 2018, to December 31, 2024. Data on the type, dosage, frequency, and duration of surgical antibiotic prophylaxis, as well as patient age, the urgency of C-section, and the attending consultant, were extracted and evaluated. Findings show a statistically significant association between the type and duration of surgical antibiotic prophylaxis and the attending consultant. This chapter highlighted unwarranted variation in the prescribing of surgical antibiotic prophylaxis, indicating the absence of an evidence-based approach.

Chapter 7: Decision-making around the use of surgical antibiotic prophylaxis for women undergoing caesarean sections at a tertiary care hospital in Antigua and Barbuda.

In this chapter, a qualitative study employing a vignette-based methodology explores factors influencing decision-making regarding the use of surgical antibiotic prophylaxis for women undergoing C-sections at a tertiary care hospital in Antigua and Barbuda. Semi-structured interviews were delivered either face-to-face or online to explore how prescribing decisions are made for women identified for C-sections. The data were analysed inductively, and it was determined that hierarchical structure is the key factor influencing decision-making regarding the use of surgical antibiotic prophylaxis. The Capability, Opportunity,

Motivation Behavioural (COM-B) Model[16] is introduced in this chapter and is applied to interview data to understand the behaviours associated with decision-making. The application of the COM-B Model highlighted several behavioural barriers to decision-making, including inadequate physical resources to facilitate appropriate prescribing and poor social support networks. The findings of this study were presented in poster format at the IOI 2025 Early Career Researcher Conference: Multidisciplinary Approaches to AMR on 21 March 2025.

Chapter 8: Global clinical practice recommendations for surgical antibiotic prophylaxis in caesarean sections

A systematic review of clinical practice recommendations for surgical antibiotic prophylaxis during C-sections is reported in Chapter 8. This chapter summarises current recommendations for surgical antibiotic prophylaxis from several prominent global clinical practice guidelines (CPGs). The methodological quality of CPGs was assessed using the AGREE II tool[17], and the evidence supporting practice recommendations was examined. Most CPGs were from the European context, and no CPGs were retrieved for the Caribbean region. All CPGs recommended the preoperative use of surgical antibiotic prophylaxis in C-sections, as it reduces the risk for post-operative infectious complications. There were some variations with the choice of antibiotic agent and the timing of administration. The quality of CPGs varied across settings, and the evidence supporting recommendations was published before 2022.

Chapter 9: Items to be included in a formulary for surgical antibiotic prophylaxis in C-sections in Antigua and Barbuda.

This chapter used a Delphi study design and generated expert-level consensus on items to include in a formulary detailing surgical antibiotic prophylaxis for women undergoing C-sections in Antigua and Barbuda. Survey criteria were developed using accumulated evidence from Chapters 3 to 8, local bacterial sensitivity profiles and hospital stakeholder input. Following two rounds of surveys, there was consensus on 13 items for inclusion in a formulary for surgical antibiotic prophylaxis. Items included the antibiotic agent, the timing of administration, the duration of prophylaxis and considerations for special patient circumstances.

Chapter 10: Discussion and conclusion

In Chapter 10, the author summarises the findings of Chapters 3 to 9 and discusses how this evidence contributes to current knowledge on antibiotic prescribing. A proposed intervention strategy, along with a programme theory, provides information on what could be done to improve prescribing in the setting and how and why the intervention is supposed to achieve its outcome. The strengths and limitations of the work reported in this thesis and implications for practice and future research are also provided.

1.5 Academic activities

1.5.1 Training and skills development

The author completed multiple training sessions and workshops organised by the Medical Sciences Division, the Nuffield Department of Primary Care Health Sciences, the Department of Continuing Education, and the Information Technology Department, some of which are listed in Table 1.2.

Table 1.2 Methods used in the thesis and associated training

Methods	Training	Date completed
Evidence syntheses	Introduction to systematic reviews and evidence syntheses:	2018-10-18
	Systematic reviews	2021-01-19
	Assessing risk of bias in randomized trials/systematic review	2021-01-28
	Mixing it up: Understanding and using mixed methods research in	2019-04
	Qualitative evidence synthesis	
	Conducting a scoping review	
Cross-sectional study/ Retrospective analysis	Spreadsheets: Good practice with pivot tables (Excel)	2020-12-01
	Bite-sized: Excel Power Query	2025-04-02
	Introduction to Statistics	2025-03-31 /04-15
	Choosing the right data analysis software: R, STATA, and SPSS	2025-05-19
	R: A first look	2025-01-23
	Introduction to R for biologists	
	Information security and data privacy	
	SPSS: Up and running for academic research course	2022-05-13
	Excel: Good practice with lookups	2025-05-20
Qualitative investigation	Interviewing for qualitative research	
	Coding in qualitative research	
	Collecting qualitative data: Interviews and Focus Groups	
	Assessing quality in qualitative research	2021-02-02
	Primary qualitative research made simple	2021-02-22
	Synthesising qualitative research made simple	2025-03-27/28
	Learning with the Book: An Introduction to Qualitative Research	Jan – March 2023
	Qualitative interviewing: An introduction	2022-01-06
	Qualitative analysis – where do themes come from?	2021-06-17
	NVivo - Walking before running: Code and retrieve	2025-05-22
Delphi study and intervention development	Surveys: Introduction to Jisc Online Surveys and Microsoft Forms.	2021-05-26
	Introduction to Behaviour Change	2023-05-01
	Implementation Research (IR) with a focus on Infectious Diseases	2019-12-08
	Utilising Social Science and Behaviour Change in Antimicrobial	2021-04-01
	Digiknow: Creating mind maps, flowcharts and infographics.	2022-02-22
	Microsoft Project	2021-03-16

General training	Word Tools, Tips and Timesavers	2025-05-06
	Word Advanced	2025-06-25
	Developing new ideas through analytical frameworks	2023-11-08
Dissemination	Improving your research posters	2020-12-07
	Presentations: Delivering with confidence (Extended)	2025-03-25
	Large group and lecturing	2024-03-14

Three behaviour change courses: Introduction to Behaviour Change, Utilising Social Science and Behaviour Change in Antimicrobial Stewardship Programmes, and Tackling Antimicrobial Resistance: A Social Science Approach, were completed via the Future Learn platform.

1.5.2 Dissemination of research findings

Three of the evidence syntheses conducted as part of this thesis have been published in the Journal of Hospital Infection, one of which is reported in Chapter 3,[5] Chapter 4,[8] and Chapter 8. The MMSR reported in Chapter 3 was presented at the EBM Live Conference in Oxford in July 2022 and the Doctoral Research seminar hosted by the Department of Continuing Education. The qualitative investigation of decision-making regarding surgical antibiotic prophylaxis for C-section patients, reported in Chapter 7, was presented as a poster at a conference hosted by the INEOS Oxford Institute (IOI) for Antimicrobial Research on March 21, 2025. Chapter 5's retrospective analysis of general systemic antibiotic prescribing was presented as a poster at the IOI Early Career Researcher Conference 2026 on March 20, 2026. The findings from all chapters of this thesis were presented at Sir Lester Bird Medical Centre, Antigua, on August 15, 2025, and to the Antimicrobial Resistance Group of the Pan American Health Organisation on September 25, 2025. The Pan American Health

Organisation has acknowledged the author on its social media platforms as an advocate in the fight against antimicrobial resistance.

1.5.3 Teaching and Research Supervision

The author is an adjunct faculty member at the School of Health and Behavioural Sciences at the University of the West Indies, Five Islands Campus in Antigua and Barbuda. Key duties include lecturing in Research Methodology to undergraduate nursing students and supervising student research projects through completion. Since 2020, the author has supervised 17 undergraduate nursing research projects.

CHAPTER TWO

Chapter 2: Introduction

2.1 Chapter aims

This chapter provides an overview of the history of routinely used antibiotics, their importance in human medicine and the consequences of inappropriate use on global health; an updated literature review on antibiotic use in the Caribbean Community; and describes an approach for developing an antimicrobial stewardship intervention to optimise antibiotic use while exploring the complexities of prescribing.

2.2 Definitions of key terms

In 1889, Jean Paul Vuillemin used the term antibiose to describe the antagonistic behaviour displayed by one microbe against another.[18] Further, in 1947, Selman Waksman introduced the term 'antibiotic' for substances which demonstrated antibacterial activity, defining it as "*a chemical substance, produced by micro-organisms, which has the capacity to inhibit the growth of and even to destroy bacteria and other micro-organisms.*"[19] This definition covered only naturally produced antibacterial agents. Several definitions have been used over the decades. The World Health Organization uses the term antimicrobials and broadens the scope to include drugs used to target all microorganisms. The definition is as follows *"Antimicrobials – including antibiotics, antivirals, antifungals, and antiparasitics – are medicines used to prevent and treat infectious diseases in humans, animals and plants*." [20] The term antimicrobial is often used interchangeably with antibiotics in the literature. The Oxford English Dictionary defines an antibiotic as "That kills, or inhibits the growth or reproduction of, microorganisms, esp. bacteria; antibacterial or antimicrobial.[21] In

this thesis, the author uses the term antibiotics in discussions about prescribing, use and resistance. The term "antimicrobial" will be used for direct quotations or when antimicrobial stewardship interventions are being discussed.

2.3 An overview of antibiotics

Thousands of years ago, microorganisms that produced antibacterial compounds were used to prevent infections. Mouldy bread poultice applications were used by many to treat open wound infections.[22] The use of beer yeasts and mushrooms has also been documented for treating infections.[23] Between 1874 to 1876, William Roberts and John Tyndall described the bacteriolytic properties of Penicillium sp.[24] In 1885, it was reported that Arnalda Cantani successfully treated a tuberculosis patient using *Bacterium termo* formulated as an inhaled spray.[24] The earliest documented widespread use of a synthetically derived organoarsenic compound, arsphenamine (Tradename-Salvarsan 606), with antibacterial activity was used from 1910 to treat infections with *Treponema pallidum*.[25, 26] Drug targeting was postulated by Paul Ehrlich in the late 19th century, arsphenamine was later developed in Ehrlich's laboratory by Alfred Bertheim in 1907, and its antisyphilitic activity was illustrated by Sahashiro Hata in 1909.[26] By 1924, resistance to arsphenamine was seen in clinics, although this had been shown via experiments 7 years earlier.[27] A major subsequent documented lab discovery was the identification of a naturally occurring antibiotic by Alexander Fleming in 1928. Fleming observed that on an old agar plate cultured with *Staphylococcus sp* there was reduced growth and cell lysis around the area where a contaminating mould, *Penicillium notatum*, had grown.[28] Further in vitro testing of *Penicillium notatum* identified a bacteriolytic substance, coined Penicillin, which inhibited the growth of Staphylococcus and

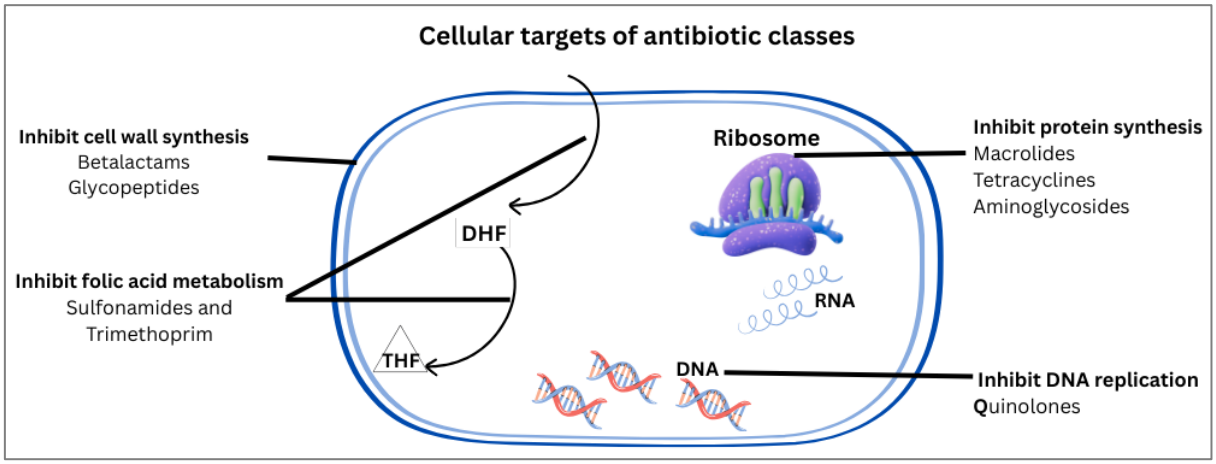
other species of bacteria when it had diffused into the agar.[28] Penicillin was later introduced into clinical treatment in 1941 after it was extracted and purified by Howard Florey, Ernst Chain and Norman Heatley. [29, 30] A sulphonamide, prontosil, developed by Gerhard Domagk in 1939, was the second documented synthetic antibiotic.[31] Prontosil was the first documented antibiotic with broad-spectrum activity.[22] Since then, several antibiotics have been synthetically formulated, and naturally occurring antibiotics have been refined for clinical management. A brief timeline of the identification/development of currently used classes of antibiotics is illustrated in Table 2.1.

Table 2.1 Timeline of antibiotic discovery, first clinical use and resistance in clinical samples

Antibiotic class	Discovery of antibacterial substance	Documented first use	Early reports of antibiotic resistance - clinical
Penicillin	1928 [28] Isolated from Penicillium notatum by Alexander Fleming	1941 [30] Clinical treatment for some groups	1942 *Staphylococcus aureus* strains in hospitalised patients were resistant to penicillin.[32]
Sulphonamides	1932 [33] Prontosil, a synthetic agent, was developed by Gerhard Domagk in 1939.	1935 [34, 35] Clinical treatment	1945 Treatment failure due to some strains of Streptococcus developing resistance [36]
Aminoglycosides	1943 [37] Isolated from *Streptomyces griseus* by Selman Waksman. Streptomycin was produced.	1944 [38] Trials in humans	1974 [39] Resistance in clinical isolates of Enterobacteriaceae and Pseudomonas.
Tetracyclines	1945[40] Tetracycline - *Streptomyces aureofaciens* isolated from soil by Benjamin Minge Duggar. Aureomycin was produced.	1948 [41, 42] Tetracycline used for clinical	1953[43] Isolated from *Shigella dysenteriae*
Cephalosporins	1945 [44] - *Cephalosporium acremonium* isolated from seawater by Guiseppe	1964 [44] Clinical	1960s[45]
Macrolides	1950 [46] *Streptomyces erythraeus* isolated from soil by J. McGuire. Ilyocin, later known as erythromycin, was derived.	1952[47] [46]	1968[48] Resistance to erythromycin by *Streptococcus pyogenes*.
Glycopeptides	1954 [22] *Amycolatopsis orientalis* isolated from soil by Edmund Kornfeld.	1958 [49, 50] Approved for	Mid 1990s – 2000s [51] First reported clinical isolates
Quinolones	1962 [52] Synthetically derived , nalidixic acid, by George Lesher.	1962 [52] Clinical trials	1987 resistance to *S.dysenteriae* reported.[53]
Azoles	1953 Azomycin was extracted from bacterium *Nocardia mesenterica* by K. Maeda, T.Osato and H. Umezawa. Synthetic metronidazole was later developed.	1959 [54] Metronidazole used for clinical treatment.	1978 [55] Treatment failure due to resistant Bacteroides fragilis. Sensitivity testing not routinely conducted for anaerobes.[56]
Carbapenems	1976 [57] Thienamycin found in culture broths of *Streptomyces cattleya* but not used clinically. Imipenem developed in 1984.	1985 [58] Imipenem approved for use- US	1991 [59] Resistance reported in *Pseudomonas aeruginosa* isolate during clinical trial for nosocomial pneumonia.

2.3.1 Pharmacology and classification of antibiotics

Antibiotics are broadly grouped into two categories, bacteriostatic and bactericidal based on in vitro activity. Bacteriostatic antibiotics inhibit bacterial cell growth while bactericidal antibiotics kill bacterial cells. Each antibiotic specifically targets an essential cellular function or component of bacterial cells.[60] In summary, the main mechanisms of action of antibiotics include the inhibition of cell wall synthesis , nucleic acid synthesis, protein synthesis and folic acid metabolism.[61] Figure 2.1 further illustrates the mechanisms of specific antibiotics on bacterial cells.



DNA-deoxyribonucleic acid, RNA-ribonucleic acid, DHF-dihydrofolate, THF-tetrahydrofolate

Figure 2.1 Cellular targets of antibiotic classes

Several factors are used to categorise antibiotics, including origin, mechanism of action, spectrum of activity, chemical structure and pharmacokinetic properties. The chemical structure, spectrum of activity and mechanism of action will be used to frame discussions on antibiotics in this thesis. Spectrum of activity pertains to the range of bacteria targeted by an antibiotic. Broad-spectrum antibiotics target a diverse range of bacteria, whereas

those antibiotics that target selected bacterial strains or groups are referred to as narrow-spectrum antibiotics. Antibiotics originating from a single source generally exhibit similar chemical structures and are classified based on these structural characteristics.

2.3.2 Antibiotics in human medicine

When used appropriately, antibiotics are essential in modern medicine. These drugs are important for the treatment of bacterial infections and for reducing the risk of infection in persons undergoing essential medical procedures such as chemotherapy, which compromises the immune system of cancer patients, and Caesarean sections (C-sections).[62]

Most adverse effects of antibiotic use are relatively minor and patient-specific. Allergic reactions, particularly to penicillins and cephalosporins, can range from mild to severe and may require antihistamines and further medical management. These adverse effects typically resolve once the treatment course is completed or discontinued following a medical consultation. Nephrotoxicity and ototoxicity are more severe complications of antibiotic use, seen with the use of aminoglycosides.[63] Heart problems, severe aches and pains, and central nervous system stimulation have been documented with fluoroquinolone use. [64, 65] Extended use of broad-spectrum antibiotics can increase the risk of Clostridium difficile infections.[66]

2.3.3 Antibiotic resistance

An unintended consequence of antibiotic use is the development of bacterial resistance to antibiotics. Antibiotic resistance develops when bacteria stop responding to drugs that once inhibited or destroyed them.[20] This usually occurs after some bacterial cells survive exposure to an antibiotic and are able to replicate and spread. Antibiotic resistance is the "temporary

or permanent ability of an organism and its progeny to remain viable and/or multiply under conditions that would destroy or inhibit other members of the strain."[67] Bacteria can be intrinsically resistant to an antibiotic, or they can acquire resistance.[68] With intrinsic resistance, some bacterial species possess low-permeability outer membranes, which prevent the entry of certain classes of antibiotics, and active multidrug efflux pumps, which reduce drug concentration within bacterial cells.[69] Bacteria acquire resistance by utilising a host of different mechanisms, including genetic adaptations, alterations of antibiotic target sites, limiting diffusions of antibiotics through biofilms, permeability barriers, enzymatic modifications and neutralisation of antibiotics.[70] With acquired resistance, it can be relative, meaning the bacteria remain susceptible to the drug, but the minimum inhibitory concentration (MIC) gradually increases over time.[68] Acquired resistance can also be absolute, in which the bacterial MIC exceeds what is safely used in clinical practice.[68] The development of antibiotic resistance has been reported since the first antibiotics were discovered, and it is a natural process carried out by bacteria to ensure their survival.[20] Therefore, the widespread utilisation of some antibiotics in hospitals inadvertently contributes to the emergence of antibiotic-resistant bacteria, which pose a significant threat to global public health and economies.[71]

2.3.4 Antibiotic misuse

Drug misuse has been defined by the World Health Organization (WHO) as "*the use of a substance for a purpose, that is, not consistent with legal or medical guidelines*".[72] Antibiotic misuse, first discussed by Fleming in the 1940s, refers to not using the right drug for the right patient, at the right dose for the right duration.[73, 74]

Concerns have been raised about the inappropriate use of antibiotics in hospitals, and it was noted that up to 50% of antibiotic use in this setting is inappropriate.[75] Further, the WHO has stated that antibiotic misuse is a principal driver of antibiotic resistance in bacteria.[20] This was confirmed in a study by Goossens et al., who reported a significant association between higher antibiotic use and bacterial resistance in some European countries.[76] Infections caused by antibiotic-resistant bacteria can be complicated to treat and life-threatening. It has been estimated that 1.27 million deaths (95% CI: 0.91-1.71) in 2019 have been attributed to infections caused by antibiotic-resistant organisms, with 27·3 deaths per 100 000 (20·9–35·3) in western sub-Saharan Africa. [77, 78] . For Latin America and the Caribbean, estimates for 2021 show that 78.1 per 1000 deaths were attributable to antibiotic-resistant bacterial infections, while 322 per 1000 deaths were associated with antibiotic-resistant bacteria.[79] The O'Neill Report projected that by 2050, the lives of 10 million people per year could be at risk due to infections caused by antibiotic-resistant organisms.[62] Low and middle-income countries will be disproportionately affected by the drivers of antibiotic resistance, and will experience both direct and indirect consequences.[20, 62] Latin America and the Caribbean were identified as one of the two regions projected to have the highest all-age mortality from AMR infections.[79]

2.3.5 Principles of antibiotic use

The British National Formulary emphasised the importance of evaluating three key factors before selecting an antibacterial agent: the patient's circumstances, the likely or known causative organism, and the risk of bacterial resistance if the antibiotic is repeatedly used.[80] Using appropriate antibiotics at the correct dose, time, and frequency helps to reduce the

risk for infectious postoperative complications and minimises the development of antibiotic-resistant organisms.[81]

Within hospitals, there is often unexplained variation in antibiotic prescribing for the same clinical condition or circumstance. In a study by Schulman et al, observed antibiotic use in a neonatal intensive care unit could not be explained by infection burden or other clearly identified indications.[82] This phenomenon has been described as unwarranted variation by John Wennberg, who explained that "*variations are unwarranted because they cannot be explained by type or severity of illness or by patient preferences*."[83] This results in the misuse of antibiotics and has serious consequences for patient outcomes and the development of antibiotic resistance. To mitigate unwarranted variations in antibiotic prescribing, context-specific hospital-wide strategies need to be designed, implemented, and monitored to improve prescribing practices.

2.4 Overview of the health structure in CARICOM States

The Caribbean Community (CARICOM), was established on 4 July 1974 and is a regional organisation in the Caribbean comprising 15 member states and 5 associate members. These countries, illustrated in Figure 2.2, collaborate to create a single market and economy, promote foreign policy and security cooperation, and improve education, living standards and health across the region. [84]



Figure 2.2 Map of the Caribbean showing the 15 CARICOM Member States highlighted with yellow markers

The Caribbean Public Health Agency coordinates regional health surveillance and policy. It has developed a regional health framework in collaboration with the Pan American Health Organization and the CARICOM Secretariat to address priority diseases and strengthen the region's health systems.[85] In a recently developed project, "Strengthening national and regional AMR detection and surveillance in CARICOM Member States 2019-2021", CARICOM States, Pan American Health Organization (PAHO) and Argentina cooperated to strengthen AMR-focused activities, particularly lab capacity for AMR detection. Although efforts are ongoing, few countries in the region have developed and implemented National Action Plans to address AMR.

2.4.1 Health system structure in Antigua and Barbuda

Antigua and Barbuda has a population of approximately 88,000 according to the 2011 census.[86] Persons aged 15-64 years account for 78.75% of the population, with a life expectancy of 76.9.[87] The Ministry of Health, Wellness and the Environment governs and finances Antigua and Barbuda's health system. In 2014, the government expenditure on health as a percentage of total government expenditure was 18.08, and 5.85 (2021) as a percentage of the Gross Domestic Product.[87] There are approximately 25 primary clinics within the country and one 158-bed public hospital, the Sir Lester Bird Medical Centre, which provides secondary and tertiary care to the population. There are no structured antimicrobial stewardship (AMS) programs at this hospital; however, there have been ad hoc activities addressing this public health threat.

2.5 Antibiotic use in the Caribbean Community

An updated literature search was done on 31 October 2025 using the search strategy first utilised in 2019 for Chapter 3's mixed-methods systematic review. The search was conducted in the databases Medline Ovid, EMBASE (Excerpta Medica Database), LILACS (Latin American and Caribbean Health Sciences Literature), and Google Scholar. Since the publication of the mixed-methods systematic review on antibiotic prescribing in CARICOM states,[5] relatively few articles on antibiotic use, prescribing, resistance and stewardship from the CARICOM States were retrieved between 2020 and 2025. Two recent studies on AMS interventions in Latin America and the Caribbean were identified, but no interventions were evaluated in CARICOM States.[88, 89] The remaining publications on AMS interventions and programs focused on Latin American countries. [88, 90-97] Multiple AMR-related studies were retrieved; two described AMR hospital surveillance data from several CARICOM countries. [98, 99] Carbapenem resistance was the focus of two studies: one on *Klebsiella pneumoniae* in Barbados, [100] and the other examined resistance in *Escherichia coli* and *Klebsiella sp* in patients from intensive care units.[101] Surveys exploring knowledge, attitude and practice regarding antibiotic resistance and use were conducted in community settings in Dominica and Trinidad and Tobago.[102-104] Two studies have investigated antimicrobial consumption (AMC) in different settings within Trinidad and Tobago.[105, 106] A third multi-country descriptive study examined AMC in Latin America and four CARICOM States, Barbados, Guyana, St Kitts and Nevis and Trinidad and Tobago.[107] AMC studies track regional and national trends of antibiotic use and enable institutional, regional and country-level comparisons when a

standard methodology is applied. The retrieved AMC studies did not yield patient-level data, limiting the ability to identify target populations for AMS efforts.

Research teams from PAHO assessed the prevalence of antibiotic use in CARICOM States using the WHO Methodology for Point Prevalence Survey (PPS) on Antibiotic Use in Hospitals.[108] In one PPS, antibiotic use was audited in hospitals of three CARICOM States: Barbados, Guyana and St. Lucia. The percentage of inpatients using antibiotics was 35.6% (95% CI -30.5, 41.0) in Barbados, 48.6% (95% CI -43.3, 54.0) in Guyana, and 47.1% (95% CI -38.4, 56.0) in St Lucia.[109] The three most prescribed antibiotics also varied by country, Barbados-Amoxicillin/clavulanic acid 21.4%, ciprofloxacin (12.6%), and metronidazole (11.9%); Guyana-Ceftriaxone (20.9%), gentamicin (10.3%), and ampicillin (9.1%); and St Lucia-Amoxicillin/clavulanic acid (18.4%), cefuroxime (18.4%), and metronidazole (18.4%)[109] In a multi-centre PPS conducted in Haiti, the overall prevalence of antibiotic use was 73% (95% CI, 68.2%–81.8 %), with equal numbers of prescriptions for therapy and prophylaxis.[110] Of all antibiotics prescribed for prophylaxis, 68% were used for medical prophylaxis.[110] PPS provide a snapshot of antibiotic use among admitted patients on each audited ward for a single day. However, they do not provide details on whether the right patient receives the right antibiotic for the right duration.

Overall, several knowledge gaps regarding antibiotic use in the CARICOM States remain, and this is compounded by the predominant use of observational study designs and the lack of follow-up studies to address identified gaps or areas for AMS interventions. The observations from this literature review were supported by Hegewisch-Taylor and

colleagues, who reported only baseline findings on antibiotic use in a few CARICOM States in their 2020 review of AMS interventions. [111]

2.6 Preserving antibiotics

The WHO has created a list of 15 families of antibiotic-resistant pathogens, categorising them as critical, high, and medium priorities.[78] This Bacterial Priority Pathogens List (BPPL) is used for public health initiatives and to guide investment for the research and development of new antibiotics to address antibiotic resistance.[78]

2.6.1 Antibiotics under development

At the end of 2023, 244 antibacterial agents were in preclinical development.[112] The WHO reported that 16 antibacterials have been approved by stringent regulatory bodies since 2017; however, only one has been approved since 2021.[113] In addition, the WHO has reported that since 2017, only two authorised antibiotics have new drug target sites.[114] Despite ongoing antibiotic development and recent clinical approvals, the pipeline is inadequate to counter the global threat of antibiotic resistance.[112]

2.6.2 Antimicrobial stewardship

Because of AMR and its impact on public health, currently available antibiotics need to be preserved, as the development of new antibiotics has slowed since the 1950s. To maintain the effectiveness of current antibiotics, strategies such as antibiotic streamlining from combination to monotherapy have been described by Briceland and colleagues as early as 1988.[115] In 2015, the World Health Assembly developed the Global Action Plan on Antimicrobial Resistance, officially adopting antimicrobial stewardship as a core component

to optimise the use of antimicrobials and prevent the emergence of antibiotic resistance.[116] The National Institute for Healthcare Excellence (NICE) defines AMS as "*an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness*."[117] At the hospital level, several strategies can be used to address antibiotic prescribing and use, as discussed by Coleman in 1998.[118] These include monitoring antibiotic use and resistance patterns, providing feedback, education and training, and targeting healthcare professionals' behaviours related to antibiotic prescribing.[118, 119] The main objectives of using these strategies are to ensure that patients are prescribed the right drug at the right dose for the right duration, to reduce antibiotic misuse and to minimise the emergence of antibiotic-resistant organisms. [120]

2.7 The prescribing of antibiotics as a complex intervention in healthcare

The prescribing of antibiotics is complex because multiple factors, including prescribers' knowledge, access to resources, motivation to prescribe, and social interactions among healthcare professionals within the hospital, can influence prescribing. Therefore, a complex intervention is required to reduce antibiotic misuse and encourage appropriate antibiotic use. The Medical Research Council (MRC) Framework for Complex Interventions was designed to guide research on complex interventions in healthcare, outlining four phases: development or identification of the intervention, feasibility, evaluation, and implementation.[6] The precept of this framework is that numerous interacting components in healthcare interventions prompt a theoretically informed systematic approach to intervention design.[121] Accordingly, a pluralistic methodological approach was essential.

2.7.1 Behaviour Change Wheel for theoretically informing a complex intervention

The prescribing of antibiotics is a behaviour which is often associated with prescriber factors.[122] Therefore, intervention development should be informed by a clear understanding of factors influencing current prescribing behaviour.[123] The Behaviour Change Wheel (BCW) is an integration of 19 behaviour change frameworks into a theoretical model of behaviour with broad reach in healthcare settings.[121] There are four behavioural science tools used in the BCW: the Capability, Opportunity Motivation – Behaviour (COM-B) model, the Theoretical Domains Framework (TDF), the BCW, and the Behaviour Change Techniques Taxonomy (BCTTv1). The COM-B Model uses a theoretical approach to understand the factors that influence antibiotic prescribing behaviour.[9, 124, 125] The determinants of prescribing behaviour can then be mapped to the appropriate intervention on the BCW.[121] Intervention functions are subsequently evaluated based on contextual factors and evidence to determine the best approach for the setting. The MRC Framework, in conjunction with the theory-informed BCW, was most suitable for systematically outlining the series of research methods to develop an intervention to optimise the use of surgical antibiotic prophylaxis in women undergoing C-sections in Antigua and Barbuda. The BCW is illustrated in Figure 2.3.[126]

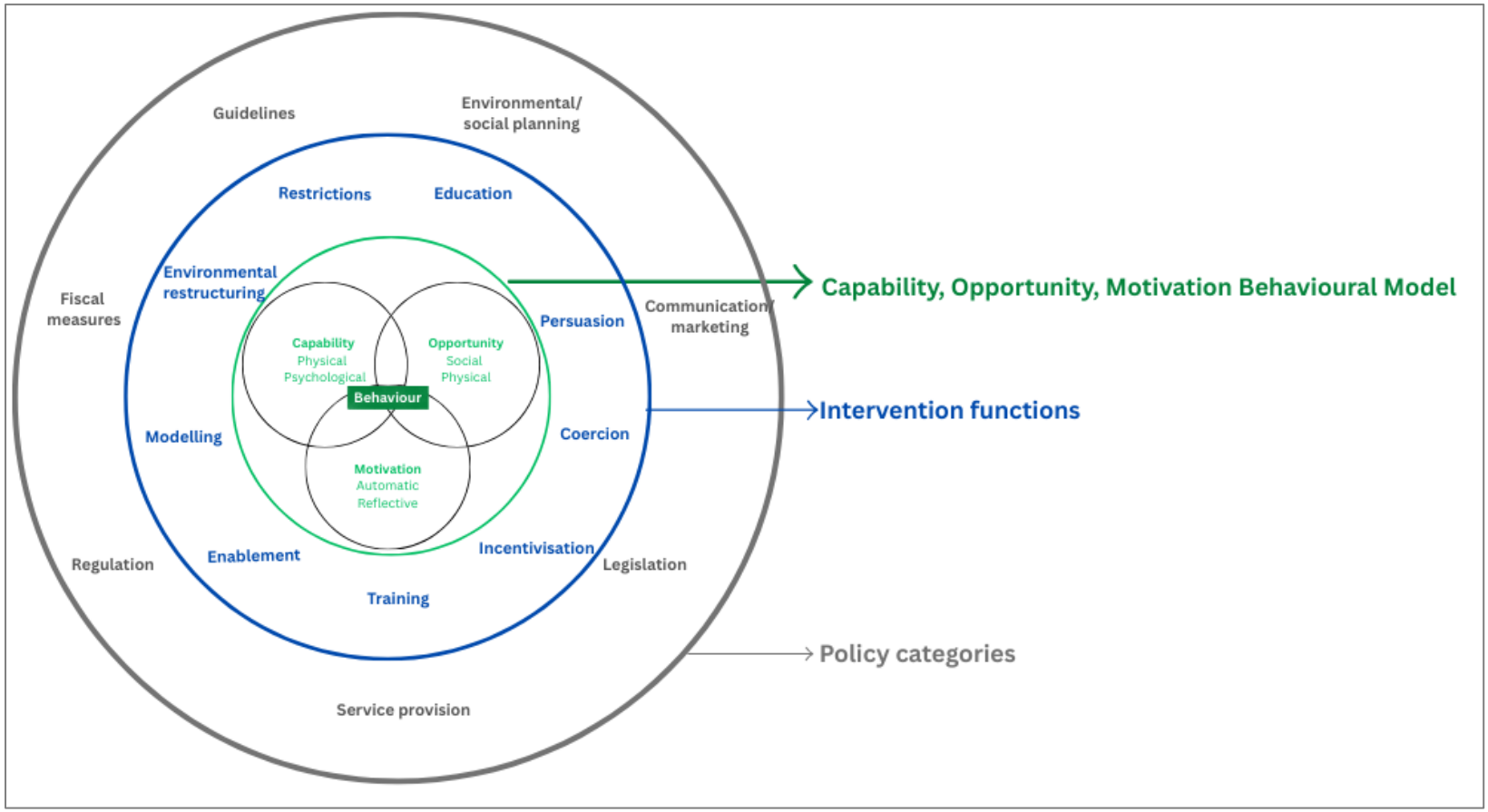


Figure 2.3 Illustration of the Behaviour Change Wheel, Adapted from Michie et al, 2014[9]

2.8 Chapter summary

- Antibiotics are produced naturally by some microorganisms or can be derived using synthetic methods and act by killing bacterial cells or inhibiting their growth.
- Bacteria develop antibiotic resistance through various mechanisms that prevent the antibiotics from inhibiting or destroying them.
- Antibiotics are essential for preventing post-operative infections and for treating active infections, which can be life-threatening.
- Antibiotics are currently being misused in hospital settings, and this can lead to poor patient outcomes and the accelerated emergence of antibiotic resistance.
- Antimicrobial stewardship is a group of strategies that can be used in hospitals to optimise the prescribing and use of antibiotics.
- There is limited research on antibiotics in CARICOM States, with retrieved studies predominantly conducted in Trinidad and Tobago and Jamaica.
- Published literature on antibiotic use in CARICOM States is primarily descriptive, focusing on antimicrobial consumption and point prevalence surveys of antibiotic use.
- The methods used and research emphasis do not provide information on the basic principles of antibiotic use.
- No evidence syntheses on the prescribing and use of antibiotics in CARICOM States were retrieved before the conduct of Chapter 3's mixed-methods systematic review.

CHAPTER THREE

Chapter 3: Prescribing of antibiotics in Caribbean Community States

3.1 Publication statement

A summary of this chapter is published in the following peer-reviewed journal:

Wade T, Heneghan C, Roberts N, Curtis D, Williams V, Onakpoya I. Healthcare-associated infections and the prescribing of antibiotics in hospitalised patients of the Caribbean Community (CARICOM) states: a mixed-methods systematic review. Journal of Hospital Infection. 2021 Apr 1;110:122-32. [5]

3.2 Chapter introduction

Information on antibiotic prescribing in hospitalised patients is generally sparse in low-resource countries. [127] The literature review in Chapter 2 shows that research on antibiotic prescribing in the Caribbean Community (CARICOM) States is limited, focuses on antimicrobial consumption in selected countries, and the methods used do not provide adequate evidence on how prescribing is conducted in hospitals. Further, no evidence syntheses of antibiotic use were retrieved for the CARICOM States at the commencement of this thesis. Synthesising the available evidence was crucial, as it provided insight into the current state of antibiotic prescribing and use and provided a foundation for further investigations in the CARICOM States.

3.2.1 Mixed-methods systematic reviews

A mixed-methods systematic review (MMSR) examines antibiotic prescribing in CARICOM States. Historically, systematic reviews collate empirical evidence according to pre-specified criteria, and when of high quality, they can guide clinical practice.[128] Given the complexity of

health systems, an evidence synthesis from a single paradigm may not provide a comprehensive picture of antibiotic prescribing and use in CARICOM States. An MMSR, which integrates qualitative and quantitative paradigms, can address complementary questions that are broadly linked to the research question.[129] They allow for an in-depth understanding of complex phenomena and provide a complete picture of the phenomena under investigation.[129] For this chapter, both qualitative and quantitative paradigms needed to be integrated, as the goal was to obtain complete information on the prescribing of antibiotics in the CARICOM States.

3.3 Chapter aims and objectives

This chapter defines the evidence base for prescribing antibiotics in CARICOM States. The main objectives were to:

- Critically appraise the existing literature on antibiotic use within CARICOM States
- Assess the methods used and findings of studies conducted in CARICOM States to assess the prescribing of antibiotics in hospitalised patients.
- Synthesise evidence on healthcare workers' knowledge, perceptions, and compliance with hospital-based interventions for the prescribing of antibiotics in CARICOM States.
- Describe barriers and limitations that may have impacted the prescribing of antibiotics in hospitals of CARICOM States.

3.4 Methods

A mixed-methods systematic review integrating qualitative and quantitative evidence was conducted to achieve the study's objectives. The protocol was prospectively registered at the International Prospective Register of Systematic Reviews (PROSPERO) on 1 April 2019 (ID

CRD42019128747). The reporting of this review was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement and the Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guidelines.[130, 131] Ethical approval was not needed to conduct this study.

3.4.1 Inclusion criteria

Population

Primary quantitative studies conducted in the CARICOM States of Trinidad and Tobago, Jamaica, and Antigua and Barbuda were included. These studies reported on hospitalised patients and healthcare providers in hospitals within CARICOM States.

Intervention/Exposure

Studies evaluating antibiotic prescribing in hospitals, including adherence to guidelines, empiric and culture-directed antibiotic use, prophylactic and therapeutic antibiotic use, antimicrobial stewardship (AMS) interventions, and physicians' views regarding antimicrobial resistance and antibiotic prescribing practices, were included in this MMSR.

Types of outcome measures

Studies reporting the rates and appropriateness of antibiotic use, patient outcomes following antibiotic use, including mortality, infections, and length of stay, and healthcare workers' knowledge and perceptions about antibiotic prescribing were included.

3.4.2 Exclusion criteria

Evidence syntheses, case studies, letters, protocols, conference abstracts and editorials were excluded. Studies were excluded if they solely assessed antimicrobial resistance in hospitals or evaluated antibiotic prescribing and use in outpatient settings.

3.4.3 Search strategy and searches

Search terms were determined based on the eligibility criteria outlined in the review's protocol, and the author performed a basic search on Medline (Ovid) and Google Scholar. The Cochrane Database of Systematic Reviews and the International Prospective Register of Systematic Reviews (PROSPERO) were examined for existing and ongoing systematic reviews. The following keywords [Anti-Bacterial Agents OR antibiotic*) AND ("quality of health care" OR guideline adherence OR practice Patterns, Physicians' OR Drug Prescriptions) AND (Caribbean OR CARICOM States)] were used by the author to develop the search strategy. The search strategy, shown in Appendix 3.1, was piloted on Medline (Ovid) by the author and refined with assistance from an information specialist (NR). Various combinations of these keywords using Boolean operators and individual CARICOM states were utilised during searches. For published research, the author systematically searched major databases MEDLINE® Daily and Ovid MEDLINE®) [1946-present], EMBASE (OvidSP)[1974-present], Applied Social Sciences Index and Abstracts (ASSIA)(Proquest)[1987-present] and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) [1997-2020]. Additional searches were conducted on the websites of regional health agencies and journals, including the Pan American Health Organization

(PAHO)-Virtual Health Library, Global Health Library-Global Index Medicus (LILACS), the Caribbean Public Health Agency (CARPHA) and the West Indian Medical Journal (WIMJ). ProQuest Dissertations and Theses Global and Oxford Research Archives (ORA) were searched for grey literature. All databases were searched from their inception date to December 2019. An updated search was performed on 30 September 2020. The reference lists of included studies were scanned for citations that met the inclusion criteria. There were no language restrictions during the search.

3.4.4 Study selection

Duplicate citations were tracked and removed using EndNote. Cochrane's Data Collection Form for Intervention Reviews [132] was piloted on three studies, modified, and used for data collection. The author and NR independently screened the titles and abstracts of all retrieved studies. Eligible studies were subjected to independent full-text review by the author and DC. Articles that did not meet the inclusion criteria following full-text screening are listed in Appendix 3.2, along with the reasons for exclusion.

3.4.5 Quality of included studies

The Mixed Methods Appraisal Tool (MMAT) [133], seen in Appendix 3.3, was used to assess the quality of studies included in the MMSR. There were two general screening questions: one on question clarity and the other on the appropriateness of the data for answering the research questions. Methodological limitations assessed for quantitative studies were based on the following domains: sampling strategy, representativeness of the target population, appropriateness of measurement, risk of nonresponse bias, and data analysis.[133] The author independently assessed the risk of bias, and a second reviewer, IO, cross-checked it. Discrepancies were resolved via discussion.

3.4.6 Data extraction

The author and a second reviewer, DC, independently applied the predetermined inclusion criteria and extracted data from primary studies using a 20-item data extraction form, shown in Appendix 3.4. The data extraction form developed by the author was piloted across five studies, and minor amendments were made before data extraction. The following information was extracted from the included studies: study design and methods, study location, patient/participant characteristics, outcome measures, including variable definitions, and barriers and limitations as described by the authors.

3.4.7 Data analysis and presentation

The discussion sections of included studies were analysed as textual documents using qualitative document analysis and thematic analysis. According to Bowen, document analysis is valuable because documents provide contextual and historical information about the

environment in which the research was conducted.[134] This approach was therefore used to identify contextual factors which may have influenced antibiotic prescribing and use in the study settings of included studies. A narrative synthesis of the reported data from quantitative studies was generated and presented in the findings, along with a thematic synthesis of the limitations and barriers reported in the included studies. The findings from the narrative synthesis and document analysis were then integrated into the discussion section to generate contextual interpretations of prescribing behaviours. The author used an approach to data synthesis described by Thomas and Harden, in which the independent synthesis of the qualitative and quantitative strands preceded the integration of the two paradigms.[135] The flow of the MMSR is illustrated in Figure 3.1.

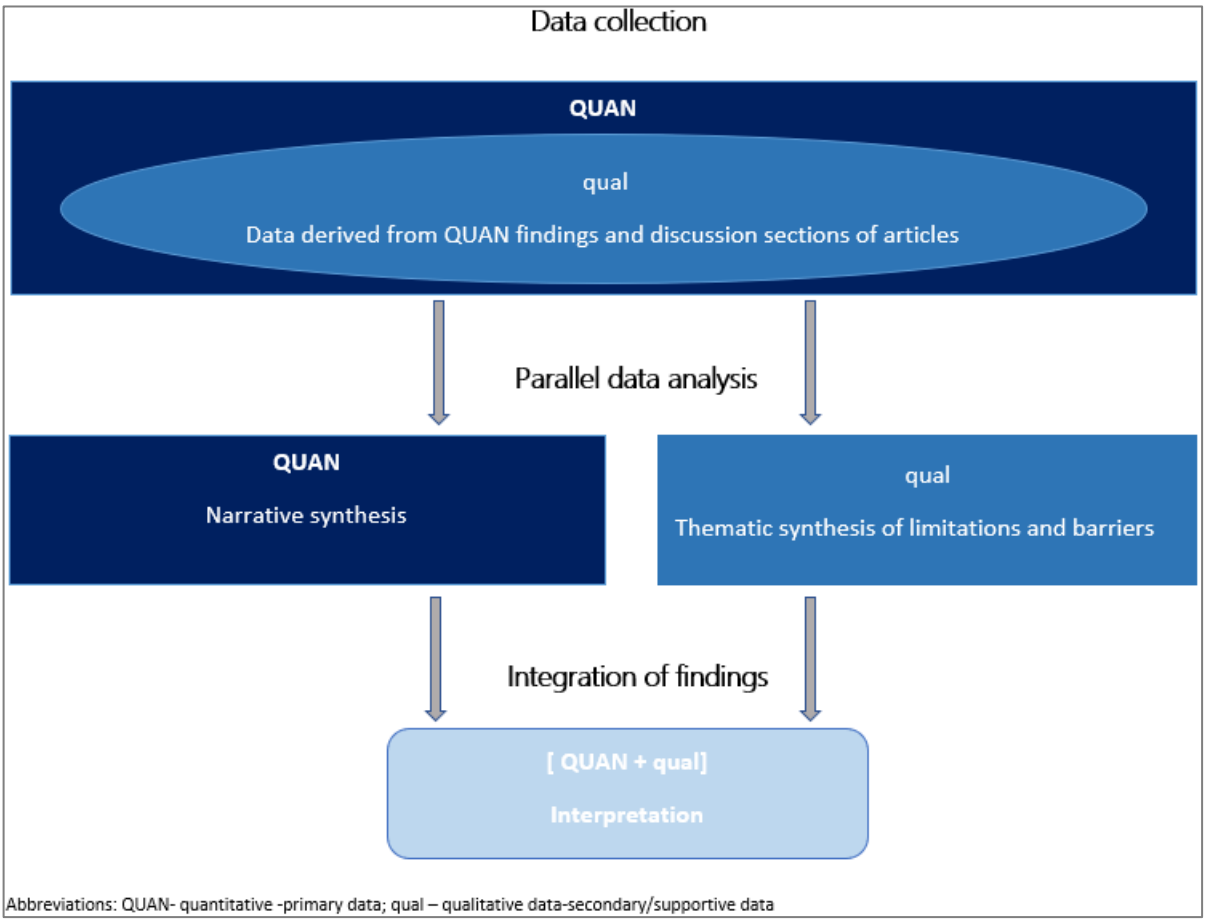


Figure 3.1 Flow diagram of mixed-methods systematic review [136]

Assessment of Heterogeneity

The data were examined for clinical and methodological heterogeneity by performing a side-by-side comparison of characteristics across included studies. The investigation of statistical heterogeneity was not planned, as few comparable studies were anticipated, and the inclusion criteria encompassed diverse populations and outcomes to maximise the scope of the retrieved literature.

Quantitative synthesis

The author grouped the extracted data and presented a narrative synthesis of the study types, target populations, methods, measurement instruments, and findings. Due to the diversity of measurement tools, summary estimates of the quantitative findings could not be presented, as the results would be misleading.

Thematic synthesis

Barriers and limitations were systematically extracted during data collection. Articles were reread to better understand the barriers and limitations in context before conducting the thematic synthesis. Descriptive themes were generated using the extracted evidence from quantitative studies. A codebook outlining descriptive themes, definitions and illustrative examples was created and is presented in Appendix 3.5. The codebook ensured consistency in data coding by standardising definitions, an approach described in the literature.[137, 138]. Using QSR International's NVivo software (Version 12)[139], textual data was extracted and grouped under the most appropriate theme. Textual data, in this instance, were the authors' accounts of the factors that may have affected the rational prescribing and monitoring of

antibiotics in study settings. Three candidate themes were identified, and extracted information was thematically synthesised as described by Thomas and Harden's publication on thematic synthesis. [140]

3.5 Findings

3.5.1 Results of the search

A total of 380 references were retrieved following the initial and updated electronic and reference searches. After duplicate removal, the titles/abstracts of 124 publications were screened. Forty-one primary articles were eligible for full-text screening, of which eight met the inclusion criteria. The PRISMA flow diagram [131] shown in Figure 3.2 illustrates the screening and study selection process.

