

**PERCEPTIONS AND ATTITUDES OF HEALTH PROFESSIONALS ON THE
ESTABLISHMENT OF AN ANTIMICROBIAL STEWARDSHIP
PROGRAMME AT A TERTIARY HOSPITAL IN GAUTENG PROVINCE**

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DECLARATION

I, Hermenegilda Madeira, declare that this research report is my original work. It is being submitted for the degree of Master of Public Health in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University. I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong. I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.

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Signature:

A handwritten signature in dark ink, reading 'Hermenegilda Madeira', written in a cursive style.

Date:

9 November 2020

DEDICATION

In loving memory of my mother Maria Madeira 1952-2005 who believed that I could before I even started.

I also dedicate this work to my loving husband who has supported me throughout this journey. To my father who continuously inspires me to thrive for the best and who taught me the importance of working hard to achieve your dreams from a young age. To my children Kiyan and Kenzo for being the reason why I could never give up. Without God by my side, this would not have been possible.

The completion of this thesis amidst the ongoing COVID-19 pandemic was a challenging achievement and I would like to acknowledge my colleagues in the health sector that are doing all that they can in the fight to overcome it while putting their own lives at risk.

LIST OF ABBREVIATIONS AND ACRONYMS

AMR - Antimicrobial Resistance

AMS - Antimicrobial Stewardship

ASP - Antimicrobial Stewardship Programme

FIDSSA - Federation of Infectious Diseases Societies in Southern Africa

GAP - Global Action Plan

GARP - Global Antibiotic Resistance Partnership

HAI - Health Care Associated Infection

HCW - Health Care Worker

ICU - Intensive Care Unit

ID - Infectious Diseases

ICSSA – Infection Control Society of South Africa

IDSSA - Infectious Diseases society of Southern Africa

IPC - Infection Prevention and Control

KAP - Knowledge, Attitudes and Perceptions

MRSA - Multidrug resistant staphylococcus aureus

PAF - Prospective Audit with Feedback

SAASP - South African Antibiotic Stewardship Programme

SASCM - South African Society for Clinical Microbiology

SASPID - South African Society of Paediatric Infectious Diseases

VRE – Vancomycin resistant enterobacteriaceae

WHA - World Health Assembly

WHO - World Health Organization

DEFINITION OF CONCEPTS

Antimicrobial: an agent such as a drug that destroys or inhibits the growth of a microorganism (1).

Antibiotic: A drug used to treat bacterial infections (2).

Note that in this study, the terms **antibiotic** and **antimicrobial** may occasionally be used interchangeably but **this research report focuses specifically on resistance to antibiotics** and **excludes resistance to other antimicrobials** such as antivirals, antihelminthic, antiprotozoal drugs and antimycobacterials.

Antimicrobial resistance: the ability of a microorganism to withstand treatment with an antimicrobial drug (1)

Antimicrobial stewardship: a multidisciplinary, systematic approach to optimizing the appropriate use of all antimicrobials to improve patient outcomes and limit the emergence of resistant pathogens whilst ensuring patient safety (3).

Clinical pharmacist: A clinical pharmacist is a specialist pharmacist who has undergone additional training and is able to assess a patient's health problem and determine whether prescribed medications are optimal. Clinical pharmacists can recommend changes in therapy to the treating physician and are part of the clinical team (4).

Formulary restriction: limiting which antimicrobial agents are available to prescribers at a given institution or requiring the prescriber to indicate the rationale for the selection of a particular agent or requiring prior approval for use by an infectious diseases (ID) or pharmacist (i.e., preauthorization-based restriction) (3).

Inappropriate antibiotic use: the use of antibiotics when no health benefit is possible, such as to treat upper respiratory tract infections caused by viruses or the suboptimal use of antibiotics for responsive conditions, such as the choice of drugs with an unnecessarily broad spectrum, incorrect dosage or duration, or poor patient adherence to the prescribed treatment (5).

Medical Registrar: A hospital doctor senior to an intern but junior to a consultant who is specializing in Internal Medicine.

Specialist Consultant: A doctor who has completed specialist training in a particular field of medicine and has attained the position of consultant.

ABSTRACT

Background

Antibiotic resistance is a global health threat that arises primarily from the inappropriate use of antibiotics. The establishment of antimicrobial stewardship programmes in health care facilities is recommended to curb the misuse of antibiotics. It is important to understand the existing antibiotic prescribing practices and to identify potential barriers and facilitators to the establishment of antimicrobial stewardship programmes at the level of the health care facility in order to implement tailored solutions. Therefore, this study aimed to get an in-depth understanding of the perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme (ASP) in a tertiary hospital in Gauteng province. The study also describes perceived barriers and facilitators regarding the implementation of an ASP at the hospital

Methodology

An exploratory qualitative study design was used. The study was conducted in a public sector tertiary care academic hospital in Gauteng province. Sixteen face-to-face in-depth interviews were conducted with professional nurses, medical interns, registrars, consultants and pharmacists using a semi-structured interview guide. Thematic analysis was conducted and codes were identified and grouped into major themes and subthemes.

Results

Both appropriate and inappropriate antibiotic prescribing practices were described in this hospital. Prolonged antibiotic use, inappropriate combinations of antibiotics and antibiotics prescribed for non-infectious conditions such as cardiac failure were some of the inappropriate prescribing practices described. Appropriate practices described were the prescription of antibiotics based on microbiological culture results and clinical criteria. Inappropriateness in the administration of antibiotics by nursing staff was also described and included workaround behaviours such as the administration of antibiotics in a way that differs from what was prescribed such as through an incorrect route and for an incorrect duration. Drivers of antibiotic prescribing included health care worker knowledge, the fear of poor patient outcomes, laboratory delays, staff shortages, availability of antibiotics and the antibiotic prescribing culture. Patient demand was not cited as a driver of antibiotic prescribing in this study.

There was a widespread perception that the composition of an antimicrobial stewardship committee should consist of a multidisciplinary team which is in keeping with local and international recommendations. The categories of health care workers that were nominated include specialist physicians, infectious diseases specialists, infection prevention and control

practitioners, registrars, interns, professional nurses, pharmacists and hospital management. The interventions proposed for the ASP include prospective audit with intervention and feedback, education on antibiotic prescribing through bedside teaching, formal lectures and guidelines.

Perceived barriers to ASP implementation include lack of resources, namely human resources, drugs and information technology systems, poor communication and resistance to change. Perceived facilitators were the existence of experts in AMS, managerial support of the ASP, a willingness to learn and the availability of diagnostic facilities such as imaging and microbiology laboratories.

Conclusion

The establishment of an ASP is welcomed by the health professionals in this hospital. This study has explored their perceptions and attitudes with regards to the establishment of an ASP and identified barriers and facilitators that can inform the implementation of the ASP in this hospital.

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1 CHAPTER 1: INTRODUCTION

1.1 Background

Antimicrobial resistance (AMR) has become a significant public health threat affecting both high and low income countries (6-9). The development of drug resistant micro-organisms causing disease can have detrimental effects on health systems especially in resource poor settings (6). Health systems become overburdened because AMR results in a prolonged hospital stay as well as increased morbidity and mortality (10). Furthermore, the cost of treating patients with antimicrobial resistant infections is significantly higher than that of treating patients infected with susceptible micro-organisms (11). These costs are high due to the need for more expensive drugs to treat resistant micro-organisms, increased use of diagnostic tests and increased length of hospital stay (6). The increased bed space and time needed from health care workers (HCWs), additional training of personnel on the use of newer drugs, and the development of new treatment guidelines also places an additional burden on health care facilities(6). Health care associated infections (HAIs) which consist mostly of infections with drug resistant organisms are a significant source of litigation costs for health facilities and these can be reduced by interventions that reduce the incidence and prevalence of HAIs (12). The patients also incur significant financial costs arising from loss of productivity and income due to extended hospitalizations which can negatively impact the overall economy (6, 10, 13). Some infections with resistant bacteria such as multidrug resistant staphylococcus aureus (MRSA) have severe complications which result in higher morbidity and mortality (14).

Of particular concern is the fact that the rate of development of new antimicrobials is not keeping up with the emergence of drug-resistant strains implying that common infections could become untreatable with the existing antibiotics if the problem is not addressed (15). Modelling studies estimate that if AMR is left unchecked, there will be a significant increase in mortality due to infections with resistant micro-organisms and a decrease in the world's gross domestic product(9). Furthermore, a recent study by Ekwanzala et al (16) found concerning evidence that antibiotic resistant bacteria such as vancomycin resistant enterobacteriaceae (VRE) from hospital wastewater could contaminate other water sources that the public consumes emphasizing the need to address the root cause of antibiotic resistance.

It is important at this stage to make a clear distinction between antibiotic resistance (ABR) and antimicrobial resistance (AMR) as these terms are usually used interchangeably in the literature. Antibiotics are drugs used to prevent and treat infections caused by bacteria and not other micro-organisms such as viruses, fungi, helminths and parasites(17). These bacteria can develop resistance to the antibiotics used to treat them rendering these antibiotics ineffective and this is referred to as antibiotic resistance (17). Antimicrobials on the other hand are a broader group of drugs which include antibiotics and others such as antifungals, antivirals, anthelmintics and antiprotozoal drugs (17). Therefore the term antimicrobial resistance refers to resistance in any microorganisms which includes viruses, fungi, helminths, parasites and is not limited to resistance in bacteria (17). In 2015, according to the WHO Global Action Plan against AMR, ABR was viewed as more of a priority than AMR but this is changing as broader resistance is increasingly becoming more prevalent and this is reflected in the change of the WHO's world antimicrobial awareness week slogan from "Antibiotics: Handle with Care" to "Antimicrobials: Handle with Care" in 2020 (17). My study focused specifically on antibiotics and not on other forms of antimicrobials.

It has been well described in the literature that the inappropriate use of antimicrobials is one of the major risk factors for the development of AMR (18, 19). Antimicrobials are often prescribed unnecessarily and inappropriately by HCWs (20). Although HCWs are aware that AMR is an important problem resulting from the misuse of antibiotics (21, 22), this awareness has often not been translated into more mindful antibiotic prescribing. The inappropriate prescription of antibiotics is a problem that affects all countries regardless of socioeconomic status (23-25). The data show that there was a 35 % increase in the consumption of antimicrobials between the years 2000 and 2010 and South Africa was amongst the 5 countries responsible for 76% of this increase (26). There have been several efforts to address AMR globally such as a number of World Health Assembly (WHA) resolutions since 1998, and initiatives from the WHO including the 2001 WHO Global Strategy for containment of AMR and the 2011 World Health Day campaign 'Combat drug resistance - no action today, no cure tomorrow' but there has been very slow progress made globally and nationally(27). At the 67th WHA in 2014, delegates of member states signed a pledge to adopt the resolutions that were made which emphasized the institution of measures to support the development of national policies on antibiotic stewardship, and infection prevention and control (28). At this WHA the WHO was mandated to develop a Global Action Plan (GAP) against AMR by 2015 and this

action plan was later on adopted at the WHA in May 2015(15). The GAP outlined five objectives which are to improve awareness and understanding of AMR through effective communication, education and training, to strengthen the knowledge and evidence base through surveillance and research, to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, to optimize the use of antimicrobial medicines in human and animal health and to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools and, vaccines and other interventions (15). The GAP highlights the action that needs to be taken by member states, secretariat, international and national partners in order to attain each objective and urged that countries should develop national action plans on antimicrobial resistance(15). In 2016, the heads of state of the United Nations General Assembly sanctioned a political declaration in which they pledged to address AMR, this was the fourth time in the history of the UN that a health issue was discussed at the general meeting (29). However, only seven countries in the WHO African region were found to have national AMR plans by 2017 namely, South Africa, Ethiopia, Sierra Leone, Zimbabwe, Kenya, Mauritius and Tanzania (30).

The 2015 WHO GAP against AMR recommended the development of antimicrobial stewardship programmes (ASP) as one of the cornerstone strategies to curb the misuse of antibiotics, the other two pillars are surveillance and infection prevention and control (15). An ASP in a health facility is usually run by a multidisciplinary team whose role is to control and reduce the misuse of antibiotics through the implementation of various interventions (3). ASPs were found to be effective in decreasing antibiotic utilization in both well and poor resourced settings (31, 32). For example, surveys in Peru and Congo found that ASPs were viewed as favorable in resource poor settings where HCWs had sub-optimal knowledge on the correct use of antibiotics (21, 33). Furthermore, ASPs have resulted in both short-term and long-term reduction in antibiotic associated hospital costs (34). In addition, ASPs have resulted in an increase in the appropriate use of antibiotics, a decrease in the rates of drug resistant mutations, and a decrease in *clostridium difficile* infections (*clostridium difficile* infections typically occur in patients that have received antibiotics) (35). In South Africa, the introduction of an antibiotic prescription chart and a weekly AMS ward round resulted in a 35% cost reduction in the antibiotic budget in an academic hospital in the Western Cape (32). However, the effectiveness of ASPs can be influenced by the perceptions and attitudes of those affected by the interventions being implemented (36).

Over the years, there has been an increase in the establishment of ASPs in health facilities to promote safe and effective antibiotic use, however, these have primarily been implemented in high income countries (HICs) (37, 38). Also, most of the available studies on antimicrobial stewardship focused on doctors and pharmacists and not so much on other cadres of health care workers that might be affected by the implementation of ASPs. In South Africa, some hospitals in the public and private sectors have instituted ASPs (32, 39, 40). A scoping review by Chetty et al (40) analysed all the South African published literature on AMS initiatives in the public and private health sectors. They found 18 studies published between the year 2000 and 2019 that met their inclusion criteria of which only one study was a qualitative study (40). This indicates that limited local qualitative studies exist that provide insights into what it takes to establish antibiotic stewardship programmes, who should form part of their team, what interventions they should implement, as well as how they are accepted by health professionals affected by them. Therefore, my study aimed to explore perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme at a tertiary hospital in Gauteng province.