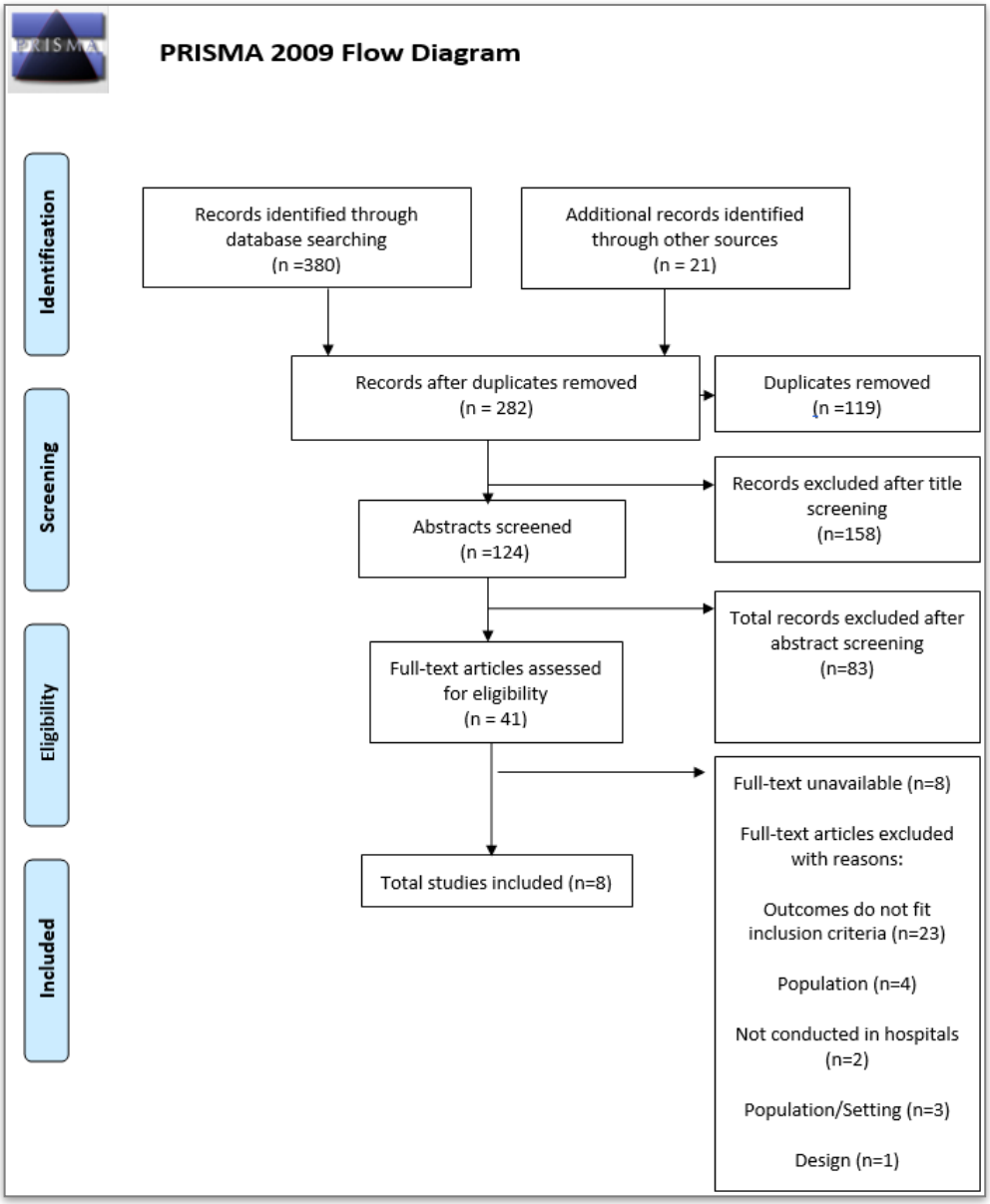


Figure 3.2 Prisma flow diagram for mixed-methods systematic review

3.5.2 Characteristics of included studies

From 1985 to 2013, 8 studies on antibiotic prescribing were retrieved through a comprehensive literature search, with only 20% (n=3) of CARICOM States represented, as shown in Figure 3.3. Fifty per cent (n=4) of the articles originated in Trinidad and Tobago [141-144], and 38% (n=3) were from Jamaica. [145-147]

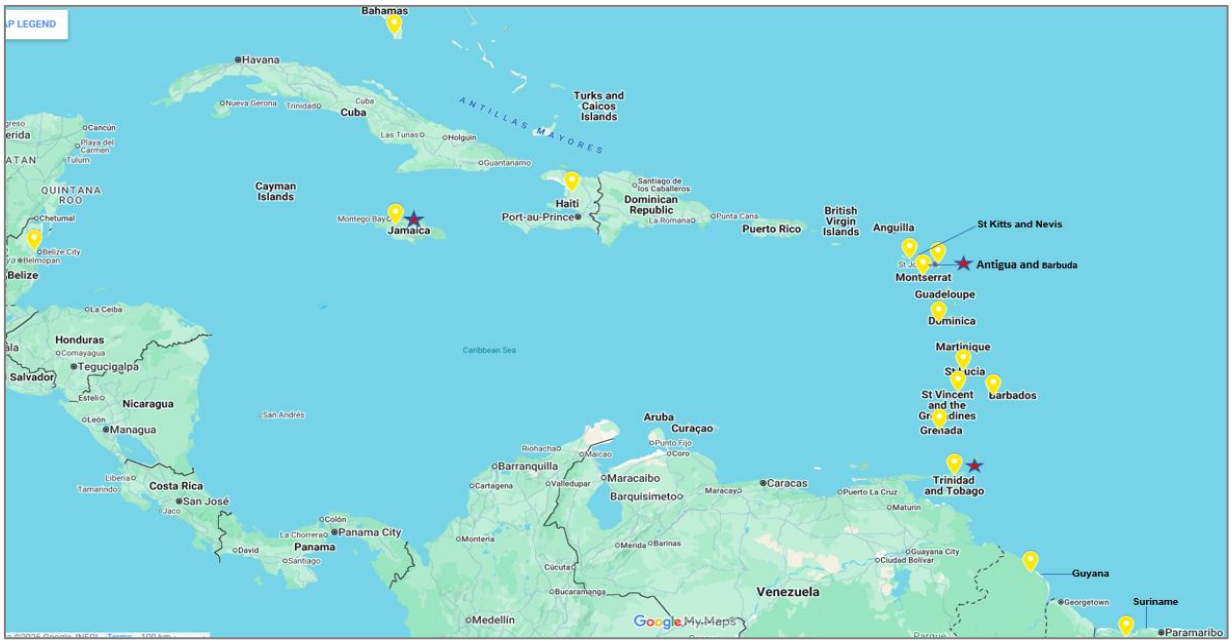


Figure 3.3 Distribution of published articles on antibiotics across CARICOM States (represented by red stars)

Eighty-eight per cent (n=7) of the studies assessed antibiotic use in several patient populations[141-145, 147, 148], as seen in Table 3.1.

Table 3.1 Characteristics of included studies (By order of study ID)

Study ID	Setting	Study design	Objectives	Sample size	Population	Outcome (pre-specified in protocol/methods of study)
Chin 2010	Jamaica	Cross-sectional analytical study	To determine antibiotic usage patterns in the ICU at the UHWI and to compare the practices with international standards to identify areas for improvement.	109	ICU patients	Antibiotic usage patterns Comparison of practices with international standards
Hariharan 2009	Trinidad and Tobago	Prospective observational study	To determine the prescribing patterns and the usage of antimicrobial agents.	335	All inpatients admitted to general wards.	Appropriateness of antibiotic usage Antimicrobial consumption
Hariharan 2013	Trinidad and Tobago	Prospective observational study	To study the prescribing patterns and usage of antimicrobials in the Neonatal Intensive Care Units of Trinidad & Tobago.	353	All patients receiving antimicrobials	Prescribing patterns of parenteral and oral antimicrobials
Macfarlane 1985	Jamaica	Chart review	To assess the effect of these (listed factors) and other factors on the incidence of bacteraemia and on the mortality from bloodstream infections.	222	All patients with positive blood cultures	Identification of community or nosocomial bacteraemia Antibiotic therapy
Martin 2006	Antigua and Barbuda	Retrospective review	To review appendicectomy cases at Holberton Hospital with respect to antibiotic use and outcome.	88	Appendicectomy patients	Post-operative wound infection rate Antibiotic use Length of hospital stay. Mortality
Orrett 2001	Trinidad and Tobago	Survey	To assess the patterns of antimicrobial use in a large rural hospital.	527	Discharged patients	Total antimicrobials used

Study ID	Setting	Study design	Objectives	Sample size	Population	Outcome (pre-specified in protocol/methods of study)
Pinto Pereira 2004	Trinidad and Tobago	Cross-sectional	To assess the appropriateness of prescribing 3GCs and to determine the direct cost of treatment.	192	Inpatients > 13 years receiving cefotaxime/ ceftriaxone/ceftazidime	Appropriate antibiotic prescriptions Cost of antibiotic treatment
Tennant 2010	Jamaica	Cross-sectional survey	To identify physicians' knowledge and attitudes regarding antimicrobial resistance and current antibiotic prescribing practices.	240	Physicians	Physicians' perceptions on the magnitude of antibiotic resistance Prescribing practices Physicians' opinion of their scope of knowledge and interest in further education

ICU-Intensive Care Unit, 3GCs--Third-generation cephalosporins, UHWI-University Hospital of the West Indies

One study investigated physicians' knowledge and attitudes on antibiotic prescribing and antibiotic resistance.[146] Data for 88% (n=7) of the studies were collected during chart reviews.[141-145, 147, 148]. Only 26% (n=2) of the studies used prospective data.[142, 143] The studies assessed several outcomes, including the appropriateness of antibiotic use relative to standard guidelines, post-operative infection rates, the number of antibiotics prescribed per encounter, and length of hospital stay. None of the studies was published in the five years preceding this review, and 42% (n = 3) were published between 2010 and 2013.

3.5.3 Quality of included studies

The methodological quality of all eight studies included in this MMSR was assessed across the seven domains defined by the MMAT Tool. The findings are illustrated in Figure 3.4.

Study ID	Are there clear research questions?	Do the collected data allow to address the research questions?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question?
Chin 2010.	✓	✓	✓	✓	!	NA	!
Hariharan 2009	✓	✓	✓	✓	✓	NA	✓
Hariharan 2013	✓	✓	✓	✓	!	NA	!
Martin 2006	!	✓	✓	✓	✗	NA	!
Orrett 2001	✓	✓	!	!	✓	NA	!
Pinto Pereira 2004	✓	✓	✓	✓	✓	NA	✓
Tennant 2010	✓	✓	✓	✓	!	!	!
Mafarlane 1985	!	!	!	!	!	NA	!

Unclear	Low	High	NA
!	✓	✗	Not applicable due to study design

Figure 3.4 Risk of bias for included studies

Two studies had low ROB for all assessed indicators of the MMAT Tool. [143, 144] The appropriateness of the measurements used in 50% (n=4) of the studies had an unclear ROB; [142, 145-147], and 75% (n=6) had an unclear or high ROB for the use of appropriate statistical analyses to answer their research questions.[141, 142, 145-148]

3.5.4 Appropriateness of antibiotic prescribing

The misuse of antibiotics was documented in 6 of the 7 studies that evaluated the appropriateness of antibiotic use against several national and international guidelines. In Antigua and Barbuda, 97% of patients undergoing an appendectomy received surgical antibiotic prophylaxis for an average duration of five days (range 2-12 days) with no consideration for disease severity.[148] As shown in Table 3.2, 73% of surgical antibiotic prophylaxis was inappropriate when assessed against the Surgical Infection Society guidelines.[148, 149]

Table 3.2 Antibiotic prescribing information for included studies

Study ID	Target Population	Measurement tools-Appropriateness	Commonly used antibiotics	Inappropriate use (%)	> 1 antibiotic per encounter (%)
Chin 2010.	ICU patients	ATS/IDSA Guidelines[150]	Prophylactic-ceftriaxone (31.7%) and metronidazole (19.0%). Therapeutic-piperacillin/tazobactam (32.1%), ceftazidime (27.5%), or metronidazole	88.9*, 29 *	-
Hariharan 2009	Paediatric and adult inpatients of ICU, medical, surgical, paediatric wards.	Hospital Antimicrobial Policy	Amoxicillin-clavulanate was the most common (32%). First-line meropenem and gentamicin. Hospital protocol recommends piperacillin-tazobactam as first-line treatment.	36.3	100
Hariharan 2013	NICU patients receiving antimicrobials.	1. CDC-Prevention of perinatal Group B Streptococcal Disease 2002[151] 2. WHO. Explore Simplified Antimicrobial Regimens for The Treatment of Neonatal Sepsis. 2002[152]	The first-line antibiotic of choice was a combination of ampicillin and gentamicin (85.8 %). The second-line antibiotic of choice was cefotaxime.	14.2	-
Macfarlane 1985	Patients with positive blood cultures.	Garrod et al- Antibiotic and chemotherapy, 5th ed. Edinburgh: Churchill Livingstone, 198l.[153]	Not stated	43	-
Martin 2006	All cases of appendicectomy	SIS Guidelines[149]	Gentamicin, metronidazole and ampicillin/penicillin/ cloxacillin/cephradine (81.8%).	73	88.6
Orrett 2001	Discharged inpatients	Not stated	Ampicillin and gentamicin are frequently prescribed across wards. Paediatric most frequently prescribed-chloramphenicol and ampicillin.	-	22
Pereira 2004	Adult inpatients receiving+ 3GC	2000 Sanford Antibiotic Guide[154]	Ceftriaxone most prescribed cephalosporin.	64.6	49.6

ICU, intensive care unit; ATS/IDSA, American Thoracic Society and the Infectious Diseases Society of America; NICU, neonatal intensive care unit; CDC, Centers for Disease Control and Prevention; WHO, World Health Organization; SIS, Surgical Infection Society; 3GC, third-generation cephalosporin. *Prophylactic. *Therapeutic

Similarly, a high rate, 88.9%, of inappropriate antibiotic prophylaxis was documented in Jamaica in patients admitted to an intensive care unit when evaluated against the guidelines of the American Thoracic Society and the Infectious Diseases Society of America.[145, 150] An assessment of the appropriateness of therapy with third-generation cephalosporins against the Sanford Antibiotic Guideline 2000[154] showed that 62% of prescriptions were inappropriate in Trinidad and Tobago, with the inappropriate use of cephalosporins significantly higher in gynaecology units.[144] Inappropriate use was reported in one setting, although local hospital policies guided antibiotic use.[143]

3.5.5 Selection of antibiotics

The types of antibiotics selected for both prophylaxis and therapy varied across institutions and countries. During hospitalisation, up to three antibiotics may be given concurrently in some settings.[148] Empiric treatment with intravenous administration was most common, with culture-directed therapy infrequently used. In some instances, the initially prescribed empiric treatment was continued alongside culture-based recommendations.[143] Discontinuation in some settings occurred either upon completion of the course or upon the patient's death.[145] Regarding antibiotic use and resistance, respondents in one study did not perceive resistance as a national or institutional threat.[146]

3.5.6 Thematic synthesis of limitations and barriers

Several authors reported challenges, including limited resources, inadequate or poorly developed guidelines, and reliance on physician discretion in prescribing decisions.

Decisions on antibiotic use

Decisions about antibiotic prescribing were based on clinical coverage for the suspected pathogen and the origin of the patient's infection.[145] In some settings with guidelines, prescribing antibiotics was based on the attending physician's preference or experience.[143, 145] Extended antibiotic use was attributed to physicians' lack of monitoring or reluctance to discontinue treatment.[142, 145]

Lack of data to support the prescribing of antibiotics

It was noted by several studies that culture and sensitivity reports are usually delayed [142, 143, 145] and as a result, some physicians may choose not to pursue sensitivity testing. Surveillance data were not up to date, and monitoring of antibiotic use was not generally practised.[144, 145] Some authors noted that the human resource shortage accounted for inadequate monitoring and surveillance efforts.[141, 143]

Deficiencies in guideline development and content

Local guidelines for antibiotic use were developed in some settings. Although local guidelines were developed, dissemination and implementation were not done in the intended settings.[143, 144] Diagnosis-specific antibiotics were listed in some guidelines, but the guidelines were incomplete because they did not document guidance on the dosage, route, or duration of antibiotics.[143] Some guidelines were also outdated and needed review.[144]

3.6 Discussion

3.6.1 Summary of findings

In this MMSR, eight quantitative descriptive studies, published between 1985 and 2013, met the inclusion criteria. Fifty per cent of the studies were conducted in Trinidad and Tobago, and 38% in Jamaica. These trends persist, as most antibiotic-related studies published between 2017 and 2025 in CARICOM States were quantitative and primarily conducted in Trinidad and Tobago.[98, 105, 106, 155] These studies focused on antibiotic consumption at regional levels,[105, 106] antibiotic resistance[98] and hospital-based prescribing patterns.[155] Point prevalence surveys led by the Pan American Health Organization, and Sati and colleagues described antibiotic use in hospitals of Barbados, Guyana and St Lucia[109], and Haiti[110], respectively. Quantitative descriptive methods were also employed, consistent with the approaches used in the studies included in this MMSR.

The emphasis of global antibiotic research is on antimicrobial stewardship interventions and the use of behaviour theory to understand and improve antibiotic use.[156-161] Recently published studies from low-and-middle-income countries have focused on drivers of misuse in community settings[159] and over-the-counter dispensing of antibiotics.[162] Qualitative methods have examined prescribing influences on antibiotic use in low and middle-income settings, [157, 162], unlike the predominant descriptive methods employed in CARICOM States.

Evaluating the appropriateness of antibiotic use is central to antimicrobial stewardship, and multiple frameworks and methods for assessing appropriateness have been discussed in the literature.[163-165] In the studies included in this systematic review, various tools have been used

to assess the appropriateness of antibiotic use in different patient groups.[149, 150, 154] This may be explained by the deficiencies in guideline development identified by the document analysis of factors influencing antibiotic use in the settings. Although tools varied, a key finding was the misuse of antibiotics through overprescribing and prolonged use. These prescribing practices may be partially explained by insufficient diagnostics, guidelines and human resources. Additionally, physician preference and inadequate monitoring practices were highlighted as reasons for prescribing practices. The prudent use of antibiotics is high on the global agenda due to rising antibiotic-resistant infections; however, studies evaluating antibiotic prescribing in CARICOM hospitals remain few and localised. Findings from the included publications provide a starting point for antibiotic research in the CARICOM States and highlight the need for additional research and diverse methodologies to investigate antibiotic use.

3.6.2 Strengths and limitations of this MMSR

Although few studies were included in this MMSR, the information gathered has contributed to the evidence base for antibiotic prescribing in CARICOM States. A broad and systematic approach was adopted to search the literature since very few studies were retrieved during an initial search on Google Scholar. The literature search was conducted on several databases and regional websites to ensure that all relevant literature was captured. Conducting ROB assessments was another strength of the MMSR since it provided useful data on the types of methodological flaws in the included studies. Knowing the most common insufficiencies would enable better planning for future research. It is possible that unpublished literature may have been missed during our comprehensive literature search. Additionally, qualitative

studies on antibiotic prescribing were not retrieved for the CARICOM States; therefore, a synthesis of primary qualitative and quantitative data was not possible. No studies on the implementation of interventions to improve antibiotic prescribing were retrieved. The current situation regarding antibiotic prescribing could not be determined, as none of the included studies was published within the 5-year period preceding the updated literature search for this MMSR. Since the included studies used various assessment tools, the author was unable to provide a meaningful synthesis of the findings. However, it was established that the prescribing and use of antibiotics are poorly researched in many CARICOM States, and that reliance is placed on international guidelines to assess appropriate antibiotic use. The thematic synthesis of the barriers and limitations was invaluable, as it not only highlighted inadequacies in physical resources to support prescribing but also suggested that the region's approach to antibiotic use may not be evidence-based.

3.6.3 Implications for research

This MMSR includes a small number of studies on antibiotic prescribing in CARICOM States. These studies were predominantly conducted in 13% (n=2) of CARICOM States, Trinidad and Tobago and Jamaica. As misuse, in the form of overuse, can contribute to the emergence of antibiotic resistance, resulting in poor patient outcomes, it is paramount that further research be conducted in this region. Considering this, CARICOM States must conduct both qualitative and quantitative primary research, individually or collectively, to investigate antibiotic prescribing. Specific outcomes related to the principles of antibiotic use, such as the appropriate antibiotic agent, dose, route, and duration of antibiotic prescriptions, as well as the targeting of systemic antibiotics, should be considered in hospital settings. Understanding

current prescribing practices is crucial for selecting effective AMS interventions to improve antibiotic prescribing in these settings, particularly if evidence suggests antibiotic misuse. Furthermore, synthesising evidence on globally implemented and evaluated AMS interventions would help identify contextually adaptable and feasible strategies for low-resource settings.

3.7 Chapter summary

- Antibiotic use in hospitals of some CARICOM States is inappropriate when evaluated against international guidelines.
- International guidelines are relied on to assess the appropriateness of antibiotic use in CARICOM States, and locally developed guidelines in some states have not been adequately developed or disseminated.
- Empiric prescribing is common in some hospitals in CARICOM States and remains that way until patient discharge.
- Antibiotics are overused in the form of extended durations or the number of antibiotics administered per patient encounter.
- Hospitals across some CARICOM States have inadequate resources to support rational antibiotic prescribing, including prescribing guidelines and diagnostics.
- The approach to prescribing antibiotics in CARICOM States does not appear to be evidence-based.
- There is no published evidence on the use of antimicrobial stewardship interventions to improve the prescribing of antibiotics in CARICOM States.
- The prescribing of antibiotics is poorly researched in CARICOM States, and published primary studies are limited to Trinidad and Tobago and Jamaica, outdated, and do not provide adequate information to determine if the right patient is receiving the right antibiotic at the right time.

- Primary qualitative and quantitative studies should be conducted in additional CARICOM states to provide a better understanding of how systemic antibiotics are prescribed and used for different cohorts of hospitalised patients.
- A synthesis of globally implemented antimicrobial stewardship interventions is necessary for identifying the evidence base of what works best in low-resource hospital settings and low and lower-middle-income countries.

CHAPTER FOUR

Chapter 4: Global evidence base of healthcare worker-targeted antimicrobial stewardship interventions used in hospitals.

4.1 Publication statement

A summary of this chapter is published in the following peer-reviewed Journal:

Wade T, Roberts N, Ban JW, Waweru-Siika W, Winston H, Williams V, Heneghan CJ, Onakpoya IJ. Utility of healthcare-worker-targeted antimicrobial stewardship interventions in hospitals of low-and lower-middle-income countries: a scoping review of systematic reviews. *Journal of Hospital Infection*. 2023 Jan 1; 131:43-53.

4.2 Introduction

In Chapter 3, the evidence base for prescribing antibiotics to hospitalised patients in CARICOM States was explored through a mixed-methods systematic review (MMSR). From a limited number of CARICOM States, evidence showed that antibiotic use was predominantly empiric, with reports of excessive and inappropriate antibiotic use in hospitals. Further, there was no published evidence of antimicrobial stewardship (AMS) interventions in CARICOM hospitals, and poor antibiotic use was attributed to prescribers' behaviours. Reflecting on the association between antibiotic misuse and antibiotic resistance, and the consequences of antimicrobial resistance on global health, there is an urgent need to implement effective AMS interventions to preserve the effectiveness of available antibiotics. Using the systematic approach outlined by the Medical Research Council,[6] the second area of inquiry in this thesis was identifying the evidence base for the types of AMS intervention components used to target healthcare workers in hospitals. The

focus was on AMS intervention components that would be feasible and sustainable for low and lower-middle-income countries (LLMICs).

4.2.1 Scoping review of systematic reviews

Scoping studies, as described by Arksey and O'Malley, explore the extent of the literature on a particular phenomenon of interest.[166] Referred to as scoping reviews, they are used to identify knowledge gaps, present a summary of the evidence, and the overall state of research on a topic, notwithstanding the quality of the included studies.[166, 167] Because of its exploratory nature, scoping reviews are iterative and allow the researcher to refine the search strategy to ensure comprehensive literature searches.[166] An unlimited search of Google Scholar using the key terms 'antimicrobial stewardship interventions' generated citations for 17,900 publications. When the search was restricted from 2010 to 2020 and conducted using the keywords (review) AND (antimicrobial stewardship interventions), the first 50 retrieved publications were predominantly systematic reviews. Since both primary and secondary literature on antimicrobial stewardship is extensive, a scoping review of systematic reviews was utilised to provide a quick overview of the synthesised evidence of globally implemented antimicrobial stewardship interventions.

4.2.2 Effective Practice and Organisation of Care (EPOC) Taxonomy

The classification of health system interventions is not universally standardised. The Effective Practice and Organisation of Care (EPOC) Taxonomy of health systems interventions affords a standardised way to classify AMS intervention components.[15] The Cochrane EPOC Group developed this classification based on practical or conceptual similarities of intervention

components in 2002 and revised it by 2015. This taxonomy consists of four domains of interventions: delivery arrangements, financial arrangements, governance arrangements, and implementation strategies.[15] The implementation strategies domain of the EPOC taxonomy was applied to classify intervention components presented in the publications included in this scoping review. Within this domain, change interventions targeting healthcare facilities, healthcare professionals' behaviour, and healthcare service use can be classified.[15]

4.3 Chapter aim and objectives

This chapter presents the evidence base for evaluated healthcare worker (HCW)- targeted AMS interventions implemented in hospitals. The primary objectives were to systematically identify and summarise the components of hospital-based AMS interventions targeting healthcare workers; summarise the effects of intervention components on process and clinical outcomes; and critically evaluate the quality of systematic reviews on HCW-targeted AMS interventions.

4.4 Method

For this chapter, a scoping review of systematic reviews was used to gather information on antimicrobial stewardship interventions implemented globally. Protocol development was guided by the Joanna Briggs Institute's (JBI) Manual for Evidence Synthesis.[168] The protocol was preregistered on Figshare.[169] The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Extension for Scoping Reviews was used to guide the reporting of this review.[170]

4.4.1 Eligibility criteria

The population, concept and context mnemonic described by JBI was used to specify the inclusion criteria, which is less restrictive for scoping reviews due to their broad scope.[168]

Types of evidence sources

This scoping review included published SRs, with or without meta-analysis, conducted from 2010 to 2021. All other study designs were excluded, including nonsystematic literature reviews, overviews and scoping reviews.

Concept

Evaluated healthcare-worker-targeted interventions that can be categorised according to the EPOC taxonomy were sought out in the systematic reviews. The included systematic reviews assessed the effectiveness of AMS interventions targeting HCWs who prescribe antibiotics to hospitalised patients or monitor antibiotic use within hospitals. Emphasis was placed on interventions with persuasive or educational functions, as these may be more feasible and sustainable in low-and lower-middle-income countries. Reviews were considered if they reported on clinical outcomes, including infection and mortality rates, process outcomes such as guideline compliance, and evidence of unintended consequences associated with individual AMS intervention components. Excluded were studies that reported only microbiological or financial outcomes, or the outcomes of restrictive interventions such as expert approval and automatic stop orders. Studies that focused solely on technologically advanced AMS interventions, such as point-of-care testing, electronic surveillance, and artificial intelligence, were excluded. The systematic review was excluded if

it presented an overall finding without discussing the impact of the AMS intervention components.

Context

The interventions assessed in the SRs were those implemented in hospitals providing inpatient care. All systematic reviews that evaluated interventions in outpatient settings, including community clinics, field hospitals and general practitioners' offices, were excluded.

4.4.2 Search strategy

A three-step approach, as described by JBI, was utilised to search for reviews on AMS interventions.[171] The author developed a search strategy for Medline (Ovid) and performed a limited literature search. The search strategy was adapted and applied to CINAHL, JBI Evidence Synthesis, and the Cochrane Library, as shown in Appendix 4.1. Google Scholar (GS) and ProQuest Dissertations and Theses were searched for grey literature. Information Specialist (NR) assisted in developing the final search strategy, which was reported in accordance with PRISMA-S, an extension of the PRISMA reporting guidelines for systematic reviews, as shown in Appendix 4.2.[172] The final search strategy included a combination of title/abstract keywords and subject headings for antimicrobial stewardship, surveillance/monitoring, and hospital-acquired infection, based on the preliminary search. Language filters were not applied to the searches. However, publications not written or translated into English during title screening were excluded due to time constraints and the lack of resources required for translation. The reference lists of included systematic

reviews were searched for additional systematic reviews. The final search was run on September 17, 2021.

4.4.3 Evidence selection

Results were imported into EndNote X9 for deduplication, and the author and a second reviewer, WWS, independently screened the titles and abstracts of retrieved studies. A third reviewer, JWB, arbitrated discrepancies. Full-text articles that fit the inclusion criteria were independently assessed against the inclusion criteria by the author and JWB, and disagreements were resolved via discussion.

4.4.4 Quality Assessment

The Assessment of Multiple Systematic Reviews (AMSTAR) Tool was used to objectively assess the quality of the included systematic reviews. [173] This version of the AMSTAR Tool, presented in Appendix 4.3, comprises 11 items and was designed to assess the methodological quality of systematic reviews.[173] The author and JWB independently examined the quality of the systematic reviews using the AMSTAR Tool. When discrepancies could not be resolved via discussion, a third reviewer, IJO, arbitrated.

4.4.5 Data extraction

JBI's template source of evidence details, characteristics, and results extraction instrument was modified, piloted and used for data extraction.[174] Data on primary objectives, search methods, search time frames, intervention components and clinical and process outcomes were extracted. When outcomes for intervention bundles (interventions comprising more than one intervention component) were reported, the primary articles were retrieved. This

was done to examine the articles for details of intervention components, as they may have been excluded by the systematic reviews. If components were exclusively addressed, associated process and clinical outcomes, including unintended consequences, were extracted. The author and HW independently extracted the data, and discrepancies were resolved through discussion.

4.4.6 Presentation of findings

A narrative summary presented the information on intervention components evaluated in the included studies. Components were categorised according to the EPOC taxonomy of interventions listed under the domain Implementation Strategies, Category (and related subcategories) for interventions targeting HCWs.[175] Outcome measures used to assess the impact of AMS interventions were graphically represented.

4.5 Results

During the literature search, 6,519 citations were retrieved. Following the removal of duplicates and title/ abstract screening, 35 publications were identified for full-text review. Of these, 18 systematic reviews met the inclusion criteria. The review selection process is illustrated in Figure 4.1. Excluded studies (n=17) and reasons for exclusion are shown in Appendix 4.4.

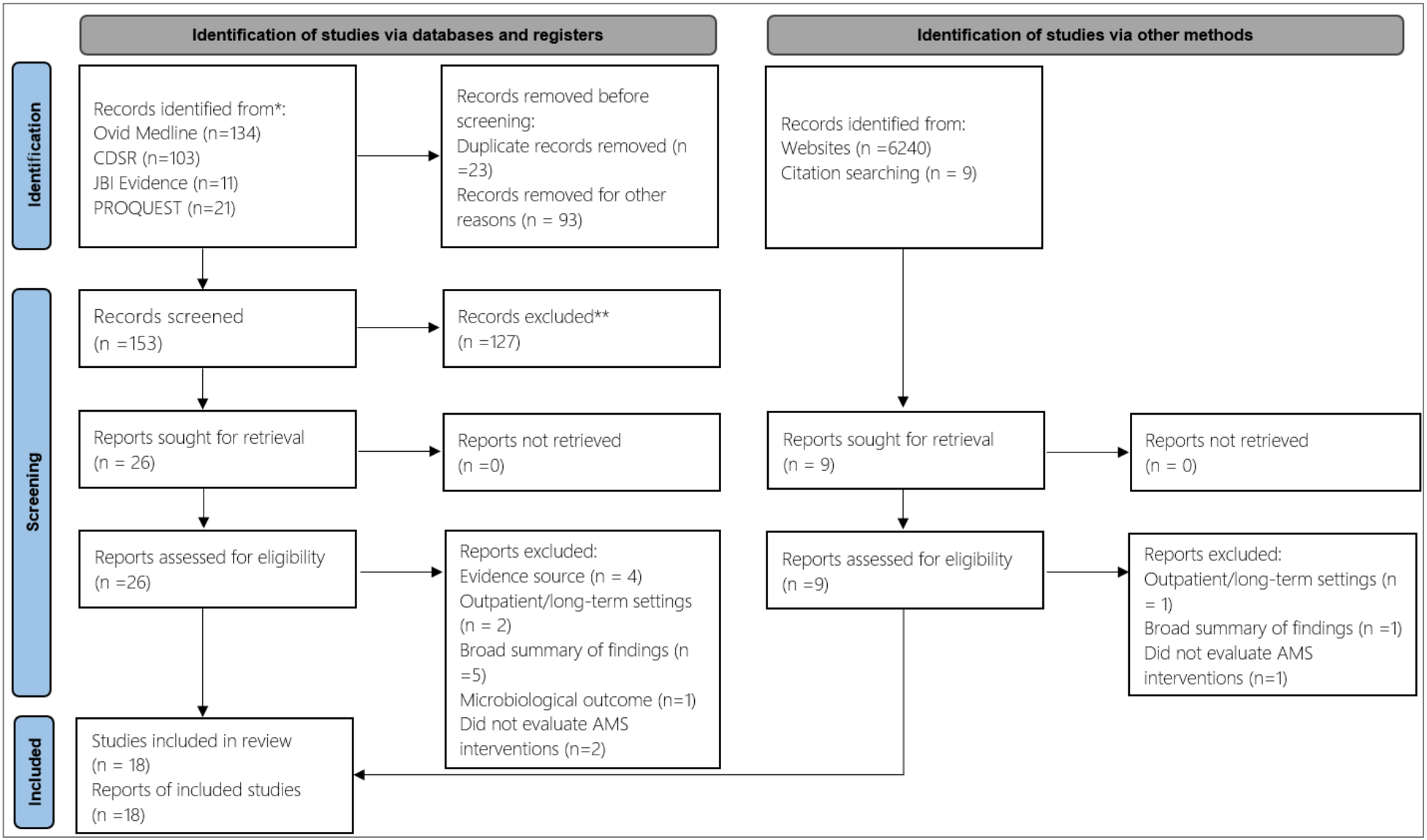


Figure 4.1 Prisma Flow Diagram showing the review selection process[131]

4.5.1 Characteristics of included studies

Systematic reviews included a variety of study designs, most commonly before-and-after studies, interrupted time series, and randomised controlled trials. Multiple quality assessment tools were employed to evaluate the methodological quality of primary studies. In total, 547 primary studies were included in the 18 SRs. Of those studies, only 2% (n = 12) were conducted in LLMICs.[176-184] Eight of these studies assessed intervention components targeting healthcare workers in hospitals; three were conducted in Kenya,[177, 180, 184] and two in India.[178, 183] As presented in Table 4.1, the number of included primary studies ranged from a minimum of 9 in a review by Araujo and colleagues[185] to 221 in a Cochrane review by Davey et al.[186]

Table 4.1 Characteristics of systematic reviews by order of study ID

Study ID	Search method (time frame)	Included studies	Evidence assessment tools
Akpan 2020 [187]	PubMed, Scopus, Cochrane library, African Journal Online, CINAHL, Google scholar, references of included papers and reviews (1990 and March 2019)	13	NHLBI quality assessment tool for before and after studies [188]
Araujo 2020 [185]	PubMed, SciELO, EMBASE, Cochrane Database, articles from cross-referencing January 2000–April 2019)	6	ICROMS Quality criteria for review of multiple study designs [189]
Araujo 2017 [190]	PubMed, CDSR, two additional from reference articles (1 January 2007–31 March 2017)	9	ICROMS[189]
Baur 2017 [191]	PubMed, CDSR, CENTRAL, WoS. Reference lists of included studies (1 January 1960–31 May 2016)	108	NIH Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group.[192]
Bertollo 2018 [193]	Scopus, LILACS, and SciELO (1 January 2012 –4 January 2017)	26	None. Assessed based on two study designs considered appropriate for evaluating the impact of ASPs: randomized controlled trials and quasi-experimental studies [186]
Charani 2011 [194]	MEDLINE, ASSIA, Business Source Complete, Cochrane Library, PsycINFO, DARE, HMIC (January 1999–April 2011)	10	CASP tool[195] for evaluating qualitative research , Cochrane Risk of Bias Tool [196], EPOC Model[197] The 3 tools were used to develop quality criteria for review of included studies.
Davey 2017 [186]	CENTRAL, Cochrane Library, MEDLINE, EMBASE. Bibliographies of included articles and personal files (1946–22 January 2015)	221	2013 EPOC 'Risk of bias' criteria, ROBINS-I Tool[198], ORION statement: Guidelines [199]
Kaki 2011 [200]	OVID MEDLINE, EMBASE, Cochrane Library (January 1996–December 2010)	24	1.Cochrane Risk of Bias tool [128] 2. Newcastle–Ottawa Quality Assessment Scale[201] for nonrandomized studies.
Karanika 2016 [202]	PubMed, EMBASE, Google Scholar, reference lists of the retrieved articles (To 8 July 2015)	26	Newcastle–Ottawa Quality Assessment Scale[201]

Study ID	Search method (time frame)	Included studies	Evidence assessment tools
Lindsay 2018 [203]	MEDLINE, EMBASE, CINAHL, Web of Science, CENTRAL (Inception–October 2017)	11	EPOC Risk of Bias Assessment Tool [128]
Monmaturapoj 2021 [204]	Medline (OvidSP), Embase (OvidSP), CENTRAL, reference lists of retrieved articles (February 2015 and July 2020)	52	1. Cochrane risk of bias tool[128] 2. ROBINS-I Tool[198]
Mijovic 2018 [205]	Medline, PUBMED, Cochrane Library, EBSCO, manual search for original articles in relevant journals. (27 April–1 April 2017)	24	BEME Collaboration Guide[206]
Nasr 2016 [207]	MEDLINE, EMBASE, International Pharmaceutical Abstracts, Google, Google Scholar, reference lists of identified articles (1948–February 2016)	20	None
Pitiriga 2017 [208]	EMBASE, MEDLINE, Web of Science, reference tracking to identify further papers (Inception–November 2016)	21	None
Roque 2014 [209]	MEDLINE-PubMED January (2001–December 2011)	65 total-31 in hospital	None
Smith 2015 [210]	PubMed, WoS, bibliographies of all retrieved studies (Through March 2014)	17	None
Van Dijck 2018 [211]	CENTRAL, EMBASE®, MEDLINE®, Global Index Medicus, WHO-VHL, reference lists of selected studies and of relevant reviews, consulted experts for additional literature. (Inception–5 December 2017)	27	2017 quality criteria for randomized controlled trials and quasi-experimental studies of the Effective Practice and Organisation of Care Review Group[212]
Wagner 2014 [213]	MEDLINE (Ovid), additional studies from systematic reviews, reference lists of retrieved articles, suggestions made by experts in the field. (2000–2013)	37	Cochrane EPOC, AMSTAR,[173] AHRQ [214]

CINAHL (Cumulative Index to Nursing and Allied Health Literature) NHLBI-National Heart, Lung and Blood Institute, SCIELO-Scientific Electronic Library Online, EMBASE-Excerpta Medica Database, ICROMS- Integrated Quality Criteria for Review of Multiple Study Designs, CDSR-Cochrane Database of Systematic Reviews, CENTRAL- Cochrane Central Register of Controlled Trials, WoS-Web of Science, NIH- National Institutes of Health, LILACS Latin American and Caribbean Health Sciences Literature, ASP-antimicrobial stewardship programs, ASSIA-Applied Social Sciences Index and Abstracts, DARE-Database of Abstracts of Reviews of Effectiveness, HMIC- Health Management Information Consortium, CASP- Critical Appraisal Skills Programme, EPOC-Effective Practice and Organisation of Care, ROBINS-I-Risk of Bias in non-randomised in intervention studies, ORION-0utbreak Reports and Intervention Studies of Nosocomial Infections,,BEME- Best Evidence Medical Education, WHO-VHL-World Health Organization's Virtual Health Library, AHRQ- Agency for Healthcare Research and Quality and the Effective Health Care Program, AMSTAR-A Measurement Tool to Assess Systematic Reviews.

4.5.2 Quality of included systematic reviews

AMSTAR evaluation revealed variable methodological quality across systematic reviews. Seventy-eight per cent (n=14) met the criteria for comprehensive literature searches, and 83% (n=15) for documenting the characteristics of included studies, as listed in Table 4.2.

Table 4.2 Overall methodological quality of included systematic reviews.

AMSTAR Item	Description	% of reviews meeting criterion
1	A priori design provided	22
2	Duplicate study selection and data extraction	56
3	Comprehensive literature search	78
4	Inclusion of grey literature	6
5	List of included and excluded studies	11
6	Characteristics of the included studies	83
7	Quality assessment	39
8	Consideration of quality in conclusion	28
9	*Methods used to synthesise findings are appropriate.	100
10	*Publication bias assessed	75
11	Conflict of interest included	6

AMSTAR-A Measurement Tool to Assess Systematic Reviews *Only applicable to included systematic reviews with meta-analyses (n=4)

Twenty-two per cent (n=4) of reviews did not conduct comprehensive literature searches, as their reports indicate that they either searched only one database or conducted no database searches. Only one systematic review included grey literature as part of its inclusion criteria. [186] The quality of the included primary studies was assessed in 39% (n = 7) of the included systematic reviews. The proportion of AMSTAR criteria met across the remaining eight items ranged from 6% to 56%. Based on the risk of bias assessments, the average quality of the included systematic reviews was 6.6. As shown in Appendix 4.5, 67%

(n=12) of the systematic reviews were deemed low quality (rating 0-4), and 28% (n=5) were of moderate quality (rating 5-8). One Cochrane review by Davey and colleagues[186] was judged as high quality.

4.5.3 Antimicrobial stewardship intervention components in hospitals

Based on the implementation strategies domain of the EPOC Taxonomy, seven AMS intervention components were evaluated in the selected SRs. These included audit and feedback, clinical practice guidelines (CPGs), continuous quality improvement, education materials, educational outreach visits or academic detailing, educational meetings and reminders. The impact of these intervention components was primarily measured by antibiotic use (indicators: number of prescriptions, defined daily doses), infection risk (indicators: rate of healthcare-associated infections, rate of Clostridium difficile infections), appropriateness of antibiotic use (drug type, dose, duration), guideline compliance and cost reduction. Overall, antibiotic use and the appropriateness of use were the most common impact measures, accounting for 87% (n=6) of AMS intervention components, as shown in Figure 4.2. Meta-analyses were performed in three of the included reviews [186, 191, 202] but results were pooled across all interventions and did not provide details on the impact of individual AMS intervention components. Outcomes related to intervention components are presented in Appendix 4.6.

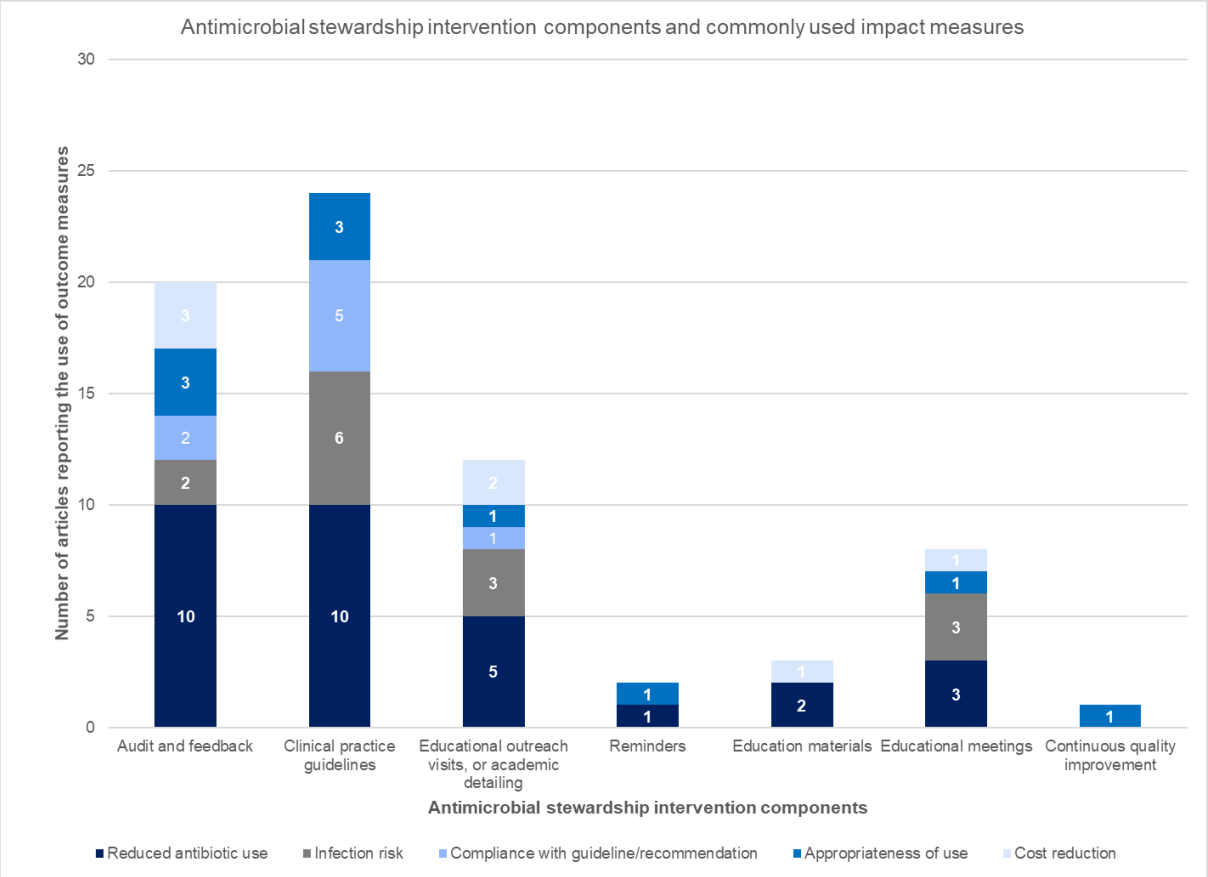


Figure 4.2 Antimicrobial stewardship interventions with commonly used impact measures

4.5.4 Impact of healthcare worker-targeted antimicrobial stewardship interventions

All included reviews reported positive outcomes following the implementation of AMS intervention components. However, there were reports of non-significant changes or unintended consequences following intervention implementation. The majority of unintended consequences were reported in the review by Davey et al, as its objectives included evaluating the safety of interventions in addition to their effectiveness.[186]

Audit and feedback

Improvements in several clinical and process outcomes were documented by 93% (n=13) of the SRs that evaluated audit and feedback as an intervention component. Audit and

feedback interventions reduced the duration and rate of inappropriate antibiotic prescribing to zero in some settings following implementation.[185, 207, 213] Results on improvements in the appropriate use of antibiotics differed across two reviews, with one showing improvement and the other showing no difference following audit and feedback. [207, 213] Compliance with the time elapsed between antibiotic order and administration improved from 41.2% to 78.4% following audit and feedback.[187] Antibiotic therapy was discontinued for 90% of patients whose doctors received formal feedback.[200] Reductions were observed in total antibiotic consumption, most frequently measured as defined daily doses (DDD). One study also found no compensatory increase in the use of other antibiotics.[200] Wagner reported that patient outcomes, including mortality, length of stay and readmission, were generally unaffected following audit and feedback, but the authors noted that the studies were not adequately powered.[213] An unintended consequence, increased vancomycin use, was reported by one study in the review by Davey and colleagues.[186]

Clinical practice guidelines

Implementing clinical practice guidelines improved both clinical and process outcomes across all hospitals where the guidelines were applied. When used to guide surgical antibiotic prophylaxis, improvements were observed in the appropriate initiation of first-line therapy and in the reduction of broad-spectrum antibiotic prescribing.[213] Improvements in antibiotic use, including reductions in inappropriate use and in the timing of antibiotic use, were reported following the implementation of clinical practice guidelines.[210, 211, 213] Wagner and colleagues reported mixed outcomes from studies without a feedback component following

guideline implementation, including increased mortality in an ICU setting and no difference or decreased mortality in other settings.[213]

Educational outreach/academic detailing

Twenty-seven per cent (n = 5) of the included SRs evaluated educational outreach/ academic detailing. Evidence suggests that educational outreach/academic detailing can reduce total and inappropriate antibiotic use, as well as the duration of antibiotic therapy.[215] However, prescription errors were reported during the implementation of this intervention. During the first year of this intervention component, dose-related prescription errors were observed, with 48% classified as significant, 25% as severe, and 27% as minimal.[210] Five per cent of children developed infections after recommended therapy changes were followed.[215]

4.6 Discussion

4.6.1 Summary of Main Findings

This scoping review of systematic reviews included 18 publications on interventions for AMS. Audit and feedback, and clinical practice guidelines were the most frequently reported AMS interventions targeting healthcare workers. Seventy-eight per cent of reviews reported on audit and feedback, while 61% reported on clinical practice guidelines. Educational interventions were the third most reported AMS strategy in this review, but were identified as the leading intervention in a scoping review of AMS interventions in Latin America and the Caribbean.[111] This implies that AMS programs in LAC rely on educational initiatives, possibly due to limited resources for more complex AMS interventions.

Evidence from this scoping review suggests that audit and feedback, clinical practice guidelines, and educational interventions may improve numerous clinical and process outcomes in hospitals. AMS interventions are critical for addressing AMR, however, results vary following implementation. This variation may reflect differences in the inclusion criteria of reviews, geographical settings, outcome measures, and patient populations, highlighting the importance of considering these factors when translating evidence into AMS intervention development.

A limited number of studies from LLMICs were included in the systematic reviews used in this scoping review. Research from these countries accounted for 2% (n=12) of all studies included in the systematic reviews and, therefore, did not provide substantial evidence on implementation and impact in LLMICs. Similarly, the scoping review of AMS interventions in Latin America provided information only for upper-middle-income and high-income countries, but included no AMS data for the Caribbean Community (CARICOM) States.[111] This highlights a significant evidence gap from LLMICs and CARICOM States.

4.6.2 Strengths and Limitations

In this scoping review, the author synthesised findings from 18 systematic reviews evaluating AMS interventions in hospitals, collectively drawing on evidence from 547 studies. An extensive literature search was conducted with input from an information specialist to maximise the retrieval of published evidence and grey literature on AMS interventions. For the reported AMS intervention components, it was unclear which taxonomy was used in the systematic reviews, and details of the interventions were rarely provided. The EPOC

Taxonomy was used to standardise the reporting of the intervention components in this scoping review, enabling a uniform presentation of the findings. In many of the systematic reviews included in this review, interventions from primary studies were bundled, and findings were pooled or presented in aggregate form. It was challenging to classify some intervention components presented in secondary studies; therefore, the author consulted primary studies to inform this review. In cases where components were clearly described, quantifying the number of times an intervention was reported or an impact measure was used was problematic because several systematic reviews included the same primary studies. The author of this scoping review documented reported intervention components and their outcomes, but could not confirm from the included systematic reviews whether those components were frequently implemented in hospitals. Furthermore, several low-quality studies were included in the systematic reviews, which may reduce the credibility of the evidence they presented.

4.6.3 Implications for research

The findings of this scoping review suggest that there is limited evidence on AMS interventions from LMICs. This finding is supported by evidence from the mixed-methods systematic review in Chapter 3 of this thesis, which revealed that no studies were retrieved on AMS interventions in CARICOM States. This highlights the need for further primary research to investigate the status of AMS interventions in LLMICs, specifically reporting on the impact of all intervention components. Based on the findings of the evidence syntheses in Chapters 3 and 4 of this thesis, the author assumes that AMS interventions are rarely implemented in hospitals of LLMICs because evidence on antibiotic prescribing and use is

not readily available. Therefore, evaluating antibiotic prescribing and use in these settings is crucial for establishing a foundation for developing targeted interventions.

4.7 Chapter Summary

- Findings suggest that some AMS interventions targeting healthcare workers in hospitals can improve a range of clinical and process outcomes.
- Audit and feedback and clinical practice guidelines were the most frequently reported AMS interventions.
- Antibiotic use, infection risk, appropriateness of use, guideline compliance, and cost reduction were the most used outcome measures following the implementation of AMS interventions.
- An unintended consequence of AMS interventions is an increase in antibiotic use.
- Evidence on AMS interventions and their impact on clinical and process outcomes in low and lower-middle-income countries is severely limited.
- Future research in LLMICs and low-resource settings should investigate the status of antibiotic prescribing and use, and utilise this information to develop and evaluate targeted AMS interventions based on the local context.