1.1.1 Overview of South Africa's response to antimicrobial resistance

The Federation of Infectious Diseases Societies in Southern Africa (FIDSSA) was created in 2005 and it is an amalgamation of existing societies that represent infectious diseases, federation member societies include the Infectious Diseases Society of Southern Africa (IDSSA), Infection Control Society of South Africa (ICSSA), South African Society for Clinical Microbiology (SASCM) and Southern African Society of Paediatric Infectious Diseases (SASPID) (1). In 2012, the South African antibiotic stewardship programme (SAASP) was formed, SAASP was borne from FIDSSA (41). A SAASP working group that consisted of a multidisciplinary team of experts from fields of infectious diseases, pharmacy, microbiology, intensive care and infection control based both in the public and private sector that were selected to provide leadership and institute antimicrobial stewardship programmes in different health care facilities (41). The goals of the SAASP working group are to direct appropriate training on antibiotic stewardship, coordinate the dissemination of information regarding antibiotic stewardship, develop antibiotic prescribing guidelines, to identify and carry out research that would overcome gaps in knowledge on antibiotic stewardship and engage with the National Department of Health to look into issues that could be obstacles to

antibiotic stewardship efforts (41). Over the years the SAASP has achieved most of its goals, including advocacy, the creation of national antibiotic prescribing guidelines and they have led several research projects and educational programmes including an online course on antibiotic stewardship that is free and easily accessible on the FIDSSA website to anyone that wishes to take it (42). In response to the rising threat of AMR, the South African National Department of Health drafted a National AMR Strategy Framework in 2014 (1). The South African government committed to combat AMR and a multidisciplinary inter-sectorial Ministerial Advisory Committee (MAC) was established in 2014 (1). The MAC was mandated to advise the minister of health on matters relating to AMR as well as to monitor and evaluate the implementation of the AMR Strategic framework (1).

During the conceptualization phase of this study in 2018, the academic hospital participating in this study was in the process of establishing an ASP and had created a working AMS committee however, no formal activities had commenced. This was the third time that an AMS committee had been created in this facility, the previous committees had been established in 2014 and 2017. These previous committees did not reach a stage of implementing any substantial AMS activities, both committees were short-lived and did not go past the planning phases. Following the resignation of the respective committee chairpersons these committees were inactive until 2018 when a new chairperson was nominated. The AMS committee followed the mandate that was given to hospitals from the Provincial AMS committee. The committee adhered to the principles outlined in the National Guidelines for the containment of AMR in South African Hospitals (43). These guidelines provide comprehensive guidance with regards to AMS structures including the composition of the hospital's AMS committee and team, and the roles of the AMS teams. The current AMS committee consists of members from multidisciplinary backgrounds which included representatives of hospital management, infectious diseases specialists, microbiologists, intensivists, specialist physicians, infection prevention and control practitioners as well as hospital pharmacists.

This pre-implementation stage of the third attempt to form an ASP provided a window for one to conduct a study to establish what the existing perceptions and attitudes were with regards to ASPs among the different cadres of health care workers in the hospital. However, since 2019, there have been some developments with regards to the antimicrobial stewardship activities implemented in this academic hospital and these are detailed below:

As part of a pilot project, antimicrobial stewardship ward rounds were conducted in selected internal medicine wards between November 2018 and April 2019. The AMS team that attended

the rounds consisted of an Infectious Diseases specialist that led the rounds, infection prevention and control practitioners, pharmacists and microbiologists and the attendees were the doctors and nurses in the respective wards. This pilot project had ended when I was collecting data for my study, some of the study participants had experienced the rounds before while others had not. The hospital pharmacy had recently implemented restrictions to broad spectrum antimicrobials such as some carbapenems. Access to a salvage antibiotic called colistin that is used to treat infections caused by bacteria that are resistant to carbapenems had always been restricted even before the establishment of the ASP and these restrictions remained in place. The restricted antibiotics were only dispensed upon receipt of the microbiology results and a motivation form that had to be signed by a consultant. Pre-authorization of antibiotics was applied to colistin as well and a consultant's signature was one of the pre-requisites for the antibiotic to be dispensed. This information allowed the pharmacist to assess the appropriateness of the antibiotic prescriptions that they received.

Despite these developments, the findings of this study are still beneficial in informing the ongoing implementation of the antimicrobial stewardship programme in this facility.

1.2 Literature Review

Antimicrobial resistance and antimicrobial stewardship have been the focus of a lot of research in recent years all over the world. This literature review explores issues pertaining to antibiotic prescribing practices, the composition and activities of antimicrobial stewardship committees and the facilitators and barriers to the establishment of ASPs in high-, middle- and low-income countries. Literature from South African studies that looked into issues of AMR and ASPs is growing rapidly but there is still a need for more local research (40).

1.2.1 Antimicrobial prescribing practices

Deciding whether a patient requires an antibiotic and choosing the most appropriate one is a challenging decision that doctors make frequently. In order to assess antibiotic prescribing patterns, one has to be able to distinguish between appropriate and inappropriate prescribing. According to the Centers for Disease Control and Prevention (CDC) appropriate antibiotic prescribing occurs when antibiotics are prescribed only when they are needed (44). In addition,

the right antibiotic should be selected, at the right dose and for the correct duration (44). Furthermore, antibiotic prescribing should be in line with evidence based local guidelines if these are available (44). Conversely, inappropriate antibiotic prescribing occurs when antibiotics are prescribed unnecessarily, when the wrong antibiotic is selected, or the wrong dose is prescribed or when an antibiotic is prescribed for the wrong duration (44).

A qualitative study done in pulmonary medicine in two teaching hospitals in Australia found that doctors struggled with deciding if an infection was viral or bacterial and distinguishing between colonization and infection which could lead to the misuse of antibiotics (45). In another study conducted in six hospitals in the United States (US), there was a significantly high rate of unnecessary antibiotic use (46). This prospective observational cohort study showed that broad-spectrum and extended-spectrum antibiotics were widely used as an initial treatment and that there was a shortfall in terms of the use of laboratory and imaging tests before initiation of antibiotics (46). The latter study also looked at the rates of de-escalation or discontinuation of therapy in cases in which the tests were done and found these to be inadequate as well (46).

An Ethiopian study conducted in a teaching hospital found that participants admitted to prescribing empiric antibiotics for longer than three days which is not the recommended practice (47). In another study in Egypt, 51% of physicians prescribed antibiotics for colds, this study as well as a study from India, showed that the use of two or more antibiotics concurrently was commonly practiced (48, 49). A cross sectional survey in Lesotho also identified several inappropriate antibiotic prescribing practices with only 17% of the participants reporting that they always send a sample for microscopic identification before prescribing antibiotics and only 32% reporting that they always send a sample for culture sensitivity tests (24). Furthermore, a Cambodian study demonstrated that only 58% of doctors who worked in hospitals that have microbiology services used results from microbiology to guide antibiotic prescribing (22). In Gambia health practitioners reported using microbiological results to guide antibiotic prescribing in less than 25 % of their patients with infections (50).

Antibiotic prescribing practices were also assessed in South Africa and it was found that there was an overuse of antibiotics as well (39, 51). Antibiotics were used when there was no indication for them in a significant proportion of patients, there was a lack of microbiological verification in several patients who received antibiotics, there were inappropriate combinations

of antibiotics prescribed and a prolonged duration of antibiotic use (39, 51). However, the antibiotic dosages and dosing intervals were correct (51). In primary health care facilities in the Western Cape, inappropriate prescribing practices were described such as prescribing an antibiotic when it was not indicated, use of an incorrect dose and incorrect duration of therapy (52). In a paediatric ward in a public sector hospital in the Limpopo province of South Africa, health professionals prescribed antibiotics without requesting laboratory tests therefore they predominantly prescribed antibiotics empirically (53). When the use of the antibiotic colistin was assessed in four private South African hospitals in Gauteng, it was found that there was adherence to taking of blood cultures before starting an antibiotic, prescribing a loading dose and prescribing the colistin with another drug as recommended in the guidelines (54). Poor practices that were observed included incorrect doses being prescribed, non- adjustment for renal dysfunction and not de-escalating the drug following culture and susceptibility results (54). Inappropriate prescribing practices have also been demonstrated in an oral health centre in Gauteng indicating that the problem is not limited to doctors (55). In South Africa, inappropriate antibiotic prescribing practices have been demonstrated in both the public and private health sectors, the public sector teaching hospitals were found to do better than other public sector hospitals when they were evaluated for compliance with South African paediatric guidelines for surgical antibiotic prophylaxis (56).

The majority of third and fourth year medical students from a medical school in the North East of South Africa believed that antibiotics were overused in hospitals and outpatient areas (57). Similarly in a KAP conducted on medical students across three universities in South Africa, 92 % of respondents perceived that antibiotics are overused in South Africa (58).

Overall, the referenced studies show that inappropriate prescribing practices are prevalent in high, low- and middle-income settings.

1.2.2 Factors influencing antibiotic prescribing behavior

Drivers of antibiotic prescribing behavior are well described in the literature and are quite similar among different settings. A Norwegian qualitative study conducted on hospital doctors found that they relied on advice from their senior colleagues such as infectious diseases specialists as well as microbiologists when choosing antibiotics (59). In a UK study, peer norms were shown to affect antibiotic prescribing, with some junior doctors simply mimicking the

antibiotic prescribing practices of their senior colleagues without consulting guidelines (60). A culture of hierarchy in which junior doctors prescribe what their senior counterparts suggest without questioning it and without understanding the rationale for it is also described by Charani et al and Sikkens et al (36, 61). Another UK study showed that the opinion of senior colleagues significantly influenced prescribing practices, this study included all levels of non-consultant hospital doctors, not just junior doctors (62). In yet another UK study it was shown that junior doctors felt unsupervised and lacked support from seniors when prescribing antibiotics which led them to commit errors when prescribing (63). A similar hierarchical prescribing culture was described in low income settings in an Ethiopian study (47). A root-cause analysis of inappropriate antibiotic prescribing was carried out in a Dutch hospital which identified inadequate physician knowledge and fear of infectious complications as drivers of poor prescribing and cultural factors such as rejection of interference.

Furthermore, delays in the availability of microbiological results influenced antibiotic prescribing in the Norwegian study (59). Similarly, low-income countries also found that a delay in obtaining laboratory results was a significant determinant of prescribing behaviour which increased prescription of broad-spectrum antibiotics, also, the study participants had a mistrust of the laboratory results which was not a factor in the studies conducted in high income countries (47) (64).

Doctors also rely on their clinical assessment to guide antibiotic prescribing but the appropriateness of this was found to be dependent on one's clinical experience and could result in inappropriate prescriptions by less experienced doctors (59). More senior doctors were more likely to rely on their personal experience when prescribing antibiotics in another UK study (62). Charani et al (61) also found that doctors have decision-making autonomy when prescribing antibiotics and feel that their decisions cannot be challenged. Sikkens et al (36) had a similar finding and described this behaviour as a rejection of interference by doctors. In a study that focused on low income countries, antibiotic prescribing did not differ based on the level of knowledge as there was no difference in prescribing behaviour when doctors were compared to medical assistants (64). Antibiotic guidelines or policies were found to be more useful to inexperienced doctors compared to experienced doctors in the Norwegian study, the inaccessibility of guidelines was also identified as a determinant of antibiotic prescribing and could be overcome by having them in print format or in an app in addition to an online platform (36, 59). Charani et al (61) found that policies were sometimes not used because doctors

believed that they did not cover all the possible scenarios encountered in clinical practice. Sikkens et al (36) also found that inappropriate prescribing occurred when guidelines contained incorrect or conflicting information. A heavy workload in health facilities has been described as a determinant of antibiotic prescribing as well (36).

Findings from LMICs such as Ethiopia, the Democratic Republic of Congo (DRC) and Peru revealed additional factors that influence antibiotic prescribing. These were, poor laboratory infrastructure, economic incentives given to prescribers for prescribing certain antibiotics, the cost of antibiotics, the availability of antibiotics, fear of poor patient outcomes and patient demand for antibiotics (21, 33, 47, 64). A study from Lesotho found that the decision to prescribe antibiotics and the selection of appropriate antibiotics was influenced by individual attitudes and perceptions (24). A survey from Peru found that poor knowledge of antibiotic guidelines and the inability to identify the correct antibiotic to treat specific infectious organisms were drivers of prescribing behaviour (33). In a Gambian study, health practitioners cited the unavailability of laboratory support and inadequate supervision as the main reasons for inappropriate antibiotic prescribing (50). Farley et al (65) conducted a KAP survey on primary health care providers in South Africa predominantly from the private sector and in their study, 67% of participants felt pressure from patients to prescribe antibiotics. The same study also reported that the participants that attained higher knowledge scores reported better prescribing behaviour than those with lower knowledge scores which demonstrated that knowledge affects prescribing behaviour (65). KAP surveys on AMR and AMS were also conducted in South Africa on pharmacy students and the students felt that education on antibiotic prescribing, antibiotic policies and institutional guidelines were the most important interventions needed to address AMR (66). Similarly, in another study in South Africa, third and fourth year medical students reported that they would like to have education on proper antibiotic prescribing as part of their curriculum (57). They also reported that they relied on advice from other physicians and handheld applications such as Epocrates when they needed to select antibiotics (57).

1.2.3 Antimicrobial stewardship programmes

Many countries have implemented ASPs with the aim of combating the misuse of antibiotics and reduce the burden of resistance (31, 32).

Composition of antimicrobial stewardship committees

The composition of ASP teams varies widely across countries and health institutions. The Infectious Diseases Society of America (IDSA) recommends that the ASP team be led by an infectious diseases physician trained in antimicrobial stewardship and a clinical pharmacist with advanced training in infectious disease (67). The South African guidelines for the prevention and containment of antimicrobial resistance distinguishes the AMS committee from the AMS team (43). These guidelines depict that the AMS committee should consist of high-ranking hospital managers such as the CEO, senior clinician, medical microbiologist, chief pharmacist, infection control practitioner and nursing service manager (43). Furthermore, they describe an AMS team as a group of people responsible for the operationalization of the AMS activities and recommend that it include a pharmacist, clinician, professional nurse, infection control practitioner, microbiologist and ID specialist (43). The guideline states that the AMS team is usually led by an ID specialist but recognizes that this cadre is scarce and may not be available in most health facilities and in that case another appropriate health professional can lead the AMS team (43). Microbiologists, ID specialists and Quality Assurance managers can also be consulted offsite if not available (43).

The scope of work of a clinical pharmacist differs from that of a hospital pharmacist. Clinical pharmacists spend more time interacting with patients at the bedside and with medical professionals compared to hospital pharmacists (68). On the other hand, hospital pharmacists spend most of their time in the pharmacy preparing medications (68). Furthermore, clinical pharmacists undergo more prolonged training with a clinical component than a hospital pharmacist (68). Some duties of a clinical pharmacist are to ensure that patients receive the correct medication for their medical condition and tracking the progress of patients whereas hospital pharmacists are involved in preparing prescription medication, completing paperwork and ordering more stock of drugs as required. These highly trained cadres of pharmacists are scarce especially in poor resource settings. In an academic hospital in Gauteng, clinical pharmacists were introduced into a surgical and trauma ICU and they implemented several different interventions that improved the monitoring of pharmacotherapy these included advising on appropriate antibiotic therapy, recommending investigations, and addressing inappropriate antibiotic doses and dosing frequencies (69). AMS team members from a private hospital in Kwazulu-Natal reported that the ICU nurse can play an advocacy role for patients in the AMS team such as by making doctors aware of the duration of antibiotics, they can also have a clinical role such as emphasizing on IPC principles and a collaborative role by being

involved in discussions with the AMS team (70). Additional cadres of health professionals recommended by the IDSA guidelines unlike the South African guidelines are information systems specialists and hospital epidemiologists, these two cadres of health professionals do not exist in the tertiary hospital where my study was carried out (71). The involvement of an information systems specialist would be relevant for data management in a setting in which electronic data systems for antibiotic prescribing and dispensing are in place (71).

The role of pharmacists in AMS as described by Parente et al (72) includes conducting prospective audits with feedback on inpatients and advising clinicians on appropriate interventions. Pharmacists can also be involved in the transition of patients from in-patient to an out-patient settings and in the outpatient setting (72). The involvement of facility leadership is also recommended by the CDC to support AMS activities in different ways such as by showing commitment to the programme and by providing financial support, staffing support and support in other areas where the need arises (73). Microbiologists are an integral component of AMS committees and can provide statistics of relevant infections such as *Clostridium difficile* which can be used to assess the success of the strategies being implemented by ASPs as well as introduce different diagnostic tools to facilitate stewardship efforts (74). An Australian study showed that the involvement of nurses in AMS activities resulted in improved knowledge and an increase in the switch from intravenous to oral antibiotics (75).

In a hospital in New York, the ASP team consisted of infectious disease specialists, infectious diseases trained pharmacists and clinical microbiologists (76). Conversely, ASP teams may comprise only an infectious disease physician and in other settings only pharmacists as seen in smaller hospitals in the UK and in South Africa (39, 77). In a tertiary academic hospital in Cape Town, South Africa, the core ASP team is very well resourced and consists of an infectious diseases specialist, a consultant microbiologist, an infection prevention and control nurse and a ward pharmacist (32). In a private hospital in the Western Cape a study showed that nurses have an important role to play in AMS and are a cost-effective resource and therefore should be part of the AMS team (78). Interestingly, despite the variations in composition, positive outcomes are obtained by these ASPs.

Interventions instituted by ASPs

Interventions instituted by ASPs are multiple, a survey conducted on infectious diseases specialists in the USA reported using 164 different ASP strategy combinations in different health facilities (38) but the two main interventions are formulary restriction with pre-authorization and prospective audit with intervention and feedback (PAF) (3). Supplemental interventions include education, guidelines, antimicrobial order forms, de-escalation of therapy, changing from intravenous to oral administration, switching therapy and dose adjustment (3).

One of the advantages of PAF mentioned in the literature is that the prescriber's autonomy is not lost (3). A paediatric tertiary institution in Nashville implemented PAF as their main ASP strategy and the recommendations made by the AMS team were non-binding which meant that the prescriber was free to choose whether or not to follow the recommendations given (31). In this institution there was a 77% compliance rate to the recommendations made, there was no significant difference in compliance among the different specialties but there was a difference in compliance with ASP recommendations based on the role of the provider receiving the recommendation (31). They found that pharmacists and residents were more compliant than nurses, that compliance varied with the type of recommendation given and recommendations to discontinue treatment were more likely to be followed than those advising them to consult an infectious disease physician (31). Despite the incomplete compliance, the Nashville study showed a decline in the antimicrobial use of 11.1 % per year after the institution of the ASP (31). Duane et al (79) noticed that there was lower compliance to ASP recommendations by surgical services compared to medical services.

In a tertiary hospital in Switzerland, formulary restrictions, guidelines and educational sessions were implemented in a stepwise manner and they noted a significant cost reduction in antibiotic related expenditure in the hospital (34). The educational interventions included lectures on antibiotic use, weekly ward rounds, yearly provision of hospital's antibiotic susceptibility patterns and provision of feedback to staff on antibiotic expenditures (34). Formulary restriction with pre- authorization has been associated with an increased administrative burden which can lead to delays in obtaining antibiotics because the justification for an antibiotic should be provided by the clinicians before the antibiotic can be dispensed and it can also result in the overuse of antibiotics that are not restricted as these are easier to access although may not be the appropriate antibiotic for the infection being treated (43).

Davey et al (80) compared the efficacy of restrictive versus persuasive interventions, the persuasive interventions that they looked at included advising physicians on how to prescribe antibiotics or providing feedback on how they have prescribed them whereas restrictive interventions included the need for preauthorization by an infectious disease specialist before an antibiotic can be prescribed (80). They found that restrictive interventions worked faster than persuasive interventions in changing the antibiotic prescribing habits for hospital inpatients (80). These findings suggest that the former may be useful when fast results are needed but the effects can be short-lived and therefore there is a need to supplement with the latter (80). In addition, these authors demonstrated that restrictive interventions had a better microbial outcome at six months when compared with persuasive interventions (80). Black and colleagues (81) also found that restrictive interventions were negatively viewed as “policing” and led to poor relationships. The authorization of prescriptions for restricted antibiotics by antimicrobial stewardship teams can be done in different ways, it was done telephonically and through an electronic system in two hospitals in Australia (45). PAF resulted in an increase in antibiotic consumption and length of hospital stay compared to prior authorization in a tertiary hospital in Philadelphia (82).

Developing and disseminating guidelines on antibiotic prescribing based on the local resistance patterns is another way in which ASPs achieve appropriate antibiotic prescribing. A South African study that assessed the resistance profiles of bacterial isolates from different levels of care hospitals in Kwa Zulu Natal demonstrated that the resistant patterns of bacteria varied amongst facilities that provide different levels of care. Isolates from tertiary hospitals displayed resistance to more antibiotics than those from regional and district hospitals, this study demonstrated that showed that prescribing antibiotics based on a national guideline is not likely to be effective and that each facility should create its guidelines based on the resistance patterns in that facility (83). In a UK study, it was noted that the hospital had guidelines on antibiotic prescribing but some of the doctors were not aware that they existed and those that knew felt that they were too elaborate and would have preferred simplified straightforward guidelines (62). Broom and colleagues (60) found that in addition to providing guidelines, the rationale for guideline recommendations should be communicated to the clinicians to improve compliance.

Education is one of the supplementary strategies recommended by South African guidelines and IDSA, they recommend that teaching on antibiotic stewardship is included in the medical curriculum but that it should be accompanied by the core strategies formulary restriction with pre-authorization and prospective audit with intervention and feedback (43, 67, 71). The South African national strategic framework for antimicrobial resistance recommends the inclusion of antimicrobial stewardship teaching into the undergraduate and curriculum of health professionals as a strategy to combat resistance in addition to in-service training of the existing workforce (84). South African medical students and pharmacy students reported that they would like to have education on appropriate antibiotic prescribing incorporated into their university curricula(57, 66). Medical students from three universities in South Africa reported that they would like more education on antibiotic prescribing and felt like they had inadequate knowledge on the matter (58).

A qualitative study on junior doctors in the UK found that first year doctors would like to have education on antibiotic prescribing (63). Their needs included informal ward based teaching rounds in which decision making processes are shared with the junior doctors, an induction pack with important information that they would receive when starting their rotations in a specific department and more supervision of their prescriptions such as countersigning of prescriptions written by junior doctors by a senior (63). In another UK based study, doctors reported that they would like to have continued medical education on antibiotic prescribing (62).

In a tertiary hospital in South Africa, a comprehensive ASP package that included weekly antibiotic stewardship ward rounds, a new antibiotic prescription chart and online education sessions was introduced in 2012 in an academic hospital in Cape town (32, 85). This ASP also instituted restrictions on some antibiotics and imparted education on AMS during the ward rounds (85). Over four years, this ASP had a sustained reduction in antibiotic consumption and expenditure in the hospital indicating that these interventions can be effective in similar settings to this (85). Furthermore, in South Africa a pharmacist-led PAF intervention across 47 private hospitals resulted in a significant reduction in the consumption of antibiotics, this finding provides an alternative way of running ASPs in settings where there are limited infectious diseases resources (39). In addition, Brink et al (86) showed that a pharmacy-led process improvement strategy that included audit and feedback resulted in a reduction in rates of surgical site infections and improved compliance to antibiotic prescribing recommendations in

a study that included 34 private South African hospitals. In an academic hospital in Ethiopia, a mixed-methods study found that participants believed that prospective audits with feedback would be more labour intensive than formulary restriction and should be implemented only in certain wards (47).

1.2.4 Facilitators and barriers to the establishment and implementation of an ASP

Implementation is a continuous and interactive process rather than a static event and to implement one intervention it may be necessary to change some existing ways of doing things (87). The overall aim of antimicrobial stewardship is to change prescribing behaviour. Various facilitators and barriers to the establishment of a successful antimicrobial stewardship programme extracted from the existing literature are discussed in the ensuing section.

Facilitators to the establishment of an antimicrobial stewardship programme

The use of antibiotic guidelines to overcome the knowledge deficit on antibiotic prescribing has been identified as a facilitator for the successful implementation of ASPs and is one of the recommended interventions (88). A survey in Congo indicated that having local antibiotic guidelines instead of international ones could facilitate the success of an ASP (21). Similarly, the findings of a qualitative study in which ASP pharmacists and physicians representing 21 academic medical centers in the USA were interviewed, indicated that using evidence-based guidelines was useful for the success of ASP strategies particularly for communication purposes, to gain buy-in from clinicians and even in conflict resolution (89). A mixed methods study conducted in rural hospitals in Australia identified the free availability of national antibiotic prescribing guidelines as a facilitator (90). Promotion of antibiotic policies by hospital management was found to be an important facilitator as well, Skovdin et al (59) found that the lack of promotion of antibiotic guidelines by hospital management resulted in uncontrolled antibiotic use.

The findings by Thriemer et al (21) also point to the fact that having additional training on antibiotic prescribing would also be a facilitator to a successful ASP. Establishing good relationships and good communication amongst colleagues is important for the success of an ASP, in particular a face-to-face non-confrontational communication style improved the receptiveness of prescribers to recommendations made by AMS team members (89). A study

conducted in the Netherlands found that preserving the prescriber's autonomy and having a participatory approach in choosing ASP interventions was successful in improving the appropriateness of antibiotic prescriptions (36). Having a sense of pride in their health care facilities was also described as a facilitator to the implementation of ASPs (90).

Pakyz et al (89) conducted a study on health professionals employed in the university health systems consortium in the USA and found that including non-ASP committee members in the programmes' activities and gathering support from different clinical specialties and the institutional leadership was very useful in increasing the uptake of ASP recommendations. An Ethiopian study identified that the existing prescribing hierarchy in the hospital and the national initiative to implement ASPs was as facilitator (47). Similarly, in the UK study, the hierarchy of instruction was seen as favorable to making informed prescribing decisions and may facilitate ASPs (62). In a study conducted in a hospital in Madrid, Bouza and colleagues (74) described how a microbiology laboratory created a system for fast-tracking laboratory results by identifying patients whose specimens needed to be prioritized and assigning these specimens to a specific microbiology team that ensured rapid processing and reporting of results to the clinicians allowing for directed antibiotic therapy to be instituted. Therefore an efficient and supportive microbiology laboratory is a facilitator to establishing an ASP.

Barriers to the establishment of an antimicrobial stewardship programme

There is a paucity of knowledge regarding optimal antibiotic use in low- and middle-income countries which is a challenge to ASPs and this is due to the lack of capacity to conduct surveillance activities in some institutions that do not have access to microbiology laboratories (91). Broom et al (60) found that a lack of communication between AMS teams and clinicians limited the opportunity for the team to explain the rationale behind the antibiotic guidelines that they had implemented and as a result clinicians found them confusing and did not adhere to them. Junior doctors in particular, displayed a lack of knowledge needed to make decisions regarding antibiotics and were more likely to prescribe broad-spectrum antibiotics due to a lack of knowledge and following trends (47). This lack of knowledge can pose as a barrier to ASP activities as they would require a significant amount of support.

Broom and colleagues (60) in the UK found that there was a reluctance from consultants to accept antimicrobial advice from microbiologists with the reasoning that microbiologists are laboratory-based and not at the bedside of the patient. Therefore, these consultants believed

that the ultimate decision should be made by the treating clinician disregarding the advice given by a microbiologist (60). This way of thinking can pose as a barrier to ASP implementation as the members of an AMS team will need to advise clinicians on antimicrobial choices during prospective audits and in stewardship ward rounds. The same study also found that advice from infectious diseases (ID) specialists was believed to be more relevant compared to that of microbiologists even though consultants were not always receptive of both (60). The reluctance of consultants to adhere to advice from ID specialists and microbiologists coupled with the senior consultants teaching junior doctors how to prescribe antimicrobials based on their experience and not on guidelines can potentially result in serious non-adherence to AMS guidelines and advice. In addition, the fear of antagonizing collegial relationships is also described as a barrier to successful ASPs as it may result in the ASP team not recommending changes where they deem necessary (92). In an Australian study, a lack of confidence in AMS guidelines was brought up as a barrier by specialist pulmonology doctors who did not think that guideline recommendations were applicable to their specialized patients and would prefer to make decisions based on individual patients (45). Furthermore, in the same study, the pulmonologists were not involved in the development of the guidelines which added to the lack of confidence (45).

Pakyz et al (89) noted that a shortage of personnel to carry out programme activities was a significant barrier to the success of an ASP. In particular, the shortage of physicians to provide oversight to the programme and the unavailability of infectious disease physicians to make decisions regarding restricted antibiotics in a timely fashion (89). Particularly, they noted that a mismatch between the workload and the dedicated time that physicians had to work on ASP activities was a challenge (89). A lack of information technology is another barrier to ASPs success and this includes shortages of electronic systems for resource allocation, real-time feedback, clinical surveillance and tools for clinical support (89). Specifically the inability to have electronic surveillance of strategies, and to incorporate real-time microbiological and clinical data when implementing ASP strategies (89). The lack of remuneration of infectious disease physicians for their participation in ASPs has also been cited as a barrier to ASPs' success (92). In rural hospitals in Australia, it was identified that the lack of access to infectious diseases and microbiological support, the lack of access to education, lack of pharmacists with AMS skills and difficulties in retaining qualified staff in rural facilities were significant barriers (90).