CHAPTER FIVE

5 The prescribing of antibiotics for systemic use in hospitalised patients at a tertiary care public hospital in Antigua and Barbuda

5.1 Publication statement

A summary of this chapter is currently being prepared for publication in Antimicrobial Stewardship and Healthcare Epidemiology.

5.2 Chapter Introduction

One of the most frequently prescribed drugs in hospitals is antibiotics, which are essential for reducing the risk of infection, severe infection, and death. The use of antibiotics has increased in many settings, and often, the reasons for their use are unjustified. This type of prescribing has contributed to the accelerated emergence of antibiotic-resistant organisms in hospitals and poses a serious threat to patient safety.[216] In Chapter 2, the mixed-methods systematic review (MMSR) found that evidence on antibiotic prescribing and use in hospitals was outdated and had been conducted in only two Caribbean Community (CARICOM) States: Trinidad and Tobago and Jamaica. The MMSR findings indicate that prescribing is predominantly empiric, with few instances of de-escalation based on bacterial culture and sensitivity reports in CARICOM States.[5] Health bodies have been calling for improvements in prescribing and antibiotic use through antimicrobial stewardship programmes, but it is first necessary to understand local prescribing practices.[217] To add to the evidence base for antibiotic prescribing in CARICOM States, the author investigated prescribing patterns of systemic antibiotics at a tertiary care hospital in Antigua and Barbuda. The only retrieved

study from a tertiary care hospital in this setting, published in 2006, reported antibiotic overuse among patients undergoing appendectomies.[148]

5.3 Chapter aim and objectives

This chapter examines trends in antibiotic prescribing for systemic use among hospitalised patients at a tertiary care public hospital in Antigua and Barbuda from January 1, 2014, to September 30, 2021. The primary objectives were to characterise antibiotic prescribing by class, spectrum, and route of administration, and to assess temporal trends in systemic antibiotic prescribing.

5.4 Methods

A cross-sectional review of antibiotic prescriptions dispensed by the pharmacy for patients 16 and older who were hospitalised in the surgical, medical and maternity units was conducted to achieve the objectives of this chapter. The protocol for this study was registered on the Open Science Framework OSF Registries | The prescribing of antibiotics for systemic use in hospitalised patients. As shown in Appendix 5.1, the local Institutional Review Board of the hospital in Antigua and Barbuda granted written permission to conduct this study. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines.[218]

5.4.1 Inclusion criteria

Prescriptions for patients hospitalised in the medical, surgical, and maternity units from 1 January 2014 to 31 December 2021 were eligible. Included were complete inpatient prescriptions with at least one antibiotic for systemic use. Antibacterials for systemic use

(J01) as classified by the World Health Organization's (WHO) Anatomical Therapeutic Classification (ATC) index, shown in Appendix 5.2, were included.[219]

5.4.2 Exclusion criteria

Prescriptions for patients hospitalised in the paediatric and intensive care units were excluded, as antibiotic prescribing for these patients may differ due to age-related factors and greater clinical complexity. Prescriptions issued in outpatient settings, including the accident and emergency, dialysis, and oncology units were also excluded. Additional exclusions comprised topical, anti-tuberculosis, incomplete and repeat prescriptions issued to hospitalised patients within 6 months of a previous prescription.

5.4.3 Sampling approach

For surveys investigating prescribing patterns, the World Health Organization's manual on investigating drug use in health facilities has suggested that more than 600 encounters should be examined.[220] In this study, data on all eligible antibiotic prescriptions were collected to ensure a complete and representative picture of antibiotic prescribing in the setting. The pharmacy drug-dispensing data record was used to identify prescriptions for systemic antibiotics for patients from the medical, surgical, and maternity units who were hospitalised during the study period, from January 1, 2014, to December 31, 2021.

5.4.4 Data extraction and management

The author obtained the pharmacy's drug-dispensing records and filtered the dataset in Microsoft Excel, manually extracting all data on antibiotic prescriptions for hospitalised patients. The data were cleaned, and the names of all antibiotics were standardised to

generic names to enable accurate grouping for analysis of drug-class frequencies. To ensure consistency in data collection, the WHO's Form to record antimicrobial treatments,[221] presented in Appendix 5.3, was piloted, modified, and applied to extract data from pharmacy records. Demographic data, including sex, age and unit of admission, were collected. Data on antibiotics included the date of prescription, the generic name of the prescribed antibiotic, dose, route of administration, frequency, and prescribed duration. No identifying data was included in the final dataset for analysis. All entries were coded, and the dataset was stored in the university's OneDrive for Business, shared only with members of the research team involved in data cleaning, sorting, and analysis.

5.4.5 Data Analysis

Antibiotics were analysed according to the WHO Anatomical Therapeutic Chemical classification system, a tool used in research and drug utilisation monitoring.[219] Antibacterials for systemic use have been classified under J01 in this system. Descriptive statistics were used to summarise data on antibiotic prescriptions, including the mean, range, frequency and percentages. Prescription rates were used to track yearly trends in antibiotic class usage and patterns of use across inpatient units. The chi-squared test was used to determine whether the proportion of intravenous antibiotic prescriptions differed from that of oral prescriptions across the assessed inpatient units. Prescriptions associated with a switch to oral antibiotics were excluded from the overall prescribing analysis to prevent duplication. R Software and Microsoft Excel were used to visualise prescribing patterns.

5.5 Results

Between January 1, 2014, and September 30, 2021, 28,781 prescriptions for oral and parenteral antibiotics were reviewed. Four per cent (n=1,104) of these prescriptions indicated a switch to oral antibiotics. 27,676 initial prescriptions were subsequently used to assess the prescribing trends. Of these prescriptions, 52% (n=14,285) were from the Surgical Unit, 38% (n=10,556) were from the Medical Unit, and 10 % (n=2,835) were from the Maternity Unit.

5.5.1 General prescribing patterns

As shown in Figure 5.1, the most frequently prescribed subgroup of antibacterials for systemic use (J01) was 'other beta-lactam antibacterials' (J01D), representing 41% (n=11,337) of all prescriptions. Ninety-two per cent (n = 10,377) of the prescriptions from this subgroup were cephalosporins, and the remaining 8% (n=960) were the carbapenems, meropenem and imipenem.

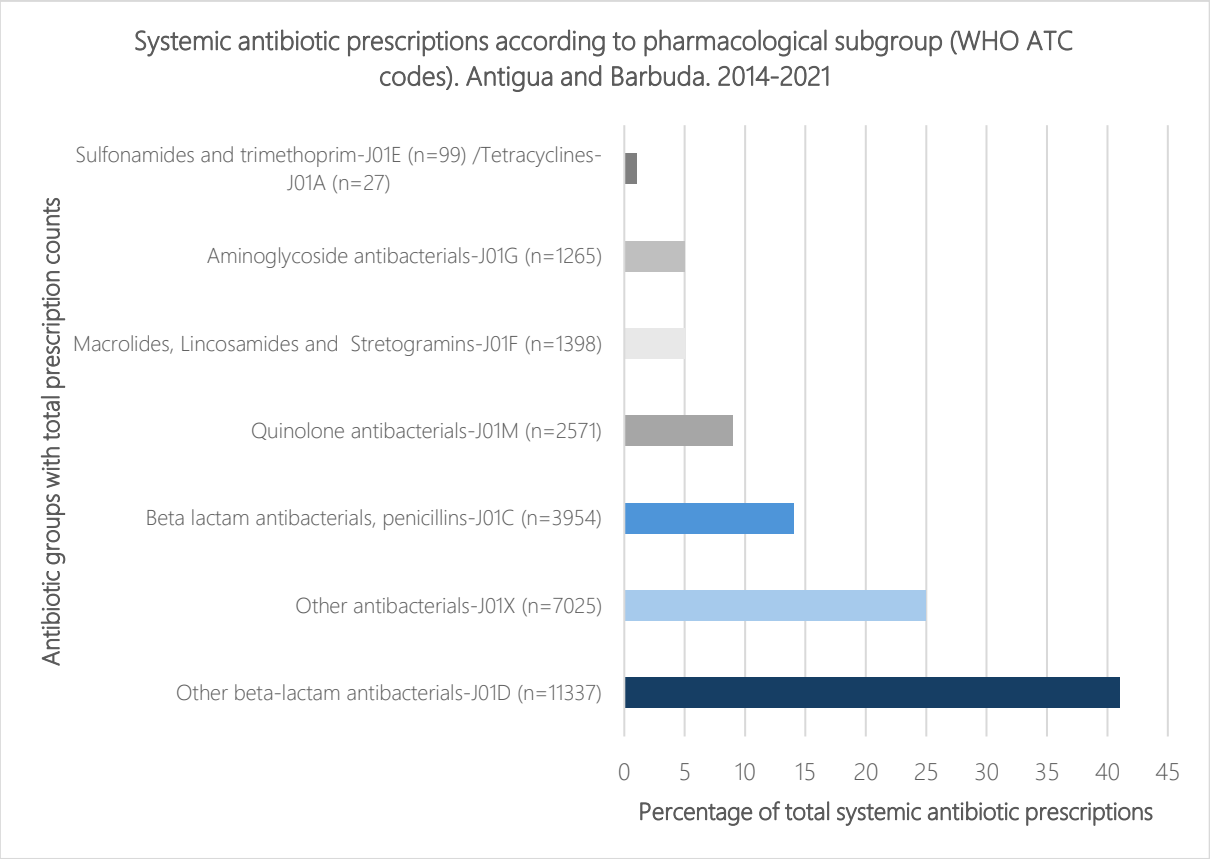


Figure 5.1 Distribution of systemic antibiotic prescriptions (% of total) according to pharmacological subgroup World Health Organization Anatomical Therapeutic Chemical (WHO ATC) Code. Antigua and Barbuda 2014-2021

Of all prescribed cephalosporins, 60% (n=6207) were third-generation and 37% (n = 3817) were cefuroxime, a second-generation cephalosporin. Only 3% (n=344) of these prescriptions were for the first-generation cephalosporin cefazolin. Ceftriaxone was the most prescribed cephalosporin at 39% (n=4051) and the second most prescribed antibiotic in this setting, accounting for 15% (n=4051) of all prescriptions, as shown in Figure 5.2.

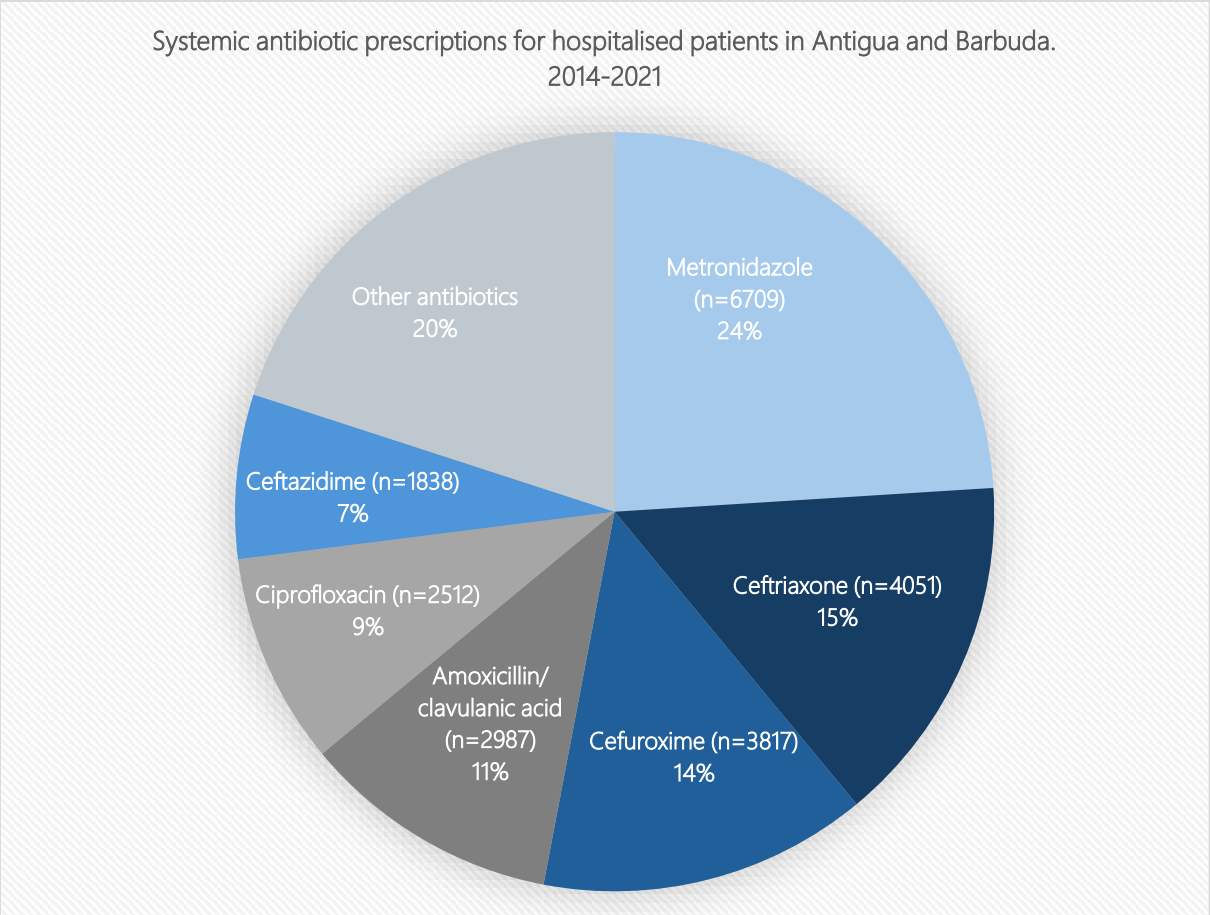


Figure 5.2 Percentage of commonly prescribed systemic antibiotics for hospital inpatients in Antigua and Barbuda

'Other antibacterials' (J01X) were the second most prescribed group of antibiotics, accounting for 25% (n=7025) of all prescriptions. In this setting, metronidazole and vancomycin comprised this group. Metronidazole accounted for 96% (n=6709) of prescriptions in this subgroup and was the most commonly prescribed antibiotic in this setting, at 24% (n=6709). The remaining 4% (n=316) of prescriptions from the J01X subgroup were for vancomycin.

Beta-lactam antibacterials, penicillins (J01C), accounted for 14% (n=3954) of all prescriptions. Amoxicillin with clavulanic acid made up 76% (n=2987) of prescriptions from the subgroup and 11% (n=2987) of all prescriptions.

Macrolides, lincosamides and streptogramins (J01F) and aminoglycoside antibacterials (J01G) represented a smaller proportion (5%) of this subgroup. The full distribution list of systemic antibiotics by inpatient unit and ATC classification in Antigua and Barbuda is presented in Appendix 5.4

5.5.2 Administration routes of systemic antibiotics

Seventy-five per cent (n=21,538) of all reviewed antibiotic prescriptions for hospitalised patients were for parenteral use. Overall intravenous prescribing rates were 84% (n=12,021) in the Surgical Unit, 70% (n=7373) in the Medical Unit, and 76% (n=2144) in the Maternity Unit. Figure 5.3 illustrates a shift in the route of administration for systemic antibiotics in patients, with intravenous antibiotics increasingly more common than oral antibiotics from 2014 to 2021.

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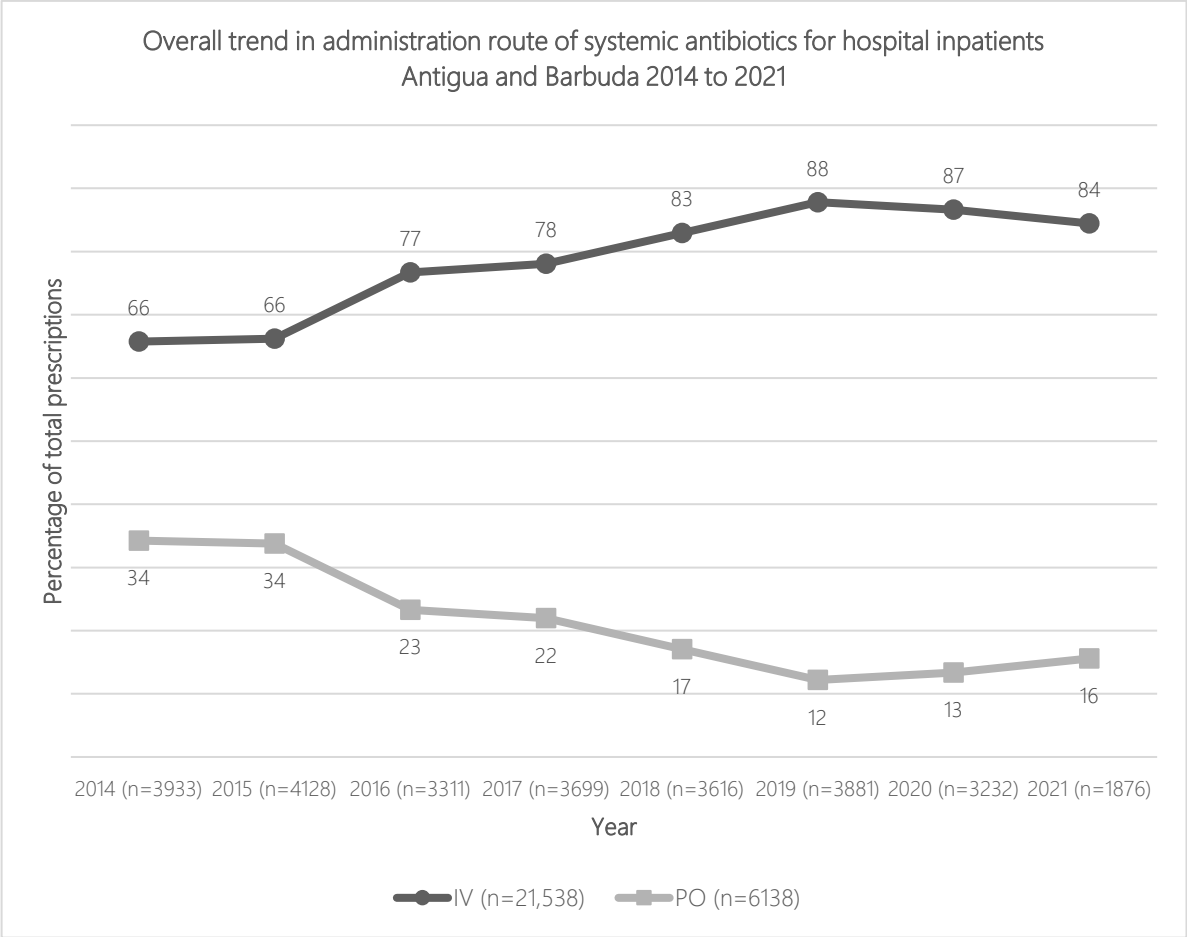


Figure 5.3 Route of antibiotic prescriptions for hospital inpatients in a tertiary care public hospital in Antigua and Barbuda. 2014-2021

When IV prescription rates were compared across inpatient units, the chi-squared test yielded a p-value > 0.05. Therefore, it cannot be concluded that the proportion of IV antibiotic prescriptions differed significantly by inpatient unit.

5.5.3 Trends in systemic antibiotic prescriptions by inpatient unit

Several antibiotics from different pharmacological subgroups have been prescribed in this setting from January 1, 2014, to September 30, 2021, as illustrated in Figure 5.4.

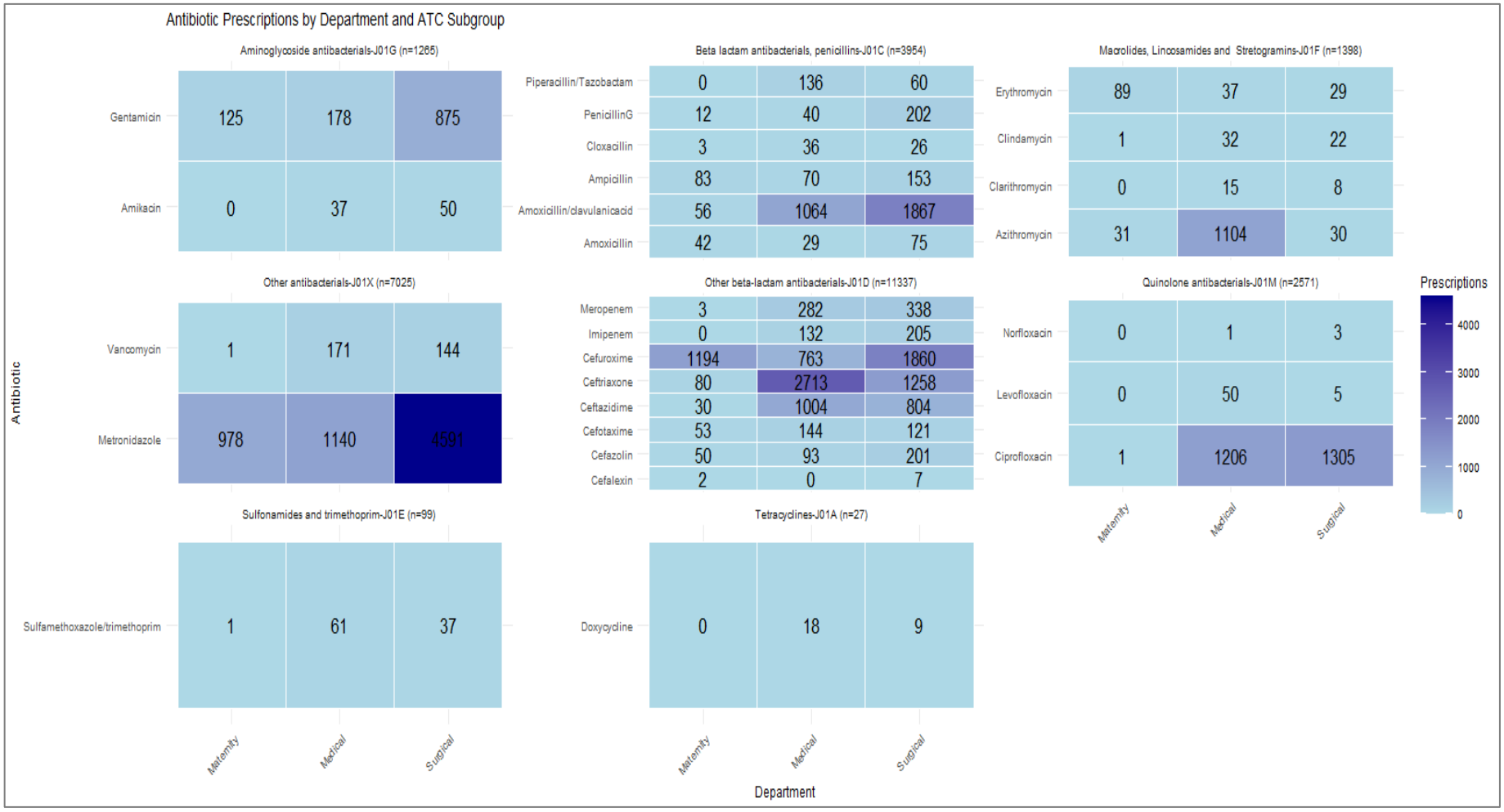


Figure 5.4 Heatmap showing the distribution of antibiotics by inpatient unit and ATC subgroup

J01A: Tetracyclines, J01C: Beta lactam antibacterials-penicillins, J01D-Other beta lactam antibacterials, J01E- Sulfonamides and trimethoprim, J01F- Macrolides, glycosamides and streptogramins, J01G: Aminoglycoside antibacterials, J01M: Quinolone antibacterials, J01X: Other antibacterials

Prescribing trends in the medical unit

Other beta-lactam antibacterials (J01D) were most frequently prescribed in the Medical Unit, shown in Figure 5.5. The annual average prescribing rate was 48%, with a range from 37 to 57%. Fifty-three per cent (n=2713) of these prescriptions were for ceftriaxone, while 20% (n=1004) were for another third-generation cephalosporin, ceftazidime.

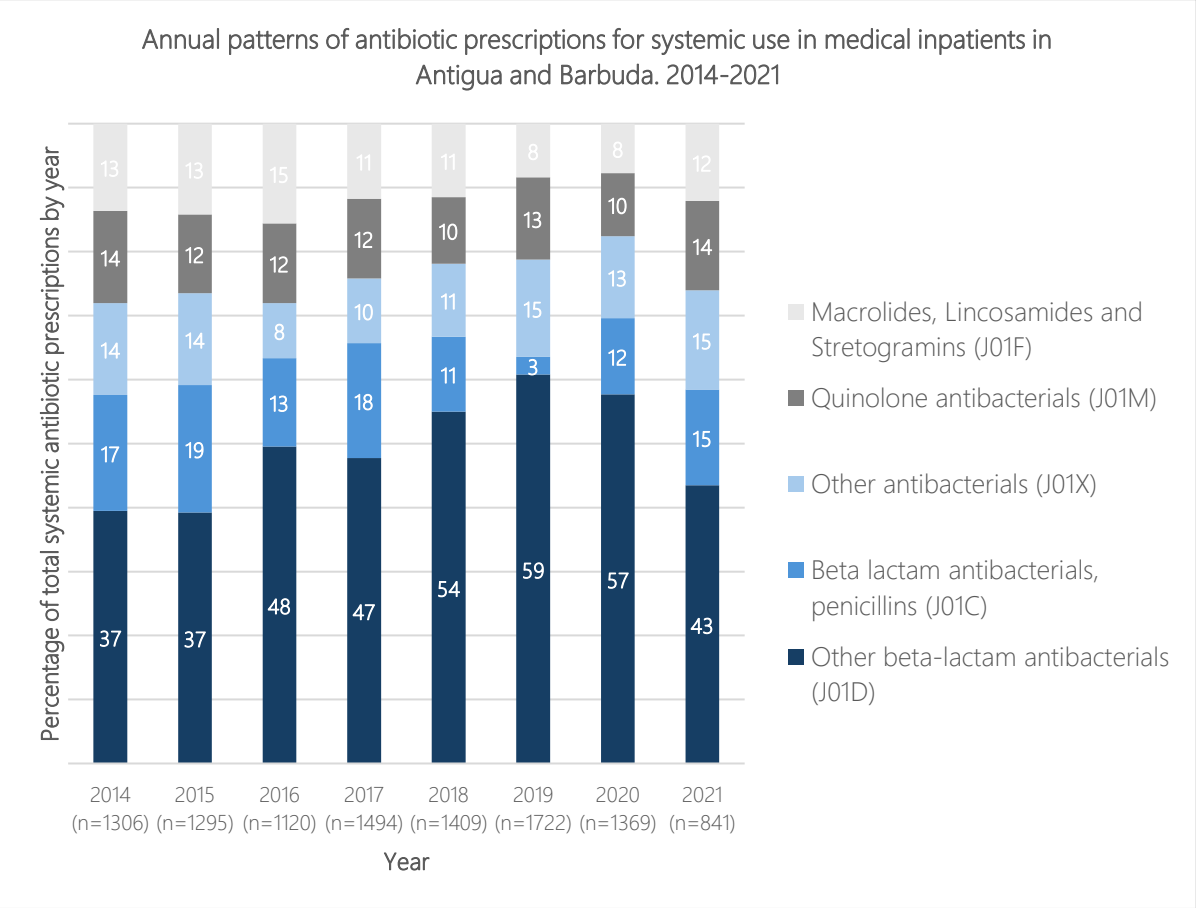


Figure 5.5 Distribution of systemic antibiotic prescriptions for medical inpatients in Antigua and Barbuda.

Prescribing trends in the surgical unit

In the surgical unit, subgroups 'other beta-lactam antibacterials' (J01D) and 'other antibacterials' (J01X) were predominantly prescribed for inpatients. Both subgroups had an annual average prescribing rate of 34%. Prescribing rates for J01X ranged from 30 to 41%, while the prescribing rate of J01D ranged from 30 to 37%, as shown in Figure 5.6. Ninety-seven per cent (n = 4591) of J01X prescriptions were metronidazole, and the remaining 3% (n = 144) were vancomycin.

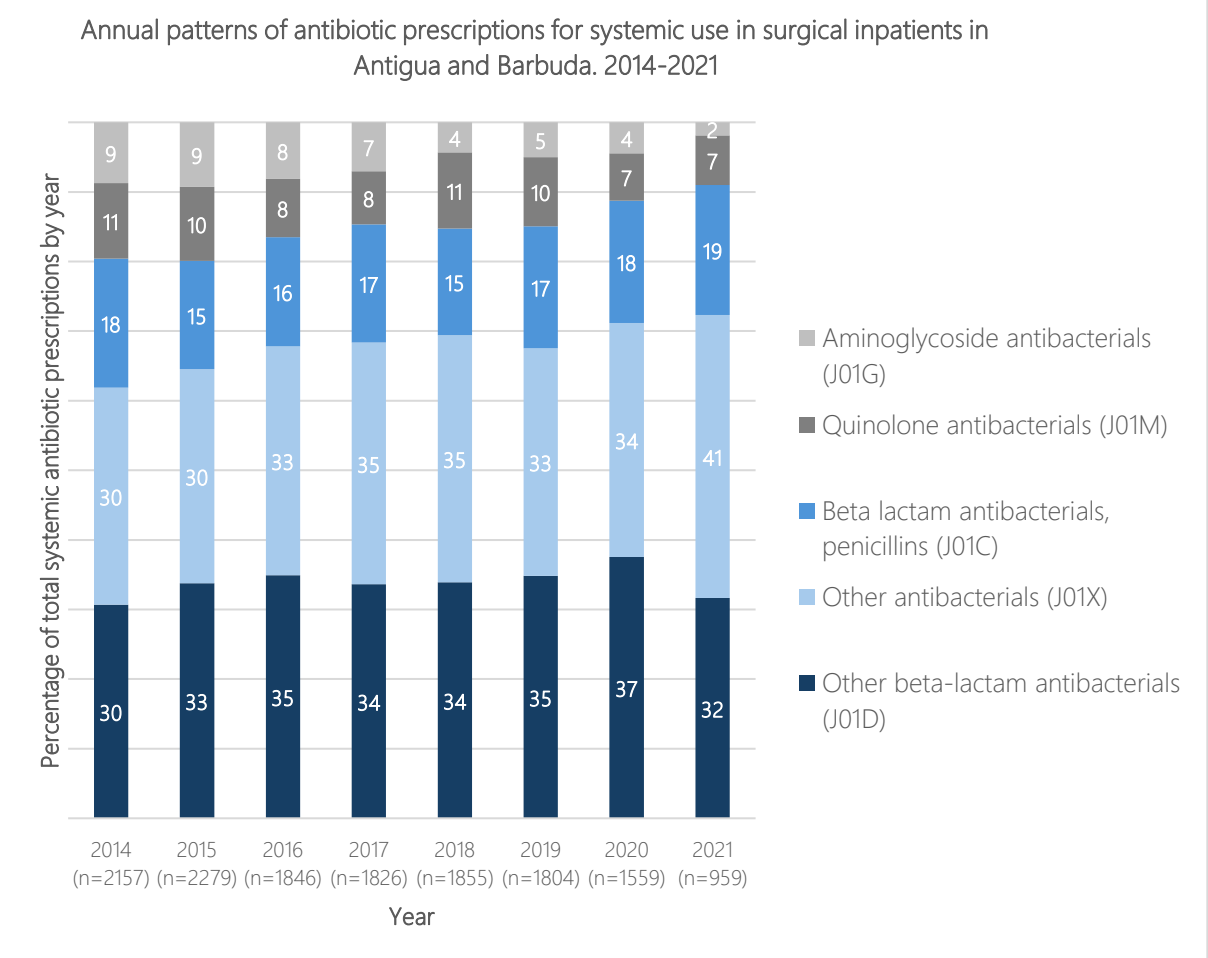


Figure 5.6 Distribution of systemic antibiotic prescriptions for surgical inpatients

Beta-lactam antibacterials, penicillin (J01C), were consistently prescribed from 2014 to 2021 with a mean annual prescribing rate of 17% and a range of 15 to 19%.

Prescribing trends in the maternity unit

The mean prescribing rate for subgroup 'other beta lactam antibacterials' (J01D) in maternity inpatients was 48%, ranging from 22% to 69% between 2014 and 2021, as shown in Figure 5.7. Eighty-five per cent (n = 1194) of prescriptions in this group were cefuroxime.

Subgroup 'other antibacterials' (J01X) was also frequently prescribed in this unit, with an annual average of 36% and a range of 21 to 57%. Metronidazole accounted for 99.8% (n = 978) of prescriptions in this subgroup.

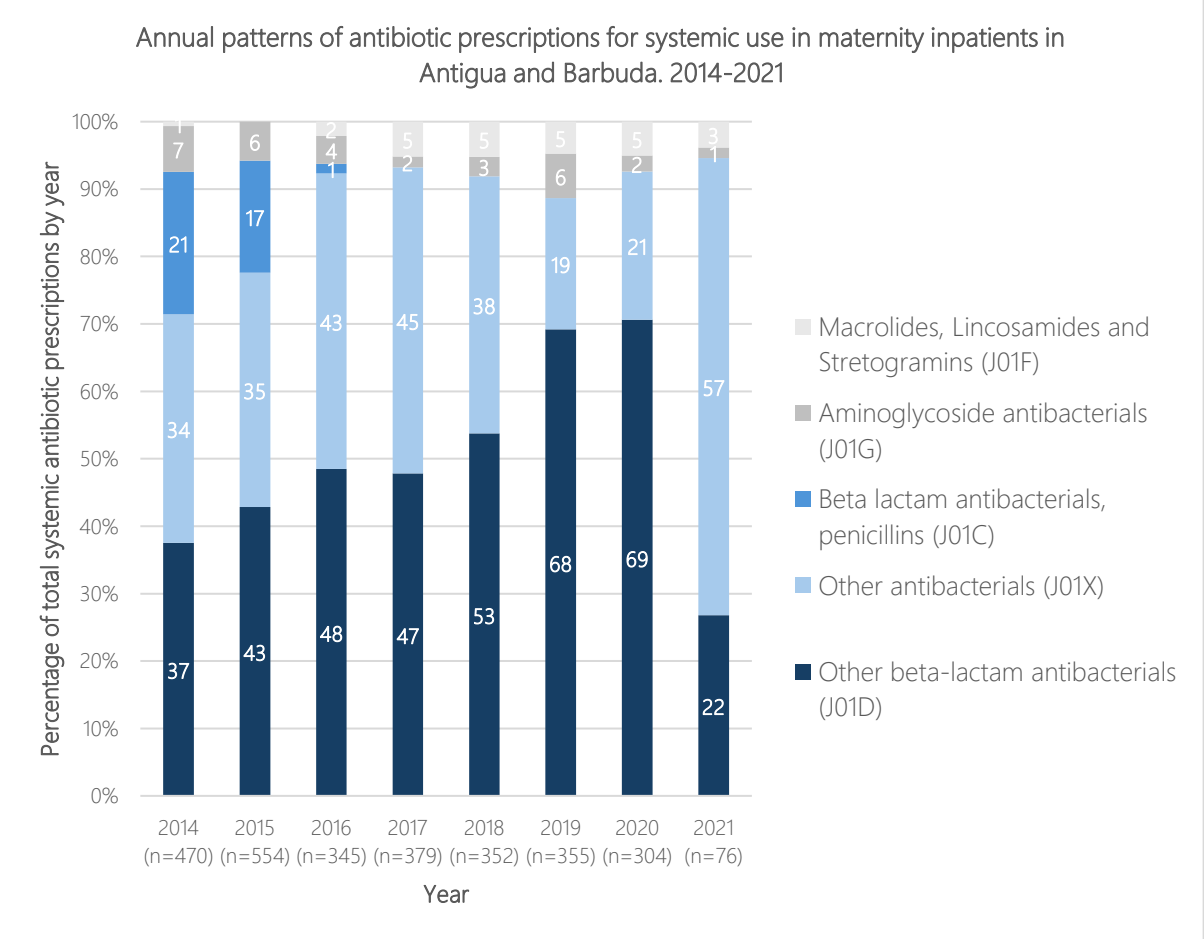


Figure 5.7 Distribution of systemic antibiotic prescriptions for maternity inpatients

There were noticeable fluctuations in the prescriptions of cephalosporins and metronidazole across the study period. In 2021, the prescription rate for J01D (predominantly cephalosporins) declined to 22% (n=17), substantially below the annual average rate of 48%.

5.6 Discussion

5.6.1 Summary of main findings

In this chapter, 27,676 antibiotic prescriptions were reviewed across three inpatient units at a tertiary care public hospital in Antigua and Barbuda. The number of antibiotic prescriptions per patient ranged from 1 to 8, a finding similar to that of Martin's 2006 study of appendectomy patients conducted at a separate tertiary care institution in Antigua and Barbuda.[148] The most prescribed subgroups were other beta-lactam antibacterials (J01D), predominated by cephalosporin prescriptions for ceftriaxone and cefuroxime. Other antibacterials (J01X) were the second-most prescribed subgroup, mainly metronidazole. Metronidazole was the most prescribed antibiotic, followed by ceftriaxone and cefuroxime. On average, 77% of antibiotic prescriptions were for intravenous administration, with use increasing over the study period. The increased use of intravenous antibiotics at hospital admission is often clinically necessary; however, antimicrobial stewardship programs recommend reviewing therapy at 48 to 72 hours to assess the possibility of switching to oral therapy.[222] An intravenous-to-oral switch was performed in only 4% of prescriptions in this setting. From 2020 to 2021, there were noticeable fluctuations in the prescribing of cephalosporins and metronidazole in the maternity unit. These fluctuations could be partially explained by local policy changes that led to the bulk distribution of antibiotics to

inpatient units during the COVID-19 pandemic. This may account for the absence of unit-specific drug dispensing data in the pharmacy dataset.

5.6.2 Strengths and limitations

To the author's knowledge, this is the first study to assess antibiotic prescribing patterns for systemic use in hospitalised patients at the Sir Lester Bird Medical Centre in Antigua and Barbuda. Prescription data spanning 8 years were analysed to illustrate prescribing patterns for different antibiotic classes across the maternity, surgical, and medical units of the only public hospital in Antigua and Barbuda. The methodology balances comprehensiveness and feasibility, with strengths including a standardised antibiotic classification system, a census sampling strategy and structured data extraction. This study contributes to the evidence base on antibiotic prescribing in Antigua and Barbuda and, by extension, in the CARICOM States. The information from this study can be used in regional and global evidence syntheses on prescribing patterns of systemic antibiotics.

Several limitations were identified in this study. Cross-sectional studies inherently limit the ability to verify uncertainties present in retrospective data during the study.[223] Patient age and sex were inconsistently reported and could not be verified because the hospital's health information system had limited capacity and was not linked to the pharmacy, thereby limiting cross-checking. This limitation prevented the inclusion of a summary of patient demographics and required the removal of some antibiotic prescription entries.

For patients with multiple antibiotic prescriptions over a 30-day period, the author was unable to determine whether they were continuously admitted or readmitted during this

period. As a result, the number of antibiotics per patient encounter could not be evaluated. Prescription records were only available from January 1, 2014, to September 30, 2021, because the COVID-19 pandemic affected the pharmacy staff complement, resulting in inadequate record-keeping. The dataset used in this study lacked clinical context; therefore, it did not reflect clinical indication, drug administration, or adherence.

As this was a single-centre study, generalisation of findings to other tertiary care hospitals in the CARICOM States is limited; however, the information presented can be used in regional and global evidence syntheses assessing systemic antibiotic prescribing patterns in hospitalised patients.

5.6.3 Implications for research

The notable increase in intravenous antibiotic use warrants further investigation in this setting, as its use is associated with catheter-related complications, healthcare-associated infections and higher treatment costs. Having additional information about the clinical context could inform antibiotic prescribing. As such, future research should focus on specific diagnoses or patient circumstances to better understand how antibiotics are prescribed within selected groups. This should include information on the specific types of antibiotics used, as well as the dose, route, frequency, and duration of use. Targeting patient groups would provide detailed information that can be acted upon if antibiotic misuse is observed.

5.7 Chapter summary

- Pharmacological subgroups 'other beta-lactam antibacterials' (J01D) and 'other antibacterials' (J01X) were most prescribed for inpatients in Antigua and Barbuda.
- Of the J01D subgroup, cephalosporins are the most prescribed antibiotics for this tertiary care hospital in Antigua and Barbuda.
- Antibiotic prescriptions for all units were predominantly for intravenous use, averaging 77%.
- From one to eight antibiotics could be prescribed per patient encounter.
- Cephalosporins were the most prescribed antibiotics in the medical unit, and this remained constant throughout the study period.
- Cephalosporins and metronidazole were frequently prescribed in the surgical unit, and this trend was consistent from 2014 to 2021.
- In the maternity unit, cephalosporins were the most prescribed antibiotics, followed by metronidazole. There were notable variations in the prescribing of these antibiotics for the study period.
- Targeted research involving well-defined patient cohorts can yield deeper insight into antibiotic prescribing practices, thereby informing strategies to improve antibiotic use.

CHAPTER SIX

6 Use of surgical antibiotic prophylaxis for women undergoing caesarean sections at a tertiary care public hospital in Antigua. And Barbuda

6.1 Publication statement

Under peer review by the journal, BMC Pregnancy and Childbirth.

6.2 Chapter introduction

It was determined in Chapter 5 that cephalosporins were the most prescribed class of antibiotics at the Sir Lester Bird Medical Centre in Antigua and Barbuda from 1 January 2014 to 30 September 2021. Although evidence on systemic antibiotic prescribing was collated, the lack of clinical context prevented the author from determining whether the right patient received the right drug for the right duration. Chapter 5 revealed that in 2021, the cephalosporin prescription rate decreased to 22%, substantially below the average of 48%. Additionally, the second-generation cephalosporin, cefuroxime, which has high selective pressure for antibiotic resistance, was most frequently used in the Maternity Unit. The author assumed that this antibiotic may be associated with Caesarean sections (C-sections) in this unit. However, some prominent clinical practice guidelines for surgical antibiotic prophylaxis in C-sections recommend using a first-generation cephalosporin.[81, 224, 225] Given the predominant use of cefuroxime, the observed reduction in cephalosporin use in 2021, the relatively uncomplicated nature of caesarean deliveries, and the feasibility of accessing records to assess surgical antibiotic prophylaxis in C-sections, the author decided that the best approach would be to investigate the targeting of surgical antibiotic prophylaxis for women undergoing C-sections.

6.3 Chapter aims and objectives

This chapter investigates the targeting of surgical antibiotic prophylaxis for women delivering via C-sections at a tertiary care public hospital in Antigua and Barbuda. Specific objectives included describing the patterns of use of surgical antibiotic prophylaxis for women who underwent C-sections and were admitted to the Maternity Unit, and determining whether maternal age, urgency for C-section, year and attending consultant were associated with regimen-type, and prescription duration from January 1, 2018, to December 31, 2024.

Definitions of independent and outcome variables

Maternal age was categorised into risk groups for pregnancy consistent with classifications described in the literature.[226, 227] Age stratifications used in this chapter were <20, 20-35, and>35. The urgency of c-section, elective or non-elective, was used to categorise patients and was based on consultant notes documented in patient charts. All surgeries reported as emergencies were categorised as non-elective. Surgical antibiotic prophylaxis was defined as administering intravenous cephalosporins preoperatively and/or postoperatively to prevent postoperative infectious conditions. These antibiotics, in addition to adjunctive metronidazole, formed the basis of primary analyses. Surgical antibiotic prophylaxis was categorised according to:

- Regimen type – Single regimen included prescriptions with a cephalosporin, while dual regimen included a prescription with a cephalosporin and adjunctive metronidazole.

- Prescription duration- less than 24 (≤24) hours consisted of cephalosporin prescriptions with one preoperative dose, one preoperative dose followed by a stat dose 12 hours after initial administration and prescriptions that indicated a duration of 1 day. Prescriptions classified as greater than 24 hours (>24) included cefuroxime and cefazolin with durations ranging from 2 to 7 days.

6.4 Methods

A retrospective analysis of patient records was used to achieve the objectives of this chapter. The STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline was used in the reporting of this study.[4] This study was registered at the Open Science Framework https://osf.io/qycma. Ethical approval was obtained from the Institutional Review Board of the Sir Lester Bird Medical Centre (Reference: March2022.UO).

6.4.1 Study subjects and data source

This study was done at the Sir Lester Bird Medical Centre, a tertiary care hospital in Antigua and Barbuda. The author performed a cross-sectional review of medical records of women who had caesarean delivery, irrespective of indication and were hospitalised for at least 24 hours. Only available and complete medical reports were used. The Maternity Admissions Logbook was first reviewed to identify women who had given birth via C-section from January 1, 2018, to December 31, 2024. The author used this information to access patient records from the maternity unit's medical records storage area. It has been suggested that more than 30 patient encounters per prescriber are necessary to describe prescribing patterns within an institution, with 100 encounters per prescriber being sufficient to provide

a more accurate estimate.[228] All patient encounters which met the inclusion criteria were included in this study.

6.4.2 Data extraction and management

The author commenced collecting the data from patient records in September 2022 and continued until February 2025. This period reflects the timing of data extraction and study activities rather than the dates of the patient records analysed. Eighty-six per cent (n=1326) of records documenting C-section deliveries were retrieved and reviewed. The remaining 14% (n = 208) were excluded because medical files were unavailable during data collection. All data were extracted from patient records using a modified and piloted version of the World Health Organization's Form to Record Caesarean Section Surgical Prophylaxis. The dates of admission, discharge, and date of caesarean delivery, as well as the attending consultant, were recorded. Extracted from the patients' files were maternal age, clinical characteristics, including indication for C-section, urgency of C-section, antibiotic allergies, types of antibiotics administered, postpartum infectious complications experienced during admission, and those requiring admission within 30 days post-procedure. Prescribing information included the name of the prescribed antibiotic, dosage, route of administration, frequency, duration and number of doses administered while the patient was admitted to the maternity unit. The pharmacy dataset was used to cross-check prescription data documented in patient charts.

All unique patient files were assigned a code using a system developed by the author to de-identify the data and protect patient privacy. The datasheets covering the period from 2018

to 2024 were consolidated into a single Microsoft Excel spreadsheet. Data was cleaned by standardising date formats, correcting antibiotic spelling, standardising antibiotic entries by relabeling them with their generic names, and formatting all cells to ensure that data was correctly identified during data analysis. Maternal age was categorised, and attending consultants were assigned numbers. The data was sorted in ascending order by year and date of C-section. Data was stored at the University of Oxford's OneDrive for Business.

6.4.3 Data analysis

Descriptive statistics

Patient characteristics and prescription data were summarised with frequency counts, percentages, and measures of central tendency and variation. This data was used to describe prescribing by year, attending consultant, regimen-type and duration of surgical antibiotic prophylaxis. Only antibiotics intended for use as part of a regimen for surgical prophylaxis were included in the analyses. Microsoft Excel was used to analyse and visualise data. R software was used for regression analysis.

6.4.3.1 Identification of factors associated with the prescribing of surgical antibiotic prophylaxis

Univariable logistic regression was used to examine the association between independent variables, maternal age, year, urgency of C-section, and consultant with the odds that a patient received a:

1. Single regimen prescription preoperatively.
2. Prescription for surgical antibiotic prophylaxis for less ≤24 hours duration

Coefficients from the regression models were exponentiated to obtain odds ratios. The year was analysed as both a continuous and a categorical variable, and the Akaike information criterion (AIC) was used to select the regression model that best fit the data. A multivariable binomial logistic regression model was then constructed to estimate the association between variables with significant observations in the univariable model with the odds of receiving a:

1. Single regimen prescription preoperatively
2. Prescription for surgical antibiotic prophylaxis for less ≤24 hours duration

Adjustments were made using sum contrasts to estimate predictor effects relative to the grand mean and to ensure that each variable contributed to the model without labelling a single reference category.[229] Type III deviance was used to examine the independent effects of each predictor while adjusting for other variables. Variables age and C-section urgency were excluded from the multivariable model because they were not significant in the univariable analyses.

6.5 Findings

From January 1, 2018, to December 31, 2024, 7123 births were recorded at the hospital, with 22% (n=1534) of deliveries done via caesarean section. Two hundred and eight files were unavailable during data collection, and seven were excluded due to incompleteness. Eighty-six per cent (n=1319) of eligible patient records were reviewed.

6.5.1 Characteristics of study subjects

Seventy-three per cent (n=965) of caesarean deliveries were non-elective. Maternal ages ranged from 14 to 46, with 6% (n=77) of c-section patients under 20, 72% (n=957) aged 20-35, and 22% (n=285) over 35, as shown in Table 6.1. The median maternal age was 30, with an interquartile range of 10.

Table 6.1 Summary of characteristics of women undergoing caesarean delivery

Year	Total patients	2018	2019	2020	2021	2022	2023	2024	% of total C-sections	Multi-year median	Interquartile range
Urgency of C-section											
Elective	354	50	43	43	70	34	60	54	27	50	14
Nonelective	965	114	134	121	148	141	140	167	73	140	27
Age Categories											
<20	77	6	13	10	13	8	13	14	6	13	5
20-35	957	126	128	109	153	130	152	159	73	130	27
>35	285	32	36	45	52	37	35	48	21	37	20

Postoperative infectious complication rate was 5% (n=71) over 7 years and included wound infections, puerperal sepsis, febrile morbidity and urinary tract infections.

6.5.2 Characteristics of antibiotic prescriptions

Ninety-nine per cent (n=1314) of women undergoing C-sections were prescribed at least one intravenous antibiotic preoperatively. Of these patients, 22% (n=287) received adjunctive metronidazole. Post-operatively, surgical antibiotic prophylaxis was given to 81% (n=1073) of c-section patients whose medical files were reviewed. Sixteen per cent (n=211) of women who received a single preoperative dose of a cephalosporin before caesarean delivery did not receive post-operative surgical antibiotic prophylaxis. Preoperative cephalosporins were prescribed to 97% (n=1271) of patients. Three per cent (n=43) of

patients who were either allergic to cephalosporins or were being treated for premature prelabour rupture of membranes received clindamycin, ampicillin, erythromycin, or gentamicin preoperatively.

Preoperative surgical antibiotic prophylaxis

Cefuroxime accounted for 75% (n=954) of cephalosporin prescriptions, while 22% (n=274) of prescriptions were cefazolin. As illustrated in Figure 6.1, cefazolin and cefuroxime usage were equal in 2023. The use of third-generation cephalosporins for surgical prophylaxis in this setting was minimal, accounting for 4% of all prescriptions from 2018 to 2024.