Some challenges that are specific to low- and middle-income countries (LMIC) are firstly that some health facilities lack the laboratory infrastructure for an accurate diagnosis to be made and for context-specific guidelines to be developed (91). Shortages of trained personnel such as microbiologists have been cited as a weakness in the current systems to address AMR in South Africa (93). An Ethiopian study identified the lack of laboratory infrastructure, delays in getting laboratory results, as well as a shortage of expertise in terms of infectious diseases specialists and clinical pharmacists as challenges to the implementation of ASPs (47). Poor regulation of antimicrobials means that their safety, quality and efficacy may not be known (91). The fact that the institutional policies did not support the implementation of ASPs and that other health facilities were not implementing them uniformly was also perceived as a challenge (47). A lack of an electronic prescribing system and a system that links the pharmacy to the laboratory and clinical data systems in the institutions in South Africa was also viewed as a weakness (93). In general, the healthcare facilities in LMIC usually have a large patient volume, poor infrastructure, and a shortage of health personnel which are significant barriers to implementing an ASP and these need to be addressed for the ASPs to be successful (91).

Box 1: Key Findings from the Literature Review

- Inappropriate prescribing practices are prevalent in both high, low and middle-income countries.
- The drivers of antibiotic prescribing are multiple and consist primarily of health systems, health worker and patient related factors. Understanding these drivers can lead to the identification of the potential facilitators and barriers to the establishment of antimicrobial stewardship programmes in health care facilities.
- Some barriers are specific to low- and middle- income settings, therefore solutions need to be tailored to specific settings.

1.3 Problem Statement and Study Justification

Antimicrobial resistance is a public health threat that is partly driven by the misuse of antimicrobials (18). Antimicrobial stewardship programmes can reduce the overuse of antibiotics and their implementation is recommended by the WHO in the Global Action plan against antimicrobial resistance (15). Although several studies have been conducted to understand health worker antibiotic prescribing practices and the facilitators and barriers to the

successful implementation of antimicrobial stewardship programmes (89), there is a dearth of research on what it takes to establish these programmes from the onset to implementation in sub-Saharan African countries. Therefore, this study aimed to explore the perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme at a tertiary hospital in Gauteng province. In particular, the study intended to provide insights into what it takes to establish an antimicrobial stewardship programme, who should form part of their team, what interventions they should implement, as well as how they are accepted by health professionals affected by them. While recognizing that each health institution may face its own unique challenges in establishing an ASP programme, understanding perceptions and attitudes of those that may influence its implementation and success is important to tailor the programme and increase its acceptability. To my knowledge, this is the first study of this nature in the Gauteng province.

1.4 Study Aim and Objectives

The overall aim of this study is to provide an in-depth understanding of the perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme in a tertiary hospital in Gauteng province. The specific objectives are to:

1. Explore the perceptions and attitudes of health professionals regarding the establishment of an antimicrobial stewardship programme in the Department of Internal Medicine at a tertiary hospital in Gauteng province in 2019.
2. Describe perceived facilitators regarding the establishment of an antimicrobial stewardship programme at a tertiary hospital in Gauteng province in 2019.
3. Describe perceived barriers to the establishment of an antimicrobial stewardship programme at a tertiary hospital in Gauteng province in 2019.

2 CHAPTER 2: METHODOLOGY

2.1 Introduction

In this chapter, the specific methods used to achieve the aims and objectives of this study are discussed. The chapter begins with a discussion of the study design used followed by a description of the study setting. Thereafter, the study population, the sampling methods used to select study participants, and the data collection procedures are discussed. The chapter will conclude with the discussion of the data management, data analysis and ethical considerations.

2.2 Study Design

An exploratory qualitative study design was used in order to get an in-depth understanding of the views of health professionals with regards to antimicrobial prescribing practices and the establishment of an antimicrobial stewardship programme. This study design allows for new concepts to emerge as each participant can elaborate on their experiences in their own words (94).

2.3 Study Setting

This study was conducted at a public sector tertiary care academic hospital in Gauteng province. The site was selected based on accessibility and feasibility to the researcher since she is currently an employee in this facility. The hospital provides inpatient and outpatient specialized health services to its catchment population and it is divided into five clinical departments: a) surgery and surgical disciplines, b) obstetrics and gynaecology, c) paediatrics, d) internal medicine, and e) allied health care services. There are three main pharmacies in the hospital which cater to adult inpatients and outpatients and the paediatric department.

At the time when this study was conceptualized, the participating hospital was in the early stages of establishing an ASP. When data collection was taking place the AMS committee was established and had completed the pilot phase of AMS ward rounds in the Department of Internal Medicine. However, at the time of writing this research report the ASP was well established, the achievements of the ASP are detailed below:

- A multi-disciplinary AMS committee had since been established;
- Ongoing antimicrobial stewardship teaching ward rounds were being carried out in the Department of Internal Medicine and obstetrics;

- Hospital-specific antibiotic guidelines based on the local antibiotic resistance patterns had been created;
- The committee held monthly meetings in which antimicrobial stewardship issues were discussed;
- Restrictions on broad-spectrum antibiotics such as carbapenems and colistin were implemented;
- AMS ward rounds were being implemented.

2.4 Study Population

The study population for this research consisted of all the medical doctors and professional nurses who worked in the Department of Internal Medicine and all the pharmacists in the hospital. The Department of Internal Medicine is subdivided into five units, with each unit consisting of one head of the unit, approximately five consultants, five registrars, six medical interns and 12 professional nurses. The registrars rotate between three academic hospitals during their four years of training and the interns rotate within the same hospital through various departments during their two-year internship programme. The consultants and professional nurses are permanently based in the same hospital. The hospital pharmacists work in either the inpatient or outpatient pharmacies within the same hospital and there are approximately 27 pharmacists in the hospital.

The Department of Internal Medicine was purposively selected as the study site because during conceptualization of this project, this department was identified as the pilot site for antimicrobial stewardship ward rounds. These ward rounds were then carried out between November 2018 and April 2019. The rationale for this choice was that the study participants were likely to provide richer information because of their prior exposure to these ward rounds compared to other departments that had not been exposed to antimicrobial stewardship.

2.5 Study Sample

Purposive sampling was used to select the participants of this study (Table 1). Ten medical doctors and three professional nurses were selected from the Department of Internal Medicine and three hospital pharmacists were selected to participate in the study. The choice of these cadres of health professionals was based on the fact that they were either affected by or could

influence the implementation of an antimicrobial stewardship programme in the participating facility.

Table 1: Summary of Study Sample

Health professional category	Number
Consultants	3
Registrars	3
Interns	4
Professional nurses	3
Pharmacists	3
Total	16

Maximum variation sampling was used to select medical doctors to ensure that the different cadres of medical doctors namely, interns, registrars and consultants were represented in the study. This sampling method is known to ensure that there is heterogeneity in the study sample (95). Furthermore, it allows the researcher to explore different perspectives from participants in different positions and provides a deeper insight into the phenomenon being studied (95). The hospital's staff allocation list was used to randomly select the participants. The three consultants that participated in the study were based in different subspecialties within the Department of Internal Medicine but for the purpose of maintaining confidentiality, these are not disclosed. Two participants had been exposed to the ASP pilot ward rounds in this hospital while some of the registrars had been exposed to antimicrobial stewardship during their rotation in another hospital.

2.6 Data Collection

2.6.1 Data collection tools

Face-to-face in-depth interviews were conducted by the researcher in English using a semi-structured interview guide (Appendix 1). Two variations of the guide were used, one that was tailored for non-prescribers such as professional nurses and pharmacists and one that was tailored to prescribers. The interview guide explored the participants' experiences with antimicrobial prescribing, their views on antibiotic prescribing practices in the hospital, their perceptions on the establishment of the antimicrobial stewardship programmes, and their perceived facilitators and barriers to the implementation of an antimicrobial stewardship

programme in the hospital. A semi-structured interview guide was chosen because it ensured that important pre-determined questions were asked while still leaving room for the elaboration of responses and exploration of other emerging issues. The questions from the interview guide were informed by the literature. Field notes were taken at each interview to capture some of the non-verbal cues that were expressed by the study participants.

2.6.2 Data collection procedures

The study participants were contacted in person and telephonically by me and were invited to participate in the study. The study information sheet (Appendix 2) was offered to them to read so that they could familiarize themselves with the objectives of the study. I then scheduled interviews with those who agreed to participate in the study. The interviews were scheduled for a date and time that was convenient for the study participants to ensure that their daily routines were not disrupted. All the participants signed informed consent before commencing with the interviews. Two potential participants did not participate in the study despite having agreed to due to time constraints on their part despite many attempts at rescheduling the interviews. This was dealt with by finding other study participants.

All the interviews were conducted between April and June 2019. Quiet areas that were not occupied within the hospital were identified to conduct the interviews. The interviews were recorded using a digital audio-recorder and they took approximately 30 to 45 minutes to complete.

2.7 Pilot Study

Due to the difficulties of seeking approval in another hospital, a pilot study was conducted in the same hospital where the study was conducted but at a different department. The interviews were conducted with five participants comprising of a professional nurse, a pharmacist, a medical intern, a registrar and a consultant. The pilot was beneficial in several ways:

- a. It emerged from the pilot that the concept of antimicrobial stewardship was not understood by everyone which made it difficult to ask questions related to its establishment. As a result, this necessitated the researcher to provide a brief description of antimicrobial stewardship to all the study participants.
- b. It assisted to estimate the time it took to complete a single interview and this information was useful for scheduling appointments.

- c. It allowed the researcher to refine her qualitative interviewing skills to obtain richer information from the study participants.

2.8 Data Management and Quality Assurance

I ensured that the audio recordings and transcripts were labelled correctly using unidentifiable codes and that they were saved in a password encrypted computer. The audio recordings were transcribed verbatim by the researcher and for quality assurance purposes, the transcripts were printed and read line by line while listening to the audio recordings. These post-transcriptional checks were conducted multiple times for each transcript to ensure that there were no transcription errors. In some cases, the quotations were edited to improve the readability and to maintain the confidentiality of the participants while retaining the original meaning of the quotation. The signed consent forms were kept in a secure location. The audio recordings and consent forms will be destroyed five years after completion of the study.

2.9 Data Analysis

After transcription was completed and the accuracy of the transcripts was checked, the transcripts were downloaded into NVivo version 12 software. Thematic analysis using both inductive and deductive approaches were used to analyze the data. Thereafter, all the transcripts were read line by line to identify dominant and subthemes. In conducting thematic analysis, I made the assumption that similar ideas expressed by a number of different participants signified that the idea was a recurring theme. Once a theme was identified in one transcript, the other transcripts were read to see if this theme was expressed by other participants and the manner in which it was described, while at the same time ensuring that dissimilarities were also recorded. As the themes emerged, I compiled a comprehensive codebook. Some of the quotations from the different codes are shared in the results chapter. The interpretation of the interviews was validated by my supervisor on various occasions.

2.10 Ensuring Rigor

In order to ensure consistency and dependability of the data, my supervisor and I each coded three similar transcripts from different groups of participants independently and thereafter met to discuss any coding discrepancies until an agreement was reached.

2.11 Reflexivity

On reflecting upon my position in the study, I considered myself an insider since I am medically qualified with experience on antimicrobials and I have been working as a doctor for many years in the same hospital where the study was conducted. I am also a member of the newly created ASP committee and I work primarily in the division of infectious diseases and infection prevention and control. I was familiar with the environment and I had a collegial relationship with most of the study participants. The advantage of my insider position was that the participants felt comfortable opening up to me as they did not feel like they were talking to a stranger. The disadvantage was that they became over-familiar at times and assumed that I shared the same sentiments as them concerning certain issues in the hospital. As a result, they did not feel the need to elaborate on some of their responses and in those cases I had to ask them to expand on their responses.

At the time when I decided to carry out this study, the hospital was in the preparatory phases of re-establishing an antimicrobial stewardship committee and had not initiated any activities. This process was led by one of the infectious diseases specialists with whom I worked closely. I was interested in understanding the perceptions and attitudes of the health professionals in the hospital as I felt that they could inform the implementation process. Since I had to undergo the lengthy process of protocol submission and assessment as well as obtaining ethical approval for the study, I missed the opportunity to get that information before the AMS committee was established and before any activities commenced. When I started conducting interviews, an AMS committee had been established and a pilot of antibiotic prescription charts and AMS ward rounds had been conducted in the Department of Internal Medicine. Nevertheless, I felt that the study would still be relevant because the pilot only included one department in the hospital. As this was the first study of its nature in this hospital, it would still provide valuable information that could be used in the implementation of the ASP in the rest of the hospital. Only three of the study participants, one pharmacist and two consultants had been involved in the pilot AMS ward rounds. Most of the study participants were unaware of my involvement in the AMS committee hence there were limited chances of bias from the participants' side. Throughout the research process, I was continuously self-aware of how my role in the hospital may influence the interviews, analysis and interpretation of the findings. I ensured that my tone of voice and body language was not judgmental and made the respondents feel comfortable enough to open up while maintaining a professional environment.

2.12 Ethics

Ethical approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (HREC) (M181172). Furthermore, permission to conduct the study was obtained from the hospital's research protocol committee, the clinical head of the Department of Internal Medicine and the hospital's pharmacy manager. Informed consent to participate in the study and to be audio recorded was obtained from the study participants before conducting the interviews. All the participants read the information sheet that explained the details of the study and the terms of confidentiality and if the participants decided not to partake in the study, their decision was respected. My contact details, those of my supervisor, and the Wits HREC were provided to the study participants in the information sheet (Appendix 3). The participants were informed that the audio-recordings would only be accessible to me and my supervisor.

All the information collected has been kept confidential and no identifying information will not be disclosed. The data has been kept anonymous and pseudonyms such as '*intern 1*', '*professional nurse 2*' have been used to represent participants in the final research report. The data has been kept in a safe and secure place. The audio-recordings will be destroyed after six years if the study is not published or two years after the publication of the research findings.

3 CHAPTER 3: RESULTS

3.1 Introduction

In this chapter, I discuss the findings of the study by starting with describing the characteristics of the participants. Thereafter, the findings related to the crux of this study are discussed. These are organized into five broad themes namely, a) *antibiotic prescribing practices*, b) *drivers of antimicrobial prescribing and administration practices*, c) *perceptions about the establishment of an antimicrobial stewardship programme*, d) *perceived facilitators to the implementation of an antimicrobial stewardship programme*, and e) *perceived barriers to the implementation of an antimicrobial stewardship programme*. From each of these themes, several sub-themes emerged as demonstrated in Table below.

Table 2: Summary of Study Themes

Broad themes	Sub-themes
Antibiotic prescribing practices	• Patterns of antibiotic prescribing ○ Appropriate antibiotic prescribing ○ Inappropriate antibiotic prescribing ○ Appropriate antibiotic prescribing reported as inappropriate • Antibiotic administration practices
Drivers of antibiotic prescribing and administration practices	• Health worker factors ○ Health worker knowledge ○ Fear of poor patient outcomes ○ Taking the easier way out • Health facility environment factors ○ Prolonged laboratory turnaround times ○ Staff shortages and heavy workloads ○ Shortage of antimicrobials ○ Antibiotic prescribing culture • Guideline factors • Patient factors ○ Patient demand for antibiotics
Perceptions about the establishment of an antimicrobial stewardship programme	• The composition of an antimicrobial stewardship committee • Activities for the antimicrobial stewardship programme ○ In-service training ○ Provision of guidelines ○ Control access to antimicrobials ○ Antibiotic prescription audits ○ Institute effective communication strategies

Broad themes	Sub-themes
Perceived facilitators to the establishment of an antimicrobial stewardship programme	• Expertise and diagnostic facilities • Willingness to learn • Support from hospital management
Perceived barriers to the establishment of an antimicrobial stewardship programme	• Heavy workload • Laboratory delays • Shortage and mismanagement of antibiotic stock • Resistance to change • Poor communication amongst stakeholders • Use of a paper-based system • Perceived availability of resources

3.2 Characteristics of Study Participants

3.2.1 Career characteristics

In this study, 16 health professionals were interviewed between April and June 2019. The different cadres of health professionals and their distribution were described in Chapter 2. Their length of service in the hospital in their current positions varied, with six reporting being employed for six months or less, seven reporting being employed for one to five years, and three had been employed for more than five years, with the longest length of service being 22 years.

Table 3: Characteristics of Study Participants

Study participant	Speciality working in	Work experience in current position in years and months
Professional nurse 1	Internal medicine	3 years
Professional nurse 2	Internal medicine	22 years
Professional nurse 3	Internal medicine	5 years
Medical intern 1	Internal medicine	4 months
Medical intern 2	Internal medicine	4 months
Medical intern 3	Internal medicine	4 months
Medical intern4	Internal medicine	4 months
Medical registrar1	Internal medicine	2 years
Medical registrar 2	Internal medicine	3 years and 6 months
Medical registrar 3	Internal medicine	1 year and 3 months

Consultant 1	Internal medicine	6 months
Consultant 2	Internal medicine	5 months
Consultant 3	Internal Medicine	19 years
Pharmacist 1	Hospital pharmacy	8 years
Pharmacist 2	Hospital pharmacy	3 years
Pharmacist 3	Hospital pharmacy	2 years

3.2.2 Roles in antibiotic management

When asked about their role in antibiotic management, as expected, all the professional nurses reported that they administered antibiotics to patients according to doctor's prescriptions. Additionally, professional nurses reported that they monitored the length of antibiotic use, checked the expiry dates of antibiotics and alerted doctors when antibiotics were not available in the hospital. They also mentioned that they requested doctors to prescribe alternative antibiotics when the ones prescribed were not in stock in the hospital pharmacy. One nurse reported that she stopped administering antibiotics once the prescription chart was full. This was unexpected as the decision to stop an antibiotic is normally determined by a doctor.

"If we have given (an antibiotic) for 7 days, the prescription guides us to start from day 1 to 7 and then if it's the end of the page on the prescription, we don't continue giving. We stop it." (Professional Nurse 1).

All the cadres of medical doctors reported that they were responsible for prescribing antibiotics and additionally the senior consultants reported that they also checked the appropriateness of antibiotic prescriptions written by the junior doctors. One of the consultants, who is a member of the hospital's antimicrobial stewardship committee reported being involved in conducting antimicrobial stewardship ward rounds and authorizing the release of restricted antimicrobials. The pharmacists reported that their primary role was to dispense antimicrobials to patients and to the wards. Pharmacists also reported that they restricted access to antibiotics and requested microbiological proof that patients required an antibiotic before dispensing restricted antibiotics such as carbapenem. In addition, one senior pharmacist reported that she was also responsible for ordering antibiotics for the hospital from drug companies. Furthermore, the pharmacists reported that at times they attended ward rounds in which the use of antibiotics was discussed and gave input on the availability of stock.

3.3 Antibiotic Prescribing Practices

When the participants were asked to share their understanding of antibiotic resistance, their responses indicated that they all had a good understanding of antibiotic resistance. They were also aware of the link between resistance and the misuse of antibiotics. As illustrated by the quotations below, the respondents reported that antibiotic misuse consisted of practices such as the use of antibiotics for an inappropriate duration, using wrong the antibiotic to treat an infectious syndrome and the overuse of broad spectrum antibiotics.

“Antibiotic resistance... There are two parts to that also... One is either you're giving the wrong medication or wrong antibiotic and you're not treating the situation or you are also not treating it for long enough creating the resistance of bacteria.” (Intern 2).

“It (resistance) happens in a case in which a particular organism that is responsible for an illness does not respond to a particular medication that might have been previously responsive to that medication but right now it's developed uhm I mean the medication is not able to work appropriately... In terms of either its concentration... or it might work in higher concentration that might be toxic to the patient. So, obviously the organism has acquired immunity to that particular medication. So, it's not working and you are not getting the desired outcomes.” (Registrar1).

3.3.1 Patterns of antibiotic prescribing

In this section, the responses of the study participants regarding the antibiotic prescribing patterns in the hospital are reported according to three sub-themes: a) *appropriate antibiotic prescribing*, b) *inappropriate antibiotic prescribing* and c) *appropriate antibiotic use reported as inappropriate*. These are expanded further below.

Appropriate antibiotic prescribing

This study found that five out of ten doctors were of the view that antibiotics were prescribed appropriately in the hospital. They reported that the indications for initiating antibiotics were appropriate most of the time and that reasonable antibiotic choices were made based on guidelines. The following quotations reflect these views.

“I know that with us, with me and the registrars that I have worked with so far, I haven't seen inappropriate antibiotic use, I must say. We will cover with a broad spectrum until we've got a culture then we'll change and we really give antibiotics where we think it is absolutely necessary” (Intern 1).

“More often than not, the antibiotics would have been initiated by a junior staff and most of the time they're reasonable and all that and you hardly ever ever interfere until you've got... obviously a proper result...” (Consultant 3).

Inappropriate antibiotic prescribing

Overall, the misuse of antibiotics was far more commonly reported than the appropriate use. Interestingly, all the non-medical participants and the remainder of medics reported that antibiotic use was inappropriate. However, 2 doctors reported both appropriate and inappropriate use. The different types of antibiotic misuse provided by the participants were: inappropriate duration of antibiotic prescriptions, very quick and multiple changes of antibiotics, inappropriate combinations of antibiotics, simultaneous use of multiple antibiotics, antibiotics given pre-emptively for non-infectious conditions, use of last-line antibiotics empirically, antibiotic use where it is not indicated, wrong choice of antibiotic for the infections being treated, rapid escalation of antibiotic classes without any evidence of clinical deterioration. Some of these different forms of misuse were expressed in several quotes illustrated below:

Prolonged antibiotic use: *“I mean... I've noticed a few people who would give out a particular antibiotic for more than the prescribed number of days... Like some people would let's say with pneumonia which is common here they can prescribe azithromycin for more than a week; people give augmentin for more than 12 days. And then you could find someone prescribing an antibiotic and the patient is not getting better and they're not talking about possible switching, or the culture results... That's happening sometimes” (Registrar 1)*

Inappropriate combination of antibiotics: *“...Where I was working before... They didn't prescribe augmentin and rocephin together. They started with augmentin, and if augmentin was not working they would complete 7 days of augmentin before they stopped it and started rocephin, but here they can give the two together.” (Professional Nurse 1)*

Antibiotics are given pre-emptively for non-infectious conditions: *“... It's happened a few times actually with patients that we're suspecting of having possible pneumonia but their inflammatory markers are flat and the patient is actually quite well and then there's a cover that's given with the broad spectrum antibiotic when it turns out to be mild congestive cardiac failure or bi-ventricular failure... So, we cover that with antibiotics...” (Intern 1)*

Appropriate antimicrobial prescribing reported as inappropriate

Three doctors described experiences in which they had given an antibiotic empirically based on their clinical findings. However, they reported this as inappropriate when they were asked to describe instances when they had prescribed antibiotics inappropriately as is shown in the quotes below:

“It does happen (inappropriate prescribing) like for example old people or confused patients where there's no obvious cause and clinically they're tachycardic, they are very warm to the touch. When you think for an example it's meningitis or an HIV positive patient comes in with the symptoms of meningitis and clinically has meningism then I would start prophylactic antibiotics on those patients” (Registrar 3).

“Let's take pulmonary TB but I think it's a community acquired pneumonia and I start them on antibiotics. Only to find out that they don't respond but when the gene Xpert comes then I change them” (Intern 3)

“So, sometimes you'd have a patient in an outpatient setting who is coughing and you really don't know if they have a pneumonia or not, clinically. So, you may do the bloods, do an x-ray; an x-ray may not help you, the bloods may not yet be available. So, sometimes in those patients you may have to prescribe.” (Consultant 1)

One intern was not sure of which category to classify the prophylactic use of antibiotics into:

“But I wouldn't call prophylaxis inappropriate... Well, maybe it is [laughter] you are actually treating an infection with an antibiotic but are you trying to prevent an infection or are you just going to make the situation worse... So, ja... maybe that's far as it gets inappropriate.” (Intern 4)

3.3.2 Antibiotic administration practices

Several participants described experiences pertaining to antibiotic administration in the hospital. Doctors reported that there is a prolonged hang time which is the time that it takes for a patient to receive the first dose of an intravenous antibiotic after it has been prescribed. Furthermore, a professional nurse mentioned that at times, nurses would administer antibiotics through a route that was not prescribed such as giving oral antibiotics when intravenous was prescribed. This was attributed to situations where the patient did not have an intravenous line in place for the administration of the antibiotic and also if the intravenous antibiotic was not available in the ward and needed to be collected from the pharmacy. The nurse also complained

that some nurses do not attempt to source the intravenous antibiotic from other areas in the hospital when it ran out in a specific ward.

“The other thing would be: there is no consistency in the use of antibiotics, especially when it comes to IV antibiotics. For example, we nurses, know that as an alternative to augmentin IV, we can give augmentin oral but the doctor will order 1.2g of augmentin IV TDS, then there's no IV line. You are failing to put up the IV line, there's no time to call the doctor. You give the patient oral whereas oral does not match the strength of the IV. You give 375mg whereas you omit the others because of this one or two... So I'll opt for the easier option. If there's augmentin oral; I'd give the patient augmentin oral. In my mind, I'd be thinking: at least she got something.” (Professional Nurse 3)

Another practice that was quoted by another professional nurse was the administration of double the dose of an antibiotic at a given time to avoid having to administer a dose later. Some participants also mentioned that antibiotic prescription charts were sometimes signed to indicate that an antibiotic had been given to a patient in cases where it actually had not been given and was known to be out of stock in the entire hospital. One pharmacist described her experience during a ward round in which an antibiotic had been signed for as given when she knew that it was not available in the hospital at the time:

“I went on a ward round last year, I went randomly one day out of the blue and the nurse had signed off that they had given flucloxacillin, and then me being me I said but flucloxacillin has been out of stock for 3 weeks and the nurse has been signing it off every day... Either the nurse thought she was giving something that she wasn't or maybe they have it in the ward... but as far as I know, it was out of stock at that time. So, I know ward stock didn't have... maybe she thought she was giving that and then was wrong but I could be wrong but there is no way that she could have been giving it...” (Pharmacist 3).

3.4 Drivers of Antibiotic Prescribing and Administration Practices

The participants were asked about the drivers of the aforementioned antibiotic prescribing and administration practices, and their responses have been grouped into four categories a) *health worker factors*, b) *the health facility environment factors*, c) *guidelines factors* and d) *patient factors*.

3.4.1 Health worker factors

Health worker knowledge and clinical judgement

According to some respondents, some doctors lacked the knowledge needed to make a clinical judgement of whether antibiotics are indicated in certain situations. One consultant commented as follows:

“I think it relates a lot to the turnaround of laboratory data as well as being unsure of the patient’s clinical presentation that they warrant antibiotics or not.” (Consultant 1)

Participants also reported that most doctors relied on the knowledge that they acquired during their medical training and make a clinical judgement to start a patient on an antibiotic. They seldom referred to guidelines or protocols when prescribing antibiotics. Some doctors expressed that when antibiotics were started empirically, they were always based on clinical judgement and that appropriate microbiological cultures were taken before initiating antibiotics. Furthermore, they mentioned that antibiotics were tailored according to the culture results once these were available. A quote reflecting the effect of health worker knowledge on antibiotic prescribing is shown below:

“You use your clinical judgment, which is utmost because sometimes you see the patient and you have the diagnosis at the back of your mind but at that point in time you don’t have, like microbiological confirmation of what might be wrong with the patient, but if you look at the patient clinically you can decide... If someone comes in and they look like they got pneumonia... they’ve got a fever, they are tachypnoeic and the x-ray shows infiltrates or a consolidation basically... you know that this is pneumonia... Then obviously you use your judgment and then there’s an EDL that guides... even when the test has not been done, then you can actually start the patient on empiric treatment while you’re still waiting for your sputum or blood cultures that would... probably... then you can change the antibiotics probably later afterwards.” (Registrar 1)

Only one consultant mentioned that he relied on experience when prescribing antibiotics.

“Like for instance, if you have to use vancomycin we tend to use it a bit liberally perhaps... But that’s really being based on our experience.” (Consultant 3).

Fear of poor patient outcomes

A few participants reported that they would rather give an antibiotic than miss an opportunity to treat patients with a potential bacterial infection and risk increasing their morbidity and

mortality. As such, these respondents reported prescribing antibiotics a lot more than may have been necessary. This was found to be more common in the medical admission wards where the majority of patients were initiated on antibiotics.

“I think that those that are started empirically it’s often because they think the patient looks incredibly sick on admission, and they think they will benefit from it and it’s not always the case.” (Registrar 2)

“So, I think it’s the risk of a patient developing a nosocomial sepsis or patients who’ve been in hospital before... like they’ve been transferred from the other hospital and there’s a risk of having a nosocomial infection from elsewhere” (Intern1)

Taking the easier way out

An intern and two registrars mentioned that sometimes antibiotics were given because it was the easier thing to do as it avoids having to fully investigate the patient for sepsis.