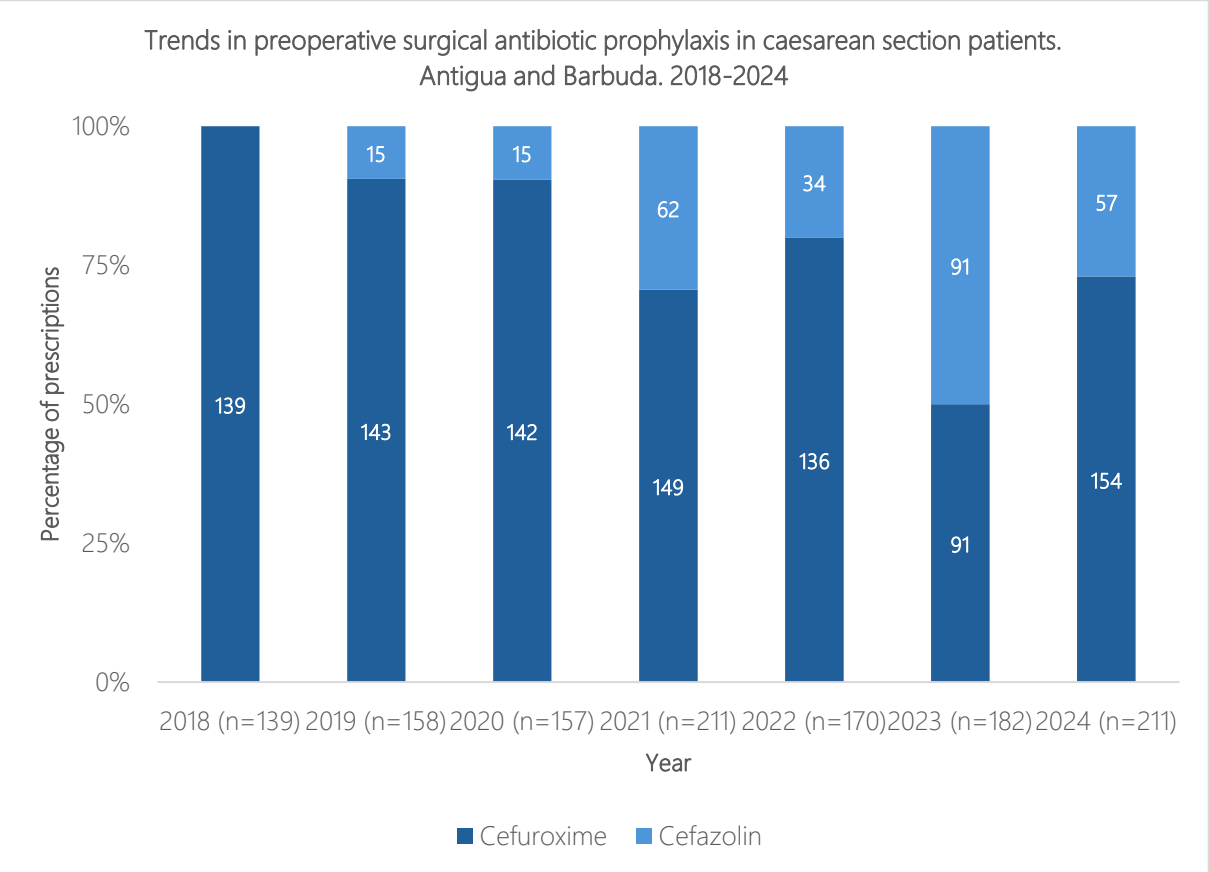


Figure 6.1 Trends in preoperative surgical antibiotic prophylaxis in women undergoing caesarean delivery. Antigua and Barbuda. 2018-2024

Overall, 77% (n=984) of preoperative surgical antibiotic prophylaxis prescriptions were single regimens.

As shown in Figure 6.2, there was a rapid decline in the use of dual regimens and a corresponding sharp increase in the use of single regimens in 2019. The upward trend in single regimen use persisted through 2020 and was followed by a steady decrease between 2021 to 2024.

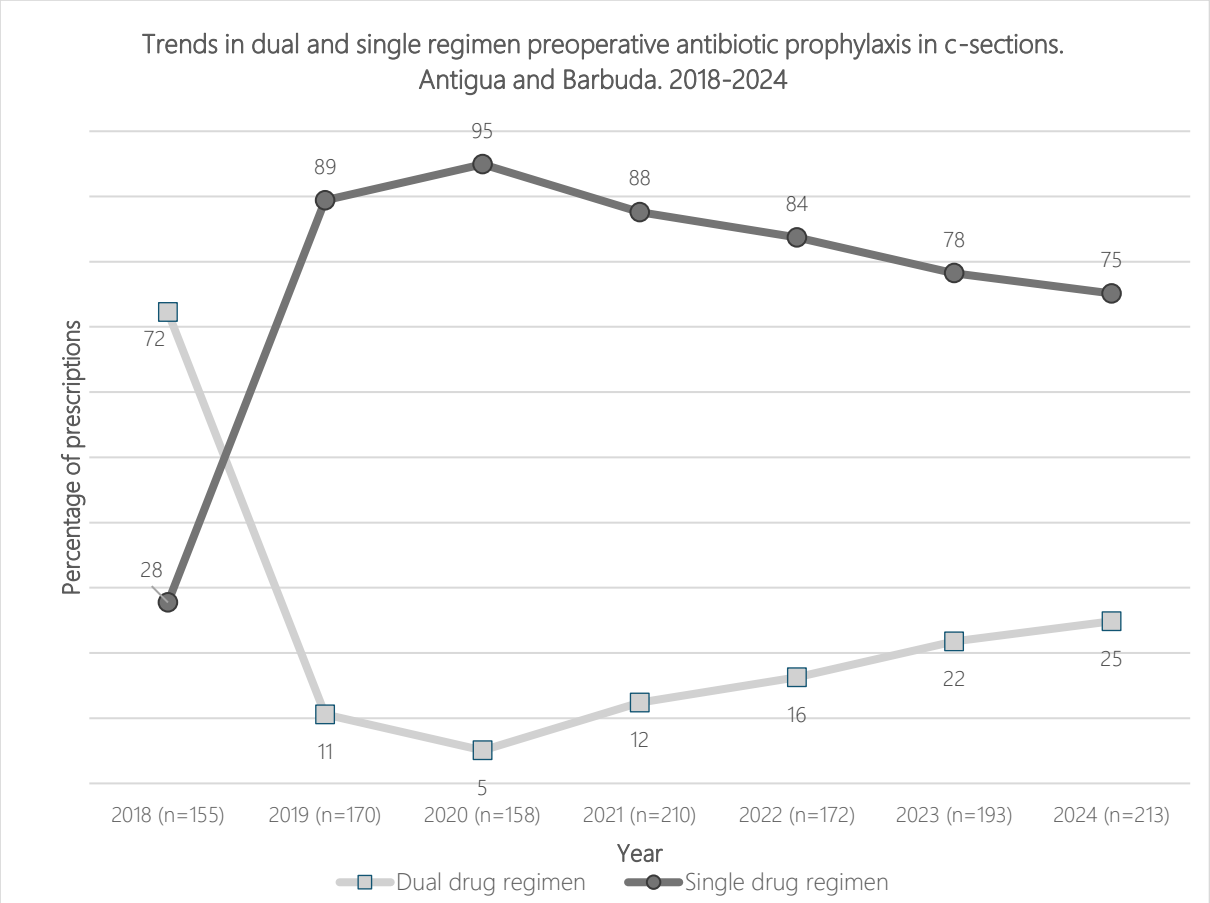


Figure 6.2 Trends in dual and single regimen preoperative surgical antibiotic prophylaxis in caesarean delivery. Antigua and Barbuda. 2018-2024

The use of single- and dual-regimen surgical antibiotic prophylaxis varied among attending consultants. As presented in Figure 6.3, more than 90% of all preoperative prescriptions by

consultants 1, 4 and 6 were single regimen, while 62% of all prescriptions by consultant 2 were dual regimen.

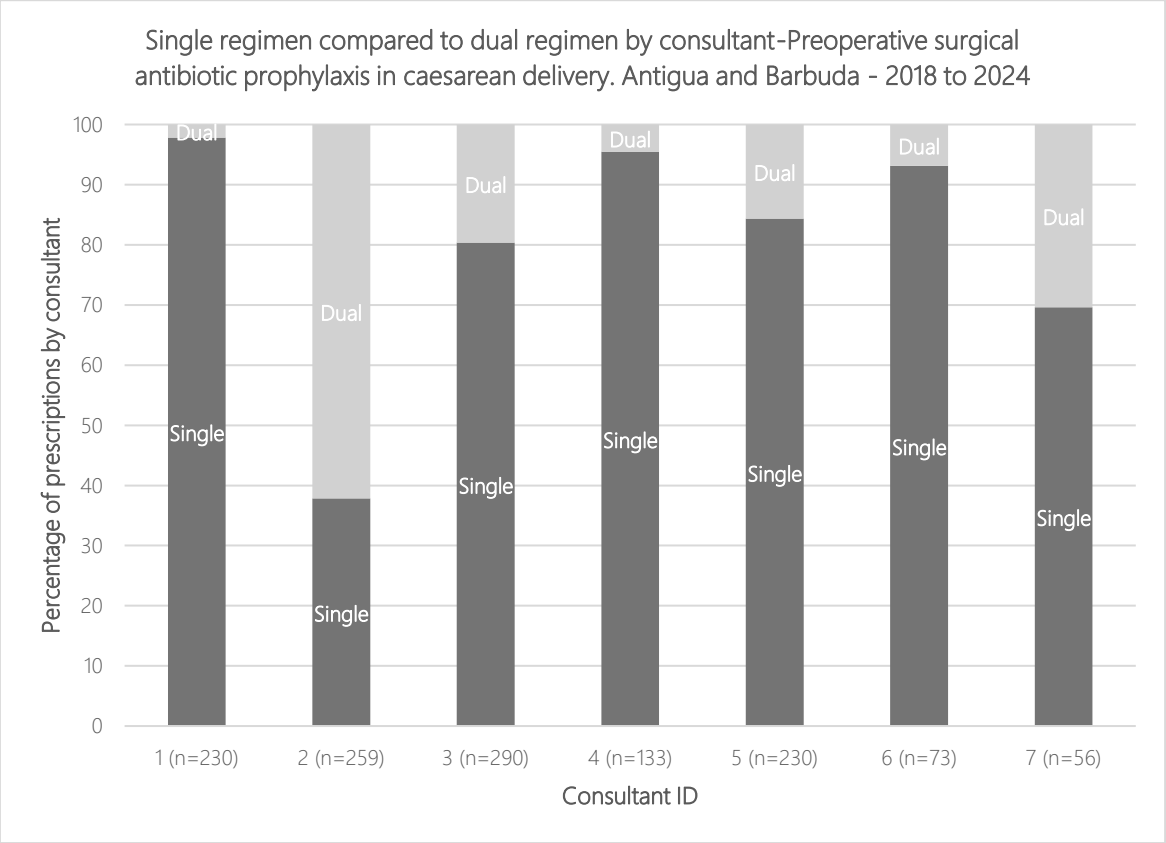


Figure 6.3 Single regimen compared to dual regimen by the consultant: Preoperative surgical antibiotic prophylaxis in caesarean delivery. Antigua and Barbuda - 2018 to 2024

When regimen type was evaluated according to maternal age categories and the urgency of C-section, prescribing patterns appeared similar across groups. Single-regimen prescriptions accounted for 77 % (n=717) of non-elective C-sections and 78% (n=267) of elective C-sections. Similarly, single-regimen prophylaxis predominated across all age categories; 81%(n=61) for patients aged <20 years, 76% (n=701) for patients 20-35, and 80% (n=222) for patients >35.

Postoperative surgical antibiotic prophylaxis

There were 1829 post-operative prescriptions for surgical antibiotic prophylaxis. Of these, 17% (n=309) were administered orally, reflecting a switch from intravenous to oral administration. The remaining 83% (n=1520) were for parenteral use. Seventy-one per cent (n=1073) of intravenous antibiotics were cephalosporins, and the remaining 29% (n=447) were metronidazole. Cefuroxime accounted for 88% (n=946) of postoperative cephalosporin prescriptions, while cefazolin accounted for 12% (n=127). Adjunctive metronidazole was administered to 42% (n=447) of patients with a post-operative prescription for surgical antibiotic prophylaxis. Ninety-seven per cent (n=922) of cefuroxime prescriptions were 750 mg, and 83% (n=106) of cefazolin prescriptions were 1000 mg. The most frequently observed administration frequency was three times daily, documented in 95% (n=1018) of cephalosporin prescriptions.

In 2018, 84% (n=125) of patients with post-operative prescriptions received a cephalosporin with metronidazole as an adjunct. As illustrated in Figure 6.4, single-regimen prescribing sharply increased from 16% (n=24) in 2018 to 77% (n=131) in 2019. From 2021 to 2023, single-regimen prescriptions gradually decreased, then plateaued.

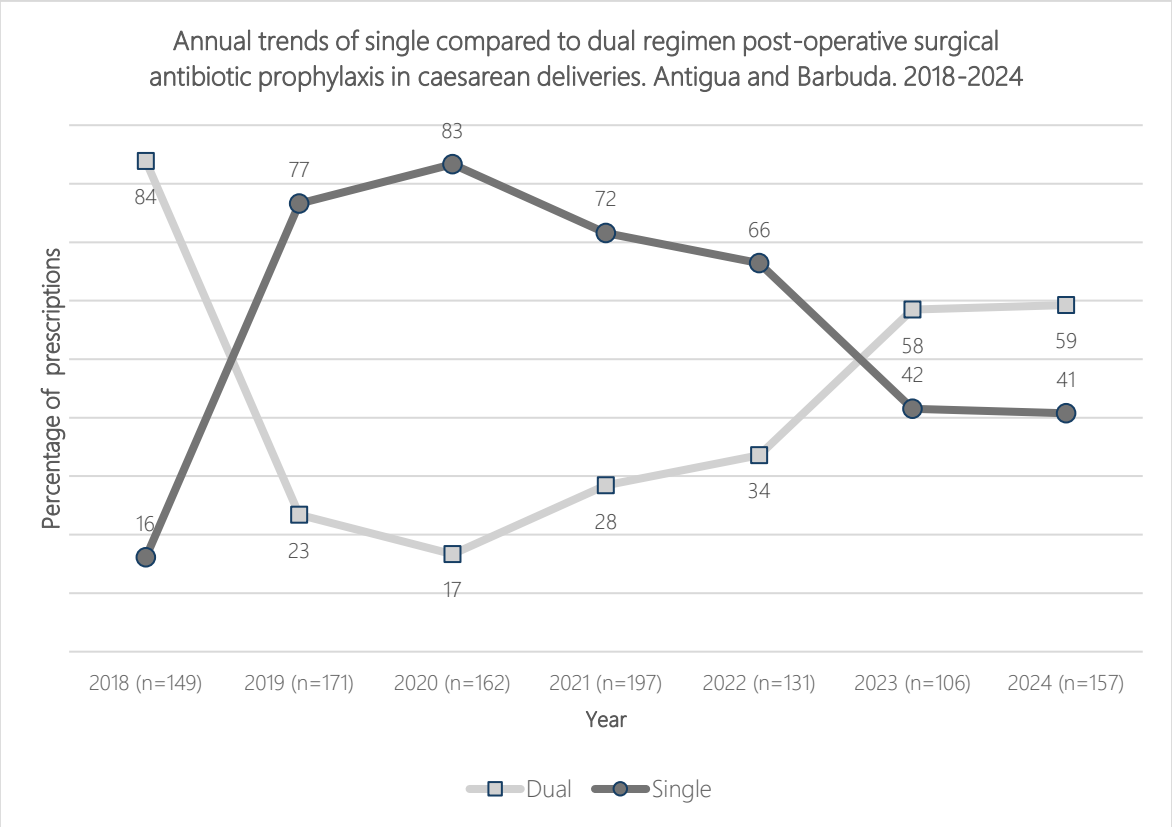


Figure 6.4 Trend in single and dual regimen post-operative surgical antibiotic prophylaxis in caesarean deliveries. Antigua and Barbuda. 2018-2024

Overall, 91% (n=211) of post-operative prescriptions for consultant 1 were single regimen as shown in Figure 6.5. In contrast, 53 % (n=259) of patients covered by consultant 2 received a single regimen post-operatively.

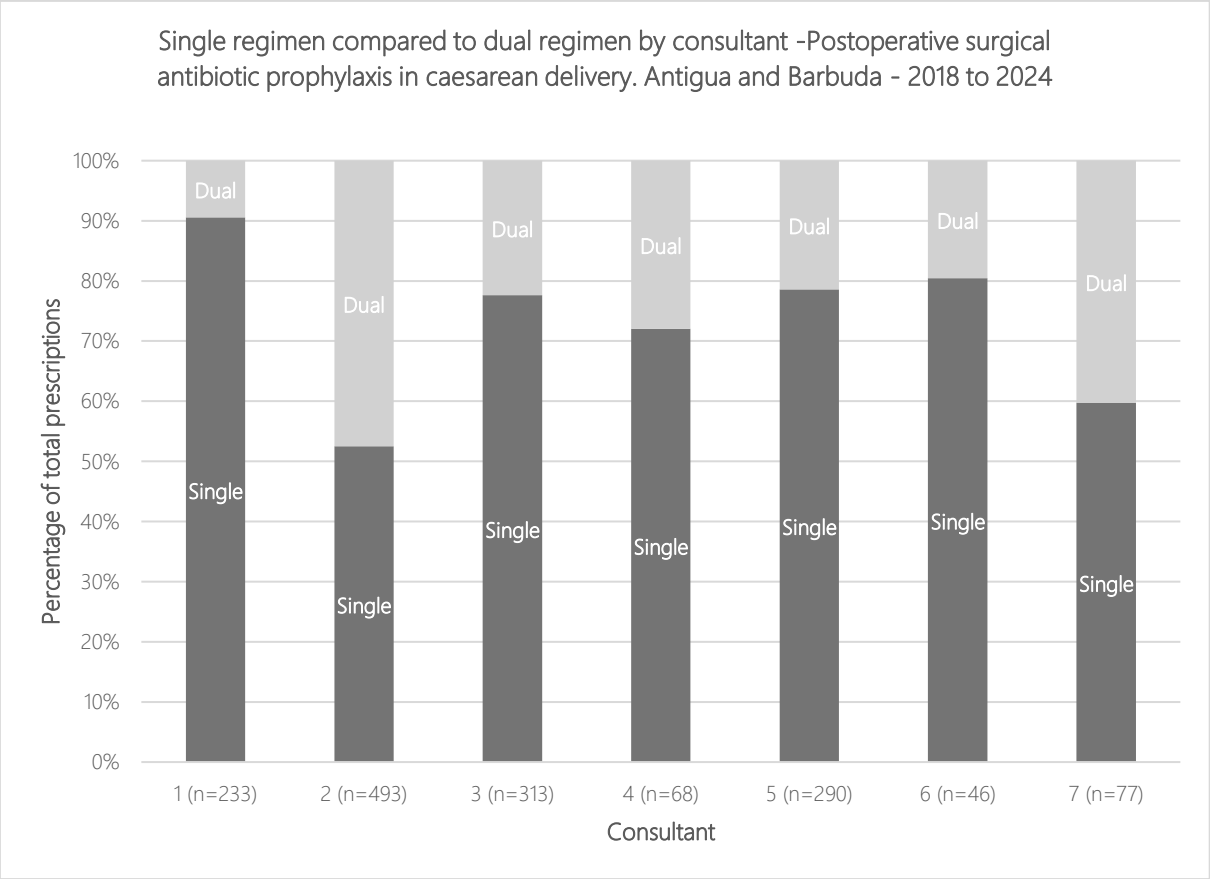


Figure 6.5 Single regimen compared to dual regimen by consultant -Postoperative surgical antibiotic prophylaxis in caesarean delivery. Antigua and Barbuda. 2018 to 2024

Prescription duration for surgical antibiotic prophylaxis

The duration of surgical antibiotic prophylaxis ranged from a single dose preoperatively to 7 days postoperatively, as shown in Figure 6.6. The mean duration for postoperative prescriptions was 4 days, and the most prescribed duration was 7 days.

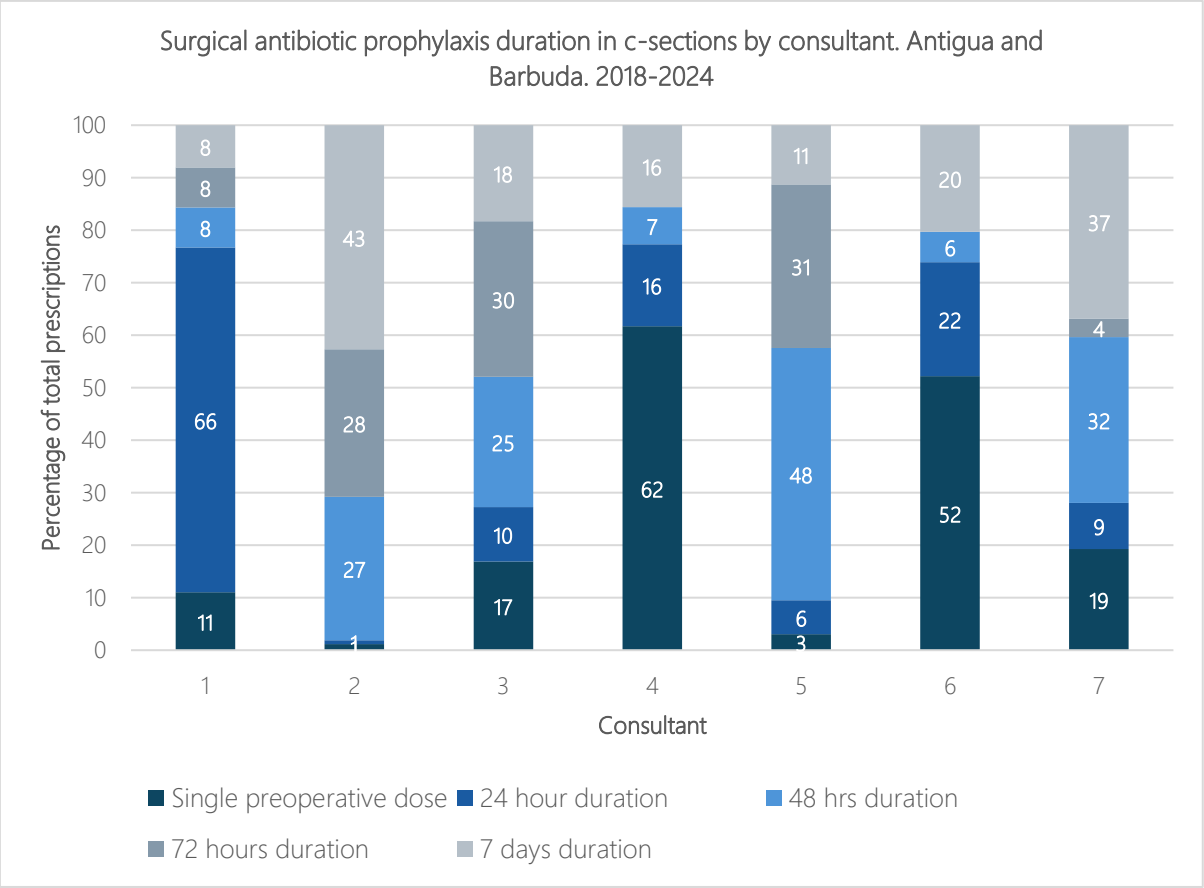


Figure 6.2 Duration of surgical antibiotic prophylaxis by consultant. Antigua and Barbuda. 2018-2024

Over 70% of prescriptions for consultants' 1, 4 and 6 had durations of less than 24 hours, whereas for consultants 3 and 7, fewer than 30% were ≤24 hrs. For consultants 2 and 5, fewer than 10 % of prescriptions were ≤24 hrs.

6.5.3 Factors associated with surgical antibiotic prophylaxis use

Type of regimen prescribed for preoperative surgical antibiotic prophylaxis

In univariable logistic regression, patient factors were not associated with the use of surgical antibiotic prophylaxis. The use of a single regimen was not associated with maternal age (p = 0.54) nor urgency of C-section (p = 0.92). However, there was strong evidence that single

regimen preoperative prescribing was significantly associated with both consultant and year, as shown in Table 6.2.

Table 6.2: Adjusted and unadjusted odds ratios for single regimen prescribing across consultants and years

ID	Single regimen prescriptions N (%)	Dual regimen prescriptions N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value
Consultant ID					
1	225 (98)	5 (2)	7.13 (5.53-17.6)	20.44 (8.66-57.0)	<0.001
2	98 (38)	161 (62)	0.1(0.07-0.13)	0.04 (0.03-0.06)	<0.001
3	233 (80)	57 (20)	0.65 (0.46-0,91)	0.91 (0.59-1.42)	0.68
4	127(95)	6 (5)	3.35 (1.72-7.70)	1.82 (0.90-4.26)	0.13
5	194(84)	36 (16)	0.85 (0.58-1.26)	1.38 (0.78-2.52)	0.28
6	68(93)	5 (7)	2.16 (1.04-5.4)	1.64 (0.75-4.25)	0.26
Year					
2018	43(28)	112 (72)	0.09 (0.06-0.13)	0.02 (0.01-0.04)	<0.001
2019	152(89)	18 (11)	2.0 (1.31-3.21)	3.08 (1.81-5.40)	<0.001
2020	150(95)	8 (5)	4.4 (2.51-8.9)	7.3 (3.76-15.56)	<0.001
2021	184(88)	26 (12)	1.68 (1.15 -2.5)	2.3 (1.42-3.78)	<0.001
2022	144(84)	28 (16)	1.22 (0.84-1.81)	1.21 (0.73-2.0)	0.46
2023	151(78)	42 (22)	0.85 (0.61-1.20)	0.97 (0.63-1.52)	0.90

*OR Odds ratio

In a multivariable logistic regression model using contrast sums, consultants differed significantly in prescribing behaviour when compared to the average consultant. The odds of Consultant 2 prescribing a single regimen as preoperative surgical antibiotic prophylaxis were very low (OR: 0.04, 95% CI: 0.03 to 0.06, p-value <0.001). In contrast, consultant 1 was 20.44 (95% CI: 8.66 to 57.0, p-value <0.001) times more likely to prescribe a single regimen than the average consultant. As illustrated in Table 6.2, no statistically significant differences were observed for consultants 3 to 6 after adjustment for year. Moreover, there were significant variations in prescribing patterns across observed years in the multivariable model. The odds of prescribing a single-regimen prescription were significantly lower in

2018 (OR: 0.02, 95% CI: 0.01 to 0.04, p-value <0.001). However, a marked increase in odds (OR: 7.27, 95% CI: 3.76 to 15.56, p < 0.001) was observed in 2020. Overall, the type III deviance analysis indicated that consultant and year were independently associated with single-regimen preoperative prescriptions for surgical antibiotic prophylaxis, even after model adjustment (p-value < 0.001).

Duration of prescriptions for surgical antibiotic prophylaxis

Univariable regression showed no significant association between maternal age (p=0.97) or urgency of c-section (p=0.20) and the duration of surgical antibiotic prophylaxis. However, significant associations were observed between independent variables, consultant and year, and prescription duration. The odds of prescribing for durations ≤24 hours were significantly lower for consultants 2 (OR: 0.04,95% CI: 0.01 to 0.07, p <0.001), 3 (OR:0.73,95% CI:0.55 to 0.98, p=0.03) and 5 (OR:0.22,95% CI:0.14 to 0.32, p<0.001) when compared to the average consultant. When the association between year and the duration of surgical antibiotic prophylaxis were examined, the odds of receiving a prescription with a duration ≤24 hours were significantly lower in 2018 (OR:0.40, 95% CI: 0.27 to 0.59, p<0.001) and 2019 (OR:0.46, 95% CI: 0.32 to 0.64, p<0.001) when compared to the average year.

Significant associations between consultants and prescription duration were observed in the multivariable model. Consultants 1, (0R:11.4, 95% CI 7.82 to 16.99, p<0.001), 4 (0R:5.89, 95% CI 3.83 to 9.28, p<0.001), and 6 (0R:3.17, 95% CI 1.84 to 5.64, p<0.001) had significantly higher odds of prescribing surgical antibiotic prophylaxis for less than 24 hours when

compared to the average consultant. The model showed that the year was also a significant predictor of prescription duration, as seen in Table 6.3.

Table 6.3 Adjusted and unadjusted odds ratios for surgical antibiotic prophylaxis duration across consultants and years

ID	Prescriptions ≤ 24 hrs N (%)	Prescriptions > 24hrs N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-value
Consultant ID					
1	181 (77)	55 (23)	6.35 (4.63-8.84)	11.4 (7.82-16.99)	<0.001
2	5 (2)	266 (98)	0.04 (0.01-0.07)	0.03 (0.01-0.06)	<0.001
3	81 (27)	214 (73)	0.73 (0.55-1.0)	0.92 (0.66-1.27)	0.59
4	96 (77)	28 (23)	6.61 (4.46-10.08)	5.89 (3.83-9.28)	<0.001
5	24 (10)	214 (90)	0.22 (0.14-0.32)	0.34 (0.21-0.53)	<0.001
6	54 (75)	18 (25)	5.79 (3.6-9.67)	3.17 (1.84-5.64)	<0.001
Year					
2018	25 (17)	126 (83)	0.40 (0.27-0.59)	0.42 (0.25-0.67)	<0.001
2019	32 (18)	143 (82)	0.46 (0.32-0.64)	0.39 (0.25-0.62)	<0.001
2020	36 (22)	125 (78)	0.59 (0.41-0.82)	0.43 (0.27-0.67)	<0.001
2021	78 (33)	161 (67)	0.98 (0.76-1.28)	0.95 (0.66-1.37)	0.8
2022	88 (51)	85 (49)	2.11 (1.60-2.80)	2.25 (1.52-3.34)	<0.001
2023	111 (61)	71 (39)	3.18 (2.41-4.24)	5.59 (3.7-8.57)	<0.001

However, consultant effects explained the greatest proportion of the observed variation (Likelihood Ratio Test-LRT 563.0), compared with year (LRT 106.5).

6.6 Discussion

6.6.1 Summary of findings

This retrospective analysis of medical records for women undergoing C-sections showed that 99% of these patients were prescribed preoperative surgical antibiotic prophylaxis. Similar results were obtained in a cross-sectional study conducted in Zambia. [230] High rates of preoperative surgical antibiotic prophylaxis are critical, as timely administration is essential for preventing postoperative infectious complications. Seventy-eight per cent of preoperative prescriptions consisted of a single regimen of cephalosporin, while the remaining 22% included adjunctive metronidazole. Cefuroxime was the most prescribed antibiotic, a finding dissimilar to other studies, which reported the use of third-generation cephalosporins in India [231] and combinations of aminoglycosides, penicillins and ceftriaxone in Zambia.[230] Variations in antibiotic selection may reflect contextual influences, such as bacterial resistance patterns, antibiotic availability, and guidelines for surgical antibiotic prophylaxis.

Surgical antibiotic prophylaxis was administered to 81% of patients after C-section, and 42% of this group received adjunctive metronidazole. The effects of postoperative prophylaxis have been studied in other settings; obese patients were the target population,[232, 233] or the timing of administration differed from this study.[234] The prescribing of single regimens preoperatively, sharply increased from 2019 to 2020 but decreased from 2021 to 2024. A similar trend was seen regarding postoperative prescriptions.

Univariable regression analysis showed no significant association between maternal age or urgency of C-section and prescribing patterns ($p > 0.05$). However, significant associations were observed for consultants and year of practice. A multivariable regression model with year and consultant mutually adjusted showed that both variables were significant predictors of the type of regimen prescribed and the duration of prescriptions for surgical antibiotic prophylaxis. Pronounced odds ratios across years indicated a significant shift in prescribing patterns over time. Observed variations in consultant prescribing patterns indicate heterogeneity in decision-making regarding surgical antibiotic prophylaxis use in women undergoing C-sections.

6.6.2 Strengths and limitations

Through an in-depth review of patient records for women undergoing C-sections, this retrospective analysis provided a comprehensive evaluation of antibiotic prescribing and use for the prevention of postoperative infectious complications over a 7-year period. This study utilised regression analysis to objectively examine the association between selected variables and the prescribing of surgical antibiotic prophylaxis. There were some limitations to this study, specifically related to the retrospective nature of the data. The timing of preoperative antibiotic administration could not be verified for some patients because documentation was incomplete and files were up to 7 years old. This prevented a thorough assessment of the timing of preoperative antibiotic administration. Third-generation cephalosporins were infrequently used for preoperative prophylaxis, but when indicated postoperatively, they were excluded from analyses because it was difficult to verify whether they were used therapeutically. Data on comorbidities, specifically diabetes, were extracted

from patient records. However, the author was unable to include this as a variable in the multivariable regression analysis due to poor documentation practices. Additionally, prescribing information was not available for all consultants for all reviewed years because they were employed at different points over the study period.

6.6.3 Implications for research

Findings suggest that individual and temporal factors influence decisions regarding the prescribing of surgical antibiotic prophylaxis. Overall, there is significant variation in the prescribing of surgical antibiotic prophylaxis at the consultant level, which patient characteristics, including maternal age and the urgency for C-section cannot explain. Further qualitative exploration is warranted to determine factors influencing how prescribing is conducted for women undergoing C-sections in this setting.

6.7 Chapter summary

- Ninety-nine per cent of women undergoing caesarean delivery received antibiotics preoperatively.
- The second-generation cephalosporin, cefuroxime, is the most prescribed antibiotic to prevent post-operative infectious complications following C-sections.
- Adjunctive metronidazole was prescribed preoperatively for 22% of patients, and this addition was most pronounced in 2018.
- Post-operative prophylaxis was given to 81% of patients, with 42% of them receiving adjunctive metronidazole.
- Single regimen prophylaxis increased from 2019 to 2020 and showed a downward trend from 2021 to 2024 for both preoperative and postoperative prescriptions.
- Maternal age was not significantly associated with regimen type or with the duration of prescriptions in univariable regression analysis.
- Univariable logistic regression showed no association between the urgency of c-section and regimen type or prescription duration.
- Multivariable logistic regression with mutual adjustments for year showed a significant consultant effect for single regimen prescribing, and prescription durations of less than 24 hours.
- Future investigations should focus on understanding the influences on decision-making around surgical antibiotic prophylaxis for women undergoing caesarean deliveries.

CHAPTER SEVEN

7.0 Decision-making around the use of surgical antibiotic prophylaxis for women undergoing caesarean sections at a tertiary care hospital in Antigua and Barbuda.

7.1 Publication statement

Under review in the journal, BMC Pregnancy and Childbirth.

7.2 Chapter introduction

Surgical antibiotic prophylaxis is crucial for preventing post-operative infections following Caesarean sections (C-sections). In Chapter 6, the retrospective analysis of surgical antibiotic prophylaxis showed that 99% of C-section patients received it before the skin incision. This is consistent with practice recommendations from obstetrics/gynaecology guidelines worldwide.[81, 224] Significant variation in preoperative regimen type and the duration of surgical antibiotic prophylaxis was demonstrated in the regression analysis conducted by the author in Chapter 6. Most of this observed variation was explained by the attending consultant. These variations are unwarranted because they cannot be explained by patient characteristics, including the severity of the patient's condition, a phenomenon described by Wennberg.[83]

7.2.1 The Behaviour Change Wheel- Capability-Opportunity-Motivation Behaviour (COM-B) Model

For antimicrobial stewardship interventions to be successful, they should be systematic and theory-based.[235] Using a behavioural approach can improve interventions targeting antibiotic use.[194] This guidance is consistent with the Medical Research Council's

recommendations for developing complex interventions.[6] Numerous theories of behaviour change exist, but the behaviour change wheel (BCW), a synthesis of 19 behavioural change frameworks, is well-designed to theoretically analyse behaviours related to antibiotic use by health professionals.[236] Behavioural analysis is a necessary step that should precede the design of interventions. The Capability-Opportunity-Motivation Behaviour (COM-B) Model, with its premise that behaviour occurs only when there is an interaction among capability (knowledge and skills), opportunity (physical and social), and motivation (automatic, reflective), is an approach used to understand behaviour around prescribing antibiotics.[235] This model of behaviour is central to the BCW and has been successfully applied in studies examining behavioural influences on antibiotic prescribing.[237, 238] For evidence-based clinical practice to exist, health professionals must change their behaviour. [236]

7.3 Chapter Aims and Objectives

This chapter identified drivers of decision-making on the prescribing of surgical antibiotic prophylaxis for women undergoing C-sections at a tertiary care hospital in Antigua and Barbuda. The specific objectives were to explore factors which influenced decision-making on the use of surgical antibiotic prophylaxis in women undergoing C-sections; and to apply the COM-B Model to understand the behavioural influences on decision-making around the use of surgical antibiotic prophylaxis in women undergoing C-sections.

7.4 Methods

This study's protocol was registered at the Open Science Framework.[239] As shown in Appendix 7.1, ethical approval was obtained from the Oxford Tropical Research Ethics Committee (OxTREC) (Reference: 513-24) and the Institutional Review Board of the study

hospital (Reference: January2024: UO) before data collection commenced. The Standards for Reporting Qualitative Research guidelines were used to guide the reporting of this study.[240]

7.4.1 Approach

In this study, the author uses a qualitative, vignette-based methodology to explore physicians' decision-making process regarding surgical antibiotic prophylaxis in C-sections. According to Finch, vignette-based methodology entails presenting respondents who are knowledgeable about a particular topic with a hypothetical scenario and inviting them to discuss how they would respond.[241] Vignette-based methodology was used in this study since it creates a buffer that minimises discomfort when discussing sensitive issues".[242, 243] Although the use of surgical antibiotic prophylaxis is not known to be a sensitive topic, there may be a blame culture in the study context, and the author felt compelled to adopt this approach to address the research question. Vignettes were delivered face-to-face or on Microsoft Teams to individual respondents.

7.4.2 Researcher characteristics and reflexivity

The author, a public health, antimicrobial stewardship and infection prevention and control practitioner within the study setting, had limited knowledge of how clinicians made prescribing decisions for patients. However, insights into the institution's hierarchical structure and the dynamics between senior and junior staff members informed the study's design. Prior to vignette development, the author documented assumptions in a reflexive diary. These assumptions were revisited throughout the vignette's development to examine

how the author's commitment to antimicrobial stewardship may have influenced the selection of issues incorporated into the vignette. Efforts were made to ensure that the scenario was clinically relevant while avoiding language or framing that might lead participants to respond in a particular way. Draft vignettes were reviewed by a senior qualitative researcher, VW, to challenge the author's assumptions. During the interviews, the author was mindful that her professional status, understanding of institutional dynamics, knowledge of antibiotic misuse, and her commitment to evidence-based clinical decision-making could influence her interactions with participants, her expectations of responses, and the interpretation of data. Therefore, respondents were informed through the participant information sheets that all identifiable information would be removed from study records and that their identities would be kept confidential. During interviews, the author adopted an open and non-judgemental stance to encourage respondents to speak openly, provide rich and detailed responses, and explore participants' perspectives rather than seeking confirmation of pre-existing assumptions. Follow-up questioning and prompts were carefully phrased to maintain neutrality. Following each interview, reflective notes were recorded to document initial reactions, assumptions and other potential biases. When analysing interview data, the author ensured that themes were grounded in participants' accounts rather than preconceived beliefs about evidence-based decision-making and antimicrobial stewardship. The author reviewed original transcripts and repeated the data coding and analysis three times over a 12-month period. Assumptions recorded in a reflexive diary during the interviews were regularly examined against the coded data to minimise the risk of confirming pre-existing assumptions and to ensure that interpretations were data-

driven. Some interviews elicited strong emotional accounts of challenging clinical experiences, and repeated analysis over time also helped the author to distinguish participants' emotions from her own response to respondents' expressed emotions. This was important for enhancing the credibility and trustworthiness of the interpretations during data analysis. To enhance self-reflection throughout the data analysis process, regular discussions were held with an independent, senior qualitative researcher, VW, who reviewed and challenged the conduct of data coding and interpretation. A reflective journal was kept during vignette development, data collection and analysis to record personal introspections and methods used to gather responses.

7.4.3 Context and eligibility criteria

This study was conducted with physicians and nurses assigned to the obstetrics/gynaecology unit of a mid-sized tertiary care hospital in a Caribbean Community (CARICOM) State. It was essential to include this group of healthcare professionals, as they had the knowledge and direct experience with surgical antibiotic prophylaxis in C-sections. At the time of the interview, the maternity unit had six full-time obstetrics/gynaecology consultants and six house officers (general physicians).

Healthcare workers were selected based on their current or recent assignment in the Obstetrics/ Gynaecology Unit and were all involved in prescribing or administering prophylactic antibiotics to C-section patients. Respondents included junior and senior nurses and nursing students, obstetrics/gynaecology consultants, house officers and physician interns. Diversity in qualifications, roles, and experience was important to this study as it

broadened the range of perspectives on surgical antibiotic prophylaxis in C-sections. General physicians, nurses and consultants not assigned to the Obstetrics/Gynaecology Department were excluded.

7.4.4 Sampling strategy

Purposive sampling was used for this qualitative investigation, as rich, diverse and targeted insights of healthcare professionals in the obstetrics/gynaecology unit were needed to answer the research question. The number of respondents was determined by the concept of information power, which considered the study's aim, sample specificity, theoretical background, quality of dialogue, and analysis strategy.[244] Given the narrow research aim, the repetition of the case vignette during individual interviews, a sample of respondents knowledgeable on and routinely involved with prophylaxis use, and the rich data provided by the respondents, a final sample size of sixteen was considered sufficient. As the interviews proceeded, the author and supervisors monitored the adequacy of the sample size. By interview 10, key themes were consistently reiterated, and the presentation of additional information in subsequent interviews did not add another layer to the ideas already presented on decision-making. At this point, the author determined that the respondents' information was sufficient to answer the research question. The importance of having sufficient rich information to adequately address research questions in qualitative inquiries has been discussed in the literature.[245]

Eligible participants were identified by contacting the heads of the Obstetrics/Gynaecology and the Human Resources Department. Email addresses were collected, and email

invitations, which included the informed consent form and a participant information sheet detailing the study and the author's contact information, were sent to these eligible individuals. Hard copies of the participant information sheet and informed consent forms were distributed by the author in the main reception area of the obstetrics/gynaecology unit, following a lack of response to initial email invitations. The researcher followed up with interested persons via email to address questions about the study. For persons expressing interest in participating, a suitable time for the interview and a delivery method were arranged.

7.4.4 Development and piloting of vignettes

Vignettes can be used in qualitative research to present fictional situations in which respondents are asked to describe the actions they would take under those circumstances.[242] Research vignettes, shown in Appendix 7.2, were initially developed by the author and were based on knowledge of local clinical practice regarding surgical antibiotic prophylaxis in C-sections. The first vignette focused on decisions regarding pre-operative surgical antibiotic prophylaxis, while the second explored decisions about stopping or extending surgical antibiotic prophylaxis post-delivery. Vignettes were reviewed by the author's doctoral supervisors, an obstetrics/gynaecology consultant, and a maternity department nurse manager, who provided feedback on the relevance, clarity and applicability of the scenarios to the local setting. Vignettes were piloted by interviewing three non-participating hospital-employed doctors and nurses and were delivered via individual interviews on Microsoft Teams

7.4.5 Data collection

Semi-structured individual interviews with open-ended questions were used for an in-depth exploration of decision-making regarding surgical antibiotic prophylaxis in C-sections. As presented in Appendix 7.3, the topic guide was based on the constructs of the COM-B model: capability, opportunity and motivation. Based on the author's knowledge of the setting, individual interviews were deemed most appropriate, as respondents may be concerned that their responses could be repeated by other respondents in non-research settings. This could negatively affect workplace relationships, especially between department heads and front-line staff. Informed consent was obtained verbally and in writing for all interviews. Respondents were interviewed once by the author, who was previously trained in qualitative interviewing methods. Most interviews (n=12) were conducted face-to-face in a quiet hospital setting and lasted 10 to 30 minutes. The remaining interviews (n=4) were conducted via Microsoft Teams and ranged from 15 to 27 minutes. The first clinical vignette was presented to all respondents in the interviews. However, some respondents addressed the second vignette before the author presented it. Probes were used to elicit additional information pertinent to constructs of the COM-B Model. As suggested by Braun and Clarke,[246] the first few interviews were examined for sufficient detail in the provided responses. When new ideas were expressed, the probes used to gather additional information were slightly modified. Demographic information on sex, age, professional category, prescribing authority and years of experience was collected from respondents. Data collection was discontinued when interviews yielded no new insight into the emerging concepts or their relationships to the COM-B Model. The topic guide was

adjusted based on respondents' job categories, but key concepts remained the same. All online interviews were recorded on the University's secure server using Microsoft Teams, while face-to-face interviews were recorded using an offline recorder.

7.4.6 Data processing and management

Audio recordings and transcripts were de-identified by omitting all participant names and specific details about their job titles, given the study's small setting and the risk of easy identification. Pseudonyms devised by the researcher were assigned to each recorded file. Each recording was assigned a unique code consisting of the respondent's professional category and a number. This code was used to name the stored files and to refer to respondents in transcripts. To protect the confidentiality of the respondents, the recordings were not shared with any members of the research team, as their voices might be recognisable. Audio recordings of face-to-face interviews were stored on the University of Oxford's Nexus365 OneDrive for Business until transcription was completed. Transcription was completed immediately after each interview to reduce the time the recordings were stored. Recordings were transcribed using the "Transcribe feature in Word for web" application. The author verified the transcriptions for accuracy by reviewing the recordings and updating all segments that the software program had incorrectly transcribed. The transcripts were de-identified by removing all respondents' identifying details and retaining the pseudonyms assigned to their corresponding original recordings. Transcripts were stored on the University's OneDrive for Business and subsequently entered into QSR NVivo Version 12 software for data analysis. Signed paper-based informed consent forms were

placed in a folder in a locked security cabinet in the researcher's office and will be stored for up to 3 years after thesis submission in accordance with university policy.

7.4.7 Data analysis

Data analysis began during the interview process but was conducted in greater depth after each interview. This early analysis was valuable for informing subsequent data collection by allowing the author to identify emerging areas of interest that were explored in later interviews. There were two phases of data analysis. First, an inductive analytical approach guided by Braun and Clark's six phases of thematic analysis [247] explored respondents' perspectives on surgical antibiotic prophylaxis in C-sections. Thematic analysis was selected because it offers a rigorous yet flexible approach for identifying and interpreting patterns within qualitative data, [246] enabling the exploration of factors influencing decision-making regarding surgical antibiotic prophylaxis in C-sections. Inductive codes were content-driven and based on respondents' views. As recommended by Green and Thorogood, transcripts were read multiple times to better understand the data.[248] Using an inductive approach, the author derived initial codes from the interview data, and as described by Auerbach, the interview transcripts were systematically searched for all data relevant to the study's objectives.[249] Segments of text conveying conceptually similar meanings across transcripts were filtered, compared and grouped.[249, 250] These groupings were used to develop themes based on the essence of respondents' accounts and were reviewed against coded extracts and the complete dataset to ensure their representativeness. Themes were constructed in alignment with the study's aim to ensure analytical relevance and coherence. Data adequacy was evaluated throughout the data collection and analysis process by repeatedly reviewing

interview transcripts and monitoring the development and continuous refinement of themes. This reflexive and iterative approach, as recommended in qualitative methodology, ensured the dataset was sufficiently rich, capturing nuances of respondents' experiences related to the research topic.[244, 251] Adequacy was considered achieved when themes were sufficiently supported by multiple examples across the data, there was a strong understanding of the relationship between themes and the study objectives and rich explanatory insights into participants' decision-making processes when prescribing prophylaxis for C-section patients were provided. This aligned with the principles of Sims and Cilliers, in which conceptual depth, information power and theoretical insufficiency should be considered collectively to assess data adequacy. [252] Coding and thematic analysis were completed by the author and cross-checked by an experienced qualitative researcher, VW, to enhance accuracy and consistency. Subsequently, inductively developed codes were deductively mapped to the components of the COM-B Model to explore the data through a theoretical lens. A codebook, presented in Appendix 7.4, was developed to provide clear definitions of the codes and ensure a systematic approach to coding. To understand current prescribing behaviour in context, the COM-B model guided the behavioural analysis of the interview data. Inductively identified codes relevant to factors influencing decision-making on surgical antibiotic prophylaxis were deductively mapped to the capability (psychological and physical), opportunity (social and physical), and motivation (reflective and automatic) constructs of the COM-B Model. This was performed to support theory-driven interpretation and identification of behaviour change targets. The language used by health professionals was used to represent themes.[253]

7.5 Findings

7.5.1 Study context

This qualitative study focused on factors influencing decision-making around surgical antibiotic prophylaxis for C-section patients. It was based on interviews with physicians and nurses in a public tertiary care institution in a Caribbean country. At the time of this study, six consultants and six house officers were permanently assigned to the Maternity Unit, and four interns had recently completed clinical rotations in the department. All physicians can prescribe surgical antibiotic prophylaxis. Although house officers and interns are permitted to prescribe, they are supervised by consultants, who hold the final authority to initiate and discontinue antibiotic regimens. House officers also supervise interns who assist them with routine functions, including developing antibiotic treatment plans for patients. Nurses do not have the jurisdiction to prescribe antibiotics in this setting. Still, they play a key role in administering prophylactic antibiotics, providing feedback on unintended patient consequences, and informing physicians of the unavailability of prescribed antibiotics. Anaesthesists sometimes administer prophylactic antibiotics depending on the clinical situation of C-section patients.

7.5.2 Respondent characteristics

Sixteen respondents assigned to the Maternity Unit and responsible for prescribing or administering antibiotics were interviewed. This included four physician interns (I), four consultants (C), four house officers (P), one senior nurse (N1) and three junior nurses (NS)

(recently graduated nursing students). Respondents' demographic details have been aggregated in Table 7.1, to minimise the risk of participant identification.

Table 7.1 Respondent characteristics

Code	Professional category	Number	Gender	Professional experience (range)	Experience in the maternity unit (range)
C	Consultant	4	Male and female	6 to >50 years	2 to 32 years
P	House Officer	4	Male and female	3 to 5 years	2 to 4 years
I	Interns	4	Male and female	9 to 10 months	3 months
NS	Junior Nurse	3	Female	4 months	2 months
N	Senior Nurse	1	Female	10 years	5 years

Thirty-one per cent (n=5) of respondents were male, and 69% (n=11) were female. Sixty-nine per cent (n=11) of the respondents were aged 20 to 35, 19% (n=3) were from 36 to 50, and the remaining 12% (n=2) were older than 50. Respondents' years of experience within the local maternity unit ranged from 2 months to 32 years. Some consultants have worked outside the current setting for several years, including in hospitals in other Caribbean countries and outside the region. Thirty-three per cent (n=4) of the physicians received specialised training in obstetrics and gynaecology, some at regional institutions and others outside the CARICOM States. Most house officers and interns were trained at Cuban institutions. All nurses were locally trained.