“Sometimes we treat because it is easier to give the medication and then you will see the response quickly if it is right, if it’s correct. If it’s not it doesn’t really harm the patient, not necessarily... Uhm, in that sense it’s difficult to say we need to wait for the right culture before we give medication.” (Intern 2)

“You find that sometimes you know the right thing, but sometimes doing the right thing becomes much more difficult...” (Registrar 1)

“I think because they’re not sure what else to do... I think people panic (when) they see a rise in the septic markers and... uhm, I think it’s easier to treat the blood result rather than to look for a source, and to look for the cause ...” (Registrar 3)

3.4.2 Health facility environment factors

Prolonged laboratory turnaround time

Prolonged turnaround time for microbiological culture results to be received by the clinicians resulted in the prescription of antibiotics that may not have been appropriate, this was reported by some of the study participants although they did not specify what the exact time delay was. This registrar described his frustration in the quote below:

“Sometimes you have bloods and then the bloods are not ready for days maybe the labtrak is off for days... And you see the patient in front of you is deteriorating, you need to take action even prior to having results ready.” (Registrar 1)

Staff shortages and heavy workload

Staff shortages and a heavy workload resulting in time constraints for the doctors, nurses and pharmacists were brought up many times by the participants. The professional nurses mentioned that they would give antibiotics orally instead of intravenously because they would be overstretched with many patients to attend to; therefore would not have time to put up intravenous lines or phone a doctor to come and insert one. Time constraints were also brought up as a reason for doctors not reviewing antibiotic scripts and ending up with prolonged antibiotic use. The quote below expresses the views of professional nurses:

“That [being overworked] is the big challenge with doctors because... I feel for them; yes! They are under a lot of strain, they're doing a whole lot of work. Especially with interns, because some registrars will leave the intern to do everything on their own. And then they will just say: Okay, I ordered this, do this, take that... forgetting that this person might have 60 patients around the whole of medical [wards]. So, they have to go from this ward to that ward to that corridor. So, this thing of... Sometimes doctors... Some respond positively when you call them and say: ‘doctor you haven’t seen this patient, you haven’t reviewed a certain script can you come back’... Some respond positively, some don’t even come to do that.”(Professional Nurse 3)

“Sometimes at work you are just one person looking after 66 patients... So, you are exhausted ... And you must cover everybody. So, sometimes you just do your job just to finish...” (Professional Nurse 1).

Shortage of antimicrobials

The antibiotic supply in the hospital influenced antibiotic prescribing practices to a certain extent. According to one of the pharmacists, there were insufficient antibiotics available for the number of patients that needed them and this was a limitation in terms of choices of antibiotics for the doctors, leading to some of them prescribing an inappropriate antibiotic for the condition that they were treating. A nurse and a pharmacist described this as illustrated in the quotes below:

“If for instance we had it (an antibiotic) last month, we might not get it the next month. We don’t have more stock... So, they end up... maybe the doctors are not happy because if they want meropenem specifically but meropenem is out of stock then they are forced to give something else yet the sensitivity may show that you need meropenem and they have to come and change it to another antibiotic.” (Professional Nurse 1)

“I mean appropriate resources in terms of medication availability... That’s a big one... We don’t have enough medication to accommodate the number of patients we have in the hospital.” (Pharmacist 2).

Antibiotic prescribing culture

An interesting finding was that doctors based their antibiotic prescribing on the existing practices that they observed when they first started working in the hospital. One medical registrar and pharmacist describe this in the quotes below:

“From my own experience, what I see is... I mean if you walk into a hospital now and you see that people do stuff this way here... And after a while you find yourself doing the same... It might not be completely correct but because it is what they do there... It’s the same with what they say when you get to Rome you behave like a Roman... So, I feel like there’s a lot of people following what is being done in that setting... I feel like a lot of that happens around here...” (Registrar 1)

“I don’t think most decisions are made on their specific clinical experience because most of them are interns. So, some of them just go with what they learnt or what they’ve seen the practice is and that’s why I’m challenged all the time.” (Pharmacist 1)

In addition, there is an existing hierarchy of prescribing in which the registrar’s decisions override the intern’s and the consultant’s decisions override both the registrar’s and intern’s decisions on whether to prescribe an antibiotic and on the choice of an antibiotic. This hierarchy underpins the junior doctors’ prescribing practices as this intern described:

“...there are times when I think [antibiotics are not indicated] ... There was one incident with a patient that was hospitalized recently we thought it was a PE (pulmonary embolism) but we still covered him with tazocin for a few days...” (Intern 2)

“A lot of them [doctors] are finding it difficult to challenge a prescription. So, if a consultant or somebody senior says: I would give this. Nobody wants to step back at that moment and say: Is this the right thing to do?” (Pharmacist 1)

“It’s more, to be honest, based on previous experience from seniors. So, they often do that, I’ve noticed. And even if you don’t put the patient on antibiotics... I find that most often on the first intake the consultant will just say cover empirically with antibiotics.” (Registrar 3)

An intern described an instance where he did not think that antibiotics were warranted but he had to prescribe them because the registrar thought otherwise:

“Well I'm always following the order of the registrar but I thought that at the time if it was conclusive... The thing is we didn't have any signs and stuff on the chest, so I didn't think it was necessary [antibiotics]. (Intern 2)

Furthermore, the junior doctors mimic the antibiotic prescribing practices of seniors because they do not want to cause conflict and also because sometimes when they withhold an antibiotic, they find that the seniors prescribe them anyway. One medical intern described this as a “*see one and do one*” phenomenon in which you do as you see others doing whether or not it is the right way to do it.

3.4.3 Guideline factors

Most of the participants reported that there were no hospital antibiotic prescribing guidelines or policies in place at the time of the study. One professional nurse expressed this in the quote below:

“No, there aren't [policies], since I was a student nurse I have never known a policy regarding that. The only thing is the 5 rights of which they apply to every medication. They're not specific to these antibiotics.” (Professional nurse 3)

Conversely, one intern seemed to be convinced that hospital guidelines were available, but that they had not read them as the quote below illustrates:

“So... there are policies available in the unit but I'm going to put myself into a corner if I said that I have read them but as far as I know there are policies available” (Intern 1).

Very few participants reported that they referred to guidelines when prescribing antibiotics. Some of the guidelines that the participants reported referring to are the *National Essential Medicine Lists* and the *South African Thoracic Society Guidelines for the Treatment of Community Acquired Pneumonia*. Many participants wished that the hospital antibiogram could be used to create tailored hospital-specific antibiotic guidelines that they could use.

“I think local guidelines, hospital based guidelines would go a long way as well, you know... informed guidelines looking at the, microbial patterns in the hospital and then informing local guidelines within the hospital, would go a long way.” (Consultant 1)

3.4.4 Patient factors

Patient demand for antibiotics

In this hospital, patients requesting for antibiotics to be prescribed for them was not a problem as many participants reported that they had not experienced any patient pressure and one doctor felt that this was more likely to occur in the private sector.

“In private, if you work as a GP, you know that people come to you and pressure you... but probably because of... I don’t know if it’s the level of education or the type of patients that we see. Most of the patients we see are not economically in the top ... I mean there might be a barrier in them advocating for you to prescribe antibiotics. Basically, from my experience here I’ve not really had someone telling me I need to start them on antibiotics. I suppose that happens more in private compared to the public sector.” (Registrar 1).

Those that reported having experienced pressure from patients did not succumb to it.

Occasionally, I experience (patient pressure), but if I think it’s [antibiotic] not warranted I never succumb to that... I guess being in the public sector, this is driven by other factors. If I feel that an antibiotic is unwarranted I don’t give it. (Consultant 3)

3.5 Perceptions about the Establishment of an Antimicrobial Stewardship Programme

When the participants’ views were sought on the establishment of an antimicrobial stewardship programme, two sub-themes emerged namely a) *views regarding the composition of an antimicrobial stewardship (AMS) committee* and b) *suggested activities to be carried out by the antimicrobial stewardship committee.*

3.5.1 The composition of an antimicrobial stewardship committee

In general, the majority of the participants expressed that there was a need for the establishment of an ASP as a mechanism to curb the development of antimicrobial resistance. A senior registrar, who had an experience with ASPs in another academic hospital, shared that its establishment would be useful in this hospital:

“So, I think it would be very good actually (ASPs)... because they have it at (name of hospital), they’re quite stringent about antibiotic use and they’re quite strict and I think just to have someone overlooking that would help a

lot in terms of; less resistance, less misuse of antibiotics... Just so we can get some kind of approval before it gets escalated.” (Registrar 3)

There was consensus amongst the majority of participants that the AMS committee would have to consist of a multidisciplinary team. The categories of staff that were most commonly recommended to be part of the committee were specialist physicians, specifically infectious diseases (ID) specialists. Most participants alluded to the fact that the ID specialist would be the most knowledgeable on antimicrobials and therefore would be able to provide important input on ASP matters. Furthermore, two consultants agreed on the involvement of infection prevention and control practitioners in the committee and recognized the link between ASPs and infection prevention and control in reducing resistance. The quotes reflecting this are shown below.

“So, it [the AMS committee] should be pretty diverse so that you get a maximum impact. You definitely need input from IPC practitioners, you need pharmacy input, you need obviously doctors to be involved, microbiology are very important as well.” (Consultant 1)

“So, infectious diseases consultants, the pharmacists, the infection control nurses, heads from each department should be included ...or someone that can link meetings information to the other people and every time there is a meeting of this committee the information can be easily disseminated to other members of the team.” (Consultant 2)

“The pharmacy, infection control nurses, ID physicians, general physicians and the registrars form a great percentage of the actual prescribers in this facility, so if they're represented in that committee it can make the difference.” (Registrar 1)

A few participants suggested that there should be an intern and registrar representative in the committee. The reasoning behind this was for them to be educated on the correct antimicrobial prescribing habits while they are still at an early stage of their medical career with the hope that they will practice appropriate antibiotic prescribing in their future employment. This view is illustrated in the comment below:

“...I think they should start with young doctors coming in so that this change starts there and it goes up all the way.” (Intern 4)

However, one participant was of the view that interns did not have to be part of the committee as they were always supervised and did not make decisions independently.

In addition to the infection control nurses, one intern, three professional nurses and two pharmacists recommended that general enrolled and professional nurses should also be included in the committee because they work closely with patients and are involved in the administration of antibiotics. Furthermore, one consultant explained that having representation in the committee would empower the nurses to question inappropriate antibiotic prescriptions that they may come across in their clinical practice. The quote below reflects the recommendation for nurses to be in the committee

“In the nursing practice I would choose enrolled nurses and professional nurses because they're the ones who are mostly involved with giving antibiotics, whether it's oral or IV, so I would say those ones. I would also include doctors whether it's registrars or interns so that they know that: Yes, I have to do 1, 2, 3, 4 so that my patient can get better.” (Professional Nurse 3)

Seven participants consisting of interns, consultants, registrars and pharmacists agreed that pharmacists have a role to play in the committee. However, the involvement of pharmacists was not supported by one professional nurse who questioned the pharmacists' knowledge of antibiotics. In the quotation below, this nurse made an argument that pharmacists were unfit to be involved in antibiotic stewardship as they were not in direct contact with patients and therefore should not make any decisions with regards to antibiotics particularly in terms of restricting access to antibiotics:

“I feel that the pharmacists don't have enough knowledge because (with) antibiotics you cannot just change because you feel like it. There are tests that are being run. As nurses we see the patient; they don't see the patient. We are the ones who see the patient from admission. We take this journey with the patient, we are with the patient every day. We see how they react or how they respond to a certain medication.” (Professional Nurse 3)

On the other hand, one pharmacist expressed that they do interact with patients particularly in the outpatient setting and experience issues related to antibiotic prescriptions and would therefore need to be part of the committee as described below:

“We are the last line, before they [patients] go home, we are the last line that they see. We are the last face that they become angry at. Because they were waiting for hours and hours until they get to us and then we say: but why are there three antibiotics written on this prescription? Augmentin, Azithro and Amoxyl on one

prescription. Is it written because maybe something is out of stock? Is there an actual reason why?” (Pharmacist 3)

Only a small subset of participants proposed that the hospital management should be part of the committee and they thought that management has the capacity to provide support with regards to resources needed to overcome challenges such as staff and antibiotic shortages. The administrative staff was suggested to be involved in the committee to enable them to track the readmission of patients into the hospital as an outcome measure of the activities of the AMS committee. One pharmacist suggested that there should be a representative from all cadres of hospital staff including the general staff such as porters and the administrative staff. This pharmacist rationalized that every hospital staff member has a role to play in preventing antibiotic resistance:

“Honestly everybody! I feel like everybody in the hospital has a role for the recovery of the patient. So, from top managers, the CEO right to the bottom, cleaners, porters, everyone plays a role in the outcome of the patient. No matter how big (or) how small the role is but any small practice in any position can affect the patient’s outcome and recovery. And I mean you can think about it in a sense if you have a porter coming in and out of the ward who is transporting patients who are infective and are highly contagious and is going from one patient to another or walking amongst the wards and meeting people and spreading, this is another way.” (Pharmacist 1)

Furthermore, one professional nurse brought up the idea that it would be preferable for committee members to have certain personal attributes that are separate from their occupation. She expressed that individuals considered for inclusion in the committee needed to be willing participants who are committed and ready for change. However, she noted that those regarded as “rotten potatoes” should also be included in the committee with an intention to change their mindsets. This is elaborated in the quote below.

“You know the first thing that came to my mind... I wanted to say people who are ready for change, (people) who are committed, who want to be there. But at the same time, I'm thinking: even those ones, the rotten potatoes. They should come because if you can change one person’s mind, you can also influence them to change the next person’s mind.” (Professional Nurse 2).

3.5.2 Activities of the antimicrobial stewardship programme

When participants were asked to describe the kind of activities that they would like the ASP to implement, they mentioned four broad categories of activities namely, a) *in-service training*,

b) *provision of guidelines*, c) *control of access to antibiotics*, and d) *prospective audits with feedback*. These are discussed in detail below.

In-service training

Education on appropriate antibiotic prescribing was the most common suggestion given by all participants who believed that the lack of education was a significant contributor to the inappropriate prescribing practices in the hospital. Interns in particular, indicated that there were variations in the manner in which their seniors prescribed antibiotics, making it difficult for them to understand the rationale behind the prescriptions. Therefore, they proposed that in-service sessions could cover issues such as the identification of patients that require antibiotics as well as specifics on antibiotic prescribing.

Different forms of in-service training were suggested, such as antibiotic stewardship ward rounds that are based on teaching on appropriate prescribing. Those that had experienced antibiotic stewardship ward rounds in other hospitals found them particularly useful. Some participants mentioned that they would like to have in-service training sessions that focused specifically on issues related to antibiotic prescribing while others wanted to have educational material displayed on the walls. One consultant suggested that an antibiotic prescribing course could be offered to the staff in the hospital and that those that have attended the course could in turn train others. The quotes below depict some of these findings.