7.5.3 Factors influencing decision-making around surgical antibiotic prophylaxis

Decision-making regarding surgical antibiotic prophylaxis is driven by several factors in this setting, including hierarchical dynamics, systemic gaps, and contextual influences.

Hierarchical dynamics shape prescribing behaviours

The decision about the type and duration of surgical antibiotic prophylaxis appears to be largely consultant-driven, thus reflecting a hierarchical influence on the clinical management of c-section patients. Most respondents noted that the decisions on prophylactic antibiotic use depended on the preference of the attending consultant, with one intern noting that, "*Specific guidance is more consultant-based, so whichever guideline a consultant uses is what they use on their patient, and that's how we go forward with it…* "(I3).

Prescribing norms were reinforced via consultant instruction, with junior staff learning individual prescribing patterns through repetition. Decisions on the duration of surgical antibiotic prophylaxis were also consultant-dependent, and pattern recognition was internalised by junior staff,

"… they [some patients] just get the full day course of IV antibiotics … two other consultants who say send their patients home on a week of oral antibiotics." (P2)

In this setting, consultants rotate daily or every two days. This creates confusion for junior physicians and reflects tension about the best approach to antibiotic prophylaxis on any day, as there was no uniform guidance from consultants. Junior staff felt that they had no opportunity to intervene or were hesitant to question the consultants about divergent prescribing decisions,

"*Once the consultant says this is this, if another consultant would come and change the other consultants* [prescription], *you were like, oh ok and just go ahead with it. So, there's not much of a room to say, doc, why don't you use this*?" (I2)

Nurses recognised that consultant preference guides antibiotic prophylaxis

"*…antibiotic administration is dependent on the consultant.*" (N1)

and their familiarity with these patterns allowed them to anticipate antibiotic orders and prepare prophylactic antibiotics for administration before receiving formal prescribing instructions

"*… sometimes, before the doctors start to even give the orders, we know to pull it* [antibiotics] *up*." (NS3)

Some respondents perceived that consultants' experience in their private practices and on the maternity ward may affect how prophylaxis was prescribed. Adaptation to consultant decisions appeared to be the tacit norm in this setting,

"*… They've [consultants] experienced some resistance … that changed their prescribing habits, and when they change their prescribing habits, we will adapt to that*." (I1)

One consultant expressed disappointment at the lack of reaction from junior physicians during practice, while acknowledging and relaying their fear of repercussions if they spoke out. With the current prescribing method, there is no logical rationale behind decision-making and no ownership of decisions made by junior staff.

Systemic gaps undermine evidence-based decision-making

Respondents were aware of the importance of surgical antibiotic prophylaxis in C-sections. However, their psychological capability was limited due to insufficient support tools for informed decision-making.

Absence of a uniform guideline for surgical antibiotic prophylaxis

All respondents shared that there was no standardised guideline for the prescribing of prophylactic antibiotics for women undergoing C-sections, while highlighting poor monitoring systems,

" There's no unified protocol. There's nobody who's going to say, you know, yes, you follow this, or you follow that, there's nobody." (C4)

Junior physicians appeared wary of the instability in prescribing decisions,

"*It shouldn't be, ok well, who's doing the surgery this day, or what are their preferences, …* " (P1)

Some consultants openly expressed their frustrations with the lack of guidelines and current variations in prescribing practices, noting that patients suffer as a result. All consultants were aware of the department's varied prescribing practices. When asked, some explained that their prescribing practices are based on the guidelines of the obstetrics and gynaecology organisations that certified them. Many physicians believe that evidence-based guidelines, such as those published by the American College of Obstetricians and Gynaecologists (ACOG) and the Royal College of Obstetricians and Gynaecologists (RCOG), should guide prophylaxis. They perceived that complying with guidelines was one of their responsibilities, noting that this step could improve the level of care offered in this setting

"I think I'm responsible to follow the guidelines, you know, that are put in place, so we can see Improvement in patients and decrease the rate of wound infections." (P3)

Legacy prescribing appeared to be frustrating and a point of contention for some respondents,

"... from the time they graduate, they are doing the same thing they've been doing from before. So how are we going to get any change? "(C4)

Some respondents believed that precedence had already been established, and they were skeptical about the adoption of evidence-based guidelines in the setting,

"... if you are using the same medication for the last 10 to 15 years, it's very hard for us to get somebody to change their mind." (I1)

There seems to be a pragmatic reliance on clinical experience, background training and external guidance in the absence of local evidence,

"I do think it's important always to consider your experience in your clinical setting. But until that information [infection rate] *is available, to be guided by international standards. I would also say that what influences this, you know, decisions that we make. Our own training backgrounds, right? (C2)*

Inadequate access to local surveillance data

According to respondents, antimicrobial resistance rates are infrequently disseminated. If resistance rates were regularly shared, participants expressed an openness to modify decision-making around surgical antibiotic prophylaxis,

"that's something [resistance rates] *that is broadcast to us, and it is not as frequent as it should be. And I feel like if we are more, we are more aware of the numbers, we can then tailor our care to reflect that*." (P4)

Respondents deemed feedback on surgical site infection rates inadequate. There was a conditional willingness to change practice if evidence is provided,

" … if you're arguing that some people are prescribing for too long, then you have to be able to provide evidence that people who don't prescribe for as long do not have a higher rate of surgical site infection." (C3)

Respondents felt that surveillance data would provide an opportunity for improving the use of prophylactic antibiotics.

Shortcomings in the curriculum and continued professional education

When prompted, physicians discussed the education they received on antibiotic use and microorganism coverage while studying for their medical degrees. Junior physicians revisited knowledge gained in medical school or sought out online guidelines to provide some reassurance for current practice. There is also tacit learning through peer-level processing and collective sense making of consultants' decisions,

" we do discuss reasons as to why certain consultants would choose certain antibiotics … on who might have you know better reasoning, so you gather your own personal opinion." (P1)

One consultant held the view that physicians' knowledge was limited and spoke of a trial-and-error approach to prescribing,

"most of the doctors are like poor with pharmacology and where which bacteria is located. So, it's just based on this doesn't work, then you go to this one". (C4)

Some junior physicians lamented the lack of continuing medical education on antibiotics after graduating from medical school. Both consultants and junior staff agreed that their hands-on experience and training during clinical rotations and residency greatly contributed to their understanding of the use of preoperative antibiotics. Nurses had different experiences in nursing school as their education predominantly focused on the administration of different antibiotics,

"*… we learned quite a few techniques in pharmacology, pretending to administer different antibiotics in the different ways, because there's different antibiotics and there's different ways you can administer them to the patient*" (NS1)

with few details on other aspects of antibiotic use,

" *the only thing that I would say I was educated about, what's basically antibiotic resistance … other than the education about resistance and what prophylactic antibiotics can do, no*." (NS3)

Inter- and intra-departmental tensions influence prescribing decisions

Respondents emphasised the need for coordination between the nursing staff in the maternity ward and the staff in the operating theatre,

" I think the problem is not necessarily prescribing it [antibiotics], it's making sure it's done…there just needs to be better coordination…" (I4)

Although some doctors requested the administration of prophylaxis before the patient is admitted to the operating theatre, it is sometimes done beyond the recommended time frame,

"*... nurses don't give the antibiotics in time. So, a lot of times the patient will be on the operating table, operation starts, and that's when the anaesthesist will give it. Although it's written in the orders ...*" (C1)

As a result of delays, some consultants have extended the duration of prophylaxis post-incision. There were conflicts with the current timing and location of prophylactic antibiotic administration in this setting. Nurses mainly administer surgical antibiotic prophylaxis, and as explained by a junior nurse,

"*Usually we don't give them prophylaxis on the ward. Prophylaxis is given when they get to the operating theatre. But we pull it [antibiotics] up on the ward. So mix and prepare it*." (NS3)

Nurses reported that antibiotics could be administered later than prescribed due to a nursing shortage. The administration of prophylaxis on the operating table was also perceived as best practice for infection prevention, especially for patients using spinal anaesthesia,

"*So in my training ... antibiotics were given when the patient was on the table in the operating theatre by the anaesthesia team, here they are often unwilling to do so. ...*" (C3)

In this instance, redosing is performed if the perceived time between the initial administration and skin incision is prolonged. Respondents appeared dissatisfied with

pharmacy collaboration. Respondents believed that pharmacists did not assist enough with decision-making,

"*...They just get the treatment chart, and it is just like a machine to fill it back up. You know, there is no discussion ...*" (I2)

One nurse noted that patient information is not shared with the pharmacy, which may explain the pharmacy's lack of input.

Contextual influences on prescribing

Several local factors, including inconsistent antibiotic supply, patient pressure, patient circumstances, and environmental factors, influenced prescribing practices.

Inconsistent availability of antibiotics

Respondents appeared reassured by the reliable access to cephalosporins when prophylactic antibiotics are needed. Despite general availability, respondents raised concerns about inconsistent stock of preferred cephalosporins, noting that wait times for out-of-stock antibiotics could last weeks. One physician with working experience in hospitals outside of the region commented on the limited selection of prophylactic antibiotics in the setting, and some consultants shared that their selection is based on which antibiotic is available,

"*It's inconsistent, so your agents change depending on what's available. You may not be able to use the agent that you'd want to use*." (C2)

Similar concerns were echoed by a nurse who described antibiotic choice as being constrained by availability,

"*…sometimes we don't have it* [preferred antibiotic*] in stock, so we would be forced to use what is present*." (NS2)

Patient pressure

Experiences varied when discussing patient pressure and prophylactic antibiotic use. Physicians with shorter-term assignments said client pressure for antibiotics is uncommon. There were instances where physicians spoke of clients' reluctance to use antibiotics because of poor experiences in the past. Physicians explained that some clients refused postoperative antibiotics because they had just given birth and felt that they didn't need them because they were breastfeeding. One physician spoke of pressure from the "*Google patients*" (I2) who didn't want antibiotics because of information they found on the search engine. Conversely, physicians with more experience in the setting did recount episodes of client insistence. However, respondents explained that patients did not influence decision-making, explaining their strategy for defusing patient pressure,

" …I educate them on why I make the choices that I do, and we move on." (C3)

Some physicians were also of the opinion that the treatment plan ultimately lies with the physician, but did acknowledge patient rights,

"*Well, the patients already don't have much of a say in terms of what to treat them with because they come to the doctor because the doctor is the one with the knowledge. They have the autonomy to refuse treatment…"* (I4)

Patient circumstances

The patient's clinical circumstances were also taken into consideration when deciding on the type of antibiotic and the duration of antibiotic prophylaxis. Respondents explained that patients with allergies are usually given alternative antibiotic prophylaxis depending on the type of allergy. Patients with comorbid conditions such as diabetes were cited as a group that may be given an extended duration of prophylactic antibiotics since their healing process is slower. The patient's weight was also identified as a factor which could influence the dosage of the prescribed antibiotic.

Hospital environment and local climatic conditions

Modifications are also made when hygiene issues have been identified as an infection threat. Some respondents shared that the duration of prophylactic antibiotics is extended post-surgery when there are environmental hygiene challenges in the hospital. If there is a noticeable increase in post-operative infections, some physicians clearly stated that they wanted to,

"*err on the side of caution and just give them [patients] the antibiotics to be safe.*" (I1) However, other respondents disagreed with this rationale. The local climate was perceived as a contributor to postoperative infections. One consultant reflected on decision-making regarding the climate,

"*You know, we live in a hot, humid country. … I think that may cause us to sometimes not strictly follow the guidelines in terms of duration of antibiotics and our choice of antibiotics. You know whether you use one agent or two …*" (C2)

7.5.4 Behavioural analysis using the Capability, Opportunity, Motivation Behaviour Model

All constructs of the COM-B Model were identified during the analysis of text relevant to decision-making around surgical antibiotic prophylaxis in C-sections.

Capability

Roles related to prescribing and administering prophylactic antibiotics were clear to all respondents who performed functions associated with surgical antibiotic prophylaxis. Respondents were knowledgeable about prophylactic antibiotic use and its importance in reducing the risk of postoperative maternal infections. However, differences in psychological capability were evident in respondents' knowledge of an appropriate regimen and duration of surgical antibiotic prophylaxis in C-sections.

Opportunity

There is some behavioural modelling within the consultant group and peer-to-peer learning among junior staff. However, several barriers were identified for the COM-B construct, opportunity, as shown in Table 7.2. Notably, deficiencies in physical opportunity, particularly the absence of clinical support tools, such as a standard guideline for surgical antibiotic prophylaxis, were evident.

Table 7.2 Behavioural analysis of decision-making around surgical antibiotic prophylaxis for c-section patients

Constructs of the COM-B Model	Barriers (B) / Enablers (E) to decision-making around surgical antibiotic prophylaxis for c-section patients	Quotes
Psychological capability- the capacity to engage in the necessary thought processes- comprehension, reasoning.	All respondents recognised the importance of the timely administration of surgical antibiotic prophylaxis for infection prevention. **(E)**	C1 "*...if you can give a patient antibiotic prior to surgery, then you're going to have less likelihood of them getting a wound infection...*"
	The presumed regimen and duration of surgical antibiotic prophylaxis to prevent post-operative infections differ among consultants. **(B)**	P3 "*Some give two antibiotics which is cefuroxime or flagyl, while others just give one, which is just a cefuroxime or another cephalosporin, which is a cefazolin*"
	Participants know the procedures involved in the prescribing/administering of surgical antibiotic prophylaxis. **(E)**	
	Participants understand the importance of having surveillance rates to inform prescribing practices **(E)**	
	The importance of following uniform guidelines to standardise patient care is understood. **(E)**	P4 "*We need protocols, written protocols that everybody has to follow. That way we will have a much better outcome.*"
	Physicians demonstrate cognitive flexibility by selecting appropriate alternative antibiotics depending on patient circumstances or if the preferred medication is unavailable. **(E).**	C2 "*If the patient is allergic, then we may have to look at alternatives. If the patient umm has been in labor for a long period of time and we need additional coverage then you know we add metronidazole because we don't have azithromycin available parenterally.*"
	Lack of clinical reasoning by junior staff as they prescribe according to consultant preference **(B)**	
	Consultants prescribe based on preference and individual experience and training. **(B)**	
Physical capability- Physical skill, strength or stamina	Healthcare workers know techniques for preparing and administering surgical antibiotic prophylaxis. **(E)**	
	Healthcare workers know how to conduct a risk assessment before making prescribing decisions. **(E).**	C2: "*you have to always be careful that there's proper risk stratification of patients, so it's important that the context in which those decisions are made, are appropriate and you're not withholding antibiotics in a patient who is actually at increased risk for developing infection perioperatively.*"
Physical Opportunity afforded by the	Evidence-based guidelines are not available in the setting. Consultants follow various guidelines from international obstetrics	P1 "a*t the hospital, our department itself, we don't have a specific guideline that the department follows ... there's specific ones for each consultant*"

Constructs of the COM-B Model	Barriers (B) / Enablers (E) to decision-making around surgical antibiotic prophylaxis for c-section patients	Quotes
environment involving time, resources, locations, physical barriers.	and gynaecology organisations or use their clinical judgement or previous training. **(B)**	
	Continuing professional education sessions/courses on surgical antibiotic prophylaxis are unavailable in the setting and limited online. **(B)**	I1 "*The last time I did anything specifically antibiotics was during medical school. Everything else about how we prescribe is learned on the job.*"
	Inconsistent release of information on surveillance rates, bacterial sensitivity summaries, and audit and feedback reports of antibiotic use to inform prescribing practices. **(B)**	C1"*I think the most we went with something from the infectious control people every once in a while, you know, they might tell us something.*"
	Poor environmental hygiene may sometimes contribute to increased infection rates **(B)**	N1: "*Of late, we had a lot of cases who came back with the wound infections because you know the condition of the theatre at the time. But prior to that, as I said, the antibiotic administration is depending on the consultant.*"
	Inconsistent supply of antibiotics limits access to preferred treatments **(B)**	C4 "I*n this setting it depends on what you can get … one month they may get this[antibiotic], another month they get that [antibiotic].*
	The nursing department is understaffed, leading to delays in drug administration. **(B)**	N1 "They [nurses] are busy, the nursing shortage basically is usually the reason [for untimely administration]
Social opportunity-afforded by the cultural milieu that dictates the way we think about things.	The current approach to practice is not evidence-based as it varies according to the attending consultant. **(B)**	P2:" … *When it's this consultant's patients, you do this, when it's the other person with the other consultants' patient, you do a different thing.* "
	Social learning dynamic is observed among some senior staff. **(E)**	C2: "*I was able to now work in a setting where other colleagues who train in other places were comfortable and had a standard practice of sticking strictly to those guidelines, after a while I was able to change my practice …*"
	Institutional culture (hierarchy) reinforces habitual prescribing. **(B)**	
	Junior staff discuss consultants' decisions to understand the decision-making process. **(E)**	P1: "*…we do discuss reasons as to why certain consultants would choose certain antibiotics…on who might have you know better reasoning so you gather your own personal opinion.*"
	Hierarchical norms do not encourage junior staff to participate in decision-making. (B)	P2 "*The consultants. No, you just come and they* [consultants] *just tell you what is done and what is not done.*"
	Pharmacists do not provide adequate support for decision-making. **(B)**	
Reflective motivation-reflective	Staff believed that other healthcare workers are set in their habits and will not want to change prescribing behaviour. **(B)**	

Constructs of the COM-B Model	Barriers (B) / Enablers (E) to decision-making around surgical antibiotic prophylaxis for c-section patients	Quotes
processes involving plans and evaluations (beliefs about what is good and bad).	Junior physicians indicated they are not responsible for making prophylactic prescribing decisions. **(B)**	
	Intent to use evidence-based guidelines to guide prescribing **(E)**	
	Intending to change practice if local evidence is provided **(E)**	C2 "*if the persons that use no antibiotics or one agent, or a particular agent are seeing more surgical site infections then the rest of us will be guided to know that approach may not be the best approach in preventing surgical site infections…*"
	Junior physicians want to learn by questioning decisions, but exercise caution when approaching consultants. **(B)**	I2 "*If you're going to question, you can't just go direct and say doc have you tried this? You have to be very careful because remember they have years of experience you would have to be careful how you gonna have the discussion. Yeah, be careful*."
	Participants felt it was their responsibility to follow standardised guidelines. **(E)**	
	Respondents are processing the alignment of research with practice **(E)**	C1, "*research has shown that if you can give a patient antibiotic prior to surgery, then you're going to have less likelihood of them getting a wound infection, since you are making an incision.*"
Automatic motivation involves emotions and impulses that arise from associative learning and/or innate dispositions.	Focus is on remembering the memorised prescribing patterns of consultants. **(B)**	I3, "*We kind of just memorise what to give each patient …*"
	There is habitual adaptation to authority. **(B)**	I1,"*They've experienced some resistance, so they believe there may be some resistance for this specific type of antibiotic. And therefore, that changed their prescribing habits, and when then they change their prescribing habits, we will adapt to that*"
	In the absence of local guidelines, consultants defer to their individual experiences, certifications/training during decision-making (B)	

Motivation

Respondents reflected on tailoring practice if evidence was provided. Still, junior physicians lack an explicit understanding of the evidence or knowledge behind the decision-making process, and the drive to reflect on or question consultant decisions is low.

7.6 Discussion

7.6.1 Summary of main findings

Respondents' narratives highlighted hierarchical, contextual, and systemic factors that influence decision-making regarding surgical antibiotic prophylaxis in C-sections. Respondents described a clinical culture in which consultants' individual preferences largely shaped the prescribing of surgical antibiotic prophylaxis, reflecting hierarchical decision-making. This key idea was presented in all interviews, and is similar to a finding in a qualitative study on prescribing etiquette conducted by Charani and colleagues.[254] Additionally, this finding of preference-based prescribing aligns with the results of the mixed-methods systematic review on antibiotic prescribing in Caribbean Community States presented in Chapter 3.[5] These findings raise concerns for evidence-based practice in the study setting. Further, junior staff adapt based on what is modelled by consultants and other senior physicians. The institutions' hierarchical structure reinforces this adaptation in the absence of evidence-based guidelines, further undermining evidence-based practice. Medical hierarchy has been identified in the qualitative literature as a barrier to evidence-based decision-making.[255] In this study, respondents are trying to achieve a balance between what they perceive as best practice and the norms of the context. The availability

of clinical support resources and other contextual factors, such as environmental hygiene, also shape prescribing decisions. These factors have also been identified in a qualitative study examining the drivers of postoperative antibiotic prophylaxis in an Ethiopian context.[256] There is an intention to modify prescribing if evidence on rates is provided to physicians. However, clinical inertia may persist if clinicians are not provided with evidence to inform practice. Respondents also discussed coordination challenges marked by conflicting priorities and miscommunication. These conflicts highlight the importance of implementing and reinforcing standardised, evidence-based guidelines within the hospital and of fostering discourse among healthcare professionals.

Behavioural analysis shows both enablers and barriers to decision-making around surgical antibiotic prophylaxis for c-section patients. Clinicians generally have the knowledge and skills to make decisions about surgical antibiotic prophylaxis. However, limited access to physical resources and inadequate social support systems were identified as significant barriers to decision-making, consistent with conclusions from a metasynthesis of reviews.[238] Evidence-based decision-making cannot be facilitated if physical resources and social support structures are inadequate.

7.6.2 Strengths and limitations

To date, this is the only qualitative investigation to explore how decisions about antibiotic use are made in this setting. This investigation captured in-depth information on the decision-making processes around surgical antibiotic prophylaxis in C-sections. The COM-B Model provided a nuanced understanding of the physical and social influences on

decision-making and physicians' motivations for current prescribing practices. Although the findings are specific to the Obstetrics/Gynaecology Department, the author, who has firsthand knowledge of the setting, believes that the information from this study could be used to improve decision-making around antibiotic prescribing in other units of this institution. Some limitations were encountered in this study. Only one senior nurse agreed to be interviewed. Three of the four nurse respondents were recently graduated, student nurses. However, the responses from the senior nurse were no different from those of the junior nurses.

7.6.3 Implications for research

Several influences on prescribing have been identified in the setting. A behavioural analysis revealed underlying influences on prescribing behaviour, which were assessed as barriers to and enablers of decision-making around surgical antibiotic prophylaxis use. Further application of the Behaviour Change Wheel is necessary to narrow the target behaviour and improve the precision of intervention development. This way, a behavioural analysis of the target behaviour(s) can be done to identify barriers to behaviour change. Appropriate intervention functions can then be assigned to improve the selected target behaviour.

7.7 Chapter Summary

- Hierarchical norms centralise prescribing, limiting input and clinical reasoning from junior staff and reinforcing consultant-led prescribing variations.
- Behaviours are reinforced by seeing them done by peers, and this process is socially validated in the setting.
- Situational factors such as inconsistent antibiotic availability and poor environmental hygiene influence prescribing decisions.
- Poor intra- and inter-departmental communication and collaboration influence decision-making around surgical antibiotic prophylaxis.
- Anecdotes and consultant experience guide prescribing in the absence of formal guidelines and supporting surveillance data.
- Respondents value an evidence-based approach to decision-making but are limited by the hierarchical structure and systemic gaps in the institution.
- Behavioural analysis shows multiple barriers to decision-making with primary constraints linked to physical resources and social support.
- The target behaviour should first be narrowed, and a behavioural analysis conducted to determine effective intervention functions for identified behavioural barriers.

CHAPTER EIGHT

8 Global clinical practice recommendations for surgical antibiotic prophylaxis in caesarean sections

8.1 Publication statement

A summary of this chapter was published in the Journal of Hospital Infection.

Wade T, Looby A, Burgert J, Roberts N, Heneghan CJ, Onakpoya IJ. Surgical antibiotic prophylaxis in women undergoing caesarean delivery: a systematic review of clinical practice guidelines. Journal of Hospital Infection. 2025 Nov 24..[126]

8.2 Chapter introduction

In Chapter 7, the author's analysis of respondents' accounts revealed that the selection and duration of prophylaxis were largely dependent on consultants' preferences, their individual training and experience and their preferred guideline. This corroborates the findings of Chapter 6's regression analysis, which showed a significant association between the consultant and the selection and duration of surgical antibiotic prophylaxis in caesarean sections (C-sections). Given the observed variability in prescribing practices among consultants, the author concluded that a synthesis of published evidence on surgical antibiotic prophylaxis for C-sections is essential for standardising consultants' collective knowledge. A scoping search presented in Appendix 8.1, on recommendations for surgical antibiotic prophylaxis in C-sections was conducted on December 19, 2024. Medline (OvidSP) [1946-present], Embase (OvidSP) [1974-present], and Trip Database were searched using title, abstract, author keywords, and subject headings for key concepts of caesarean and antibiotics. No recent evidence synthesis on surgical antibiotic prophylaxis was found in the

search results. However, 17 eligible systematic reviews and meta-analyses, 39 randomised controlled trials and 14 clinical practice guidelines on the topic were identified. Publication dates for trials and systematic reviews spanned from 2020 to 2025, whereas global clinical practice guidelines were published within the past decade. Due to the volume of recent publications and the constraints of this thesis, the author synthesises practice recommendations from clinical guidelines.

8.3 Chapter aims and objectives

This chapter examines global clinical practice recommendations for surgical antibiotic prophylaxis in women undergoing C-sections. To achieve the aims of this chapter, specific objectives were to summarise current recommendations on antibiotic choice, timing of administration, and duration of surgical antibiotic prophylaxis from global clinical practice guidelines (CPGs), examine the evidence underpinning these recommendations, and assess the methodological quality of CPGs for surgical antibiotic prophylaxis in C-sections.

8.4 Methods

A systematic review was used to synthesise the evidence on surgical antibiotic prophylaxis in caesarean deliveries. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guided the reporting of the reviews' findings.[257] The protocol and its modifications are available at the Open Science Framework https://osf.io/vqgpm.[239]

8.4.1 Inclusion criteria

Population

Guidelines addressing surgical antibiotic prophylaxis for C-sections published between 2015 and 2025 were included.

Interventions

CPGs that included recommendations for timing, antibiotic(s), dosage, frequency, and duration of surgical antibiotic prophylaxis in different clinical circumstances were included in the review.

Outcomes

Current practice recommendations and supporting evidence, and the methodological quality of clinical practice guidelines.

8.4.2 Exclusion criteria

CPGs were excluded if they were subnational guidelines or if they provided recommendations solely for antibiotic prophylaxis in other surgical conditions. Additionally, CPGs lacking recommendations on the timing and type(s) of antibiotics used for surgical antibiotic prophylaxis were excluded. Excluded publication types comprised observational studies, qualitative studies, randomised controlled trials (RCTs), commentary, expert opinion, systematic reviews, scoping reviews, and narrative reviews.

8.4.3 Search strategy and searches

An expanded search of the following databases was conducted from inception to 27th June 2025: Medline (OvidSP)[1946-] Embase (OvidSP)[1974-], LILACS, Cochrane Database of Systematic Reviews (Cochrane Library, Wiley) and Trip Database. The CADTH CPG filter was adapted, and the search focused on guidelines (Refs).[258] Keywords included "caesarean section", "antibiotic prophylaxis" and "guideline". No date or language limits were applied. The World Health Organisation's website was manually searched for additional CPGs, and reference lists of retrieved CPGs were reviewed for other guidelines relevant to this review. Results of the updated search were exported to Covidence.

8.4.4 Study selection

Non-English CPGs without translations, excluding those written in German and Spanish, were excluded. Using Covidence, a web-based software platform used to streamline processes in evidence syntheses,[259] the author and a second reviewer, AL, independently performed title/abstract screening and full-text review. Disagreements were resolved via discussion.

8.4.5 Quality of included clinical practice guidelines

The Appraisal of Guidelines for REsearch & Evaluation (AGREE) II Online Appraisal Tool was used to appraise the quality of the clinical practice guidelines.[17] This tool assesses six domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence and consists of 23 questions rated on a 7-point Likert scale. Some CPGs provided additional obstetrical/gynaecological practice

recommendations unrelated to the review's objectives. Therefore, only recommendations related to surgical antibiotic prophylaxis in caesarean deliveries and overall guideline development were assessed. In addition to the author, two independent reviewers, IJO and JB, assessed the quality of the CPGs.

8.4.6 Data extraction and presentation

Data were independently extracted from the guidelines by the author and AL using a tool designed to match the review's research questions and inclusion criteria. The extraction tool was piloted on three publications and modified as necessary. Recommendations for surgical antibiotic prophylaxis in C-sections, including regimen, dosage, frequency, and duration for different patient circumstances, were extracted. Additionally, the titles of the CPGs, year of publication, geographical location, objectives, evidence assessment tools, level of evidence, and strength of recommendations were collected from the CPGs. Data was stored in a Microsoft Excel Spreadsheet. Calculations for scaled domain scores for the AGREE Tool and key practice recommendations were presented in both tabular and narrative forms.

8.5 Findings

8.5.1 Results of the search

Seventeen full-text publications were reviewed against the inclusion criteria. Eleven guidelines were selected after full-text screening and a search of the reference lists. The Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram in Figure 8.1 illustrates the evidence selection process. [257] Publications excluded after full-text review, along with reasons for exclusion, are listed in Appendix 8.2.

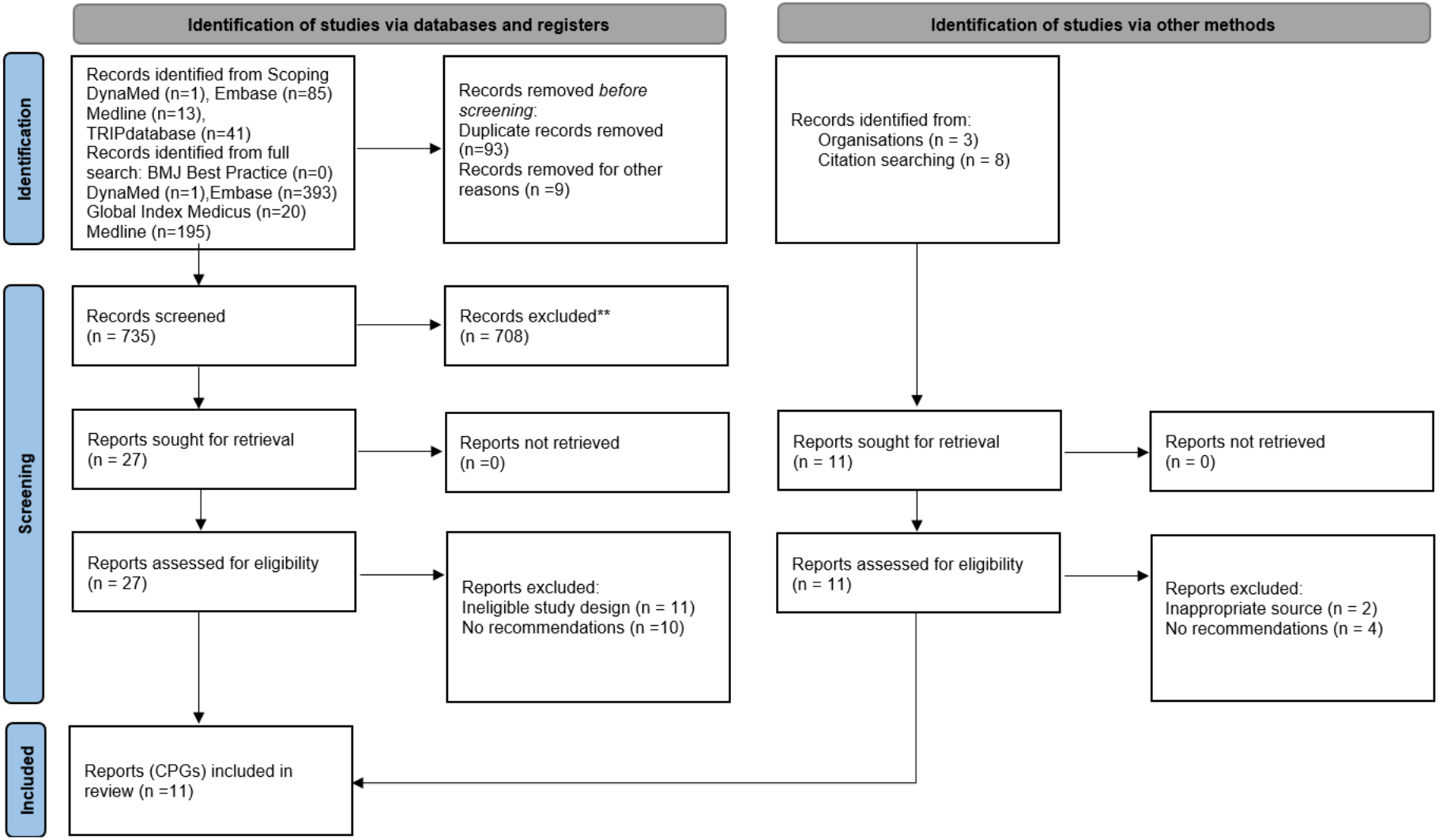


Figure 8.1 PRISMA Flow diagram showing evidence selection

8.5.2 Characteristics of included guidelines

Eleven guidelines from England-National Institute for Health and Care Excellence (NICE), France- French College of Obstetricians and Gynecologists (CGNOF), United States - American College of Obstetricians and Gynaecologists (ACOG), Canada -Society of Obstetricians and Gynaecologists of Canada (SOGC), Poland- Polish Society of Gynecologists and Obstetricians (PTGIP), Ireland- Health Service Executive (HSE), Italy - Italian Society of Gynecology and Obstetrics (SIGO), Germany/Switzerland/Austria - German Society of Gynecology and Obstetrics/ Austrian Society of Gynecology and Obstetrics/ Swiss Society of Gynecology and Obstetrics (DGGG, OEGGG and SGGG), China - Chinese Eugenics Science Association, Australia/New Zealand - The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), and one guideline from the World Health Organization (WHO) were reviewed. Seventy-three per cent (n=8) of CPGs were published in the last 5 years, and the remainder (n=3) were published in the previous 10 years. Fifty-five per cent (n=6) of the guidelines were from European countries, as shown in Table 8.1.

Table 8.1 Summary of characteristics of included clinical practice guidelines

Organisations (Country)	Title of publication	Objectives as stated in publications	Evidence assessment tool
ACOG[224] (United States, 2018)	Use of Prophylactic Antibiotics in Labor and Delivery	To present a review of clinical situations in which prophylactic antibiotics are frequently prescribed and to weigh the evidence that supports the use of antibiotics in these scenarios.	Quality according to the method outlined by the US Preventive Services Task Force
CESA[260] (China, 2025)	Expert consensus on prophylactic use of antibiotics for pregnant women during peripartum period	To standardise the prophylactic use of antibiotics for pregnant women during peripartum and reduce the irrational use of antibiotics.	*GRADE
CGNOF[261] (France,2023)	The cesarean procedure: Guidelines for clinical practice from CGNOF	To determine the surgical, but also medicinal and environmental procedures to reduce maternal morbidity during caesarean section.	*GRADE
DGGG/ OEGGG/ SGGG[262] (Germany/ Austria/ Switzerland, 2020)	Caesarean Section. Guideline of the DGGG, OEGGG and SGGG (S3-Level, AWMF Registry No. 015/084, June 2020)	To summarise the currently available knowledge on caesarean sections, focusing on its definition and classification, the information given to patients, the indications, timing and implementation of the procedure, and the impact of a caesarean birth on subsequent pregnancies and deliveries to determine the best approach in each individual case following a joint decision-making process.	SIGN 2011. DELBI
HSE[263] (Ireland, 2017) Revised 2020	Medication Guidelines for Obstetrics and Gynaecology First Edition Volume 1 Antimicrobial Prescribing Guidelines	To have a single reference document in which different options for the treatment of infections in pregnancy are presented, with some detail also regarding use of antimicrobials in lactation and teratogenicity risk.	Not stated in this document.

SIGO[264] (Italy, 2020)	Position paper on prevention of surgical site infections in obstetric and gynecological surgery	To inform healthcare personnel to strictly adopt standardized procedures and to use for antisepsis pharmaceutical specialties with specific indications.	Not stated in this document.
NICE[265] (United Kingdom, 2024)	Caesarean Birth NG (192)	To improve the consistency and quality of care for women and pregnant people who are thinking about having a caesarean birth or have had a caesarean birth in the past and are now pregnant again.	Not stated in this document. *GRADE
PTGiP[266] (Poland, 2018)	Recommendations of the Polish Society of Gynecologists and Obstetricians regarding Caesarean sections.	To improve the quality of care for all women and their offspring attending our maternity services whatever the setting.	Not stated in this document.
RANZCOG[267] (Australia, New Zealand, 2021)	RANZCOG Prophylactic antibiotics in obstetrics and gynaecology	To provide advice on the use of prophylactic antibiotics in obstetrics and gynaecology.	NHMRC Levels of Evidence [268] GRADE
SOGC[81] (Canada, 2017)	No. 247-antibiotic prophylaxis in obstetric procedures.	To review the evidence and provide recommendations on antibiotic prophylaxis for obstetrical procedures.	Canadian Task Force on Preventive Health Care
WHO 2021[225] (Global, 2021)	WHO recommendation on Prophylactic antibiotics for women undergoing caesarean section	To improve the quality of care and outcomes for women giving birth, as they relate to peripartum infection and its complications.	*GRADE CHEC checklist[269]

American College of Obstetricians and Gynaecologists (ACOG),Chinese Eugenics Science Association (CESA), French College of Obstetricians and Gynecologists (CGNOF), German Society of Gynecology and Obstetrics/Austrian Society of Gynecology and Obstetrics/ Swiss Society of Gynecology and Obstetrics (DGGG, OEGGG and SGGG),Health Service Executive (HSE) Ireland, Italian Society of Gynecology and Obstetrics (SIGO), National Institute for Health and Care Excellence (NICE),Polish Society of Gynecologists and Obstetricians (PTGIP),The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG),Society of Obstetricians and Gynaecologists of Canada. (SOGC), World Health Organization (WHO) *Grading of Recommendations Assessment, Development and Evaluation (GRADE)

The use of local susceptibility patterns to inform recommendations for surgical antibiotic prophylaxis was unclear for all reviewed guidelines. However, 36% (n=4) of CPGs suggested using local bacterial sensitivity information, and national therapeutic guidelines or formularies to inform the development of sub-national guidelines.[225, 263, 265, 267] Guidelines did not specify the healthcare professional responsible for administering surgical antibiotic prophylaxis or the specific location in the hospital where it should be administered.

8.5.3 Quality of included studies

There were notable variations in the quality of the guidelines. Upon examination, the domain, scope and purpose, showed the least variability, with a median score of 99 (range, 54-100%). Substantial variation was observed in stakeholder involvement, rigour of development, applicability, and editorial independence, as shown in Table 8.2. The median score for the domain, clarity of presentation, was 85%, ranging from 46% to 100%, with 82% (n=9) scoring above 70%. For the domain, applicability, which encompasses questions on barriers to implementation, tools to support guideline application, cost implications and monitoring, the domain score for 91% (n=10) of guidelines was below 40% (range 0-88%). WHO's 2021 guideline had the highest overall domain scores, ranging from 88 to 100%.

Table 8.2: Domain scores of clinical practice guidelines according to the AGREE II Appraisal Tool

Domain scores (%)						
Organisations	Scope and Purpose	Stakeholder Involvement	Rigour of Development	Clarity of Presentation	Applicability	Editorial Independence
ACOG[224]	83	44	36	87	7	75
CESA[260]	93	56	58	98	31	69
CGNOF[261]	100	65	75	85	0	67
DGGG/OEGGG/ SGGG[262]	100	76	56	78	14	61
HSE[263]	91	54	23	76	24	0
SIGO[264]	54	44	21	46	35	14
NICE[265]	100	67	43	93	36	58
PTGiP[266]	70	7	4	59	0	0
RANZCOG[267]	98	52	28	70	11	7
SOGC[81]	100	39	44	100	6	31
WHO 2021[225]	100	96	97	96	88	100
Median scores	98 (54-	54 (7-96)	43 (4-97)	85 (46-100)	14 (0-88)	58 (0-100)

American College of Obstetricians and Gynaecologists (ACOG),Chinese Eugenics Science Association (CESA), French College of Obstetricians and Gynecologists (CGNOF), German Society of Gynecology and Obstetrics/ Austrian Society of Gynecology and Obstetrics/ Swiss Society of Gynecology and Obstetrics (DGGG, OEGGG and SGGG),Health Service Executive (HSE) Ireland, Italian Society of Gynecology and Obstetrics (SIGO), National Institute for Health and Care Excellence (NICE),Polish Society of Gynecologists and Obstetricians (PTGIP),The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG),Society of Obstetricians and Gynaecologists of Canada. (SOGC), World Health Organization (WHO)

8.5.4 Recommendations and supporting evidence for surgical antibiotic prophylaxis in women undergoing C-sections

All CPGs recommended surgical antibiotic prophylaxis for reducing post-operative infections in women undergoing C-sections. [81, 224, 225, 260-266] This recommendation was supported by evidence from previously published systematic reviews by Smaill and colleagues.[270, 271] ACOG and SIGO also referenced the guideline on surgical site infection prevention from the Centres for Disease Control.[272] Smaill and Grivell rated the quality of

supporting evidence as moderate in their review, which was subsequently cited by 27% (n=3) of CPGs, including ACOG, CESA, and CGNOF.

Timing of surgical antibiotic prophylaxis

The general recommendation for the timing of administration was within 60 minutes of skin incision, as shown in Table 8.3. Variations within this time frame included less than 30 minutes, 30 to 60 minutes, 15 to 60 minutes, 30 to 10 minutes before skin incision, or at cord clamping.

Table 8.3 Recommendations for surgical antibiotic prophylaxis in women undergoing C-sections

Organisation	Timing of administration	Drug (dosage when indicated)	Duration
ACOG[224]	Within 60 minutes before skin incision	Cefazolin (1g)	Single
CESA[260]	30 to 60 mins before skin incision	cefazolin (1g) (or cefuroxime) ± metronidazole	Single
CGNOF[261]	No recommendation	No recommendation	No recommendation
DGGG/OEGGG/ SGGG[262]	Before the first skin incision	No recommendation	No recommendation
HSE[263]	Give 60 to 15 minutes before incision or in some cases at cord clamping.	Cefuroxime (1.5g) or Co-amoxiclav (1.2g)	Single
SIGO[264]	Before skin incision	Elective - Cefazolin Non-elective – 2nd-generation cephalosporin, an ureidopenicillin or an aminopenicillin with beta-lactamase inhibitor	It is recommended not to continue preoperative prophylaxis after suturing the surgical incision.
NICE[265]	Given up to 30 minutes before skin incision*	Cefuroxime* (1.5g)	Single or 750 mg every 8 hours if required for up to 3 doses (in high-risk procedures) *
PTGiP[266]	For penicillins and cephalosporins - between 30 and 10 minutes before the skin incision	No specific recommendation	No specific recommendation

Organisation	Timing of administration	Drug (dosage when indicated)	Duration
RANZCOG[267]	At least 30 minutes before caesarean section.	Cefazolin (2g)	Single
SOGC[81]	15 to 60 minutes before skin incision.	Cefazolin (1-2g)	Single
WHO 2021[225]	30–60 minutes before skin incision	First-generation cephalosporin or penicillin	Single

American College of Obstetricians and Gynaecologists (ACOG),Chinese Eugenics Science Association (CESA), French College of Obstetricians and Gynecologists (CGNOF), German Society of Gynecology and Obstetrics/ Austrian Society of Gynecology and Obstetrics/ Swiss Society of Gynecology and Obstetrics (DGGG, OEGGG and SGGG),Health Service Executive (HSE) Ireland, Italian Society of Gynecology and Obstetrics (SIGO), National Institute for Health and Care Excellence (NICE),Polish Society of Gynecologists and Obstetricians (PTGIP),The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG),Society of Obstetricians and Gynaecologists of Canada. (SOGC), World Health Organization (WHO) *Recommended by British National Formulary

Evidence for recommendations on the timing of administration

For the timing of surgical antibiotic prophylaxis, the evidence underpinning recommendations for 18% (n=2) of guidelines was informed by a systematic review conducted by Mackeen et al.[273] The evidence supporting the recommendation for preoperative antibiotic administration to reduce several post-operative infectious outcomes was graded by review authors as high quality.[273] A meta-analysis by Constantine[274] was cited in 18% (n=2) of CPGs. The authors did not appraise the quality of the five included studies.

Antibiotics recommended for surgical antibiotic prophylaxis

Eighteen per cent (n=2) of guidelines broadly recommended first-generation cephalosporins or penicillin as the preferred antibiotic classes for Caesarean deliveries [225, 266]. For non-elective C-sections, SIGO recommended a second-generation cephalosporin, in addition to a ureidopenicillin or an aminopenicillin-beta-lactamase inhibitor combination.[264] The CPG from NICE recommended selecting antibiotics that could

effectively reduce the risk of maternal postoperative infections, but advised against the use of co-amoxiclav as preincision prophylaxis.[265] Specific recommendations for the type of antibiotic were not evident in the NICE CPG; however, reference was made to the drug recommendations in the British National Formulary (BNF).[275] Guidelines from SOGC, ACOG, and RANZCOG explicitly recommended using a single pre-incision dose of intravenous cefazolin, with the dose varying by patient weight.[81, 224, 267] Cefuroxime or co-amoxiclav was the recommendation for surgical antibiotic prophylaxis in Ireland.[263] In the CPG from France, no recommendations were formulated on the choice of prophylactic antibiotics. The authors noted that current evidence does not support specific recommendations because the benefits and adverse effects of the compared drugs were similar.[261] Insufficient information on the comparative effectiveness of antibiotic classes was also mentioned by the Guideline Development Group of the World Health Organization.[225]

Evidence for antibiotic recommendations

For recommendations on the type of antibiotic to use as prophylaxis, 18% (n=2) of guidelines published before 2020 cited a Cochrane review by Gyte and colleagues.[276] The review's authors judged the primary evidence on the type and number of antibiotic doses needed to prevent infections to be of low quality.[276] An updated version of the review by Gyte, conducted by Williams and colleagues in 2021, [277] informed recommendations on antibiotic class in the CPGs of WHO and CESA. [225, 260] In this update, the authors reported that the evidence was of low to very low quality.

Duration of surgical antibiotic prophylaxis

Concerning the duration of surgical antibiotic prophylaxis, 64% (n=7) of guidelines recommended a single preincision dose of surgical antibiotic prophylaxis.[81, 224, 225, 260, 263, 265, 267] Considerations for extended dosing of up to 3 doses in high-risk procedures were documented by the BNF, which the NICE Guideline referenced.

Evidence supporting the duration of surgical antibiotic prophylaxis

ACOG and CESA referred to a systematic review and meta-analysis by Pinto-Lopes and colleagues when recommending a single preincision dose. Overall, the systematic reviewers judged the methodological quality of the studies included in their review as unclear.[278] Other guidelines provided no clear reference for this recommendation. The WHO guideline suggested that clinical judgement should determine if additional doses are necessary.[225]

Additional considerations for patient circumstances

Sixty-four per cent (n=7) of the guidelines made recommendations for patients with penicillin allergies. Clindamycin was generally recommended for patients with allergies; however, 36% (n=4) of the guidelines recommended a dual regimen with an aminoglycoside.[224, 260, 263, 267 *224, 267*] For blood loss greater than 1500 ml and prolonged C-sections, 64% (n=7) of CPGs recommended a second dose of the preoperative antibiotic.[81, 224, 260, 263-265, 267] A pre-incision dose of vancomycin was recommended for women who were known or suspected to be colonised with methicillin-resistant *Staphylococcus aureus* (MRSA). The reviewed guidelines provided no special considerations for women with diabetes.

8.6 Discussion

8.6.1 Summary of main findings

Retrieved guidelines were predominantly of European origin. Eleven CPGs recommended that surgical antibiotic prophylaxis be used for all C-section patients. The prevailing recommendation is to administer a single preoperative dose of prophylactic antibiotics within 60 minutes before skin incision, although variations within this time frame exist. However, supporting evidence for single-dose administration was of unclear quality. The first-generation cephalosporin cefazolin was the most recommended antibiotic, followed by second-generation cefuroxime. Some CPGs presented evidence from systematic reviews that backed the use of these antibiotics, with the most recent review published in 2021 by Williams.[277] Consideration was given to individual patient circumstances, including allergies and colonisation with MRSA, but diabetes, a risk factor for maternal peripartum infections,[279] was not addressed in CPGs. The WHO recommended infection prevention during the antenatal period for patients with diabetes.[225, 279]

Several CPGs utilised the GRADE tool [280, 281] to assess the quality of evidence and the strength of recommendations from the included systematic reviews that informed CPG development. However, multiple guideline development groups used other popular or generic appraisal tools to assess the evidence presented in their CPGs. Some CPGs cited evidence from primary studies and may have preferred other tools for assessing them, as GRADE is predominantly used to assess systematic reviews and other evidence syntheses. [257] Although some systematic reviewers judged the quality of the included primary studies as low to moderate, several guideline developers used the available evidence to generate

recommendations for prophylaxis. Contrarily, CGNOF reassessed the quality of the primary publications cited in the commonly referenced systematic reviews and did not provide recommendations on the type or timing of surgical antibiotic prophylaxis, citing that none of the available options was superior to the others.[261]

The methodological quality of CPGs varied when assessed using the AGREE II Tool. The least variation was seen in domains, scope and purpose, and clarity of presentation. However, there was considerable variation in the domains, stakeholder involvement, rigour of development, applicability and editorial independence. Several guidelines did not address stakeholder involvement and the rigour of the development process. Very few CPGs covered guideline dissemination, and most guidelines did not address supporting tools for guideline use, monitoring and evaluation. Having support tools is essential for successful guideline implementation, as guideline development does not guarantee use.[282] Overall, the WHO CPG consistently achieved higher scores across all assessed domains when compared to the other reviewed CPGs.

8.6.2 Strengths and limitations

To the author's knowledge, this is the first systematic review of clinical practice guidelines for surgical antibiotic prophylaxis in C-sections. Comprehensive literature searches were completed to identify relevant articles. Additionally, a standardised tool was used to assess the quality of the included CPGs, and the assessment was independently performed by three reviewers. Some limitations were recognised when conducting this review. CPGs not published in English may have been overlooked. It was challenging to access some external

guideline development documents referenced by the included CPGs, which would have limited the quality assessment. Where recommendations for antibiotic prophylaxis were retained from previous guidelines, supporting evidence from those guidelines could not be retrieved because the relevant documents would have been archived.

8.6.3 Implications for research and practice

Most of the retrieved CPGs originated from within the European context, with the Caribbean region underrepresented. Recommendations for surgical antibiotic prophylaxis were inconsistent across CPGs. This could be explained by differing evaluations of the evidence by guideline development groups, gaps in the evidence informing these CPGs and other contextual factors relevant to the settings for which guidelines were developed. It has been suggested that international guidelines can be adapted to external settings, but their transferability must be considered.[283],[284] Future research should focus on reconciling inconsistencies in practice recommendations to develop context-specific guidance.

8.7 Chapter summary

- All CPGs recommended the use of surgical antibiotic prophylaxis for C-section patients.
- Most CPGs recommended a single preincision dose of first or second-generation cephalosporin or a penicillin. However, the choice of agent and duration of prophylaxis varied across settings.
- Some evidence underpinning practice recommendations from various CPGs was from the same systematic reviews but was interpreted differently by guideline developers.
- The methodological quality of CPGs varied substantially for some domains of the AGREE II Tool, particularly rigour of development, stakeholder involvement and applicability.
- CPGs were primarily from Europe, and none were retrieved for the Caribbean region.
- Several systematic reviews and randomised controlled trials on surgical antibiotic prophylaxis have been published over the past 5 years warranting a review. An overview of evidence on surgical antibiotic prophylaxis from recent systematic reviews should be conducted.

CHAPTER NINE

9 Items to be included in a formulary for surgical antibiotic prophylaxis in caesarean sections in Antigua and Barbuda.

9.1 Publication statement

Under consideration at the journal, BMC Pregnancy and Childbirth.

9.2 Chapter introduction

In Chapters 6 and 7, there appeared to be tension regarding the type and duration of surgical antibiotic prophylaxis in C-sections when prescribing patterns and influences on decision-making were assessed. Further, Chapter 8's systematic review of clinical practice guidelines shows that recommendations for surgical antibiotic prophylaxis vary across geographical settings. This aligns with the findings of the qualitative investigation in Chapter 7, where respondents noted that consultants' use of several international guidelines may contribute to the variability in prescribing practices reported in Chapter 6.

Overall, Chapter 8 revealed that a single preincision dose of a first- or second-generation cephalosporin or a penicillin was recommended for surgical antibiotic prophylaxis in multiple clinical practice guidelines. This recommendation may not be generalisable to settings not considered during guideline development. As presented in Chapter 7, contextual factors such as antibiotic availability and bacterial sensitivity profiles influenced prescribing decisions. Considering these factors, the author summarised local sensitivity patterns for *Escherichia coli*, a pathogen commonly implicated in maternal post-operative infectious complications in the setting, and found that penicillins were less effective than cephalosporins, as shown in Appendix 9.1. For this chapter, the author utilises the findings

of Chapters 6, 7, and 8, along with the local formulary and bacterial sensitivity patterns, to develop criteria items for a Delphi consensus study.

9.2.1 Delphi study

Delphi techniques are helpful when there is conflicting information or limited evidence on a topic[285, 286] First described by Dalkey and Helmer in 1963, the Delphi technique is a controlled interaction involving an iterative process designed to generate reliable consensus on a topic from a panel of experts.[287] The Delphi technique has been used in healthcare and is structured to conceal the identity and opinions of each panel member to reduce bias and influence.[287, 288] The inclusion of a panel with experiential knowledge, a minimum of 2 survey rounds and the presentation of aggregated panel feedback to panellists between rounds are standard features of the Delphi technique [289] The information gathered through this method could inform the development of a simplified local protocol that guides the prescribing and use of surgical antibiotic prophylaxis in C-sections. The observation by Grimshaw et al that doctors are more receptive to locally developed guidelines,[290] underscores the importance of contextual relevance in the adoption of clinical practice guidelines.

9.3 Chapter aims and objectives

This chapter generates expert-level consensus for items to be included in a formulary detailing surgical antibiotic prophylaxis for women undergoing C-sections in Antigua and Barbuda. The key objectives were to develop a list of criteria items for surgical antibiotic

prophylaxis in C-sections and to determine, by expert consensus, a list of priority items to be included in the formulary.

9.4 Methods

The protocol for this study was registered with the Open Science Framework (OSF) registry and is available at https://osf.io/fhtkv. The study was reported in accordance with the Recommendations for Conducting and Reporting of Delphi Studies (CREDES) guidelines.[291] Ethical approval was granted by the Oxford Tropical Research Ethics Committee (OxTREC) – 1399435.

Study design

This study had two phases. In the first phase, a steering committee oversaw the development of the survey criteria and the identification of panel members. In the second phase, the survey was distributed to potential panellists for feedback.

9.4.1 Development of an electronic survey tool

The author constructed the instrument using the JISC Online Survey (Version 3) Tool, which is compliant with the General Data Protection Regulation (GDPR).[292] As seen in Appendix 9.1, the survey included structured statements and a free-text field at the end, an approach previously described by Hasson and others to gather additional comments from the panel.[293] The round one survey, shown in Appendix 9.2, consisted of 14 sections with several variations for each assessed area. Section 1 focused on the development process for formularies, while sections 2 to 7 examined the regimen, dosage, route, administration timing and duration of surgical antibiotic prophylaxis. The roles of healthcare professionals,

including antibiotic administration and associated documentation, as well as the location for administration, were assessed in sections 8 to 10. Although items in sections 8 to 10 are not usually included in a formulary, consensus was needed on these items because they have been identified in Chapter 7 as key factors influencing the use of surgical antibiotic prophylaxis. In sections 11 to 14, there were considerations for surgical antibiotic prophylaxis in exceptional patient circumstances, such as prolonged caesarean delivery and colonisation with methicillin-resistant *Staphylococcus aureus* (MRSA).

Selection of items

The author prepared a list of parameters to be considered in the first round of the Delphi. Findings from Chapters 6, 7, and 8 on variations in the selection and duration of surgical antibiotic prophylaxis were considered alongside the findings of the evidence syntheses reported in Chapters 3 and 4 and local bacterial susceptibility patterns. This information was crucial for the development of the survey criteria. An evidence summary was integrated into the data collection tool to provide the panel with additional information to be considered when making their selections. As noted by Jorm and colleagues, the quality of evidence from Delphi studies depends on the quality of evidence accessible to the panel.[294] The steering committee reviewed the list and made modifications where appropriate.

Pretesting of survey tool

The survey was piloted with three healthcare professionals. Pretesting was necessary to determine timeframes, readability, appropriateness, and clarity of statements.[286] No

modifications were made following pretesting. Pretest results were excluded from the final analysis.

9.4.2 Selection and recruitment of expert panel

The definition of an expert in Delphi studies has not been well established. It was stated that experts should be able to draw from their knowledge or personal experience with the topic being investigated [285] Since the objective of this study was to outline items for inclusion in a formulary, the author conceptualised an expert as a healthcare professional or health researcher with knowledge, experience and interest in the research topic. When clinical interventions form the basis of a study, specialists in the field under study, including persons experiencing the condition, should constitute the panel.[295] Purposive sampling was used to select a heterogeneous panel so that their diverse expertise and knowledge of the research topic could be applied during decision-making in the survey.[289, 296] Diverse perspectives can enhance the quality and acceptability of the received feedback.[297, 298] The steering committee was responsible for identifying potential panellists. Selection was based on their knowledge and/or experience in obstetrics and gynaecology, nursing, antimicrobial stewardship, infection prevention, surgery, pharmacy, medical microbiology, anaesthesiology, research experience in antimicrobial resistance and use, and persons with lived caesarean delivery experience.

Sample size

Delphi studies lack a set criterion for the number of panel members and a consensus on what constitutes a small or large sample. [299-301] According to Pluddemann et al., a panel

typically consists of around 10 to 50 members.[302] However, the sample size varies depending on the study's purpose, the researcher, and other contextual factors.[301] Based on the size and scope of the work of one hospital in Antigua and Barbuda serving a population of approximately 93,000, the plan was to recruit 15 panellists from Caribbean Community (CARICOM) States.[302]

Recruitment of expert panel

Potential panellists were sent a link via JISC online survey, inviting them to participate as panel members. Panellists were sent two reminders to complete the study, as reminders may help to optimise participation.[170] Panellists who responded to the first survey were retained for the second.

9.4.3 Data collection

Anonymity is essential when using this method, as it limits the dominance often exhibited in group settings. [303] Panel members were unaware of the identities of other panellists and freely expressed their opinions on what should be included in the formulary. As described by Taylor, to ensure anonymity, this process was coordinated remotely, with no open discussion among panellists.[300] No identifying data was collected during the rounds. There were two rounds in this Delphi study, the minimum number expected in such designs, and a consideration when establishing the evidence base to inform survey criteria.[286, 289] Only two rounds were anticipated in the design phase of the Delphi, as substantial evidence on variations in regimen type and duration, as well as drug administration details, was presented in Chapters 6 and 7. Additionally, global evidence syntheses on clinical practice

recommendations for surgical antibiotic prophylaxis, one of which is presented in Chapter 8, were used to inform the development of survey criteria. Fewer rounds were beneficial for maintaining panel participation throughout the study.[304]

Delphi process

Surveys for rounds one and two were conducted over a 4-month period from June to September 2025. The round one survey was extended due to a low response rate. Survey extension encouraged additional participation. Maximum participation through survey extension was discussed in another Delphi study.[305]

Round 1

The first round of the survey was electronically distributed to the panel for their feedback. The purpose of this round was to determine, by consensus, the priority items to add to a formulary for surgical antibiotic prophylaxis in caesarean deliveries. The survey tool, shown in Appendix 9.1, comprised 14 sections and took approximately 20 minutes for participants to complete. Based on their knowledge and/or experience, panellists indicated their level of agreement with the presented parameters on a 7-point Likert-type scale (1=strongly disagree, 2=disagree, 3= somewhat disagree,4= neutral, 5= somewhat agree, 6=agree, 7=strongly agree). Comments made in the free-text field provided insight into the non-consensus items and aided the modification and addition of new items to the round 2 survey.

Round 2

In the second round, aggregated panel feedback, including additional comments from the first-round survey, was presented to panellists. The author reintroduced items nearing consensus (>55%) in the second round, allowing panellists to reconsider their previous selections based on aggregated feedback from other panellists.[285] An additional item on administration intervals within a 24-hour period was added to the survey tool, as shown in Appendix 9.2. A 3-point Likert scale was used to assess agreement for the presented items. This modification was made to the proposed 7-point Likert scale in the original protocol, as confirmation or denial of items nearing consensus was required for the items presented in round 2.

Data analysis

Percentages were used to describe the level of agreement for each item presented.

Consensus

There is no established consensus threshold across Delphi studies. [300] Since the topic of interest is clinical management of patients, consensus on an item was considered reached if

1. ≥70% of participants provide a score of 6 to 7 (agree, strongly agree) for survey items.
2. ≥70% provide a score of 1 to 2 (strongly disagree, disagree) for a survey item they are not in favour of.

If criterion 1 was met, the items were compiled into a list for addition to a formulary. Non-consensus was established when neither threshold was met. Non-consensus items nearing consensus were presented in a modified survey in the second round. Non-consensus items following completion of round 2 of the survey were reported in the findings. Data obtained from the surveys has been stored in the university's OneDrive for Business. The author provided both narrative and graphical representations of the findings.

9.5 Findings

There was a 73% response rate (n=11) in the first round of surveys and a 91% (n=10) response rate in the second round.

9.5.1 Panel characteristics

All panellists were from CARICOM States and represented different sectors and professional categories as shown in Table 9.1. Seventy-three per cent (n=8) were from the public sector, while 27% (n=3) were from the private sector.

Table 9.1 Characteristics of expert panellists

Institution	Main professional role	Number
Public	Obstetrics/Gynaecology Consultant	4
	Obstetrics/Gynaecology-Junior physician	1
	Pharmacist	1
	Infection prevention/ antimicrobial stewardship, lab technologist	1
	Senior Nurse	1
Private	Obstetrics/Gynaecology Consultant	1
	Obstetrics/Gynaecology-Junior physician	1
	Infection prevention/ antimicrobial stewardship/consultant	1

Regarding formulary development, 91% (n=10) of respondents agreed that recommendations for surgical antibiotic prophylaxis should be evidence-based and that the local bacterial sensitivity profile and postoperative infection rates should be considered.

9.5.2 Recommendations for surgical antibiotic prophylaxis

Round one

Panel members reached consensus disagreement on the administration of antibiotic prophylaxis at cord clamping and on the continuation of antibiotic prophylaxis beyond 24 hours. For sections 2-7 of the criteria items, consensus agreement was reached on the selection, duration, route of administration, and timing of surgical antibiotic prophylaxis in C-sections, as shown in Table 9.2.

Table 9.2 Consensus items from round one of the survey on surgical antibiotic prophylaxis in C-sections.

Consensus Items -Agree	Per cent ranking agree or strongly agree
Section 1: Development of a formulary for surgical antibiotic prophylaxis in women undergoing a Caesarean delivery	
1.1 The recommendations for a formulary on surgical antibiotic prophylaxis for women undergoing a Caesarean delivery should be evidence-based. This means that high quality published evidence, expert consensus, local bacterial sensitivity profiles and locally available antibiotics should be considered during the development of the formulary.	91
1.2 Local susceptibility patterns should be used to guide the choice of agent for surgical antibiotic prophylaxis in a Caesarean delivery.	91
1.3 The local formulary should be used to guide the choice of agent for surgical antibiotic prophylaxis.	82
1.4 Local information on post-operative infectious complications should be considered when developing the formulary.	91
Section 2 Choice of antibiotic for prophylaxis in Caesarean delivery	
2.1 Cefazolin should be used as the first line of surgical antibiotic prophylaxis in women undergoing Caesarean delivery.	73
Section 5 Duration of surgical antibiotic prophylaxis	
5.1 Antibiotics should be discontinued within 24 hours of caesarean delivery unless there are indications of an infection, and it is documented in the patient's medical records.	73

Consensus Items -Agree	Per cent ranking agree or strongly agree
5.3 If surgical antibiotic prophylaxis is extended beyond 24 hours, a review for discontinuation of the course should be considered at 48 hours.	82
Section 6 Route of administration of surgical antibiotic prophylaxis	
6.1 All surgical antibiotic prophylaxis should be administered intravenously to women undergoing caesarean delivery.	91
Section 7 Timing of surgical antibiotic prophylaxis administration	
7.2 All women undergoing Caesarean delivery should be administered a prophylactic antibiotic within 30 minutes before an incision is made.	73
7.4 If pre-incision prophylaxis was not administered (for example, during an emergency caesarean delivery), it should be given during surgery.	82
Section 12 Special considerations for exceptional patient circumstances	
12.1 The first line of prophylaxis should be administered pre-incision in addition to prophylaxis for prolonged premature rupture of membranes in women undergoing Caesarean delivery.	73
13.1 Patients known or suspected of being colonised with methicillin-resistant S. aureus (MRSA) should be given a single dose of Vancomycin 15mg/kg IV pre-incision.	73
14.3 If there is bleeding in excess of 1500 ml, a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.	73
Consensus items disagree	**Percent ranking disagree or strongly disagree**
5.2 Surgical antibiotic prophylaxis for women undergoing a Caesarean delivery should be extended beyond 24 hours.	73
8.3 Surgical antibiotic prophylaxis should be administered in the ward for patients who are undergoing an elective Caesarean delivery.	73
8.6 Surgical antibiotic prophylaxis should be administered in the ward for all women undergoing a Caesarean delivery.	73
7.3 All women undergoing Caesarean delivery should be administered a prophylactic antibiotic at cord clamping.	82

For sections 8 to 10, 73% (n=8) of participants were against the administering of preoperative prophylactic antibiotics in the maternity ward. For sections 11 to 14, which assessed special patient circumstances, there was consensus agreement, 82% (n=9), for an intraoperative dose when the preincision dose was not administered in emergency situations. Seventy-three per cent (n=8) of panellists agreed that a single preoperative dose

of adjunctive vancomycin should be used for patients colonised with MRSA. There is also consensus, 73% (n=8), to add a first-line prophylactic antibiotic for C-section candidates with prolonged premature rupture of membranes who are clinically managed with other antibiotic classes.

Round 2

Open feedback from the round-one survey on the inconsistency of antibiotic use and the complexity of managing patients with allergies was shared with panellists. Consensus was reached for 6 of the 9 criteria presented in round 2. As shown in Table 9.3 panelists agreed that 1.5 g of cefuroxime should be used as prophylaxis when cefazolin is unavailable in the setting.

Table 9.3 Round 2 consensus items

Consensus items Agree	Percent ranking agree/strongly agree
2.2 Adjunctive metronidazole 500mg IV should only be considered if there is bowel injury.	80
3.1 In cases of cefazolin allergy, the attending consultant should determine the appropriate antibiotic type and dosage, guided by patient-specific circumstances and antibiotic availability. Note: Panel members provided feedback on the poor availability of antibiotics such as clindamycin and the complexities of managing patients with allergies.	100
3.2 If cefazolin is unavailable, cefuroxime 1.5g IV should be used as an alternative for surgical antibiotic prophylaxis. Note: The consideration for an alternative reflects feedback highlighting inconsistent antibiotic availability.	80
3.4 In patients with a BMI ≥ 40, the attending consultant should determine the appropriate dosage of surgical antibiotic prophylaxis.	80
4.1 The nurse should administer surgical antibiotic prophylaxis in the operating theatre holding area for all women undergoing caesarean deliveries. Note: Based on the consensus recommendation of administering antibiotic prophylaxis within 30 minutes of c-section.	70

Consensus items disagree	Percent ranking disagree or strongly disagree
2.1 Dual regimen of cefazolin plus adjunctive metronidazole should be used as surgical antibiotic prophylaxis in women undergoing a Caesarean delivery.	70

Seventy per cent (n=7) of respondents disagreed with using a cephalosporin in combination with adjunctive metronidazole as prophylaxis, agreeing instead that metronidazole should only be indicated when there is bowel injury, 80% (n=8).

Items with no consensus after rounds 1 and 2 surveys

There was no consensus on dosage or the number of doses to administer to prevent postoperative infections. Figure 9.1 shows the distribution of responses for items related to the dosage of cefazolin in round one. The level of agreement varied for all suggested doses.

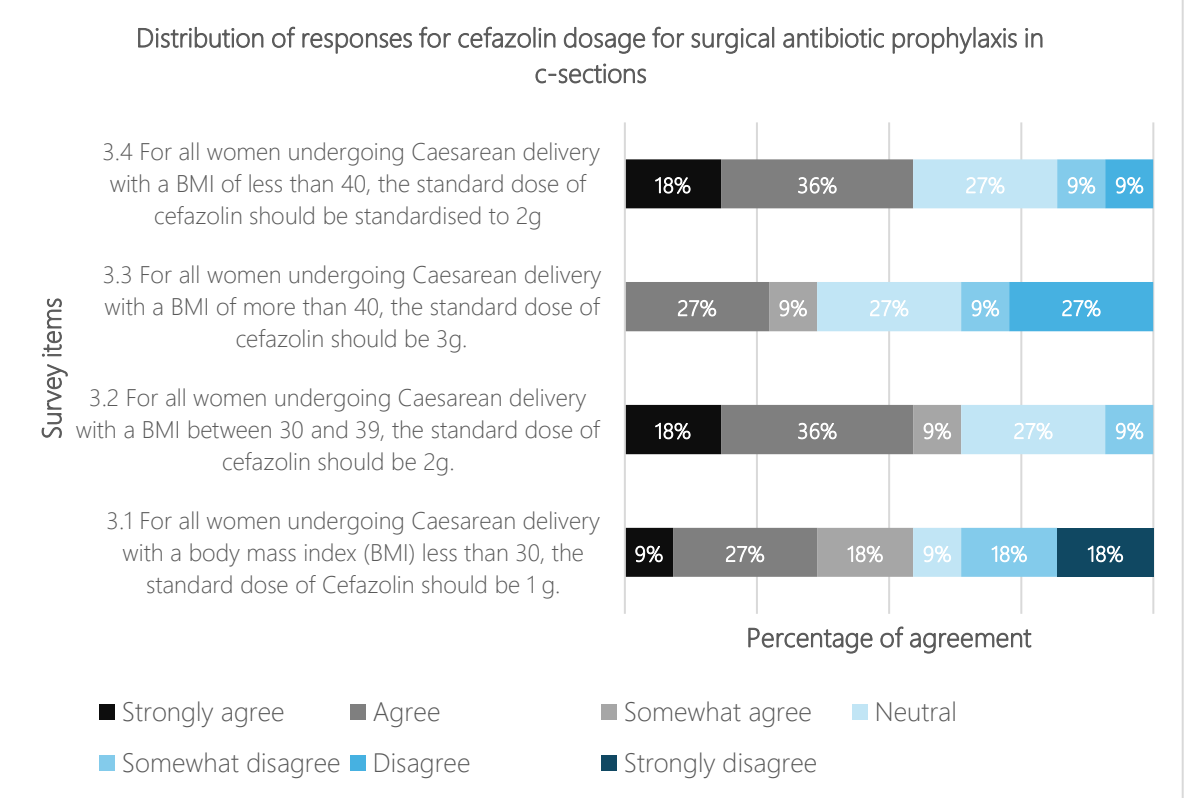


Figure 9.1 Distribution of responses for cefazolin dosage by body mass index for C-section patients

Similarly, rounds one and two showed no clear agreement on whether single or multi-dose regimens should be used within a 24-hour period. In round one, agreement on the use of 2 doses, one pre-incision and the other 12 hours after initial administration, was 55% (n=6), compared to 45% (n=5) for a single pre-incision dose. In round 2, 60% (n=6) of respondents favoured a two-dose regimen, whereas only 30% (n=3) agreed to 3 doses at 8-hour intervals, as shown in Figure 9.2.

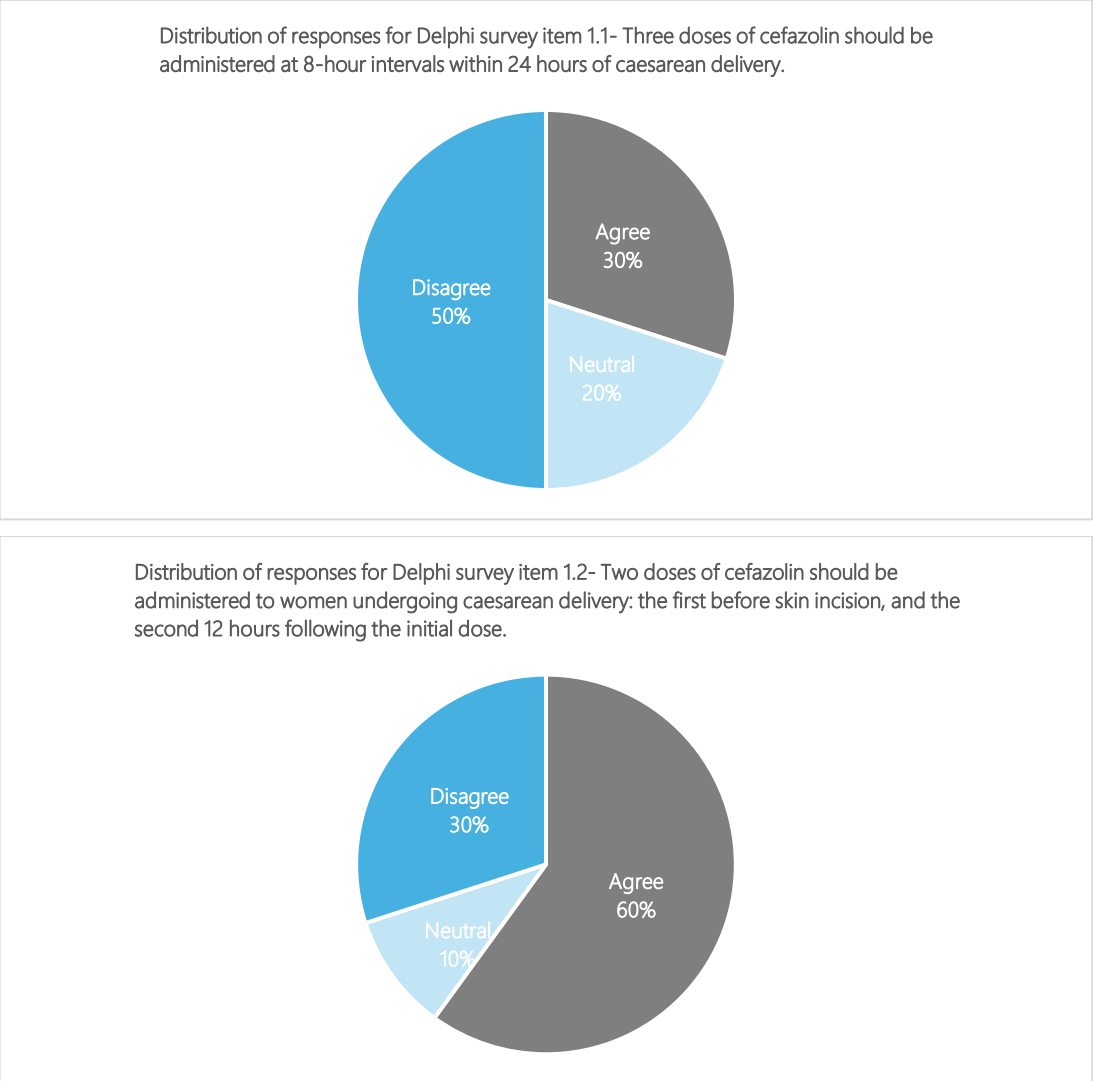


Figure 9.2 Round 2 distribution of responses on dosing

Similarly, there was no consensus on the choice or dosage of an antibiotic for patients with allergies. Panellists provided feedback on the inconsistent availability of clindamycin, which was presented as an item for consideration in the round one survey. Additionally, there was no agreement on the gentamicin dosage. Panellists described the complexities of managing patients with cephalosporin allergies. For C-sections exceeding 4 hours, there was no clear consensus on whether an additional dose was needed during surgery. However, the level of agreement was 64% (n=7) in round 1 and 60% (n=6) when reassessed on a 3-point Likert scale in round 2. No consensus was achieved for the documentation of prophylaxis administration. The final list of items generated by expert consensus is in Box 9.1.

Choice of antibiotic for prophylaxis in Caesarean delivery
Cefazolin should be used as the first-line surgical antibiotic prophylaxis for women undergoing Caesarean delivery.
If cefazolin is unavailable, cefuroxime 1.5g IV should be used as an alternative for surgical antibiotic prophylaxis.
Duration of surgical antibiotic prophylaxis
Antibiotics should be discontinued within 24 hours of Caesarean delivery unless there are indications of infection, which are documented in the patient's medical records.
If surgical antibiotic prophylaxis is extended beyond 24 hours, a review of discontinuation should be considered at 48 hours.
Route of administration of surgical antibiotic prophylaxis
All surgical antibiotic prophylaxis should be administered intravenously to women undergoing Caesarean delivery.
Timing of surgical antibiotic prophylaxis administration
All women undergoing Caesarean delivery should be administered a prophylactic antibiotic within 30 minutes before an incision is made.
If pre-incision prophylaxis was not administered (for example, during an emergency caesarean delivery), it should be given during surgery.
Special considerations for exceptional patient circumstances
The first line of prophylaxis should be administered pre-incision in addition to prophylaxis for prolonged premature rupture of membranes in women undergoing Caesarean delivery.
Patients known or suspected of being colonised with methicillin-resistant S. aureus (MRSA) should be given a single dose of Vancomycin 15mg/kg IV pre-incision.
If there is bleeding in excess of 1500 ml, a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.
Adjunctive metronidazole 500mg IV should be considered if there is bowel injury.
In cases of cefazolin allergy, the attending consultant should determine the appropriate antibiotic type and dosage, guided by patient-specific circumstances and antibiotic availability.
In patients with a BMI ≥ 40, the attending consultant should determine the appropriate dosage of surgical antibiotic prophylaxis.
Administration of surgical antibiotic prophylaxis
The nurse should administer surgical antibiotic prophylaxis in the operating theatre holding area for all women undergoing caesarean deliveries.

Box 9.1 Items to include in a formulary for surgical antibiotic prophylaxis in C-section patients in Antigua and Barbuda.

9.6 Discussion

9.6.1 Summary of findings

In this study, a list of items was generated based on research evidence and considered for inclusion in a formulary for surgical antibiotic prophylaxis in C-sections by a panel of experts. Seventy-three per cent (n=11) of potential panellists responded to the round one survey, while 91% (n=10) of panellists responded to the round two survey. Of the 23 items that achieved consensus, 78% (n=18) reached consensus agreement while 22% (n=5) reached consensus disagreement. Overall, 91% of panellists agreed that an evidence-based approach is important for developing a formulary for surgical antibiotic prophylaxis. Based on panellist feedback, the following key items should be included in a formulary: choice of antibiotic and alternative in the absence of the first-choice antibiotic, timing and route of administration and duration of prophylaxis. Other priority items included the use of vancomycin in MRSA colonisation, and an additional dose of antibiotic prophylaxis if there is excessive blood loss while undergoing a C-section. Recommendations for these items have been addressed in several clinical practice guidelines,[224] as reported in the evidence synthesis conducted in Chapter 8.[126]

There was no consensus on the dosage and number of doses of surgical antibiotic prophylaxis required in a C-section. For prolonged C-sections exceeding 4 hours, panellists did not agree on administering an additional dose to the patient. Multiple international clinical guidelines support the administration of an additional dose of antibiotic prophylaxis to maintain tissue concentrations in prolonged surgeries.[81, 224, 306] However, evidence for redosing is predominantly from studies focusing on other types of surgeries, including a

retrospective cohort study, which showed a higher risk for post-operative infections following prolonged cardiac surgery without redosing.[307] Similarly, the findings of Dornfield and colleagues' case-controlled series on intraoperative redosing during prolonged colorectal surgery[308] were cited as supporting evidence in the Bratzler et al. guideline. [306] Bratzler's guideline has since informed the ACOG guideline for surgical antibiotic prophylaxis in C-sections. The following items, which are not typically included in a formulary, namely, documentation of prophylaxis administration and the location where it should be administered, did not achieve consensus.

9.6.2 Strengths and limitations

This study was designed to gather expert opinions from a diverse group of healthcare professionals regarding the use of surgical antibiotic prophylaxis during C-sections. The study generated expert consensus on key items to include in a formulary for surgical antibiotic prophylaxis during C-sections. The author provided the panellists with evidence summaries of prescribing practices in the study setting, in addition to findings from an evidence synthesis of global clinical practice guidelines. The provision of this material would have informed panellists' selections. Although the sample was relatively small, perspectives from different specialities were represented. The narrow scope of this Delphi study may limit the generalisability of findings to other settings; however, the methods used and the surveys' criteria items are valuable for conducting Delphi studies on surgical antibiotic prophylaxis in other clinical settings.

9.6.3 Implications for practice

The results of this Delphi study could inform the development of a formulary for surgical antibiotic prophylaxis in C-sections in Antigua and Barbuda. Currently, there is no guidance for physicians to uniformly prescribe antibiotic prophylaxis for C-section patients. Having this guidance would provide a similar level of care for all patients, thereby improving patient outcomes and helping to minimise inappropriate prescribing. This may also help to reduce the development of antimicrobial resistance and preserve the effectiveness of antibiotics used in this setting. Next steps include translating the consensus recommendations generated by the panellists into an implementable formulary with strategies for implementation and monitoring.

9.7 Chapter summary

- Recommendations for surgical antibiotic prophylaxis should be evidence-based, with considerations for local bacterial sensitivity profiles and post-operative infection rates.
- Key items that should be included in the formulary are the choice of antibiotic, the timing and route of administration and the duration of surgical antibiotic prophylaxis.
- A cephalosporin should be used as surgical antibiotic prophylaxis in C-sections.
- Adjunctive metronidazole should only be used if there is bowel injury, and vancomycin if the patient is colonised with MRSA.
- Consultants should determine the choice of prophylaxis for patients with allergies and dosage for patients with a body mass index greater than 40.
- Recommendations should be translated into a formulary that can be implemented in the setting.

CHAPTER TEN

10 Discussion and conclusion

Antibiotics are essential for preventing post-operative infections following Caesarean sections (C-sections). However, it has been established that prescribing antibiotic prophylaxis for C-section patients varies within hospitals and can contribute to sub-optimal patient outcomes and antibacterial resistance. This variation within obstetrics undermines evidence-based practice. The overarching aim of this thesis was to use an evidence-based approach to develop an intervention for standardising the prescribing of surgical antibiotic prophylaxis for women undergoing C-sections in Antigua and Barbuda.

10.1 Summary of main findings

Chapter One introduces this thesis and provides an overview of the aims and objectives of each chapter. Research methods used to achieve the aims of each chapter were aligned with the framework of the Medical Research Council (MRC). [6, 7] Chapter Two presents background information on antibiotics, including development, its importance in modern medicine, antibacterial resistance and the role of antimicrobial stewardship (AMS) in improving antibiotic use in human medicine. An updated literature summary on antibiotic prescribing and use across the Caribbean region was conducted to provide a regional context for this thesis. Importantly, the existing literature is predominantly cross-sectional, focused on antimicrobial consumption and point-prevalence, and provides insufficient evidence on antibiotic use in clinical settings in the region. Notably, this challenge persists after the publication of the findings from Chapter Three on antibiotic prescribing and use in Caribbean Community (CARICOM) States. This limits efforts to design and implement

targeted interventions to optimise antibiotic use. In Chapter 3, the author employed a mixed-methods systematic review to establish the evidence base for antibiotic use, antimicrobial stewardship (AMS), and barriers to prescribing in CARICOM States. Findings showed that antibiotic prescribing was predominantly studied in two countries, Trinidad and Tobago and Jamaica, with overprescribing a common occurrence. An analysis of barriers and limitations showed several contextual factors influencing prescribing, including consultant experience and inadequate support resources. A noteworthy finding of this review was the limited (n=8) and outdated evidence on antibiotic use, as well as the absence of research examining AMS interventions in CARICOM States. A scoping review of systematic reviews was conducted and presented in Chapter 4 to provide an overview of AMS interventions aimed at healthcare workers. This review summarised global evidence of hospital-implemented AMS interventions targeting healthcare workers. Audit and feedback, and clinical practice guidelines were the most frequently reported AMS interventions with successful outcomes. Education, in the form of meetings, materials, and sessions, was also commonly reported as facilitating positive change. Although these interventions have been proven successful, 2% (n = 12) of the primary studies included in 18 systematic reviews were from low- and lower-middle-income countries (LLMICs). Therefore, identified interventions may not be practical or feasible in LLMICS, which are often constrained by contextual factors such as limited financial support and a lack of expertise. These factors can hinder the successful implementation and impact of AMS interventions. Findings from this scoping review further highlight the need to design, implement, and evaluate tailored AMS interventions for improving antibiotic use in these settings. However, context-specific

evidence on antibiotic prescribing patterns and practices is needed to inform the development of interventions in these settings. The author conducted a cross-sectional review of systemic antibiotic prescriptions for patients admitted to a tertiary care hospital in Antigua and Barbuda between January 1, 2014, and September 30, 2021. An analysis of 27,676 systemic antibiotic prescriptions in Chapter 5 revealed that 75% (n = 21,538) were for parenteral use. Overall, 41% of all antibiotics were classified by the World Health Organisation Anatomic Therapeutic Chemical classification system as the subgroup 'other beta-lactam antibacterials'(J01D). Cephalosporins were the most prescribed antibiotics in this subgroup, followed by metronidazole from the subgroup 'other antibacterials' (J01X). Since no clinical context was provided for the reviewed prescriptions, it was essential to focus on prescribing within a specific patient cohort to better understand prescribing in this setting. Therefore, in Chapter 6, the author undertook a retrospective analysis of prescribing patterns for surgical antibiotic prophylaxis in C-sections in Antigua and Barbuda. The records of 1,319 patients who underwent C-sections and were admitted between January 1, 2018, and December 31, 2024, were reviewed. Over 99% of patients received intravenous antibiotic prophylaxis before the C-section. Cefuroxime was the main antibiotic used as surgical antibiotic prophylaxis in this setting. However, there was variability in both the use of adjunctive metronidazole within preoperative surgical antibiotic prophylaxis regimens, and in the duration of postoperative prophylaxis. Maternal age, urgency of C-section, attending consultant, and year were included in regression analyses to determine whether these variables were associated with the use of single-regimen prescriptions and prescription duration. Multivariable regression, mutually adjusted for year and consultant,

demonstrated significant associations between these variables and the regimen type and duration of prophylaxis. The unwarranted variation observed in this setting prompted a qualitative investigation into factors influencing the use of surgical antibiotic prophylaxis in C-sections. This qualitative study utilised the Capability, Opportunity, Motivation Behavioural (COM-B) Model to understand behavioural influences on prescribing, forming the basis of Chapter 7. The author used vignette-based methodology and a semi-structured interview to conduct individual interviews with sixteen healthcare workers of different professional categories responsible for the prescribing and use of surgical antibiotic prophylaxis in C-sections. Inductive analysis showed that hierarchical dynamics, systemic gaps and contextual factors influenced surgical antibiotic prophylaxis. A behavioural analysis of interview data, using the COM-B Model, revealed barriers to and enablers of decision-making regarding surgical antibiotic prophylaxis. Respondents had the physical and psychological capability to understand and perform functions related to antibiotic prophylaxis use, but there were differing perspectives on the choice of antibiotics and the duration of prophylaxis. Physical opportunities to support decision-making were lacking, as practice guidelines and feedback mechanisms on antibiotic use and bacterial resistance profiles were unavailable. For behaviour to occur, there must be capability, opportunity and motivation. In this setting, key components for behaviour to occur are missing, which could explain observed variations in regimen type and duration of antibiotic prophylaxis in C-section patients. In Chapter 8, the author conducted a systematic review of global clinical practice guidelines (CPG) to examine recommendations for surgical antibiotic prophylaxis in C-sections. Eleven guidelines, 55% (n=6) from European countries, were retrieved and included in the systematic review.

Evidence from systematic reviews, primary studies, and other practice guidelines informed the development of CPGs, with several guidelines drawing on the same evidence sources. Evaluation with the AGREE II Tool revealed that CPG quality varied across settings, with notable deficiencies in the domains, rigour of development, stakeholder involvement, and applicability. Cefazolin was recommended by 45% (n=5) of guidelines, and 73% (n=8) of CPGs recommended a single pre-incision dose. Three CPGs made no recommendations for the antibiotic or timing of administration, with the CPG of the French College of Obstetricians and Gynaecologists explicitly stating that the evidence does not provide clear recommendations.

In Chapter 9, the author conducted a Delphi study to generate expert consensus on a list of items to include in a formulary for surgical antibiotic prophylaxis in the study setting, since patient care needs to be standardised. Two online surveys were conducted with 11 panellists in round one, and 10 in round two. Panellists had diverse professional backgrounds and knowledge and/or experience with surgical antibiotic prophylaxis use in C-sections. Eighteen items regarding the choice of antibiotics, timing of administration, and duration achieved consensus agreement for inclusion in a formulary for surgical antibiotic prophylaxis.

10.2 Methodological strengths and limitations

The strengths and limitations of each study are described in their respective chapters; however, this thesis has overall strengths and limitations. This thesis was guided by the MRC Framework for Complex Interventions[6], which provided a structured yet flexible approach to understanding and developing context-specific interventions. Centred around the

'developing a complex intervention' phase of the MRC framework, investigations were systematically conducted, with each subsequent project evidence-informed and context-aware. Evidence syntheses conducted and reported in Chapters 3, 4 and 8 of this thesis identified gaps and uncertainties in the evidence base for antibiotic use, antimicrobial stewardship and practice recommendations for surgical antibiotic prophylaxis in the Caribbean and low-resource settings. These gaps acted as catalysts for subsequent studies in this thesis. The mixed-methods systematic review showed that research on antibiotic prescribing frequently focused on two Caribbean countries. The author added to the evidence by providing antibiotic prescribing patterns for admitted patients in Antigua and Barbuda in Chapter 5 and C-section patients in Chapter 6.

Another strength of this thesis is its use of mixed-methods research to address the research question. Recent regional studies have employed population-level quantitative designs to describe antibiotic use.[105, 107] However, the author combined the strengths of different research paradigms and study designs at both the institutional and patient group levels. Applying a qualitative study design in Chapter 7 broadened the understanding of the reported variations in antibiotic prophylaxis in the retrospective analysis of Chapter 6. This mixed-methods strategy enhanced the breadth and depth of knowledge regarding the use of surgical antibiotic prophylaxis in C-sections.[136] Multiple methods also facilitated cross-validation of the findings, thereby enhancing the credibility and robustness of the results. Qualitative findings in Chapter 7 indicated that variation in surgical antibiotic prophylaxis prescribing stemmed from consultants' reliance on CPGs of different origins. This was subsequently substantiated by Chapter 8's systematic review, which demonstrated

inconsistent recommendations across international guidelines, thereby reinforcing respondents' accounts.

The COM-B Model can be adapted to different clinical contexts and has previously been applied to analyse antibiotic prescribing behaviour and used to inform antimicrobial stewardship interventions.[254, 309, 310] In Chapter 7, the COM-B Model was used to analyse behavioural influences on decision-making in surgical antibiotic prophylaxis. The application of this model provided a structured framework for the systematic exploration of prescribing behaviour. This was a novel application of the model and contributed to the existing research landscape.

This thesis has limitations. Overall, it was conducted in a country with a relatively small population, a resource-limited hospital setting, and reliance on poorly maintained paper-based medical reports and suboptimal documentation practices, which have affected data completeness in primary studies. Antigua and Barbuda has a population of approximately 93,000 people and is served by one public tertiary care hospital with 158 beds. This limited the sample sizes obtained for the studies reported in Chapters 5, 6, 7, and 9. The author considered adding data from other Caribbean countries to increase the sample size and enhance the external generalisability of the findings. However, it was not feasible to include other sovereign nations, as this would have involved international processes that would have substantially delayed the work of this thesis. As a member of the Pan American Health Organisation's Antimicrobial Resistance Group, the author is aware that similar challenges to those identified in the studies presented in this thesis are also experienced in other Caribbean countries. This indicates that the findings may be valuable in similar settings.

Other limitations were primarily due to time constraints and inadequate published guidance for evidence syntheses used in this thesis. The general pharmacy dataset, 2014 to 2021, used in Chapter Five's cross-sectional review of prescribing patterns, took several years to consolidate, clean, sort and format. Due to the time constraints of this thesis, a preliminary analysis was conducted using data from 2017 to 2021. These findings were crucial for narrowing the focus of this thesis, as antibiotic prescribing is a broad topic in hospital settings. However, when the complete dataset was analysed, the results aligned with the preliminary findings, with minor adjustments to the number of each antibiotic prescription. Similarly, the author performed a preliminary analysis of the dataset for C-section patients from 2018 to 2022. This information informed the design of the qualitative study presented in Chapter 7. The remaining dataset for 2023 to 2024 showed a reduction in the duration of prophylaxis. If this information had been available before the design of the qualitative study in Chapter 7, the interviews could have been adapted to explore potential interventions or policy changes. However, one respondent with several years of experience in the setting raised a point about being influenced by new team members to change practice. This highlights the strength of the qualitative approach used in Chapter 7, as it uncovered unsolicited information and helped explain the observed changes in prophylaxis duration.

Methodological guidance on designing and conducting mixed-methods systematic reviews (MMSRs) is still evolving and was unavailable when the MMSR in Chapter 3 was conceptualised. Since then, Hong has published methodological guidance on conducting MMSR in 2023,[129] and the Joanna Briggs Institute has published a manual for evidence

synthesis.[168] Reporting guidelines that could have provided some structure for MMSR would have assisted in protocol development and review reporting; however, reporting guidelines for systematic reviews of prevalence were also not widely available when the review was conducted [311] Therefore, guidelines generated for systematic reviews of interventions were used to guide this review. Additionally, guidelines for conducting scoping reviews of systematic reviews were unavailable when Chapter 4's review on healthcare-worker-targeted antimicrobial stewardship interventions in hospitals was conducted. The author was guided by the framework for scoping reviews as outlined in the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis. [168]

10.3 Implications of thesis

Overall, this doctoral thesis contributes to evidence-based healthcare by demonstrating that research evidence can be translated into real-world clinical practice.

10.3.1 Methodological approach used in thesis

This research extends existing evidence by moving beyond descriptive studies and studies of effectiveness to address a recognised gap in the literature: the translation of research evidence into local clinical practice. A mixed-methods approach is adopted to investigate antibiotic prescribing and guide the design of a context-specific, consensus-generated list of items for a formulary on surgical antibiotic prophylaxis in C-sections. Each selected study design was informed by the findings from preceding studies in this thesis and shaped by practical considerations, including time constraints, costs, and the availability of expertise. It provides applied evidence on the use of standardised frameworks; the MRC framework, and

the core of the BCW- the COM-B Model in evaluating the use of surgical antibiotic prophylaxis in routine C-sections in a low-resource setting. As a result of this pragmatic line of inquiry, the collective findings informed the development of a consensus-generated, context-specific list of items for a formulary on surgical antibiotic prophylaxis in C-sections.

The methodological approach employed in this thesis is transferable to closely related fields where behavioural theory and mixed-methods research evidence are valuable for advancing complex interventions. As shown in Table 10.1, alternative study designs can be employed where practical constraints have been identified.

Table 10.1 Methodological approaches to address key research questions: Advantages, limitations and alternative designs

MRC	Research questions	Thesis study designs	Advantages	Limitations	Optional study designs
Identify the evidence base	What is the evidence for the prescribing of antibiotics in hospitalised patients?	Mixed Methods Systematic review	Captures both qualitative and quantitative data, assesses the quality of evidence	Time consuming, methodologically complex, integration of findings can be challenging	Scoping review, systematic review
	What types of healthcare worker-targeted antimicrobial stewardship interventions have been evaluated in hospitals, and what outcomes have they reported?	Scoping review of systematic reviews	Provides a high-level evidence map across a broad topic area	Depends on the quality of included systematic reviews, loss of primary details, overlap of primary studies	Bibliometric analysis
Identify/ develop appropriate theory	How are systemic antibiotics prescribed for hospitalised patients and how does it vary across inpatient units and disease cohorts?	Cross-sectional study	Inexpensive to conduct.	Time-consuming in the absence of an electronic health system.	Prospective study
	How is surgical antibiotic prophylaxis prescribed for women undergoing caesarean sections, and are prescriptions dependent on patient, prescriber or temporal factors?	Retrospective analysis	Inexpensive to conduct.	Time-consuming in the absence of an electronic health system, poor record keeping limits a comprehensive analysis	Prospective cohort study
	What factors influence decision-making around surgical antibiotic prophylaxis in Caesarean sections?	Qualitative investigation	Provides contextual information on how antibiotics are prescribed.	limited generalisability, time intensive data collection, analysis	Clinicians' survey
	What international clinical practice guidelines exist for surgical antibiotic prophylaxis in Caesarean sections and what evidence forms the basis of these recommendations?	Systematic review	Systematic assessment of guideline recommendations and the quality of underpinning evidence.	Time and resource intensive, variability in study designs, populations, interventions, comparators, outcomes	Scoping review, overview of reviews
Modelling process and outcomes	What are the key antibiotics, dosages, duration and related items that experts agree should form part of a standardised formulary for surgical antibiotic prophylaxis in Caesarean sections?	Delphi study	Facilitates expert consensus from a diverse group of healthcare professionals, reduces group pressure and minimises influence of dominant personalities, valuable in formulary/guideline development	Limited depth of discussion, attrition across rounds, can take weeks or months to complete	Qualitative study with focus groups/ interviews

10.3.2 Intervention development for surgical antibiotic prophylaxis in C-sections

In Chapter 6 of this thesis, the author found unwarranted variation in the number and duration of prophylactic antibiotic use in C-sections. Respondents' accounts in Chapter 7 further supported findings of variations in prescribing at the consultant level. The inadequate access to feedback on antibiotic resistance and infection rates, and the absence of prophylaxis guidelines, further compounded this challenge. In the short term, an evidence-based formulary tailored for the setting should be developed and implemented. This could lead to consultant adherence in the intermediate phase, ultimately resulting in sustained long-term compliance.

Formulary development

The Delphi technique, as used in Chapter 9, is a powerful tool for generating expert consensus on antibiotic prescribing in settings without standard guidance. In Chapter 9, a list of evidence-informed consensus-generated items for a formulary on surgical antibiotic prophylaxis in C-sections was provided. Within the target setting, this list could be expanded into a comprehensive document using structured guidance from the World Health Organization (WHO) Handbook for Guideline Development.[312] The Appraisal of Guidelines for Research and Appraisal (AGREE II) Framework[17] could then be used to appraise the methodological quality and transparency of the formulary before it is presented to the hospital's governance structures for approval.

Application of the Behaviour Change Wheel to support formulary implementation

In Chapter 7, a behavioural analysis of interview text identified numerous barriers to decision-making at junior and senior physician levels, highlighting several intervention points for improvement. Given the presence and complexity of multi-level behavioural barriers across different categories of healthcare professionals, formulary implementation in isolation is insufficient. Further application of the BCW could help develop a focused, measurable strategy to successfully implement the formulary in the maternity department.

The author applied key stages of the BCW to establish a foundation for successful formulary implementation:

1. Narrowing the scope of the target behaviour.

Since behaviours are embedded within complex systems of other behaviours,[9] the author developed a conceptual map outlining behaviours associated with improving decision-making regarding regimen type and duration, illustrated in Figure 10.1.

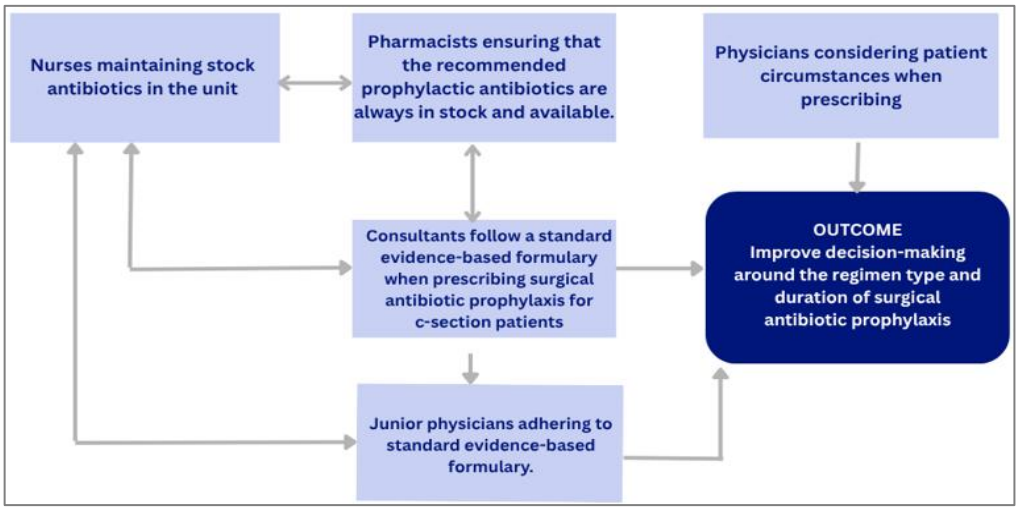


Figure 10.1 Conceptual map of behaviours related to improving decision-making on surgical antibiotic prophylaxis in caesarean sections

Behaviours from the conceptual map were prioritised using the following criteria: likely impact on the anticipated outcome, the degree to which the behaviour is amenable to change, the likely spillover impact on other behaviours, and the practicality of measuring whether the behaviour has changed.[9] Based on this assessment, shown in Appendix 10.1, and contextual findings, consultants following a standard evidence-based formulary when prescribing surgical antibiotic prophylaxis for C-section patients was selected as the starting point, having met all four evaluation parameters.