“We don’t have many ID [Infectious Diseases] or micro [microbiology] ward rounds. We get a random phone call, sometimes, about a bug that a patient has grown, but it would be nice to have [rounds] ... not necessarily every week but maybe twice a month. We could do a micro and ID round because I know from our level already, intern level. You know, you learn about the bugs at med school and then you tend to forget about them..., you tend to forget which one is which and what covers what? So, we need refresher courses.” (Intern 1)

“So, the biggest thing I feel is education... To educate the doctors that are prescribing about the risks of misuse as well as to educate them on the appropriate use of antibiotics, as well as the duration antibiotics.” (Consultant 1)

“I still have a lot to learn about antibiotics. I would appreciate it if someone taught me about antibiotics. When to use them? What to use, how much to use and how long to use it? Because we tend to figure it out in hospital, we have to learn it as we go along. And let me tell you: all the registrars have their own view on how to treat patients with antibiotics. I'm going to say: there's not a fixed standard... and I suppose

it's in any hospital when people say use this I prefer [this] ...everyone has their own likes and everything... So, it makes it a bit difficult to follow as an intern.” (Intern 4)

In-service training of pharmacists was also recommended for them to all be aware of restricted items especially for those pharmacists that work after hours:

“Another thing also from our side that is a big problem is on calls; we need to train our staff for the on-calls because... that's a big thing. For example, if you are currently working at in-patients [pharmacy], you know the rules, okay... This requires this documentation... the patient needs to be resistant to this, etc. The problem is an on-call pharmacist is getting called out at three in the morning for something, he is just going to give that medication... You want to get home, you want to sleep, you get what I'm saying.” (Pharmacist 2)

Provision of guidelines

In cognizance of the fact that the participants had different views with regards to the availability of antibiotic guidelines in the hospital, they proposed different activities that the stewardship programme could embark on. For instance, those who believed that the guidelines were not available, recommended that hospital specific guidelines need to be developed and those who believed that they were already available, recommended that they be made more accessible.

“I think local guidelines, hospital based guidelines would go a long way as well, you know... informed guidelines looking at the microbial, kind of, patterns in the hospital and then informing local guidelines within the hospital, would go a long way.” (Consultant 1)

“Indeed there is a shortage of policies. There's no policy, there is no protocol, we just work... I used to work somewhere where there was a protocol for Amphotericin B, it stated that before you give amphotericin, you must start with, saline... then potassium and after potassium you give plain saline and then you give panado and then you give amphotericin... So, here doctors just prescribe every day.” (Professional Nurse 1)

“Well I think if there's a clear cut policy... Like I've said I'm sure there are policies, but we've just not seen them... And that there should be clear cut policies that are visible in the wards... like up as posters; you know, maybe like an algorithm that we could follow on how to use antibiotics. Which ones we should start with before we head up to the stronger [antibiotic].” (Intern 1)

Two pharmacists proposed that guidelines for pharmacists should also be developed to guide them on how to substitute antibiotics when there are drug shortages and on how to carry out restrictions.

Control access to antibiotics

The majority of the participants supported the restriction of access to certain classes of antibiotics that are currently freely accessible such as carbapenems. The registrars were particularly supportive of this as they have found it to be effective in other hospitals that they have worked in during their training. One commented as follows:

“At (name of hospital), if you want to escalate to a carbapenem or you want to escalate to something other than your standard...well your first line antibiotics... you will have to review with the consultant first and get a consultant’s signature, which I think is appropriate because then not everyone gets second or third line antibiotics.” (Registrar 3)

One consultant raised concerns about the outcomes of patients and the potential increase in workload and bureaucracy that could come with restricting access to antibiotics:

“How is it going to impact patients? If you restrict the use of antibiotics, is the person who is going to give you consent for the antibiotic going to be available 24 hours a day? And can I call them? I think it will just lead to... in a busy hospital like this... If that’s going to be implemented... that’s just going to add onto the layers of bureaucracy and I think that already a system that is like overburdened with other issues. I would say that certain categories of antibiotics can be restricted, you know. For example, like vancomycin and things like those but penicillins which have been used for ages.” (Consultant 3)

Participants’ views varied in relation to the specific measures that could be used to control access to antibiotics. Two participants, one intern and one registrar expressed that the procedures that are currently being followed to access the antibiotic colistin which include submitting microbiological evidence to the pharmacy, could be used to access other classes of antibiotics.

“Like how we have to do the whole consent for colistin. There could be more antibiotics that need that kind of documentation. Like ertapenem for an example, or tazocin... We are able to prescribe that to anybody, freely. So, if more of our antibiotics had a stronger control, which might help.” (Intern 1)

Participants had mixed views regarding the restriction of access to antibiotics by pharmacists. Firstly, some participants felt that it is very cumbersome to have to go up and down to the pharmacy to resolve issues with restricted antibiotics such as submitting additional

documentation or results. This was expressed mostly by the interns who would be the ones to carry out this task. The pharmacists also mentioned that it is quite difficult to communicate with doctors about restricted items which could eventually result in patients not receiving antibiotics that they need due to the inability to get the information needed to dispense the antibiotic. Creation of an electronic system for communication between the pharmacy and clinicians was suggested:

“Healthcare professionals what we don’t do is; we don’t leave our numbers on our files and stuff. So, the pharmacy can’t call us directly. They always call consultants or things like that. Another thing is... I think... maybe an e-system where we don’t have to walk up and down because I mean this hospital is a very big place... I know [that] in radiology they have e-system now whereas we still have to run up and down.”
(Intern 2)

“Let’s be honest... getting hold of any ward is a problem. Getting hold of people in the pharmacy is a problem... I’m not calling anyone out, all sides... So, even if we have a problem with the prescription; trying to get the sisters to answer their phone in ward 60 or whatever it is, is really difficult... especially if it’s nearing 4PM. No one wants to answer the phone at that time, when a doctor leaves a hash number it’s such a blessing.” (Pharmacist 3)

Another pharmacist indicated that they experienced difficulties with the restriction of colistin because laboratory results do not always get submitted with the prescriptions and this results in them lifting restrictions based on verbal results and not formal printouts.

“It was a bit difficult getting the appropriate documents from the doctors. I think that’s where we experienced the biggest problem. It was the problem with, for an example, sometimes the microbiologists wouldn’t have submitted the right results to the doctors. So, we wouldn’t have anything but it would be like a verbal agreement with no paperwork to confirm it.” (Pharmacist 2)

One registrar favoured the restriction of all antibiotics other than first line antibiotics by the pharmacy and believed that it would reduce the inappropriate use of antibiotics.

It’s a good thing (antibiotic restrictions by pharmacy). It makes people think twice about what they’re going to prescribe, and I would support it. It’s a very good thing.” (Registrar 2)

One professional nurse did not think that restriction by the pharmacy would be effective because some antibiotics are kept in the ward (ward stock) and not in the pharmacy and therefore used freely. One intern also said that pharmacists may not be able to restrict access

to antibiotics effectively without seeing the patients. In addition, he reported that when restricting access to medication, pharmacists seem to doubt the clinicians' decision to start that treatment by requesting for submission of confirmatory laboratory results.

“Them (pharmacists) without seeing the patient uhm, it's very difficult. It's like for instance we have, let's say, one situation... I'm not sure if this applies, but a patient needs coartem and we need to motivate for it... I'm not sure, maybe there's another reason for it. But they wanted the proof of parasitemia. But the thing is we will not just treat malaria without seeing them, that it is a positive malaria or if there's a parasitemia... and yet I have to... Sometimes it's hard. They are right to do certain things... sometimes uhm, without seeing the [patient]...” (Intern 2)

Another method suggested for restricting access to antibiotics was the introduction of preauthorization, a system in which antibiotics are not dispensed unless motivated for by a consultant. Two consultants raised concerns about the need for consultants to sign the motivations as a prerequisite for the dispensing of the antibiotic from the pharmacy. They felt that there may be difficulties in getting consultants to sign motivation forms, especially outside normal working hours. In order to overcome this, one of the consultants suggested that registrars could undergo specific training to be able to sign the motivation forms themselves. This is explained further in the following quote:

“Sometimes it has caused problems [getting consultants' signatures] because sometimes on weekends if there's no signature of the consultant and they can't get hold of the consultant, that antibiotic gets delayed and that will impact on the management of the patient... So, there should always be some kind of a contingency plan of what to do in case of, you know, there's no available consultant at the time... Maybe if someone has gone through the course, like a registrar that has already gone through training and is kind of certified then they should be allowed to prescribe antibiotics and they should be released with their name.” (Consultant 2)

Another view that was raised was that the clinicians generally have the autonomy to make decisions about antibiotic use and due to this they may not be welcoming of a system that would undermine this autonomy requiring them to obtain permission from someone else before starting certain antibiotic classes.

Antibiotic prescription audits

While there was consensus amongst participants, including consultants that antibiotic prescription audits would be useful, there were varied sentiments regarding its acceptability.

Some reported that should the audit findings identify an inappropriate prescription, they would consider this as a learning experience. Others mentioned that this would be embarrassing to them.

“It’s difficult to tell how well received (prescription audits) that would be. People might think they’re being criticized, they’d think they’re being watched, but it would be for good reason and you know to try and make things better.” (Registrar 3)

However, some participants agreed with the idea of audits provided that they are conducted by a senior clinician and in a professional manner which involves collegiality and effective communication as shown in the quotes below:

“I think it is going to cause a bit of conflict between that person and the doctor. It also depends on... I don’t know...are they going to call that person? Will it be a doctor, will it be...? Probably a senior medical person who understands...” (Intern 4)

“I wouldn’t have a problem with that (audits) as long as it doesn’t become too intrusive... You know the main thing it should be collegial, it shouldn’t be like a witch-hunt...I wouldn’t have a problem with that as long as when they do that and they think that changes are appropriate, there should be direct lines of communication. I shouldn’t just go back and find out that things have been changed without my consent. No, that’d be inappropriate, there should be communication.” (Consultant 3)

Another participant commented that the audits could be more acceptable if they are conducted by people who are part of the clinical team or unit and not by an outsider that is not familiar with the team. This participant suggested that antibiotic stewardship ward rounds should be implemented before the audits and thus introduce these new activities gradually to hopefully increase the likelihood that they will be well received:

“I think if they [auditors] could be integrated into the team then it’s not going to be... because there’s also egos that tend to be at play. And no one likes someone out of their team coming out to say: Oh, but hang-on, what have you done here? So, I think if they could be integrated as part of the team. (Just) like how sub-specialties are actually part of the team.... So, if we could integrate the stewardship as part of the team, it wouldn’t be looked (at) as an outsider telling the team what to do...Maybe they should start it slow with ...things like rounds, micro rounds, ID rounds... You’re introducing those people into the team, already and when they start coming to do rounds to look at antibiotic usage... It is not a stranger that’s coming.” (Intern 1)

A registrar cautioned that audits should be carried out in cognisance of the existing unsupportive practice environments and the limitations that they pose when prescribing antibiotics:

“Sometimes it annoys you, to be frank... because sometimes they wouldn’t know your rationale for the action that you have taken or what limitations you have. In an appropriate setting, where everything works, then maybe that could be acceptable but... in our resource constraint setting... Sometimes you have bloods and then the bloods are not ready for days maybe the labtrak [software used to obtain laboratory results] is off for days... And you see the patient in front of you is deteriorating, you need to take action even prior to having results ready, so... I would appreciate it if someone could call you before they could just take a blanket action and then the patient suffers at the end of the day.” (Registrar 1)

3.6 Perceived Facilitators for the Establishment of an Antimicrobial Stewardship Programme

The preceding themes unravelled a number of facilitators and barriers for the establishment of an antimicrobial stewardship programme; however, there was a significant amount of repetition particularly in their responses on facilitators. Nonetheless, four broad themes were identified and are discussed below.

3.6.1 Expertise and diagnostic facilities

One consultant and one intern expressed that the success of the programme may be facilitated by having a team consisting of infectious diseases specialists on site, pharmacists and other medical specialties who together can form a well-rounded committee. Although the majority were not aware of the existing ASP, two that were aware indicated that it formed a good foundation to facilitate the success of the programme. Furthermore, the availability of specialized diagnostic infrastructure such as a microbiology laboratory department that allows for the thorough investigations of patients was highlighted as a facilitator to the programme. The quotes below demonstrate this:

“So, I think formalization of the committee plays a big role so that you have people who are responsible for it. And, kind of, ongoing education around prescribing practices as well as AMS rounds which were happening.” (Consultant 1)

“The infectious diseases department that’s a strong department that’s been there in the hospital and at the same time there is always commitment from the department to follow guidelines and to improve.” (Consultant 2)

“I think this hospital has the capability of doing it [antimicrobial stewardship] because it’s a big hospital with a lot of staff that have the expertise.” (Intern 2)

“Because it’s a well-structured hospital. It almost has all departments and if we have a big lab, a big number of interns... So, if it is implemented here, there will be a lot of people who will be trained to use antibiotics appropriately.” (Intern 3)

3.6.2 Willingness to learn

Some participants expressed that there is a generalized willingness to learn in the hospital and viewed this as a facilitator to the ASP as it could mean that there will not be much resistance during its implementation. One registrar explained that within the registrar body they are very keen to be taught the right way to prescribe antibiotics. Furthermore, one intern also expressed an interest in learning. The quotes below elaborate on this.

“I find that often we think that, particularly from the registrar group body, maybe think that people aren’t receptive to these things, that people are stuck in their ways and don’t want to do things but actually I think there’s a lot of capacity. People do want to... do want advice, they do want protocols, things to follow, the most up-to-date information... It would be, it would be received.” (Registrar 2)

“I’m always open to that (stewardship activities) because that’s how we grow and that’s how we improve. I don’t know about other people but I think the way medicine should be is to follow advice and any other suggestion you can get.” (Intern 2)

To illustrate their willingness to learn about antibiotic use one professional nurse used the administration of antiretroviral drugs as an example below:

“Because now for example, I know a lot of enrolled nurses who give antiretroviral treatment... they don’t even know what those treatment’s generic names are. They get confused, they don’t even know what 3TC is. They don’t know that 3TC and Lamivudine are the same things... You see... if they can get that thing to say ... They’ve been asking them: ‘Can we get in-service training? Can somebody from pharmacy come to us, or (from) infectious disease, and show us a chart where they can see: Oh, this thing and this thing are the same thing’. Because doctors would come and write AZT, uhm 3TC, so [they] don’t know what that is.” (Professional Nurse 2)

3.6.3 Support from the hospital management

Two participants reported that support from the hospital management would be essential for the success of the ASP. One participant felt that without the support of the management, the ASP may be short-lived as they would not have the necessary backing to overcoming any major challenges that they may encounter. Below is a quote that shows this:

“I think the most important thing right now to make this programme successful is a buy-in from our higher management because something can only be implemented and be successful if everybody is going to be in the same page. We cannot have the AMS committee itself saying this is what we are going to do and filter it down there... each unit that is represented is then not going to comply. So, I think that we need a lot of buy-in.” (Pharmacist 1)

A professional nurse lamented the fact that there is not much interaction between the hospital management and the staff in the clinical areas and felt that if this was addressed through holding regular meetings with management to provide feedback on the ASP implementation, it would be more likely to succeed.