2. Systematically identifying barriers of the target behaviour using the COM-B Model

Physical and social opportunities, including insufficient resources and poor communication, were identified as behavioural barriers to consultants' adherence to a standard evidence-based formulary. As illustrated in Appendix 10.2, environmental restructuring, modelling, enablement, education and restriction were appropriate intervention functions for addressing these concerns.

3. Selecting feasible intervention functions and policy categories to address barriers

Considering the local context, the affordability, practicability, effectiveness/cost-effectiveness, acceptability, side-effects/safety, and equity (APEASE) criteria, shown in Appendix 10.3, provided a systematic approach to selecting optimal intervention functions and policy categories to address the identified behavioural barriers.[9, 313] Educational and restrictive intervention functions, and policy categories- guidelines and communication satisfied all six criteria. Selected intervention functions, and policy categories aligned with respondents' perspectives (Chapter 7) on strategies to improve surgical antibiotic prophylaxis in C-sections.

Development of a complex intervention strategy

As shown in Table 10.2, the author designed an intervention strategy with delivery mechanisms that could support consultants' adherence to a standard, evidence-based formulary. This strategy could address variations in surgical antibiotic prophylaxis in C-sections, which unnecessarily contribute to the development of bacterial resistance, adverse side effects, increased healthcare costs and increased morbidity and mortality. The proposed strategy could be advanced using the Behaviour Change Technique Taxonomy.[124]

Table 10.2 Proposed intervention strategy for standardising surgical antibiotic prophylaxis in C-sections

Intervention function	Policy category	Purpose	Intervention strategy and mode of delivery
Restriction	Guidelines	Provide evidence-based recommendations for surgical antibiotic prophylaxis use in C-sections.	Develop a formulary for surgical antibiotic prophylaxis in C-sections using the priority items generated by the Delphi consensus, local research evidence and stakeholder involvement.
Education	Communication / marketing	Standardise knowledge on the recommendations for surgical antibiotic prophylaxis from recent evidence syntheses.	*Before formulary development:* a. Disseminate recently published evidence syntheses on surgical antibiotic prophylaxis in C-sections to local stakeholders via educational workshops and email. b. Disseminate findings of the Delphi study via email and workshops. *After formulary development*: c. Disseminate the formulary to department stakeholders and hospital management via email, educational reminders and meetings.
		Provide feedback on current prescribing practices and prescribing behaviour to hospital stakeholders.	Conduct educational meetings with members of the Obstetrics/Gynaecology Department to discuss findings: ▪ Prescribing of surgical antibiotic prophylaxis in C-sections. ▪ Factors influencing decision-making around surgical antibiotic prophylaxis

Formulary use was considered a potentially suitable method to support education and restriction intervention functions. Communication via email, educational workshops, and reminders was deemed a logistically feasible approach to supporting education in the setting.

10.3.3 Further application of the Medical Research Council Framework

Research on complex interventions consists of 4 phases: developing/identifying an intervention, feasibility, implementation, and evaluation, with several core components in each phase.[6] Throughout this thesis, core components of the MRC Framework, stakeholder involvement, contextual factors, identification of uncertainties, refinement of target behaviour for intervention development and economic considerations have all been considered when applying Michie's BCW.[9] Another core element of each phase of the MRC framework is the programme theory.[6] Developing a programme theory helps to clarify how an intervention could facilitate change by outlining mechanisms through which intended outcomes will be achieved.[314] The author used a theory-based perspective in this thesis and hypothesised that changes to the prescribing of surgical antibiotic prophylaxis in the maternity unit can occur if behavioural barriers to capability, opportunity and motivation are addressed. In the absence of programme theory, interpreting evaluation findings is limited, as it may be difficult to determine whether observed shortcomings reflect implementation or theory failure.[314] This is useful for evidence-based practice and allows for the modification and use of interventions in other settings, since the components and mechanisms of change will be well-defined.[6] In alignment with the 2021 MRC Framework, a programme theory was developed that links the problem, variations in practice identified in Chapters 6 and 7, the components of the intervention strategy, anticipated mechanisms of change, assumptions about contextual factors that may influence the intervention, and the outcome. As described by Skivington, a logic model presented in Figure 10.2 was developed to represent the programme theory.[6]

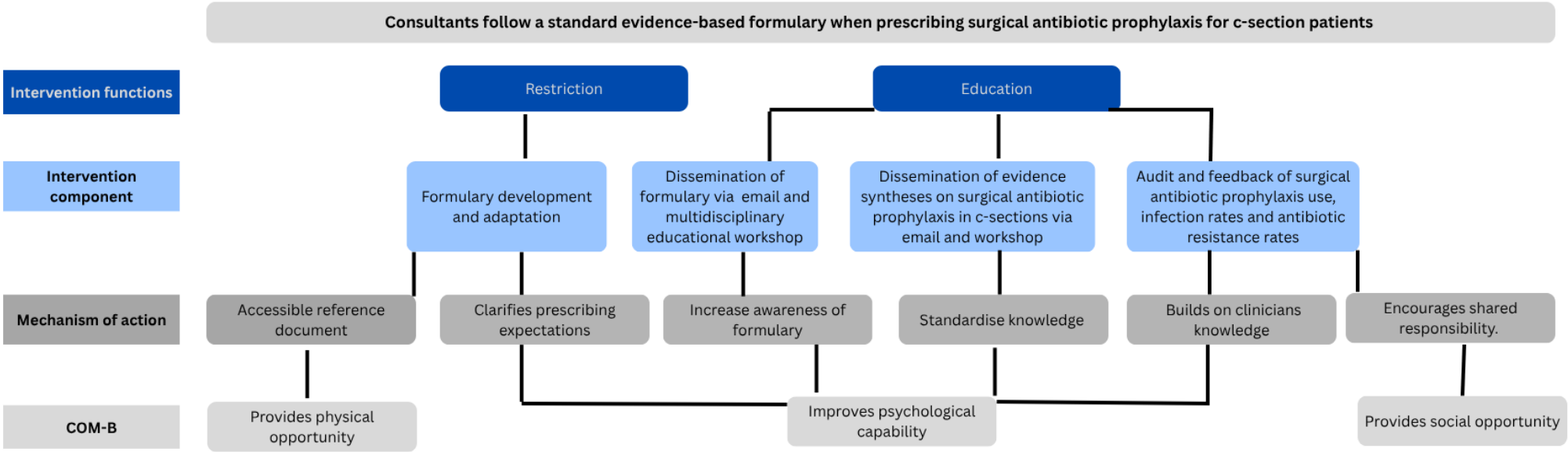


Figure 10.2 Logic model representing programme theory

For restrictive and educational intervention functions to support adherence to the evidence-based formulary, the consensus-selected antibiotic, cefazolin, must be consistently available in the hospital. For the intervention to work, institutional and departmental support is needed for the development and implementation of the formulary. Institutional support is especially crucial for sustaining behaviour change in the maternity unit. One key assumption is that consultants are willing to change practice and follow a standard formulary. In Chapter 7, there was some indication of willingness to change how surgical antibiotic prophylaxis is used. One condition was regular feedback on infection rates and antibiotic prescribing practices. Information on prescribing practices reported in Chapter 6 of this thesis was disseminated via an educational meeting with maternity department stakeholders on August 15th, 2025. Stakeholders comprised four obstetrics/gynaecology consultants, including the department head, four junior physicians, and two nurse managers. Clinicians from the paediatric department and the hospital's medical director were also present. An overall post-operative infection rate for the study period was described in Chapter 6, however, the true infection rate may have been underestimated since infection data were limited to hospitalised patients. The implementation of a system in which post-operative infections are a notifiable event would enable the capture of all infections identified during hospitalisations and those detected in outpatient follow-up. This would provide clinicians with the information needed to improve their prescribing practices and, by extension, improve patient outcomes.

10.3.4 Future research

This thesis has identified underexplored research domains in Caribbean and global literature. The findings of Chapters 3 and 4 highlight priority areas for future research: addressing knowledge gaps in antibiotic prescribing and use in the Caribbean region, promoting methodological diversification in Caribbean research, employing a theoretical approach to design AMS strategies and strengthening the global evidence base for AMS interventions. To strengthen antimicrobial stewardship efforts, future research should examine prescribing across diverse patient cohorts and common clinical conditions, including surgical antibiotic prophylaxis in uncomplicated surgical procedures and the management of community-acquired pneumonia. This would add to the evidence base for antibiotic prescribing in these regions and enable the development of targeted interventions. Since qualitative research on antibiotic prescribing in the Caribbean is limited,[5] employing qualitative methods can enhance the understanding of antibiotic prescribing by providing deeper insights into current practices in the region, as seen in Chapter 7. Future research should place stronger emphasis on behavioural theory, as this would provide a deeper understanding of prescribing practices by linking individual actions to established theoretical constructs. This approach clarifies what needs to change, which areas are amenable to change, and the mechanisms through which change can be accomplished, thus providing a structured, evidence-based framework for achieving change.

In Chapter 8, a scoping search on recommendations for surgical antibiotic prophylaxis yielded multiple primary and secondary studies, as well as clinical practice guidelines. The findings of the systematic review of clinical practice guidelines in Chapter 8 indicate that all

guidelines were informed by evidence syntheses conducted before 2022. There is an opportunity for synthesising the most recent evidence from well-conducted primary studies and systematic reviews. The author has commenced work on an overview of systematic reviews for surgical antibiotic prophylaxis in C-sections, with plans to conduct a systematic review of recently conducted randomised controlled trials. Following the completion of these reviews, stakeholders in the maternity department will be approached to advance the development and implementation of a local formulary. Completion of these additional reviews was not feasible due to the constraints of this thesis.

10.5 Conclusion

Antimicrobial resistance has been recognised as a global health threat, prompting international action. The Global Action Plan (GAP) on Antimicrobial Resistance provides a framework to guide countries in developing and implementing national action plans (NAPs) for addressing antimicrobial resistance. Although there have been global efforts to address the threat of AMR, some countries are off course in developing their NAPs. Several gaps in the literature on antibiotic prescribing and antimicrobial stewardship in the Caribbean and low and lower-middle-income countries have been identified in this thesis. Another challenge in the study setting is the limited availability of resources and opportunities for improving the use of antibiotic prophylaxis in C-sections. Antibiotic use is complex and requires adequate resources and high-level support to facilitate improvement.

This thesis has systematically addressed the intervention development phase of the MRC Framework through several research designs, as illustrated in Table 1.1. The feasibility phase

of the MRC framework was partially explored, generating critical insights to inform intervention design. In Chapter 7, respondents predominantly recommended implementing standard guidelines or protocols to improve surgical antibiotic prophylaxis in C-sections. In Chapter 10, the author developed a plan to deliver intervention components, partially advancing the implementation phase of the MRC framework. The usefulness of the intervention functions and policy categories of the BCW was assessed using the affordability, practicability, effectiveness/cost-effectiveness, acceptability, side-effects/safety, and equity (APEASE) criteria.[9] The APEASE criteria enabled the selection of an intervention strategy fitting for the study setting. Further operationalisation of this Framework will assist with the implementation and evaluation phases of the MRC framework, which was beyond the scope of this thesis. Focus should be on monitoring and evaluating the intervention, and refining the programme theory, as new evidence becomes available. This will ensure the accuracy of the mechanisms of change and help advance the intervention's scalability, sustainability, and generalisability.

Overall, the integrated findings of this doctoral thesis provide an evidence base to inform the development of an intervention strategy. This systematic line of inquiry can be applied in other clinical settings to develop evidence-based, theory-guided, and context-specific interventions for clinical management. Further, this approach can be modified and applied nationally to develop NAPs for countries considering this initiative.

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Thesis appendices

Appendix Chapter 1

Appendix 1.1 Certificates for courses undertaken

DEPARTMENT FOR CONTINUING EDUCATION
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UNIVERSITY OF OXFORD

Ms Tansy Wade
Mt Joy
ST PETERS
ANTIGUA AND BARBUDA

Date 19 Dec 2025
Registration 1811565011454

Record of CATS Points

Module	Title	Result	FHEQ	Start date	End date	Points
T19G004YOY	Mixing it up: Understanding and using mixed methods research in social sciences	63	7	23 Apr 2019	10 Jun 2019	20
					Total	**20**

Certificate of Attendance

Tansy Wade

attended

SPSS: Up and running for academic research

between

09 May 2022

&

13 May 2022

450 Minute course

The learning objectives were to:

- Be familiar with the layout and structure of SPSS
- Organise data in SPSS
- Conduct descriptive analyses, t-tests, correlations, regressions and ANOVAs in SPSS
- Interpret outputs of tests correctly
- Understand which test is appropriate for which research question
- Understand which steps are involved in the quantitative analysis research process

This certificate does not imply any specific competence

Digital Skills Manager,
IT Learning Centre

IT Learning Centre

Certificate of Attendance

Tansy Wade

attended

R: A first look

on

25 Jan 2023

180 Minute

The learning objectives were to:

- Recognise an R program
- Use an R program
- Make simple changes to an R program
- Write simple lines of R code
- Understand what the next steps are to learning more about R programming

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Introduction to statistics: group A

between

31 Mar 2025
&
15 Apr 2025

12 Hour course

The learning objectives were to:

- To get a grounding in the theory and core concepts of statistics
- How to perform some key of the statistical tests on continuous and binary data
- When you might need to use non-parametric tests, and how to do them
- How to interpret the statistical results that you have produced
- How to do sample size calculations on both continuous and binary data

This certificate does not imply any specific competence

MEDICALSCIENCES
Skills Training

Certificate of Attendance

Tansy Wade

attended

Bite-sized: Excel Power Query

on

02 Apr 2025

45 Minute

The learning objectives were to:

- Import data into Excel using Power Query
- Understand basic operations available in the Power Query Editor
- Learn how to clean data during import
- Import data in a repeatable way

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Excel: Good practice with pivot tables

on

27 May 2025

120 Minute

The learning objectives were to:

- Create Pivot Tables from different lists of data
- Group data
- Create Pivot Reports
- Create Slicers to filter data
- Create calculated fields and calculated items
- Create and work with Pivot Charts

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

NVivo - Walking before running: Code and retrieve

on

22 May 2025

180 Minute

The learning objectives were to:

- Understand the basic principles of qualitative data analysis
- Understand NVivo's capabilities
- Become familiar with the NVivo interface and simple functions
- Import a selection of data sources into NVivo
- Learn the basics of coding and annotating data sources
- Learn the basics of running queries to retrieve data out of NVivo

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Synthesising qualitative research made simple ONLINE

between

27 Mar 2025
&
28 Mar 2025

4 Hour course

The learning objectives were to:

- Making a start and deciding which method
- How (and how far) to search for studies
- How to decide if a study is good enough to include
- How to extract qualitative data
- Keeping a database and what to record in it
- How to analyse qualitative data and reporting guidelines

This certificate does not imply any specific competence

MEDICALSCIENCES Skills Training

Certificate of Attendance

Tansy Wade

attended

Surveys: Introduction to Jisc Online Surveys and Microsoft Forms

on

26 May 2021

150 Minute

The learning objectives were to:

- Gain an overview of what should be considered when selecting a survey tool
- Learn about the capabilities of JISC Online Surveys and Microsoft Forms
- Learn how to create straightforward surveys using JISC Online Surveys and Microsoft Forms
- Explore some of the options for distributing surveys and for analysing the results
- Understand the data protection issues that need to be considered when running a survey

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Digiknow: Creating mind maps, flowcharts and infographics with everyday tools

on

22 Feb 2022

60 Minute

The learning objectives were to:

- Why are mindmaps and flowcharts useful for comprehension
- How can mindmaps be used to plan your document as well as summarise it
- How to use Xmind (free mindmapping tool) to create a graphical outline for a document
- How to use outlining in Microsoft Word with Headings and navigation
- How to create flowchart from a Word outline using PowerPoint's SmartArt
- How to create infographics and interactive maps using Excel

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

IT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Excel: Good practice with pivot tables

on

27 May 2025

120 Minute

The learning objectives were to:

- Create Pivot Tables from different lists of data
- Group data
- Create Pivot Reports
- Create Slicers to filter data
- Create calculated fields and calculated items
- Create and work with Pivot Charts

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Excel: Good practice with lookups

on

20 May 2025

120 Minute

The learning objectives were to:

- Use criteria to focus calculations only on the data in a table that you are interested in
- Become familiar with Excel's lookup functions
- Gain an understanding of how table layout can affect your choice and use of lookup functions
- Discover how to combine lookup functions for more powerful searches

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Microsoft Project: Setting up a project

on

16 Mar 2021

90 Minute

The learning objectives were to:

- Plan your project
- Set up a new project
- Create a project plan
- Decipher an existing project plan
- Understand the benefits and limitations of Microsoft Project

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Developing original ideas through analytical frameworks

on

08 Nov 2023

2 Hour

The learning objectives were to:

- To apply and become familiar with the application of analytical frameworks to research datasets
- To construe how originality can emerge through data analysis
- To understand how examining data from different theoretical perspectives can facilitate the generation of a comprehensive analytical framework

This certificate does not imply any specific competence

MEDICALSCIENCES Skills Training

Certificate of Attendance

Tansy Wade

attended

Word: Tools, Tips and Time-savers

on

06 May 2025

180 Minute

The learning objectives were to:

- Use and modify styles for consistent text formatting
- Structure a document with accessible headings, using styles
- Manage pagination for a professional finish
- Manage the flow of long tables
- Use paragraph formatting to manage the space around text
- Control the flow of text around images

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Certificate of Attendance

Tansy Wade

attended

Word: Advanced

between

24 Jun 2025

&

25 Jun 2025

360 Minute course

The learning objectives were to:

- Create automatic numbering for headings
- Produce and format a table of contents, an index and a list of figures
- Manage cross references, footnotes & endnotes, headers & footers and page numbers
- Control your sections and section breaks for page layout, columns, orientation
- Design and build templates
- Assemble a set of chapters into a book
- Navigate, control and re-structure a large document

This certificate does not imply any specific competence

Digital Skills Manager,
IT Learning Centre

IT Learning Centre

Certificate of Attendance

Tansy Wade

attended

Large group and lecturing ONLINE

between

11 Mar 2024
&
14 Mar 2024

16 Hour course

The learning objectives were to:

- Plan lectures that promote learning and critical thinking
- Diagnose problems with lectures
- Engage students in active learning during a lecture
- Ask brilliant questions that engage students
- Develop the students ability to think critically

This certificate does not imply any specific competence

MEDICALSCIENCES
Skills Training

Dissemination training



Certificate of Attendance

Tansy Wade

attended

Posters: Improving your research posters

on

07 Dec 2020

120 Minute

The learning objectives were to:

- Identify the common mistakes made in poster design
- Create a layout for your poster
- The effective use of colour
- Sourcing and selecting images of suitable quality
- Making your text readable
- The poster design process

This certificate does not imply any specific competence

Emma Procter-Legg

Digital Skills Manager,
Digital Capabilities Team

iT services

UNIVERSITY OF OXFORD

Digital Capabilities Team

Appendix Chapter 3

Appendix 3.1 Search strategy (Ovid Medline)

Search date 10 January 2019

Ovid Technologies, Inc. Email Service

Search for: from 10 [8 and 9] keep 1,3,6-9
Results: 6
Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily
and Ovid MEDLINE®) 1946 to present
Search Strategy:
---
1 Anti-Bacterial Agents/ (307918)
2 antibiotic*.ti,ab. (301852)
3 1 or 2 (477134)
4 "quality of health care"/ or guideline adherence/ (96348)
5 Practice Patterns, Physicians'/ (53977)
6 Drug Prescriptions/ (26046)
7 4 or 5 or 6 (165662)
8 3 and 7 (7201)
9 (Montserrat or dominica or guyana or antigua or barbuda or st kitts or st vincent or bahamas or barbados or
trinidad or grenada or suriname or belize or jamaica or haiti).mp. [mp=title, abstract, original title, name of
substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept
word, rare disease supplementary concept word, unique identifier, synonyms] (16533)
10 8 and 9 (9)
11 from 10 keep 1,3,6-9 (6)

Appendix 3.2 Studies excluded following full article review (By order of study ID)

Study ID	Reason for exclusion
Ali 2004	Outcomes do not fit inclusion criteria
Allen 1992	Population does not fit inclusion criteria
Bell 2005	Outcomes do not fit inclusion criteria
Boulos 2017	Outcomes do not fit inclusion criteria
Cawich 2013	Outcomes do not fit inclusion criteria
Christie 1988	Outcomes do not fit inclusion criteria
Christie 1992	Outcomes do not fit inclusion criteria
Deshommes 2020	Outcomes do not fit inclusion criteria
Desinor 2004	Population do not fit inclusion criteria
Foster 2010	Outcomes do not fit inclusion criteria
Gossell-Williams 2007	Outcomes do not fit inclusion criteria
Guerrier 2016	Outcomes do not fit inclusion criteria
Kane 1992	Study type does not fit inclusion criteria
Kaseje 2018	Population does not fit inclusion criteria
Mohan 2004	Setting does not fit inclusion criteria
Mungrue 2009	Setting does not fit inclusion criteria
Nicholson 2009	Outcomes do not fit inclusion criteria
Nicholson 2016	Outcomes do not fit inclusion criteria
Orrett 1998	Outcomes do not fit inclusion criteria
Orrett 2001	Outcomes do not fit inclusion criteria
Orrett 2002	Outcomes do not fit inclusion criteria
Orrett 2007	Outcomes do not fit inclusion criteria
Ostan 2017	Population/setting does not fit inclusion criteria
O'Shea 2004	Outcomes do not fit inclusion criteria
Prabhakar 1983	Outcomes do not fit inclusion criteria
Prabhakar 1985	Outcomes do not fit inclusion criteria
Tennant 2005	Outcomes do not fit inclusion criteria
Timmins 2018	Outcomes do not fit inclusion criteria
Trotman 2006	Population does not fit inclusion criteria

Vaz 2010	Outcomes do not fit inclusion criteria
Walsh 2015	Population/setting does not fit inclusion criteria
Watson 2014	Outcomes do not fit inclusion criteria

Studies excluded prior to full article review (By order of study ID)

Study ID	Reason for exclusion
Bain 1994	Full text unavailable
Denny 1984	Full text unavailable
Francois 2019	Full text unavailable
Gardiner 1985	Full text unavailable
Hunt 2016	Full text unavailable
Nagassar 2017	Full text unavailable
St. John 1990	Full text unavailable
Riche 2016	Full text unavailable

Appendix 3.3 Mixed Methods Appraisal Tool[133]

Part I: Mixed Methods Appraisal Tool (MMAT), version 2018

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?				
	S2. Do the collected data allow to address the research questions?				
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?				
	4.2. Is the sample representative of the target population?				
	4.3. Are the measurements appropriate?				
	4.4. Is the risk of nonresponse bias low?				
	4.5. Is the statistical analysis appropriate to answer the research question?				
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Appendix 3.4 Data extraction tool for mixed-methods systematic review

Study ID (Year)	Link	Aim	Setting	Country	Duration of study	Study design	Inclusion criteria	Measurement tools	Reported outcomes/findings					Main conclusions
									1	2	3	4	5	
Martin 2006														

Appendix 3.5 Code book

Code	Definition	Purpose or meaning of code	Example
Data Integrity	Researchers describe their experience or findings in relation to data.	Identify instances where the quality, quantity and dissemination of data were substandard. Was anything affected by the data?	*Catheter use during surgical procedures may also be underreported in this review because of failure to document it in the patients records.*
Education, training, knowledge and perceptions	Researchers describe what was uncovered about people's knowledge and perception vis-à-vis HAI and the prescribing of antibiotics.	Identify instances where knowledge was lacking, and perceptions were skewed. Identify instances where education and training may have had ramifications on preventing HAI and improving the prescribing of antibiotics.	*'However, it is important to note that due to insufficient information retention, knowledge and adherence to taught practice may still be deficient in spite of training and education.''*
Hospital practices	Researchers describe the different hospital practices they observed or those reported by respondents.	Identify situations where hospital practices may deviate from protocol.	*'Gloves were consistently used except when doing venepuncture or performing intravenous (IV) access insertion''*
Resources	Researcher describes different types of resources that are needed at the hospitals	Identify instances where the lack of resources could have negative impacts on improving the prescribing of antibiotics and the prevention of HAI.	*'Staff often are frustrated by inadequate supplies of paper towels, delays in obtaining handwashing soaps, and the common use of bed linens to dry hands.* ''

Appendix Chapter 4

Appendix: 4.1 Modified initial search strategy

CINAHL (search date 24th March 2021)

Antimicrobial stewardship

TI (antibiotic prescribing or antimicrobial stewardship or antibiotic stewardship) AND TI (interventions or strategies or best practices) (95 retrieved)

Cochrane Library (search date 24th March 2021)

Antimicrobial stewardship

antimicrobial stewardship OR antibiotic stewardship or antibiotic prescribing in Title Abstract Keyword AND interventions or programs or strategies or best practices in Title Abstract Keyword (51 retrieved)

JBI Evidence Synthesis (search date 24th March 2021; seven results)

Showing four results for: *2. (antibiotics or antimicrobial and antibacterial) and (surveillance or monitoring) and hospital*

Showing five results for: *antimicrobial stewardship" AND hospital*

Appendix 4.2 Final search strategy

MEDLINE via Ovid (Search Date 30th May 2021; 116 (based on https://bestpractice.bmj.com/info/toolkit/learn-ebm/study-design-search-filters/)

1. exp Cross Infection/ and hospital*.mp.

2. ((nosocomial or healthcare-associated or healthcare associated or health-care acquired or healthcare acquired or hospital-acquired or hospital-associated) adj5 infection*).ti,ab,kw.

3. (("infection prevention and control" or infection control) and hospital*).ti,ab,kw.

4. hospital*.ti.

5. 1 or 2 or 3 or 4

6. Antimicrobial Stewardship/

7. ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj steward*).ti,ab,kw.

8. 6 or 7

9. Anti-Bacterial Agents/

10. (antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*).ti.

11. 9 or 10

12. Public Health Surveillance/ or Behavioral Risk Factor Surveillance System/ or Population Surveillance/ or Sentinel Surveillance/

13. (surveillance or monitoring or audit*).ti,ab,kw.

14. 12 or 13

15. 11 and 14

16. ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj5 (surveillance or monitoring or audit)).ti,ab,kw.

17. 8 or 15 or 16

18. education, professional/ or mentoring/

19. exp Inservice Training/

20. Reminder Systems/

21. Decision Support Systems, Clinical/

22. practice guideline/

23. (educat* or train* or mentor* or workshop? or seminar? or learn* or "audit and feedback").ti,ab,kw.

24. (reminder* or prompt* or decision support*).ti,ab,kw.

25. (campaign? or meeting? or outreach or promot*).ti,ab,kw.

26. (guideline? or guidance or protocol? or strateg* or initiative? or program* or framework?).ti,ab,kw.

27. intervention?.ti,ab,kw.

28. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27

29. 5 and 17 and 28

30. limit 29 to "systematic review"

31. ((systematic or scoping) and (review or overview)).ti.

32. 29 and 31

33. 30 or 32

34. limit 33 to yr="2010 -Current"

35. review.pt.

36. (medline or medlars or embase or pubmed or cochrane).tw,sh.

37. (scisearch or psychinfo or psycinfo).tw,sh.

38. (psychlit or psyclit).tw,sh.

39. cinahl.tw,sh.

40. ((hand adj2 search$) or (manual$ adj2 search$)).tw,sh.

41. (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.

42. (pooling or pooled or mantel haenszel).tw,sh.

43. (peto or dersimonian or der simonian or fixed effect).tw,sh.

44. (retraction of publication or retracted publication).pt.

45. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44

46. 35 and 45

47. systematic review.pt.

48. meta-analysis.pt.

49. meta-analysis.sh.

50. (meta-analys$ or meta analys$ or metaanalys$).tw,sh.

51. (systematic$ adj5 review$).tw,sh.

52. (systematic$ adj5 overview$).tw,sh.

53. (quantitativ$ adj5 review$).tw,sh.

54. (quantitativ$ adj5 overview$).tw,sh.

55. (quantitativ$ adj5 synthesis$).tw,sh.

56. (methodologic$ adj5 review$).tw,sh.

57. (methodologic$ adj5 overview$).tw,sh.

58. (integrative research review$ or research integration).tw.

59. (scoping adj5 (review$ or overview$)).tw.

60. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59

61. 29 and 60

Other searches

Google Scholar (search date 25th May 2021)

1.antimicrobial stewardship OR antibiotic stewardship or antibiotic prescribing AND interventions or program or strategies or best practice or policy or protocol or guideline or control or surveillance (30 pages screened)

2.(antibiotics OR antimicrobials AND antibacterials) AND (surveillance OR monitoring) AND hospital AND ("scoping review" OR systematic review" OR overview) (10 pages screened)

Cochrane Database of Systematic Reviews (search date 25th May 2021; 100 results)

100 Cochrane Reviews matching antimicrobial stewardship OR antibiotic stewardship or antibiotic prescribing in Title Abstract Keyword AND interventions or program or strategies or best practice or policy or protocol or guideline or control or surveillance in Title Abstract Keyword - (Word variations have been searched)

Cochrane Database of Systematic Reviews

Reference lists of included reviews and retrieved scoping reviews were searched for additional systematic reviews

Updated search using final search strategy

22nd August 2021

Based on https://bestpractice.bmj.com/info/toolkit/learn-ebm/study-design-search-filters/

Search for: 29 and 60
Results: 119

Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present
Search Strategy:
---
1 exp Cross Infection/ and hospital*.mp. (35795)
2 ((nosocomial or healthcare-associated or healthcare associated or health-care acquired or healthcare acquired or hospital-acquired or hospital-associated) adj5 infection*).ti,ab,kw. (27498)
3 (("infection prevention and control" or infection control) and hospital*).ti,ab,kw. (10863)
4 hospital*.ti. (341435)
5 1 or 2 or 3 or 4 (382059)
6 Antimicrobial Stewardship/ (2359)
7 ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj steward*).ti,ab,kw. (6330)
8 6 or 7 (6956)
9 Anti-Bacterial Agents/ (358261)
10 (antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*).ti. (200477)
11 9 or 10 (434809)
12 Public Health Surveillance/ or Behavioral Risk Factor Surveillance System/ or Population Surveillance/ or Sentinel Surveillance/ (74404)
13 (surveillance or monitoring or audit*).ti,ab,kw. (867280)
14 12 or 13 (908246)
15 11 and 14 (19512)
16 ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj5 (surveillance or monitoring or audit)).ti,ab,kw. (6530)

17 8 or 15 or 16 (26641)
18 education, professional/ or mentoring/ (5599)
19 exp Inservice Training/ (29697)
20 Reminder Systems/ (3660)
21 Decision Support Systems, Clinical/ (8646)
22 practice guideline/ (28986)
23 (educat* or train* or mentor* or workshop? or seminar? or learn* or "audit and feedback").ti,ab,kw. (1513179)
24 (reminder* or prompt* or decision support*).ti,ab,kw. (176909)
25 (campaign? or meeting? or outreach or promot*).ti,ab,kw. (1308091)
26 (guideline? or guidance or protocol? or strateg* or initiative? or program* or framework?).ti,ab,kw. (3185044)
27 intervention?.ti,ab,kw. (1060497)
28 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (5889629)
29 5 and 17 and 28 (3062)
30 limit 29 to "systematic review" (65)
31 ((systematic or scoping) and (review or overview)).ti. (172367)
32 29 and 31 (69)
33 30 or 32 (80)
34 limit 33 to yr="2010 -Current" (79)
35 review.pt. (2848107)
36 (medline or medlars or embase or pubmed or cochrane).tw,sh. (264684)
37 (scisearch or psychinfo or psycinfo).tw,sh. (44177)
38 (psychlit or psyclit).tw,sh. (916)
39 cinahl.tw,sh. (33578)
40 ((hand adj2 search$) or (manual$ adj2 search$)).tw,sh. (14506)
41 (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh. (45127)
42 (pooling or pooled or mantel haenszel).tw,sh. (121372)
43 (peto or dersimonian or der simonian or fixed effect).tw,sh. (8660)
44 (retraction of publication or retracted publication).pt. (19491)
45 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 (411087)
46 35 and 45 (175465)
47 systematic review.pt. (165924)
48 meta-analysis.pt. (140260)
49 meta-analysis.sh. (140260)
50 (meta-analys$ or meta analys$ or metaanalys$).tw,sh. (239713)
51 (systematic$ adj5 review$).tw,sh. (246324)
52 (systematic$ adj5 overview$).tw,sh. (2715)
53 (quantitativ$ adj5 review$).tw,sh. (8993)
54 (quantitativ$ adj5 overview$).tw,sh. (353)
55 (quantitativ$ adj5 synthesis$).tw,sh. (3530)
56 (methodologic$ adj5 review$).tw,sh. (7190)
57 (methodologic$ adj5 overview$).tw,sh. (478)
58 (integrative research review$ or research integration).tw. (154)
59 (scoping adj5 (review$ or overview$)).tw. (10512)
60 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 (457548)
61 29 and 60 (119)

Other searches

JBI Evidence Synthesis (search date 17th September 2021; nine results)

Showing 4 results for: *2. (antibiotics or antimicrobial and antibacterial) and (surveillance or monitoring) and hospital*

Showing 5 results for: *antimicrobial stewardship" AND hospital*

Cochrane Database of Systematic Reviews (search date 17th September 2021; 102 results)

102 Cochrane Reviews matching antimicrobial stewardship OR antibiotic stewardship or antibiotic prescribing in Title Abstract Keyword AND interventions or program or strategies or best practice or policy or protocol or guideline or control or surveillance in Title Abstract Keyword - (Word variations have been searched)

Cochrane Database of Systematic Reviews

Issue 9 of 12, September 2021

Ovid Technologies, Inc. Email Service 27th May 2022

Search for: 29 and 60

Results: 134

Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present
Search strategy:
---
1 exp Cross Infection/ and hospital*.mp. (36809)
2 ((nosocomial or healthcare-associated or healthcare associated or health-care acquired or healthcare acquired or hospital-acquired or hospital-associated) adj5 infection*).ti,ab,kw. (28969)
3 (("infection prevention and control" or infection control) and hospital*).ti,ab,kw. (11644)
4 hospital*.ti. (357103)
5 1 or 2 or 3 or 4 (399558)
6 Antimicrobial Stewardship/ (2967)
7 ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj steward*).ti,ab,kw. (7219)
8 6 or 7 (7938)
9 Anti-Bacterial Agents/ (377232)
10 (antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*).ti. (212036)
11 9 or 10 (456669)
12 Public Health Surveillance/ or Behavioral Risk Factor Surveillance System/ or Population Surveillance/ or Sentinel Surveillance/ (76141)
13 (surveillance or monitoring or audit*).ti,ab,kw. (919204)
14 12 or 13 (961032)
15 11 and 14 (21157)
16 ((antimicrobial* or anti-microbial* or antibiotic* or anti-biotic* or antibacterial* or anti-bacterial*) adj5 (surveillance or monitoring or audit)).ti,ab,kw. (7116)
17 8 or 15 or 16 (29174)
18 education, professional/ or mentoring/ (6291)
19 exp Inservice Training/ (29907)
20 Reminder Systems/ (3742)
21 Decision Support Systems, Clinical/ (9077)

22 practice guideline/ (29856)
23 (educat* or train* or mentor* or workshop? or seminar? or learn* or "audit and feedback").ti,ab,kw. (1624519)
24 (reminder* or prompt* or decision support*).ti,ab,kw. (187686)
25 (campaign? or meeting? or outreach or promot*).ti,ab,kw. (1399260)
26 (guideline? or guidance or protocol? or strateg* or initiative? or program* or framework?).ti,ab,kw. (3418418)
27 intervention?.ti,ab,kw. (1139012)
28 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (6296178)
29 5 and 17 and 28 (3362)
30 limit 29 to "systematic review" (78)
31 ((systematic or scoping) and (review or overview)).ti. (200964)
32 29 and 31 (80)
33 30 or 32 (92)
34 limit 33 to yr="2010 -Current" (91)
35 review.pt. (2989677)
36 (medline or medlars or embase or pubmed or cochrane).tw,sh. (294953)
37 (scisearch or psychinfo or psycinfo).tw,sh. (50492)
38 (psychlit or psyclit).tw,sh. (918)
39 cinahl.tw,sh. (37877)
40 ((hand adj2 search$) or (manual$ adj2 search$)).tw,sh. (15484)
41 (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh. (50361)
42 (pooling or pooled or mantel haenszel).tw,sh. (131675)
43 (peto or dersimonian or der simonian or fixed effect).tw,sh. (9457)
44 (retraction of publication or retracted publication).pt. (22522)
45 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 (455105)
46 35 and 45 (192523)
47 systematic review.pt. (197039)
48 meta-analysis.pt. (161003)
49 meta-analysis.sh. (161003)
50 (meta-analys$ or meta analys$ or metaanalys$).tw,sh. (264854)
51 (systematic$ adj5 review$).tw,sh. (278898)
52 (systematic$ adj5 overview$).tw,sh. (3073)
53 (quantitativ$ adj5 review$).tw,sh. (9662)
54 (quantitativ$ adj5 overview$).tw,sh. (383)
55 (quantitativ$ adj5 synthesis$).tw,sh. (3911)
56 (methodologic$ adj5 review$).tw,sh. (7752)
57 (methodologic$ adj5 overview$).tw,sh. (511)
58 (integrative research review$ or research integration).tw. (161)
59 (scoping adj5 (review$ or overview$)).tw. (14451)
60 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 (508208)
61 29 and 60 (134)

JBI Evidence Synthesis (search date 27th May 2022; 11 results)

Showing 4 results for: *(antibiotics or antimicrobial and antibacterial) and (surveillance or monitoring) and hospital*

Showing 7 results for: *antimicrobial stewardship AND hospital*

Cochrane Database of Systematic Reviews (search date 27th May 2021; 103 results)

103 Cochrane Reviews matching antimicrobial stewardship OR antibiotic stewardship or antibiotic prescribing in Title Abstract Keyword AND interventions or program or strategies or best practice or policy or protocol or guideline or control or surveillance in Title Abstract Keyword - (Word variations have been searched)

Cochrane Database of Systematic Reviews

Issue 5 of 12, May 2022

Appendix 4.3 Amstar tool

Table 2: AMSTAR is a measurement tool created to assess the methodological quality of systematic reviews.

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable

Appendix 4.4 List of excluded studies after full-text-review (By order of study ID)

Study ID	Reason for exclusion
de Melo 2020	Evidence source does not fit inclusion criteria
Fanelli 2020	Evidence source does not fit inclusion criteria
Feazel 2014	Broad summary of findings
Honda 2017	Broad summary of findings
Huebner 2019	Did not evaluate AMS interventions
Hulscher 2017	Evidence source does not fit inclusion criteria
Lee 2018	Outpatient/long-term care setting
Martinez-Sobalvarro	Broad summary of findings
Mas-Morey 2018	Broad findings
Nathwani 2019	Broad summary of findings
O'Riordan 2021	Microbiological outcome
Paul 2016	Broad summary of findings
Ramsay	Did not evaluate AMS interventions
Saha 2019	Outpatient/long-term care setting
Schuts 2016	Outpatient/long-term care setting
Schweitzer 2019	Did not evaluate AMS interventions
Shirazi 2020	Evidence source does not fit inclusion criteria

Appendix 4.5 Detailed quality appraisal of systematic reviews using AMSTAR Tool

AMSTAR Items	Akpan et al 2020	Araujo et al 2020	Araujo 2017	Baur 2017	Bertollo 2018	Charani 2011	Davey et al., 2017	Kaki 2011	Karanika 2016	Lindsay 2018	Monmaturapoj 2021	Mijovic 2018	Nasr 2016	Pitiriga 2017	Roque 2014	Smith 2015	Van Dijck et al, 2018	Wagner 2014
Was an 'a priori' design provided?	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1	0
Was there duplicate study selection and data extraction?	0	0	1	1	0	1	1	1	1	1	1	1	0	0	0	0	1	CA
Was a comprehensive literature search performed?	1	0	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0
Was the status of publication (i.e. grey literature) used as an inclusion criterion?	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Was a list of studies (included and excluded) provided?	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Were the characteristics of the included studies provided?	1	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	1	1
Was the scientific quality of the included studies assessed and documented?	0	1	0	1	0	0	1	0	1	*0*	*1*	*0*	0	0	0	0	1	1
Was the scientific quality of the included studies used appropriately in formulating conclusions?	0	0	0	0	0	0	1	0	1	0	1	0	0	0	0	0	1	1
Were the methods used to combine the findings of studies appropriate?	NA	NA	NA	1	NA	NA	1	NA	1	1	NA	NA	NA	NA	NA	NA	NA	NA
Was the likelihood of publication bias assessed?	NA	NA	NA	1	NA	NA	0	NA	1	1	NA	NA	NA	NA	NA	NA	NA	NA
Was the conflict of interest included?	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Total score	2	2	2	8	2	3	10	2	7	5	6	3	1	1	1	2	6	3

NA, not applicable; CA, can't answer.

Appendix 4.6 Impact of antimicrobial stewardship interventions

Commonly reported interventions (EPOC Taxonomy)	Definitions (EPOC Taxonomy)	Evidence of effectiveness	Evidence of unintended consequences
Audit and feedback	A summary of health workers' performance over a specified period of time, given to them in a written, electronic or verbal format. The summary may include recommendations for clinical action.	Reduced rate of inappropriate antimicrobial use. Reduced duration of inappropriate antibiotic use. Decreased total antibiotic use. Reduced use of broad-spectrum antibiotics. Improved rate of appropriate antibiotic use. IV -antimicrobial use switched on the appropriate day. Decrease in the hospital length of stay. Reduced risk for C.difficile infection Reduction in the number of defined daily doses of antibiotics / 100 days of hospitalization Decrease in the overall antimicrobial cost. Reduced time to antimicrobial therapy modification. Reduced duration of IV use. Reduced use of audited and evaluated antimicrobials Improved compliance with hang time (time elapsed between intravenous antibiotic order and actual administration). Increased compliance with guidelines. Enhanced therapy due to early detection of errors. Increased appropriate discontinuation of antibiotic therapy. Increased compliance with ASP recommendations Improved appropriate initial use,	Increase in antibiotic use.
Clinical Practice Guidelines*	Clinical guidelines are systematically developed statements to assist healthcare providers and patients to decide on appropriate health care for specific clinical circumstances'(US IOM)	Reduced incidence of HCAI infection. Reduced use of targeted broad-spectrum antibiotics Reduced antibiotic consumption DDD/1000/100 Reduced antibiotic cost Increase use of targeted narrow-spectrum antibiotics Reduced antibiotic use Increased appropriate first-line therapy. Increased use of surgical prophylaxis for caesarean section Decrease in incorrect timing of surgical antibiotic prophylaxis Improved initiation of antimicrobial use within 8 hours of presentation	Increase in antibiotic use. Increased mortality rate in ICU intervention group.

Commonly reported interventions (EPOC Taxonomy)	Definitions (EPOC Taxonomy)	Evidence of effectiveness	Evidence of unintended consequences
		Reduced treatment duration Reduced length of stay No increase in attributable morbidity or mortality after guideline implementation Reduced percentage of treatment failure	
Continuous quality improvement	An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem-solving approach, and use of data analysis to assess changes.	Improved use of appropriate first-line therapy Reduced IV antibiotics Reduced nursing time Reduction in cost of intravenous antibiotics Improved adherence to clinical practice guidelines. Decreased antimicrobial consumption	None reported
Educational materials	Distribution to individuals, or groups, of educational materials to support clinical care, i.e., any intervention in which knowledge is distributed.	Decreased antibiotic use Reduced antibiotic cost per patient	Increase in antibiotic use
Educational meetings *	Courses, workshops, conferences, or other educational meetings	Reduced antibiotic use Reduced MRSA bacteraemia Reduced MRSA colonization Increased appropriate antimicrobial therapy for pneumonia and diarrhoea	Decreased number of women receiving surgical antibiotic prophylaxis before a c-section.
Educational outreach visits, or academic detailing.	Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice.	Reduced antibiotic use Decreased duration of IV antibiotics Increased percentage of days of adequate antibiotic treatment Reduced duration of therapy Reduction in dosing. Increase inappropriate IV to oral switch. Reduced inappropriate antibiotic use Reduced targeted antibiotic use. Reduced IV antibiotic use Increased compliance with ASP programmes Reduced length of stay Reduced mortality rate Decreased CDI rate Reduced IV DOT	Increase in prophylactic antibiotic use for < 24 hours Increase in dose-related prescription errors during the first year of the ASP program Increase length of stay Increased mortality

Commonly reported interventions (EPOC Taxonomy)	Definitions (EPOC Taxonomy)	Evidence of effectiveness	Evidence of unintended consequences
		Reduced rate of multi-drug resistant infections Reduced DOT for restricted antimicrobials	
Reminders	Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems.	Reduced inappropriate dosing Increased appropriate administration of surgical prophylaxis Decreased days of IV therapy Reduced duration of treatment	None reported

Appendix Chapter 5

Appendix 5.1 IRB Approval Letter



MSJMC
MOUNT ST. JOHN'S MEDICAL CENTRE

Tuesday 8th March 2022

Mrs. Tansy Wade MPH
DPhil Candidate
c/o University of Oxford
United Kingdom

Mrs. Wade,

Thank you for submitting a proposal for review and consideration for approval by the Sir Lester Bird Medical Centre's Institutional Review Board titled *"Using an evidence-based approach to develop a complex intervention to reduce the duration of prophylactic antibiotic use in caesarean section patients."*

After careful review of your submission, the board recognizes that the proposal is a multi-phased design including a:

1. Quantitative study of existing datasets
2. Qualitative study of clinicians' perspectives
3. Feasibility study of an intervention for reducing the duration of prophylactic antibiotics in c-section patients.

As such, no IRB approval is required for items 1 and 3 since they include retrospective chart reviews. However, for item 2, the protocol with interview topic guide should be submitted to the IRB prior to the start of the project.

If any changes are made to the original proposal where applicable, written updates must be emailed to the irb@msjmc.org

We wish you all the best and please do not hesitate to contact the board for any further clarifications.

Regards,

Albert Duncan MD, F.A.C.S
Medical Director

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Appendix 5.2 WHO ATC Classification -WHO Access, Watch, Reserve (AWaRe) classification of antibiotics [165]

Antibiotic	Class	ATC code	Category	EML 2023
Amikacin	Aminoglycosides	J01GB06	Access	Yes
Amoxicillin	Penicillins	J01CA04	Access	Yes
Amoxicillin/clavulanic-acid	Beta-lactam/beta-lactamase-inhibitor	J01CR02	Access	Yes
Ampicillin	Penicillins	J01CA01	Access	Yes
Azithromycin	Macrolides	J01FA10	Watch	Yes
Benzathine-benzylpenicillin	Penicillins	J01CE08	Access	Yes
Benzylpenicillin	Penicillins	J01CE01	Access	Yes
Cefalexin	First-generation-cephalosporins	J01DB01	Access	Yes
Cefazolin	First-generation-cephalosporins	J01DB04	Access	Yes
Cefiderocol	Other-cephalosporins	J01DI04	Reserve	Yes
Cefixime	Third-generation-cephalosporins	J01DD08	Watch	Yes
Cefotaxime	Third-generation-cephalosporins	J01DD01	Watch	Yes
Ceftazidime	Third-generation-cephalosporins	J01DD02	Watch	Yes
Ceftazidime/avibactam	Third-generation-cephalosporins	J01DD52	Reserve	Yes
Ceftolozane/tazobactam	Fifth-generation cephalosporins	J01DI54	Reserve	Yes
Ceftriaxone	Third-generation-cephalosporins	J01DD04	Watch	Yes
Cefuroxime	Second-generation-cephalosporins	J01DC02	Watch	Yes
Chloramphenicol	Amphenicols	J01BA01	Access	Yes
Ciprofloxacin	Fluoroquinolones	J01MA02	Watch	Yes
Clarithromycin	Macrolides	J01FA09	Watch	Yes
Clindamycin	Lincosamides	J01FF01	Access	Yes
Cloxacillin	Penicillins	J01CF02	Access	Yes
Colistin_IV	Polymyxins	J01XB01	Reserve	Yes
Dicloxacillin	Penicillins	J01CF01	Access	Yes (therapeutic
Doxycycline	Tetracyclines	J01AA02	Access	Yes
Flucloxacillin	Penicillins	J01CF05	Access	Yes (therapeutic
Fosfomycin_IV	Phosphonics	J01XX01	Reserve	Yes
Gentamicin	Aminoglycosides	J01GB03	Access	Yes
Imipenem/cilastatin	Carbapenems	J01DH51	Watch	Yes (therapeutic
Linezolid	Oxazolidinones	J01XX08	Reserve	Yes
Meropenem	Carbapenems	J01DH02	Watch	Yes
Meropenem/vaborbactam	Carbapenems	J01DH52	Reserve	Yes
Meticillin	Penicillins	J01CF03	Access	Yes (therapeutic
Metronidazole_IV	Imidazoles	J01XD01	Access	Yes
Metronidazole_oral	Imidazoles	P01AB01	Access	Yes
Nafcillin	Penicillins	J01CF06	Access	Yes (therapeutic
Nitrofurantoin	Nitrofuran-derivatives	J01XE01	Access	Yes
Oxacillin	Penicillins	J01CF04	Access	Yes (therapeutic
Phenoxymethylpenicillin	Penicillins	J01CE02	Access	Yes
Piperacillin/tazobactam	Beta-lactam/beta-lactamase-inhibitor_anti-pseudomonal	J01CR05	Watch	Yes
Plazomicin	Aminoglycosides	J01GB14	Reserve	Yes
Polymyxin-B_IV	Polymyxins	J01XB02	Reserve	Yes
Procaine-benzylpenicillin	Penicillins	J01CE09	Access	Yes
Spectinomycin	Aminocyclitols	J01XX04	Access	Yes
Sulfamethoxazole/trimethoprim	Sulfonamide-trimethoprim-combinations	J01EE01	Access	Yes
Tosufloxacin	Fluoroquinolones	J01MA22	Watch	No
Tedizolid	Oxazolidinones	J01XX11	Reserve	Yes (therapeutic
Vancomycin_IV	Glycopeptides	J01XA01	Watch	Yes
Vancomycin_oral	Glycopeptides	A07AA09	Watch	Yes

Form to Record Antimicrobial Treatments

Name of unit: _____ Data collector: _____ Date: _____

Patient Information				Antimicrobial Information												
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Clinical History No.	Pneumonia Case? (Y/N)	Was Antimicrobial Prescribed? (Y/N)	No. of Days in Hospital	Was Sensitivity Test Done? (Y/N)	Name(s) of Antimicrobial(s) Prescribed	INN Used? (Y/N)	Antimicrobial on FL? (Y/N)	Dosage Form and Strength	Total Days of Treatment *	No. Antimicrobials of Same Generic Type Prescribed	Dosage Frequency per Day	Doses Prescribed	Doses Administered	Unit Cost of Dose	Cost of Prescribed Treatment	Cost of Administered Treatment
Total Cases	Total Ys	Total Ys	Total Days	Total Ys	Total	Total Ys	Total Ys	___	Total Days	Total Generics	___	Total Doses	Total Doses	___	Total Cost	Total Cost

[Instrument 2 is used to collect information for Indicators 6, 7, 8, 9, 10, 13, 14, 15, 16, and 17.]
Notes: No. = number, Y = Yes, N = No, INN = international nonproprietary name, FL = formulary list, * = TB treatment provided by central Ministry of Health program
*Total days of treatment includes inpatient treatment days and if treatment is not completed includes the number of days antimicrobials were prescribed at discharge.

Appendix 5.4 Distribution of systemic antibiotics by inpatient unit and ATC classification in Antigua and Barbuda. 2014-2021

Antibiotic	Maternity	Medical	Surgical	Grand Total
J01A Tetracyclines	**0**	**18**	**9**	**27**
Doxycycline	0	18	9	27
J01C Beta-lactam antibacterials, penicillins	**196**	**1375**	**2383**	**3954**
Amoxicillin	42	29	75	146
Amoxicillin/clavulanicacid	56	1064	1867	2987
Ampicillin	83	70	153	306
Cloxacillin	3	36	26	65
PenicillinG	12	40	202	254
Piperacillin/Tazobactam	0	136	60	196
J01D Other Beta-lactam antibacterials	**1412**	**5131**	**4794**	**11337**
Cefalexin	2	0	7	9
Cefazolin	50	93	201	344
Cefotaxime	53	144	121	318
Ceftazidime	30	1004	804	1838
Ceftriaxone	80	2713	1258	4051
Cefuroxime	1194	763	1860	3817
Imipenem	0	132	205	337
Meropenem	3	282	338	623
J01E Sulfonamides and Trimethoprim	**1**	**61**	**37**	**99**
Sulfamethoxazole/trimethoprim	1	61	37	99
J01F Macrolides, Lincosamides, Streptogramins	**121**	**1188**	**89**	**1398**
Azithromycin	31	1104	30	1165
Clarithromycin	0	15	8	23
Clindamycin	1	32	22	55
Erythromycin	89	37	29	155
J01G Aminoglycoside antibacterials	**125**	**215**	**925**	**1265**
Amikacin	0	37	50	87
Gentamicin	125	178	875	1178
J01M Quinolone antibacterials	**1**	**1257**	**1313**	**2571**
Ciprofloxacin	1	1206	1305	2512
Levofloxacin	0	50	5	55
Norfloxacin	0	1	3	4
J01X Other antibacterials	**979**	**1311**	**4735**	**7025**
Metronidazole	978	1140	4591	6709
Vancomycin	1	171	144	316
Grand Total	**2835**	**10556**	**14285**	**27676**

Appendix Chapter 6

Appendix 6.1 Form to Record Cesarean Section Surgical Prophylaxis

Form to Record Cesarean Section Surgical Prophylaxis

Name of unit: _____ Data collector: _____ Date: _____

1	2	3	4	5	6
CH No.	Surgical Procedure	Prophylaxis (Y/N)	Surgical Antimicrobial Prophylaxis for Cesarean Section in Accordance with Hospital Guidelines (Y/N)	Antimicrobial Prescribed (Name, Dosage Form, and Strength)	Number of Doses

[Instrument 3 is used to collect information for Indicators 11 and 12.]

Instructions:

1. Record in column 1 the number of each clinical history (CH) for which a cesarean section surgical procedure was performed.
2. Enter in column 2 the name of the surgical procedure.
3. Verify carefully whether antimicrobial prophylaxis was prescribed and enter *Y* or *N* in column 3.
4. Determine if antimicrobial prophylaxis for cesarean section is in accordance with hospital guidelines.
5. Record which antimicrobials were prescribed (name, form, and strength) in column 4.

Appendix Chapter 7

Appendix 7.1



MSJMC

MOUNT ST. JOHN'S MEDICAL CENTRE

Monday 29th January 2024

Mrs. Tansy Wade MPH
DPhil Candidate
c/o University of Oxford
United Kingdom

Mrs. Wade,

Thank you for submitting the proposal for the qualitative study focusing on factors influencing the use of surgical antibiotic prophylaxis for c-section patients.

After careful review of your submission, the board grants ethical approval. If any changes are made to the original proposal where applicable, written updates must be emailed to the irb@msjmc.org

We wish you all the best and please do not hesitate to contact the board for any further clarifications.

Regards,

Albert Duncan MD, F.A.C.S
Medical Director

Appendix 7.2 Vignettes

Vignette 1

Patient A decides with the Obstetrics/ Gynaecology Consultant that, due to 2 previous breech presentations during labour, she will deliver her third child via c-section. In your capacity, detail how you would prepare/manage this patient when she is admitted for surgery?

Vignette 2

Patient A has now successfully delivered via c-section. How would you manage this patient post-surgery while she is admitted to the Maternity Unit?

Appendix 7.3 Topic guide

COM-B based interview prompts if not addressed in main question

1.Capability

Psychological capability

Understanding why surgical antibiotic prophylaxis is important in c-section? What antibiotics can/cannot treat?

- What are the most important steps for you during preop/postop management?
- Why do you prescribe antibiotics for c-section patients?
- How has your medical education prepared you for the prescribing of surgical prophylaxis for c-section patients?

Use of/ awareness of guidelines for antibiotic prescribing?

- How do you decide on which antibiotic to prescribe and the duration of use? Are there any concerns in the hospital setting that contribute to decision-making around the duration of use?
- Are there local guidelines/policies available for prescribing prophylactic antibiotics for c-section patients? / Are there guidelines available on the administration of antibiotics to patients?
- How do you view the use of standard guidelines for prescribing surgical antibiotic prophylaxis for c-section patients in the Maternity Unit?

Challenges in prescribing

Are you aware of Local AMR Rates?

Physical capability

Any additional skills that would enhance your prescribing practices?

- Is there any type of feedback/training that could assist with decision-making around the use of prophylactic antibiotics?
- Are there any additional skills that the junior staff could acquire that would assist with prescribing prophylactic antibiotics?

2. Opportunity

Physical opportunity

Time available? Finances? Availability of diagnostic tests, different types of antibiotics?

- How would you describe your access to prophylactic antibiotics when they are needed?
- How would you describe your access to laboratory (susceptibility/diagnostic) testing?
- How would you describe your access to training on antibiotic use?

Social opportunity

Team working dynamics and communication? Influence of residents and their relatives, superiors other Healthcare professionals?

- How do your colleagues influence your prescribing behaviour, if at all?

- Are there any other departments in the hospital that support you when prescribing antibiotics? How do the pharmacists support you in your decision making?
- What do you think your peer's views on antimicrobial use and antimicrobial resistance are?
- Whose advice and opinion do you most respect around antimicrobial usage? And why?
- What are your experiences with client pressure and prescribing treatment plans?

3. Motivation

Consequences of prescribing vs not prescribing an antibiotic? Is promoting antimicrobial stewardship part of their role? Clinical competing priorities?

Automatic motivation

Concerns or fears around prescribing antibiotics or not?

- What do you think are the consequences of antimicrobial resistance? Do You discuss some aspects of this with your patients?
- Who do you feel is responsible for antimicrobial resistance?
- What do you think are the benefits associated with reducing antimicrobial use? Do you have access to peer support in relation to reducing antimicrobial use? Are there incentives to use antibiotics less?
- What do you think are the risks associated with reducing antimicrobial use?

Reflective motivation

- Do you know of antimicrobial stewardship activities being carried out at the hospital?
- Do you think engaging in antimicrobial stewardship activities at the hospital would make a difference to the threat of AMR?
- How do you view your professional responsibility towards the use of evidence-based guidelines for informing the use of surgical antibiotic prophylaxis?
- What do you think would be the best type of intervention (action) for improving the prescribing/administering of antibiotics for c-section patients? How can we best measure improvements following the intervention?

Appendix 7.4 Codebook

Name	Description	Files	References
Disconnect between knowledge and practice	Respondents discuss gaps between knowledge and decision-making in practice	2	2
Education to reduce patient pressure	Respondents discuss pressure from patients to either increase or reduce the use of antibiotics and how it is handled in the clinical setting.	10	12
Evidence as prerequisite for changing practice	Respondents discuss the need for evidence to change current prescribing behaviour.	3	5
Frustrations with interprofessional coordination	Respondents discuss challenges working and coordinatiing with members of other departments.	12	23
Consultant preference influences prescribing	Respondents discuss how prescribing decisions are made.	11	21
Improving decision making	Respondents discuss interventions that may help to enhace surgical antibiotic prophylaxis use	10	21
Intentions for evidence-based practice	Respondents provide statements which indicate an evidence-based rationale for prescribing.	12	22
Legacy prescribing practices	Respondents describe prescribing practices that are outdated and informed by recent evidence.	5	6
Peer influence on antibiotic prophylaxis prescribing	Respondents discuss their views on how their peers or other clinicians influence prescribing in the setting	3	3
Perceived best practice for surgical antibiotic prophylaxis	Respondents discuss how prescribing is done when a patient is admitted for a caesarean delivery.	12	17
Perceptions of antimicrobial resistance in the setting	Respondents discuss their thoughts on whether antimicrobial resistance is a challenge in the setting.	1	4
Prescribing according to patient circumstances	Respondents describe variations in prescribing due to patient circumstances.	7	9

Name	Description	Files	References
Automatic motivation	Automatic motivation involves emotions and impulses that arise from associative learning and/or innate dispositions	3	3
Physical capability	Physical capability-Physical skill, strength or stamina	2	3
Physical opportunity	Physical Opportunity afforded by the environment involving time, resources, locations, physical barriers.	13	33
Psychological capability	Psychological capability- the capacity to engage in the necessary thought processes- comprehension, reasoning etc Having the knowledge, psychological skills, strength or stamina to perform the behaviour.	13	29
Reflective Motivation	Reflective motivation - (involving self-conscious planning and evaluations (beliefs about what is good or bad)	15	46
Social opportunity	Social opportunity- afforded by the cultural milieu that dictates the way we think about things(e.g words and concepts that make up our language)	5	6

Appendix Chapter 8

Appendix 8.1 Scoping search – Ovid MEDLINE

	Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present	
1	exp Cesarean Section/	55667
2	c?esarean.ti,kf.	33648
3	1 or 2	62867
4	exp Anti-Bacterial Agents/	854837
5	(antibiotic? or anti-biotic? or antimicrobial? or anti-microbial? or antibacterial? or anti-bacterial?).ti,kf.	317682
6	Antibiotic Prophylaxis/	16159
7	((antibiotic? or anti-biotic? or antimicrobial? or anti-microbial? or antibacterial? or anti-bacterial?) adj5 (prescri* or administ* or prophyla*)).ab.	57302
8	4 or 5 or 6 or 7	993260
9	3 and 8	1871
10	guideline/ or practice guideline/	39860
11	9 and 10	13
12	3 and 10	163

13	systematic review.pt. or "Systematic Reviews as Topic"/ or ("Cochrane Database of Systematic Reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or (((((comprehensive or comprehensively) adj (analysis or review or reviewed)) or ((literature or scoping) adj (search or searches))).ti,ab,kf,kw. not "narrative review".ti.) and (database or databases or cinahl or cochrane or embase or psycinfo or pubmed or medline or scopus or (web adj1 science) or ((bibliographic or literature) adj (review or reviews)) or (((electronic adj (database or databases)) or (databases adj3 searched)) and (eligibility or excluded or exclusion or included or inclusion))).ti,ab,kf,kw.) or (((comparative adj effectiveness) and (effectiveness adj review)) or ((critical adj interpretive) and ((interpretive adj review) or (interpretive adj synthesis)))).ti,ab,kf,kw. or ((diagnostic adj test) and ((accuracy adj review) or (accuracy adj reviews) or (accuracy adj studies) or (accuracy adj study)) and (meta-analysis or scoping or systematic)).ti,ab,kf,kw. or ((evidence adj assessment) and GRADE).ti,ab,kf,kw. or ((evidence adj2 gap) and (gap adj map)).ti,ab,kf,kw. or ((evidence adj mapping) or (evidence adj review) or (exploratory adj review) or (framework adj synthesis) or (mapping adj review)).ti,ab,kf,kw. or ((meta adj (epidemiological or ethnographic or ethnography or interpretation or narrative or review or study or synthesis or summary or theory)) or metaethnographic or metaethnography or metasynthesis).ti,ab,kf,kw. or ((methodological or methodology) adj1 review).ti,ab,kf,kw. or ((mixed adj methods) and (methods adj1 (review or synthesis))).ti,ab,kf,kw. or ((narrative adj1 synthesis) or (overview adj4 reviews) or ("PRISMA" adj4 (guideline or guidelines or preferred or reporting or requirements)) or (PRISMA adj "P")).ti,ab,kf,kw. or (((prognostic or psychometric) adj1 review) or ((qualitative adj (evidence or research)) and ((evidence or research) adj synthesis))).ti,ab,kf,kw. or (((rapid adj evidence) and (evidence adj assessment)) or (rapid adj realist) or (rapid adj2 (review or reviews)) or (realist adj2 (review or reviews or syntheses or synthesis))).ti,ab,kf,kw. or (((review adj economic) and (economic adj1 (evaluation	648644

	or evaluations))) or ((scoping or systematic) adj2 (review or reviews or studies or study))).ti,ab,kf,kw. or ((review adj1 reviews) or ((systematic adj evidence) and (evidence adj map)) or (systematic adj2 mapping) or (systematic adj2 literature) or (systematic adj2 (Embase or Medline or PsycInfo or PubMed)) or (systematic adj2 (review or reviews)) or ((systematical or systematically) adj2 (review or reviewed reviews)) or (systematically adj identified) or (systematized adj review) or (umbrella adj (review or reviews))).ti,ab,kf,kw. or "Meta-Analysis".pt. or "meta-analysis as topic"/ or (meta adj2 (analyse or analyser or analyses or analysis or analytic or analytical or analytics or analyze or analyzed or analyzes)).ti,ab,kf,kw. or (metaanalyse or Metaanalysen or metaanalyser or metaanalyses or metaanalysis* or metaanalytic or metaanalytical or metaanalytics or metaanalyze or metaanalyzed or metaanalyzes).ti,ab,kf,kw. or "network meta-analysis"/ or (network adj1 (meta or metaanalyses or metaanalysis or metaregression)).ti,ab,kf,kw. or (systematic and ((meta adj regression) or metagression)).ti,ab,kf,kw.	
14	9 and 13	84
15	exp randomized controlled trial/	630003
16	controlled clinical trial.pt.	95662
17	randomized.ab.	672619
18	placebo.ab.	254445
19	clinical trials as topic/	204031
20	randomly.ab.	448952
21	trial.ti.	324893
22	or/15-21	1649324
23	exp animals/ not humans/	5290499
24	22 not 23	1520144
25	9 and 24	421
26	12 or 14 or 25	616
27	limit 26 to (english language and yr="2020 -Current")	100
28	11 or 27	113

Appendix 8.2 Expanded search strategy on Ovid Medline

	Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present	
1	exp Cesarean Section/	55667
2	c?esarean.ti,kf.	33648
3	1 or 2	62867
4	exp Anti-Bacterial Agents/	854837
5	(antibiotic? or anti-biotic? or antimicrobial? or anti-microbial? or antibacterial? or anti-bacterial?).ti,kf.	317682
6	Antibiotic Prophylaxis/	16159
7	((antibiotic? or anti-biotic? or antimicrobial? or anti-microbial? or antibacterial? or anti-bacterial?) adj5 (prescri* or administ* or prophyla*)).ab.	57302
8	4 or 5 or 6 or 7	993260
9	3 and 8	1871
10	guideline/ or practice guideline/	39860
11	9 and 10	13

Appendix 8.3 List of excluded studies (By order of study ID)

Study ID	Reasons for exclusions) for exclusion
ACOG 2010[315]	Publication date (>10yrs)/ Non-English publication/subnational guideline
Bollag 2021[316]	Did not provide recommendations for antibiotic prophylaxis in csection
Bratzler 2013[306]	Publication date (>10yrs)/ Non-English publication/subnational guideline
Caughey 2018[317]	Publication date (>10yrs)/ Non-English publication/subnational guideline
EBCOG 2017[318]	Did not provide recommendations for antibiotic prophylaxis in csection
Eriksen 2011[319]	Publication date (>10yrs)/ Non-English publication/subnational guideline
Mackeen 2024[320]	Conference abstracts, trial registrations and protocols, grey literature,
Macones 2019[321]	Did not provide recommendations for antibiotic prophylaxis in c-section
McNamara 2013[322]	Publication date (>10yrs)/ Non-English publication/subnational guideline
Moron 2020 [323]	Conference abstracts, trial registrations and protocols, grey literature,
NICE[324]	Did not provide recommendations for antibiotic prophylaxis in c-section
Nordic Federation of Societies of Obstetrics and Gynecology 2015[325]	Did not provide recommendations for antibiotic prophylaxis in c-section
RANZCOG 2022[326]	Did not provide recommendations for antibiotic prophylaxis in c-section
Roofthooft 2023[327]	Did not provide recommendations for antibiotic prophylaxis in c-section
SA Maternal, Neonatal &	Publication date (>10yrs)/ Non-English publication/subnational guideline
SA Maternal, Neonatal &	Publication date (>10yrs)/ Non-English publication/subnational guideline
Schmitz 2019[330]	Did not provide recommendations for antibiotic prophylaxis in c-section
Warren 2024[331]	Conference abstracts, trial registrations and protocols, grey literature,
WHO 2016[279]	Updated version available
Wilson 2018[332]	Did not provide recommendations for antibiotic prophylaxis in c-section
Yudin 2009[333]	Did not provide recommendations for antibiotic prophylaxis in c-section

Appendix Chapter 9

Appendix 9.1 Sensitivity profile for all *Escherichia coli* isolates in urine (2025 data)

Organism	Antibiotic name	%R	%I	%S	%R 95%C.I.	%S 95%C.I.
Escherichia coli	Ampicillin	48.5	3.7	47.9	40.6-56.4	40.0-55.8
Escherichia coli	Cefazolin	13.9	1.3	84.8	9.8-19.1	79.4-89.1
Escherichia coli	Cefepime	8.1	0.8	91.1	4.2-14.8	84.2-95.2
Escherichia coli	Cefotaxime	12.9	0.5	86.7	8.8-18.3	81.1-90.8
Escherichia coli	Cefoxitin	3.1	0	96.9	0.8-9.3	90.7-99.2
Escherichia coli	Ceftazidime	8.5	2.1	89.4	5.4-13.0	84.5-92.9
Escherichia coli	Ceftriaxone	13.2	0.5	86.4	9.1-18.5	80.9-90.5
Escherichia coli	Cefuroxime	10.2	0.6	89.2	6.2-16.0	83.3-93.3

Appendix 9.2 Survey tool for round one of the Delphi study

UNIVERSITY OF OXFORD

Items to be included in a formulary for surgical antibiotic prophylaxis in women undergoing Caesarean delivery in Antigua and Barbuda V3

The purpose of this survey is to determine which items should be included in a formulary detailing the use of surgical antibiotic prophylaxis for women undergoing caesarean delivery in Antigua and Barbuda.

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. If there is anything that you do not understand, or if you would like more information, please ask us. Please take time to consider whether you wish to take part.

Participant information for online surveys or tasks

Items to be included in a formulary for surgical antibiotic prophylaxis in women undergoing caesarean delivery in Antigua and Barbuda

CUREC Approval Reference:1399435

General Information

The aim of this research is to generate expert-level consensus on the items to be included in a formulary detailing surgical antibiotic prophylaxis for women undergoing caesarean delivery in Antigua and Barbuda.

We appreciate your interest in participating in this survey. You have been invited to participate as a potential panelist because you are a healthcare professional or researcher with knowledge, experience or interest in obstetrics and gynaecology, nursing, antimicrobial stewardship, infection prevention, surgery, pharmacy, medical microbiology, anaesthesiology, antimicrobial resistance, antibiotic prescribing and use, or have lived experience of a caesarean delivery. It is anticipated that up to 15 participants will be recruited for this survey.

Please read through this information before agreeing to participate (if you wish to) by ticking the 'yes' box below.

You may ask any questions before deciding to take part by contacting the researcher (details below). The Principal Researcher is Tansy Wade, who is attached to the Continuing Education Department at the University of Oxford. This research is being completed under the supervision of Professor Carl Heneghan and Dr Veronika Williams.

If you agree to participate in this study, you will be asked to complete two (2) anonymous online surveys. The second survey will be presented to you two (2) to three (3) weeks after completing the first survey. You will be asked to indicate your level of agreement with the presented statement on a 7-point Likert scale (1=strongly disagree, 2=disagree, 3= somewhat disagree,4= neutral, 5= somewhat agree, 6=agree, 7=strongly agree). Both surveys will take approximately ten (10) to fifteen (15) minutes to complete. No background knowledge is required. The researcher will use the information gained from this project to compile a list of items to be included on a formulary for surgical antibiotic prophylaxis in caesarean delivery. This list may be presented to the Obstetrics and Gynaecology Department stakeholders at the Sir Lester Bird Medical Centre. It may be used to design a formulary for informing the prescribing and use of surgical antibiotic prophylaxis in caesarean deliveries in Antigua and Barbuda.

Do I have to take part?

No. Please note that participation is voluntary. If you do decide to take part, you may withdraw at any point for any reason before submitting your answers by closing the browser. If submission of the survey has been completed, there is no way to remove individual responses from the survey tool due to the anonymous nature of the survey.
If you prefer not to respond to a particular statement, you can move on to the following statement.

How will my data be used?

We will not collect any data that could directly identify you.

Your IP address will not be stored. We will take all reasonable measures to ensure that data remains confidential.

The responses you provide will be stored in a password-protected electronic file on the University of Oxford's secure servers. They may be used in an aggregated form in academic publications and may be presented at conferences. Research data will be stored for 3 years after publication or public release of the work of the research.

Who will have access to my data?

The aggregated data may be shared with stakeholders of the Obstetrics and Gynaecology Department at the Sir Lester Bird Medical Centre.

The results will be written up for a DPhil degree.

Who has reviewed this research?

This research has been reviewed by, and received ethics clearance through, a subcommittee of the University of Oxford Central University Research Ethics Committee, the Continuing Education Departmental Research Ethics Committee.

Who do I contact if I have a concern or I wish to complain?

If you have a concern about any aspect of this research, please contact Tansy Wade at tansy.pilewade@kellogg.ox.ac.uk or *Professor Carl Heneghan* at carl.heneghan@phc.ox.ac.uk and we will do our best to answer your query. We will acknowledge your concern within 10 working days and give you an indication of how it will be dealt with. If you remain unhappy or wish to make a formal complaint, please contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) team at rgea.complaints@admin.ox.ac.uk or on 01865 616480.

Further Information and Contact Details

If you would like to discuss the research with someone beforehand (or if you have questions afterwards), please contact:

DPhil Student
Tansy Wade
Department for Continuing Education
University of Oxford, Uk
tansy.pilewade@kellogg.ox.ac.uk

DPHIL SUPERVISORS

Professor Carl Heneghan
University of Oxford, UK
carl.heneghan@phc.ox.ac.uk

Dr Veronika Williams
Nipissing University, Canada
veronika.williams@nipissingu.ca

If you have read the information above and wish to continue please select 'Yes, I agree to continue'. If you do not wish to continue you can exit the survey. *

- ◯ Yes, I agree to continue.
- ◯ No, I do not wish to continue.

Please note that you may only participate in this survey if you are 18 years of age or over.
If you wish to participate in this survey as a panel member, please select yes if you are over 18. *

- ◯ Yes, I certify that I am 18 years of age or over
- ◯ No, I am below 18 years of age.

If you have read the information above and agree to participate with the understanding that the data you submit will be processed accordingly, please tick the box below to start. *

- ◯ Yes, I agree to take part.
- ◯ No, I do not wish to take part.

Evidence summary

The following section is for reference and provides a summary of:
1. Published evidence on the use of surgical antibiotic prophylaxis in women undergoing a caesarean delivery.
2. Unpublished evidence from research conducted at the Sir Lester Bird Medical Centre.

Based on the findings of a recent evidence synthesis, https://osf.io/5d3bh/, several international guidelines have been informed by the same systematic reviews and meta-analyses. Guideline authors have also referenced the use of other international guidelines. [1, 2] While these guidelines evaluated, synthesised, and presented the published evidence for the geographical areas they represent, they have encouraged the additional use of local therapeutic guidelines and local bacterial sensitivity profiles in the development of sub-national guidelines. [1, 3-6]

a. Cefoxitin was not included in the list of antibiotics to be considered as surgical antibiotic prophylaxis. In a study comparing cefazolin and cefoxitin, it was shown that they are equally effective, but cefoxitin is more expensive than cefazolin. [7, 8] The use of this agent may not be sustainable in this setting. Randomised controlled trials conducted within the past five years assessed the use of ceftriaxone and cefotaxime as surgical antibiotic prophylaxis in women undergoing a caesarean delivery[9-12], but third-generation cephalosporins are not recommended. [4] A first-generation cephalosporin is the most widely preferred option because of coverage, cost and it assists in containing antimicrobial resistance because of its narrow-spectrum activity.[4, 13]

b. Evidence on the use of cefuroxime as prophylaxis is limited. Only one study assessing its use has been retrieved for the study period, 2020-2025 and it was shown that a short-term regimen with cefuroxime plus metronidazole had the same effectiveness as a long-term regimen.[14] Similarly a recently conducted randomized controlled trial reported that single doses are as effective as multiple doses in reducing post-operative infections. [15]

c. Penicillins were recommended as an option for pre-incision surgical antibiotic prophylaxis, [3, 4] but in this setting sensitivity reports show that it is not very effective for some of the pathogens implicated in post-operative infections in women undergoing a Caesarean delivery. Amoxicillin with clavulanic acid is not recommended as surgical antibiotic prophylaxis because available evidence has shown that it increases the risk of neonatal necrotizing enterocolitis.[16] It was noted that this antibiotic should only be administered after cord clamping.[4] Therefore, no penicillins were suggested as preincision surgical antibiotic prophylaxis.

d. The American College of Obstetrics and Gynaecology in 2018 suggested that adjunctive azithromycin may be considered in non-elective caesarean delivery but noted that randomized controlled trials on infections were not available. [13] In 2021, the effect of a single dose of preincision cefazolin plus adjunctive therapy (azithromycin, metronidazole, or clarithromycin) was compared to a single dose of preincision cefazolin in caesarean delivery by a systematic review and meta-analysis which included 3 randomised controlled trials and one prospective cohort study. It was reported that when compared to cefazolin only, there were significant reductions in the incidence of surgical site infections. [17] Authors concluded that additional evidence is needed to assess the

effectiveness of individual adjunctive therapy. Recent randomized controlled trials (2021-2024) have assessed the use of adjunctive azithromycin and metronidazole, but no significant findings related to post-operative maternal infections were demonstrated. [18-20]

e. There has been debate on whether surgical antibiotic prophylaxis should be administered pre-incision or at/after cord clamping since there was concern that pre-incisional dosing could mask neonatal infections.[2] However, evidence has shown that there are no adverse neonatal outcomes following pre-incision prophylaxis administration. [2, 21] Recent systematic reviews/meta-analyses reported significant reductions in endometritis, and wound infections in women who were administered pre-incision prophylaxis as compared to administration at cord clamping. [21-24]

f. Based on the findings of a retrospective analysis of prescribing patterns for surgical antibiotic prophylaxis in women undergoing a caesarean delivery at the Sir Lester Bird Medical Centre, registered at https://osf.io/95c4f/, the most frequently used antibiotic was cefuroxime, followed by the use of cefazolin (recently increased usage). Adjunctive metronidazole is common in this setting. Five per cent (n=71) post-operative infectious complications were documented between January 1, 2018, to December 31, 2024, . Fifty-eight percent (n=41) were wound infections, 14% (n=10) were cases of puerperal sepsis and 13% (n=9) were urinary tract infections. Culture and sensitivity results for samples sent to the Microbiology Department indicates that most of the post-operative infections were caused by *S.aureus* and *E.coli*. A thorough analysis of the sensitivity profiles for pathogens implicated in post-operative maternal infections could not be done, since culture and sensitivity testing were not requested for all patients suspected of having a post-operative infection. Infections could not be assessed by type of surgical antibiotic prophylaxis administered since there was substantial variation in prescribing, notably with the duration of antibiotic use which ranged from a single pre-incision dose to 7 days of use. All patient information was gathered from their medical records.

g.The healthcare professional (s) responsible for administering surgical antibiotic prophylaxis was not well-defined in reviewed international guidelines. Only one guideline indicated that the anaesthesist is responsible for administering preincision surgical antibiotic prophylaxis in their setting.[25]
It was determined from a retrospective analysis of prescribing patterns on surgical antibiotic prophylaxis in women undergoing a caesarean delivery in Antigua and Barbuda that the documentation of surgical antibiotic prophylaxis administration is poor. Additionally, based on the findings of a qualitative study conducted at the Sir Lester Bird Medical Centre,https://osf.io/sje8k/, there are varying perspectives and expectations of who should administer surgical antibiotic prophylaxis, where it should be administered and when it should be administered. Physicians expressed concern about the untimely administration of pre-incision surgical antibiotic prophylaxis. Nursing personnel shared that the current forms used to document prescriptions and drug administration can create some confusion which results in the delay of antibiotic administration for women undergoing a caesarean delivery. They also noted that the workday for nursing staff is very busy and they may miss the time for drug administration.

Development of a formulary for surgical antibiotic prophylaxis in women undergoing a Caesarean delivery.

Indicate the extent to which you agree with the following statements.

1.1 The recommendations for a formulary on surgical antibiotic prophylaxis for women undergoing a Caesarean delivery should be evidence-based. This means that high quality published evidence, expert consensus, local bacterial sensitivity profiles and locally available antibiotics should be considered during the development of the formulary.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

1.2 Local susceptibility patterns should be used to guide the choice of agent for surgical antibiotic prophylaxis in a Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

1.3 The local formulary should be used to guide the choice of agent for surgical antibiotic prophylaxis.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

1.4 Local information on post-operative infectious complications should be considered when developing the formulary.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2. Choice of antibiotic for prophylaxis in Caesarean delivery

Indicate the extent to which you agree with the following statements.

2.1 Cefazolin should be used as the first line of surgical antibiotic prophylaxis in women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2.2 Cefuroxime should be used as the first line of surgical antibiotic prophylaxis in women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2.3 Dual regimen of cefazolin plus adjunctive metronidazole should be used as the first line of surgical antibiotic prophylaxis in women undergoing a Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2.4 Dual regimen of cefuroxime plus adjunctive metronidazole should be used as the first line of surgical antibiotic prophylaxis in women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2.5 Dual regimen of cefazolin OR cefuroxime plus metronidazole should only be indicated when prophylaxis was not administered pre-incision for women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

2.6 Adjunctive metronidazole should only be given to women if there is bowel injury.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3. Dosage of antibiotic for prophylaxis in Caesarean delivery

Indicate the extent to which you agree with the following statements.

3.1 For all women undergoing Caesarean delivery with a body mass index (BMI) less than 30, the standard dose of Cefazolin should be 1 g.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3.2 For all women undergoing Caesarean delivery with a BMI between 30 and 39, the standard dose of cefazolin should be 2g.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3.3 For all women undergoing Caesarean delivery with a BMI of more than 40, the standard dose of cefazolin should be 3g.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3.4 For all women undergoing Caesarean delivery with a BMI of less than 40, the standard dose of cefazolin should be standardised to 2g

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3.5 For all women undergoing Caesarean delivery with a BMI less than 40, the standard dose of Cefuroxime is 750g.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

3.6 For all women undergoing Caesarean delivery with a BMI more than 40, the standard dose of Cefuroxime should be 1.5g.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

4. Number of doses of surgical antibiotic prophylaxis

Indicate the extent to which you agree with the following statements.

4.1 Only a single pre-incision dose of the selected antibiotic (s) should be administered to women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

4.2 Two doses of the selected antibiotic should be administered to women undergoing Caesarean delivery. One pre-incision and the other 12 hours after initial administration.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree

5. Duration of surgical antibiotic prophylaxis

Indicate the extent to which you agree with the following statements.

5.1 Antibiotics should be discontinued within 24 hours of caesarean delivery unless there are indications of an infection, and it is documented in the patient's medical records.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

5.2 Surgical antibiotic prophylaxis for women undergoing a Caesarean delivery should be extended beyond 24 hours.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

5.3 If surgical antibiotic prophylaxis is extended beyond 24 hours, a review for discontinuation of the course should be considered at 48 hours.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree

- ◯ Strongly agree

6. Route of administration of surgical antibiotic prophylaxis

Indicate the extent to which you agree with the following statements.

6.1 All surgical antibiotic prophylaxis should be administered intravenously to women undergoing caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

6.2 If surgical antibiotic prophylaxis is extended beyond 24 hours, a switch to oral should be considered at 48 hours.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

7. Timing of surgical antibiotic prophylaxis administration

Indicate the extent to which you agree with the following statements.

7.1 All women undergoing Caesarean delivery should be administered a prophylactic antibiotic within 60 minutes before an incision is made.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

7.2 All women undergoing Caesarean delivery should be administered a prophylactic antibiotic within 30 minutes before an incision is made.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

7.3 All women undergoing Caesarean delivery should be administered a prophylactic antibiotic at cord clamping.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

7.4 If pre-incision prophylaxis was not administered (for example, during an emergency caesarean delivery), it should be given during surgery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

7.5 If pre-incision prophylaxis was not administered to women undergoing a Caesarean delivery, it should be given post-surgery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8. Location of surgical antibiotic prophylaxis administration

Indicate the extent to which you agree with the following statements.

8.1 The location where surgical antibiotic prophylaxis is administered should depend on the urgency of the c-section, whether elective or non-elective.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.2 Surgical antibiotic prophylaxis should be administered in the ward for patients who are undergoing a non-elective Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.3 Surgical antibiotic prophylaxis should be administered in the ward for patients who are undergoing an elective Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.4 Surgical antibiotic prophylaxis should be administered in the operating theatre holding area for women undergoing a non-elective Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.5 Surgical antibiotic prophylaxis should be administered in the operating theatre holding area for women undergoing an elective Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.6 Surgical antibiotic prophylaxis should be administered in the ward for all women undergoing a Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.7 Surgical antibiotic prophylaxis should be administered in the operating theatre holding area for all women undergoing a Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

8.8 Surgical antibiotic prophylaxis should be administered on the operating table for all women undergoing a Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

9. Healthcare professional responsible for administering surgical antibiotic prophylaxis.

Indicate the extent to which you agree with the following statements.

9.1 Surgical antibiotic prophylaxis for women undergoing caesarean delivery should be administered by a nurse before anaesthesia is given.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

9.2 Surgical antibiotic prophylaxis for women undergoing caesarean delivery should be administered by the anaesthesist before anaesthesia is given.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

9.3 Surgical antibiotic prophylaxis for women undergoing caesarean delivery should be administered by the anaesthesist during induction of anaesthesia.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

9.4 Surgical antibiotic prophylaxis should be administered by the anaesthesist during surgery if it wasn't given prior to induction of anaesthesia.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

9.5 Surgical antibiotic prophylaxis should be administered by the nurse post-surgery if it wasn't given prior to induction of anaesthesia.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

10. Documentation of surgical antibiotic prophylaxis administration

Indicate the extent to which you agree with the following statements.

10.1 The administration of pre-incision surgical antibiotic prophylaxis done by the nurse should only be documented on the front of the drug Kardex with the time clearly stated.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

10.2 The administration of surgical antibiotic prophylaxis done by the anaesthesist should only be documented on the anaesthesist records with the time clearly stated.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

10.3 The documentation of surgical antibiotic prophylaxis administration should not be documented twice, both on the anaesthesist records and the drug Kardex.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

11. Allergy

Indicate the extent to which you agree with the following statements.

11.1 Women with a normal BMI and an allergy to penicillin should be given pre-incision clindamycin 600 mg IV and gentamicin 2mg/kg IV pre-incision.

- ◯ Strongly disgree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

11.2 Women who are obese and allergic to penicillin should be given pre-incision clindamycin 900 mg IV and gentamicin 2mg/kg IV pre-incision.

- ◯ Strongly disgree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

11.3 All women undergoing a Caesarean delivery who are allergic to penicillin should be given pre-incision clindamycin 600 mg IV and gentamicin 2mg/kg IV pre-incision.

- ◯ Strongly disgree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

12. Other considerations

Indicate the extent to which you agree with the following statements.

12.1 The first line of prophylaxis should be administered pre-incision in addition to prophylaxis for prolonged premature rupture of membranes in women undergoing Caesarean delivery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree

12.2 If the prophylactic antibiotics being used for prolonged premature rupture of membranes has coverage for organisms that may be encountered during a Caesarean delivery, the first line of prophylaxis should not be added.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

13. Colonisation with an antibiotic-resistant organism

Indicate the extent to which you agree with the following statement.

13.1 Patients known or suspected of being colonised with methicillin-resistant S. aureus (MRSA) should be given a single dose of Vancomycin 15mg/kg IV pre-incision.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

14. Readministration of surgical antibiotic prophylaxis during a Caesarean delivery

Indicate the extent to which you agree with the following statement.

14.1 The timing for readministration of surgical antibiotic prophylaxis during a caesarean delivery should depend on the half-life of the antibiotic.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

14.2 If a Caesarean delivery is prolonged for more than 4 hours then a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

14.3 If there is bleeding in excess of 1500 ml then a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Somewhat disagree
- ◯ Neutral
- ◯ Somewhat agree
- ◯ Agree
- ◯ Strongly agree

Are there any other items that should be considered for addition to a formulary on surgical antibiotic prophylaxis for women undergoing a Caesarean delivery?

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Additional Comments

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Appendix 9.2 Survey tool for round two of the Delphi study

Round 2- Consensus items to be included in a formulary for surgical antibiotic prophylaxis

SECTION 1 consists of items that reached consensus among the expert panel.
SECTION 2 includes items nearing consensus that will be assessed in this round of the survey.
SECTION 3 consists of 9 items that will be assessed for the level of agreement using a 3-point Likert scale.

Seventy-three per cent (n=11) of potential panelists responded to this survey. Representation was largely from the Obstetrics/Gynaecology Department (n=7). There were representatives from nursing administration, infection prevention control/antimicrobial stewardship committees, pharmacy/purchasing, microbiology and patient representation. Expert panel members, all healthcare professionals, had experience in one or more of the listed categories.

General recommendations (>70% consensus)

· The recommendations for a formulary on surgical antibiotic prophylaxis for women undergoing a Caesarean delivery should be evidence-based.

· Local susceptibility patterns should be used to guide the choice of agent for surgical antibiotic prophylaxis in a Caesarean delivery.

· The local formulary should be used to guide the choice of agent for surgical antibiotic prophylaxis.
· Local information on post-operative infectious complications should be considered when developing the formulary.

SECTION 1 - Consensus items (> 70% consensus)

The majority of participants agreed (>70% Strongly agree/Agree) with the following statements - These items will be included in the formulary.

1. Cefazolin should be used as the first line of surgical antibiotic prophylaxis in women undergoing Caesarean delivery and should be administered intravenously.

2. All women undergoing Caesarean delivery should be administered a prophylactic antibiotic within 30 minutes before an incision is made.

3. Surgical antibiotic prophylaxis should be discontinued within 24 hours after a caesarean section.

4. If antibiotics are continued for more than 24 hours after caesarean section, it should be for therapeutic reasons, and the indication should be clearly documented in the patient's medical record.

5. If extended beyond 24 hours for suspected infection, a review for discontinuation of the course should be considered at 48 hours.

6. If pre-incision prophylaxis was not administered (for example, during an emergency caesarean delivery), it should be given during surgery.

7. If there is bleeding in excess of 1500 ml, then a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.

8. The first line of prophylaxis should be administered pre-incision in addition to prophylaxis for prolonged premature rupture of membranes in women undergoing Caesarean delivery.

9. Patients known or suspected of being colonised with methicillin-resistant S. aureus (MRSA) should be given a single dose of Vancomycin 15mg/kg IV pre-incision.

The majority of participants disagreed (>70% Strongly disagree/Disagree) with the following statements. These items will not be included in the formulary.

1. Antibiotics should be administered at cord clamping.

2. Surgical antibiotic prophylaxis for women undergoing caesarean delivery should be extended beyond 24 hrs.

3. Surgical antibiotic prophylaxis should be administered in the ward for all women undergoing a Caesarean delivery.

4. Surgical antibiotic prophylaxis should be administered in the ward for patients who are undergoing an elective Caesarean delivery.

Where the predefined thresholds were not met, no recommendation was made. Items which fall into this category include:

1. The agent of choice for patients with allergies.

2. The documentation of surgical antibiotic prophylaxis.

3. The role of the anaesthesist in administering preoperative surgical antibiotic prophylaxis

SECTION 2 Items nearing consensus

Table showing response density for items that did not reach full consensus (>70%)

Items	Strongly disagree (%)	Disagree (%)	Somewhat disagree (%)	Neutral (%)	Somewhat agree (%)	Agree (%)	Strongly Agree (%)
Dual regimen of cefazolin plus adjunctive metronidazole should be used as the first line of surgical antibiotic prophylaxis in women undergoing a Caesarean delivery.	0	55	9	18	9	9	0
Adjunctive metronidazole should only be added if there is bowel injury.	9	0	9	9	9	45	18
For all women undergoing Caesarean delivery with a BMI of less than 40, the standard dose of cefazolin should be 2g.	0	0	9	27	9	36	18
Two doses of cefazolin should be administered to women undergoing caesarean delivery: the first before skin incision, and the second 12 hours following the initial dose.	0	27	9	9	0	36	18
If a Caesarean delivery is prolonged for more than 4 hours then a second dose of the same preincision antibiotic should be administered by the anaesthesist during surgery.	0	9	0	9	18	36	27

Percentage (number of respondents)- 9 % (n=1), 18% (n=2), 27% (n=3), 36% (n=4), 45% (n=5), 55% (n=6)

SECTION 3 Items to be included in a formulary for surgical antibiotic prophylaxis in caesarean deliveries. Please indicate your level of agreement for the items listed below.

1. **1 Number of doses of surgical antibiotic prophylaxis. Indicate the extent to which you agree with the following statements.**

1.1 Three doses of cefazolin should be administered at 8-hour intervals within 24 hours of caesarean delivery. The initial dose should be given before skin incision, with subsequent doses administered at 8-hour intervals thereafter.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

1.2 Two doses of cefazolin should be administered to women undergoing caesarean delivery: the first before skin incision, and the second 12 hours following the initial dose.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

2. **Regimen Type. Indicate the extent to which you agree with the following statements.**

2.1 Dual regimen of cefazolin plus adjunctive metronidazole should be used as surgical antibiotic prophylaxis in women undergoing a Caesarean delivery.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

2.2 Adjunctive metronidazole 500mg IV should only be considered if there is bowel injury.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

3. Special circumstances

3.1 In cases of cefazolin allergy, the attending consultant should determine the appropriate antibiotic type and dosage, guided by patient-specific circumstances and antibiotic availability. Note: Panel members provided feedback on the poor availability of antibiotics such as clindamycin and the complexities of managing patients with allergies.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

3.2 If cefazolin is unavailable, cefuroxime 1.5g IV should be used as an alternative for surgical antibiotic prophylaxis. Note: The consideration for an alternative reflects feedback highlighting inconsistent antibiotic availability.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

3.3 If a Caesarean delivery is prolonged for more than 4 hours, a second dose of the same antibiotic used before skin incision should be administered by the anaesthesist during surgery.

- ◯ Disagree
- ◯ Neutral
- ◯ Agree

3.4 In patients with a BMI ≥ 40, the attending consultant should determine the appropriate dosage of surgical antibiotic prophylaxis.

- ◯ Disagree
- ◯ Neutral

Agree

4. **Administration of surgical antibiotic prophylaxis**

4.1 The nurse should administer surgical antibiotic prophylaxis in the operating theatre holding area for all women undergoing caesarean deliveries. Note: Based on the consensus recommendation of administering antibiotic prophylaxis within 30 minutes of c-section.

Disagree
Neutral
Agree

5. Additional comments.

Appendix Chapter 10

Appendix 10:1 Selection of a target behaviour for intervention

Behaviours relevant to improving decision making around surgical antibiotic prophylaxis (type and duration)	Impact of behaviour change on outcome	Likelihood of changing behaviour	Will behaviour have a positive impact on other behaviours- Spillover score	Ease of measuring behaviour- Measurement score
Consultants follow a standard evidence-based formulary when prescribing surgical antibiotic prophylaxis for c-section patients	Very promising	Promising	Very promising	Very promising
Junior physicians adhering to standard evidence-based guideline.	Very promising	Unpromising but worth considering	Promising	Very promising
Department heads supporting and enforcing the use of a standard evidence-based formulary.	Very promising	Promising	Very promising	Unpromising but worth considering
Pharmacists ensuring that the recommended prophylactic antibiotics are always in stock and available.	Promising	Promising	Unpromising but worth considering	Promising
Nursing Managers maintaining stock antibiotics in the unit.	Promising	Unpromising but worth considering	Unpromising but worth considering	Unpromising but worth considering
Physicians considering patient circumstances when prescribing	Promising	Promising	Unpromising but worth considering	Unpromising but worth considering
Target behaviour - Consultants follow standard evidence-based formulary when prescribing surgical antibiotic prophylaxis for c-section patients				

Appendix 10.2 Behavioural analysis

COM-B Model	Barriers to consultants routinely prescribing surgical antibiotic prophylaxis to c-section patients according to a standard evidence-based formulary	What needs to change for consultants to routinely prescribing surgical antibiotic prophylaxis to c-section patients according to a standard evidence-based formulary?	Intervention functions
Capability	The presumed regimen and duration of surgical antibiotic prophylaxis to prevent post-operative infections differ among consultants.	Consultants collectively select the optimal regimen and duration of surgical antibiotic prophylaxis and align prescribing with evidence-based standards.	Education
Opportunity	Consultants follow guidelines from several international obstetrics and gynaecology organisations or use their clinical judgement or previous training.	An evidence-based formulary for the prescribing of surgical antibiotic prophylaxis for women undergoing Caesarean delivery is implemented in the setting.	Environmental restructuring, Restriction
	Standard evidence-based guideline use is not enforced in the setting.	The institution enforces the use of a standard evidence-based formulary.	Restriction
	Continuing professional education sessions/courses on surgical antibiotic prophylaxis are unavailable in the setting and are limited online.	Continuous education/training on antibiotic use and antimicrobial resistance is offered in the professional setting.	Environmental restructuring
	No access to information on surveillance rates, bacterial sensitivity summaries, and audit and feedback reports of antibiotic use to inform prescribing practices.	Adequate interdepartmental communication on surveillance of AMR, infection rates and monitoring of surgical antibiotic prophylaxis use is needed.	Environmental restructuring
	Poor environmental hygiene may contribute to increased infection rates.	Adequate environmental hygiene needs to be maintained in the setting.	Environmental restructuring

COM-B Model	Barriers to consultants routinely prescribing surgical antibiotic prophylaxis to c-section patients according to a standard evidence-based formulary	What needs to change for consultants to routinely prescribing surgical antibiotic prophylaxis to c-section patients according to a standard evidence-based formulary?	Intervention functions
	Inconsistent supply of antibiotics limits access to preferred treatments.	The pharmacy stocks recommended antibiotic for surgical antibiotic prophylaxis.	Environmental restructuring
	Communication and collaboration among professional groups are inadequate.	Physicians, nurses and anaesthesists communicate about the administration, discontinuation and documentation of administration of surgical antibiotic prophylaxis.	Environmental restructuring, Modelling, Enablement
Psychological capability, physical and social opportunity need to change for consultants to follow a standard evidence-based formulary when prescribing surgical antibiotic prophylaxis for c-section patients.			

Appendix 10.3 APEASE assessment of intervention functions for improving consultants' adherence to a standard guideline.

Intervention functions	Does the intervention meet the APEASE criteria?
Education	Yes
Restriction	Yes
Training	This is neither affordable, practical, nor cost-effective. We would need the funding to organise training, and staff would need to have the time to attend these training sessions. Multiple training sessions would also be required to accommodate staff.
Environmental restructuring	Not affordable, practicable, cost-effective or acceptable to restructure the environment.
Modelling	Modelling can be done, but it depends on the further development, adoption and implementation of an evidence-based formulary in the setting. Additionally, consultants must demonstrate guideline concordance when prescribing. This is not practicable to deliver in this setting until a standard formulary is created and implemented.
Enablement	Standard guidelines/ protocols can be used to reduce barriers to drug selection and duration. However, it is not practicable as it is dependent on the existence of a guideline.
Selected intervention functions: Education, Restriction	

Appendix 10.4 APEASE assessment of policy categories for intervention functions

COM-B Component	Intervention function	Potential policy categories that could deliver intervention function	Does the policy category meet the APEASE criteria?
Opportunity	Restriction	Guidelines	Yes
		Regulations	Rules would be made at the Board level. Long-term possibility.
		Legislations	Not practicable in the maternity unit or hospital setting.
Capability	Education	Guidelines	Yes
		Communication/ marketing	Yes
		Service provision	Not practicable.
Selected policy categories: Guidelines and Communication/marketing			