“For an example, I have been working at [name of hospital] since 2015, (yet) I don’t know the CEO of the hospital. Even [participant mentions the name the nursing manager], I only saw her in the corridors. Even with orientation, we didn’t get a proper orientation. Whereby you go to the medical [department] and they show you that this is the medical [section], this is the paedics section, you know. Even the matrons wouldn’t come and... You will not be taken and get introduced to other matrons. You have to ask: ‘who is this one, and who is that?’ And that is wrong.” (Professional Nurse 2)

3.6.4 Effective communication strategies

Participants felt that the ASP should use effective communication strategies. The pharmacists felt that having a pharmacist who communicates to the wards staff regularly about out-of-stock antibiotics would improve the effectiveness of the ASP. In addition, having clear communication channels between the pharmacy and the prescribing clinician would help to discuss prescriptions timeously. They also suggested that implementing a system in which documentation can be submitted electronically to the pharmacists would avoid the difficulties in contacting doctors that have been described.

Another aspect of communication that was discussed was between the AMS members and clinicians, specifically during the prescription audits. One consultant felt that there should be clear communication prior to any changes being made to the prescriptions:

“I wouldn’t have a problem with that (prescription audits) as long as when they do that and maybe they think that changes are appropriate there should be direct lines of communication. I shouldn’t just go back and find out that things have been changed without my consent. No, that’d be inappropriate there should be communication.”
(Consultant 3)

Furthermore, participants were keen on having an electronic prescribing system that is linked to the laboratory and the pharmacy which would reduce a lot of the communication barriers mentioned.

Another suggestion given was to have regular discussions on AMS matters within clinical units instead of the existing practice in which AMS issues are only being discussed in the monthly committee meeting as was raised by this pharmacist:

“I have to establish a meeting every week to say: In my unit we will have an AMS meeting every week and a once a month (meeting) to say: What is the update, what are the practices you see, what have you found, what have you done about it. Because I don’t want it to be at the point of where now you’re going to bring a problem that happened to you in the beginning of the month but I’m meeting you at the end of the month and you didn’t do anything about it” (Pharmacist 1).

One pharmacist also recommended that doctors should use official medical language when communicating with others as they have experienced doctors using abbreviations to bypass the restrictions because the pharmacists would not understand the non-official terms used:

“But also when we get called out, I feel that the doctors often use a lot of abbreviations and they try to overwhelm us because they want to confuse us... Now we are not trained in abbreviations and diagnosing... We know that diagnosing is your baby but the medication is our baby... So, we get abbreviations thrown at us and you get such a fright because you’re like: Oh, this patient is dying... but the abbreviation just means they refused treatment... It’s just random abbreviations that we don’t know... We get so scared we just dispense especially the younger pharmacists... And you don’t know the condition... So, then often you go to your phone and you Google and you’re like: it’s just eczema this is not an emergency, you know simple things like: Oh, it’s just this condition... the antibiotic can wait or let’s just get the lab results, make sure we’re giving the right thing.” (Pharmacist 3)

3.7 Perceived Barriers to the Establishment of an Antimicrobial Stewardship Programme

The perceived barriers to the establishment on an ASP identified in this study have been grouped into seven subthemes that are explored further below.

3.7.1 Heavy workload

The findings of this study show that across all health professions categories that were interviewed, the heavy workload in this facility was commonly perceived as a barrier to antimicrobial stewardship initiatives. The participants were of the opinion that it would be difficult to find time to attend antimicrobial stewardship activities such as ward rounds and lectures due to the demands of their daily work. The size of the hospital in comparison to private hospitals, lack of time and the fact that the staff is already overwhelmed by the workload, were raised as concerns for the antimicrobial stewardship programme. The following quotes referred to some of these issues:

“We are often overwhelmed by the number of patients that we see in this hospital and overwhelmed in terms of work... but I think it’s something that could be overcome, something that we could work around.” (Registrar2)

“I am just saying I think already (Name of hospital), most of the time people are already working at almost like capacity, most of the time. Now if I have to sort of add another layer of bureaucracy that might be problematic.” (Consultant 3)

One professional nurse pointed to the fact that due to the heavy workload, she just aims to be able to complete all the tasks assigned to her for the day and lacks the drive to do anything beyond that. Another professional nurse was concerned that the interns in particular were too overburdened with work.

“Sometime you work... And you are just one person looking after 66 patients... So, you are exhausted ... And you must cover everybody. So, sometimes you just do your job just to finish...” (Professional Nurse 1)

“That is the big challenge with doctors because ...they are under a lot of strain, they’re doing a whole lot of work and at the same time. Especially with interns, because some registrars will leave the intern to do everything on their own.” (Professional nurse 3)

One consultant expressed that the antimicrobial stewardship prescription chart that was rolled out in the AMS pilot is laborious and may be poorly completed in the setting of a heavy workload:

“Well filling the form is tedious. It takes a lot of time because now you fill out two forms rather than one. So, sometimes it’s a bit difficult (and) it’s time consuming. So, we don’t have enough human resources and you have to fill out a new form every time you write a new antibiotic or the days have finished... So, it is... It can be a bit tedious. So, I don’t know how that can be overcome...” (Consultant 2)

3.7.2 Laboratory delays

Another barrier expressed by the participants was a delay in getting laboratory results. They cited this as being critical for the antimicrobial stewardship programme’s success as AMS emphasizes the importance of directed antimicrobial therapy. One intern describes this below:

“It takes around at least 6 to 10 days for a culture to come back. Only to find out the patient cannot wait for that time before getting an antibiotic...So, maybe if they [antimicrobial stewardship team] can try to work out with the lab so that the results can come earlier, so that there’ll be no inappropriate use of antibiotics. For an example, if we know that this person has this type of bug and then from there we treat it appropriately.” (Intern 3)

However, according to one participant, in an attempt to combat these delays a Whatsapp group was created in which microbiology results reached the clinicians quicker and this could form part of the solution to this problem.

“I mean they’ve actually, they’ve been added (results) to the Whatsapp group now and flag patients early sometimes you do a blood culture on Friday, you don’t get results until Monday. So, you cannot cover for any ... I see that nowadays they send the results straight to the registrar group and you can actually check if your patients are amongst those that are flagged and you can take proper action...” (Registrar1)

3.7.3 Shortages and mismanagement of antimicrobial stock

Some participants, especially the professional nurses, pharmacists and a few doctors raised the fact that shortages of antibiotics often occur in this hospital and sometimes affect one’s antibiotic choices.

“I mean we need appropriate resources in terms of medication availability... That’s a big one... We don’t have enough medication to accommodate the number of patients we have in the hospital...” (Pharmacist 2)

One reason given for these shortages was the delayed renewal of contracts with the suppliers. The implications of this are that if the ASP advocates for the use of a particular antibiotic as their first or second-line antibiotic of choice, this antibiotic may run out. This would then lead to the use of other less optimal antibiotics as described below.

“Most companies are not being able to manufacture to the numbers we need sometimes the company tells us: ‘But we’ve over-supplied you when we’ve been only mandated to give you so many.’ And then we have to try and find it and use extra resources, extra money from us and you have our narrow-spectrum being used more than it should.” (Pharmacist 1)

In addition, the pharmacists reported that there is no control over the use of restricted antibiotics such as colistin once they are dispensed in the wards. The pharmacists reported that some nurses hide restricted antibiotics in the wards and request more stock from the pharmacy making the pharmacists believe that they have used it all when it may not have been the case. Another issue reported was that nurses do not return any leftover stock of restricted antibiotics to the pharmacy as expected when a patient dies or when the antibiotic is stopped prematurely. The existing policy requires that any colistin that is not being used for the patient that it was authorized for should be returned to the pharmacy, but in order to have extra stock in the wards the nurses do not always return it. The quote below demonstrates this.

“They hide the stock, they hide stock. So, when the next shift comes out... They don’t want to get into trouble to say: Oh, I didn’t have medicine. So, they’re hiding them in their locker and we will say we’ve already issued colistin and they’ll be like: No. there’s no colistin available. Because they don’t want to be the person in trouble that there is no colistin there for the patient... So, they hide it.” (Pharmacist 3)

3.7.4 Resistance to change

There was a general view that there was resistance to change in this hospital. The participants that reported this anticipated that it would not be easy for people to change their behavior with regards to antibiotic prescribing and administration practices. One professional nurse felt that this resistance to change was prominent in the nursing field as she explains in the quote below:

“The thing with nursing is that there’s so much cultural inertia that... People are so stuck in the old ways of doing things. And if a new way is introduced; they’re so resistant to learning. So, I think if there could be more programmes which are focusing on looking forward into things. You cannot have the same problem you had

last year, you understand. So, you must have programmes that are new, new developments ...we cannot be stuck in the past.” (Professional nurse 3)

One intern believed that people in general simply do not like change and that this could affect the programmes’ implementation as there will be some resistance. Moreover, one pharmacist and one intern felt that overcoming this resistance would be a lengthy process that would require one to adopt a slow implementation style:

“I believe people have become too comfortable. So, it’s going to take a while to change their ideas and to get them out of those comfort zones... Because now... Let’s be honest, they are getting things easy... And changing how the entire process works is going to take a while but it can be done. I think it can be done. It should be done not: it can, it should be done I don’t think it’s like: Can they do it? It has to be done. Whether or not you want it the wards are breaking out with colistin resistance or antibiotic resistance and then everyone is on colistin in the ward. How is that acceptable?” (Pharmacist 2)

3.7.5 Poor communication amongst stakeholders

The findings of this study indicate that poor communication amongst different stakeholders could be a major barrier to establishing a successful ASP in this facility. For example, two pharmacists described their experience with the existing AMS committee and PTC meetings in which the outcomes of the meetings are not communicated to the staff on the ground. The quotes below illustrate this:

“Most of the time we have a representative from each unit [at the AMS committee meeting] ... We have a representative from higher management as well but I feel that what is happening there is not filtered down properly but then again that also comes in for how important AMS is to them.” (Pharmacist 1)

“You know the information that was discussed in PTC (Pharmaceutical Therapeutic Committee) wasn’t distributed to all the doctors. So, for an example, in the case of micafungin, we were only giving it to patients with candida auris, right... but you would have doctors coming from ICU for normal candida, albicans for an example, saying that the patient is not responding to amphotericin or fluconazole, we want micafungin.” (Pharmacist 2)

Poor communication between the pharmacists and the doctors was highlighted by pharmacists and interns as a factor that can be a barrier to the ASP. For instance, two pharmacists reported having difficulties in contacting doctors when they needed clarification on a prescription or to

request for additional documentation needed to dispense an antibiotic. Furthermore, one intern stated that they did not put down their contact details on the prescription charts for the pharmacists to be able to reach them should there be a need. Similarly, one pharmacist said that getting hold of nurses and pharmacists was also a challenge.

“Let’s be honest... getting hold of any ward is a problem. Getting hold of people in the pharmacy is a problem... I’m not calling anyone out all sides [are implicated] ... So, even if we have a problem with the prescription, trying to get the sisters to answer their phone in ward 60 or whatever it is really difficult...” (Pharmacist 3)

3.7.6 Use of a paper-based system

One consultant and one pharmacist noted that the hospital used a paper-based system for record keeping including the pharmacy records. Firstly, this was perceived as a barrier to the ASP because one of the outcome measures of an ASP is the consumption rate of antibiotics.

“I think one of the important things that maybe hasn’t been done in this hospital is the pharmacy. Making sure that the pharmacy records are computerized... for an example they’re all now run on paper... So, we actually don’t know in terms of DDDs [Defined Daily Doses] what we are doing... So, AMS doesn’t really have a fixed outcome in this hospital until you know your prescribed daily doses.” Consultant 1)

Second, the paper-based system was seen to be one of the reasons for poor communication between the pharmacists, the nurses and the doctors. Some participants reported that the introduction of an electronic system to replace the paper-based one would reduce the communication challenges they experienced. Furthermore, two pharmacists reported that they would like to access patients' results electronically to avoid having to try to get hold of the doctors to get outstanding results.

3.7.7 Perceived unavailability of resources

When participants were asked to elaborate on whether the hospital has the resources to implement a successful ASP, many could not say whether the financial resources were available. It was not clear whether they were not aware of the financial standing of the hospital or were unwilling to comment on it.

However, most participants reported that there is a shortage of human resources of different cadres. One consultant believed that there were insufficient infectious diseases (ID) specialists

to run an antimicrobial stewardship programme considering the size of the hospital, but was of the view that other health professionals could undergo training and be up-skilled to run the programme as well:

“I don’t think we do [have enough human resources]. I think it needs to be disseminated through something like a course so that the rounds could be run by different practitioners (and) not just rely on ID department. So, you really are relying on 1 or 2 people from each department to run a massive programme. So, it really does need to be a lot of up-skilling within departments. So, that you have a couple of people in departments who are aware of it and willing to run with that. Because, for an example, if one person goes on leave then you have no pharmacy representation.” (Consultant 1)

One pharmacist also reported that more human resources were needed to make this programme a success even without additional financial resources. Furthermore, another pharmacist noted that there are no qualified clinical pharmacists in the hospital and one pharmacist was currently undergoing training to become one. She wished that once one pharmacist completes the training, they can then train the others. The absence of clinical pharmacists in the hospital was raised as a possible barrier to the ASP as it implies that the pharmacists’ ability to analyse antibiotic prescriptions and advise clinicians is limited. One pharmacist also reported that the staff working after hours in the pharmacy were unfamiliar with the restrictions implemented by the antimicrobial stewardship team and would require training:

“Another thing also from our side that is a big problem for us. For example, on-calls [pharmacists on call]; we need to train our staff for the on-calls because for example if you are currently working at in-patients; you know the rules, okay... This requires this documentation... the patient needs to be resistant to this, etc. The problem is an on-call pharmacist is getting called out at three in the morning for something and he is just going to give that medication ... You want to get home, you want to sleep, you get what I’m saying.” (Pharmacist 2)

In addition to human resources, printing was cited by one consultant and two pharmacists. The consultant cited that the difficulties with printing hindered the ASPs ability to implement the use of a prescription chart for AMS ward rounds and education activities. The pharmacists rely on the print-out of results to release the restricted antibiotics and if they cannot access printing, that would impair their ability to carry out restrictions.

The image below demonstrates the interrelationships and processes that emerged in this study and how they directly or indirectly have an impact on the establishment of an antimicrobial stewardship programme in this hospital.

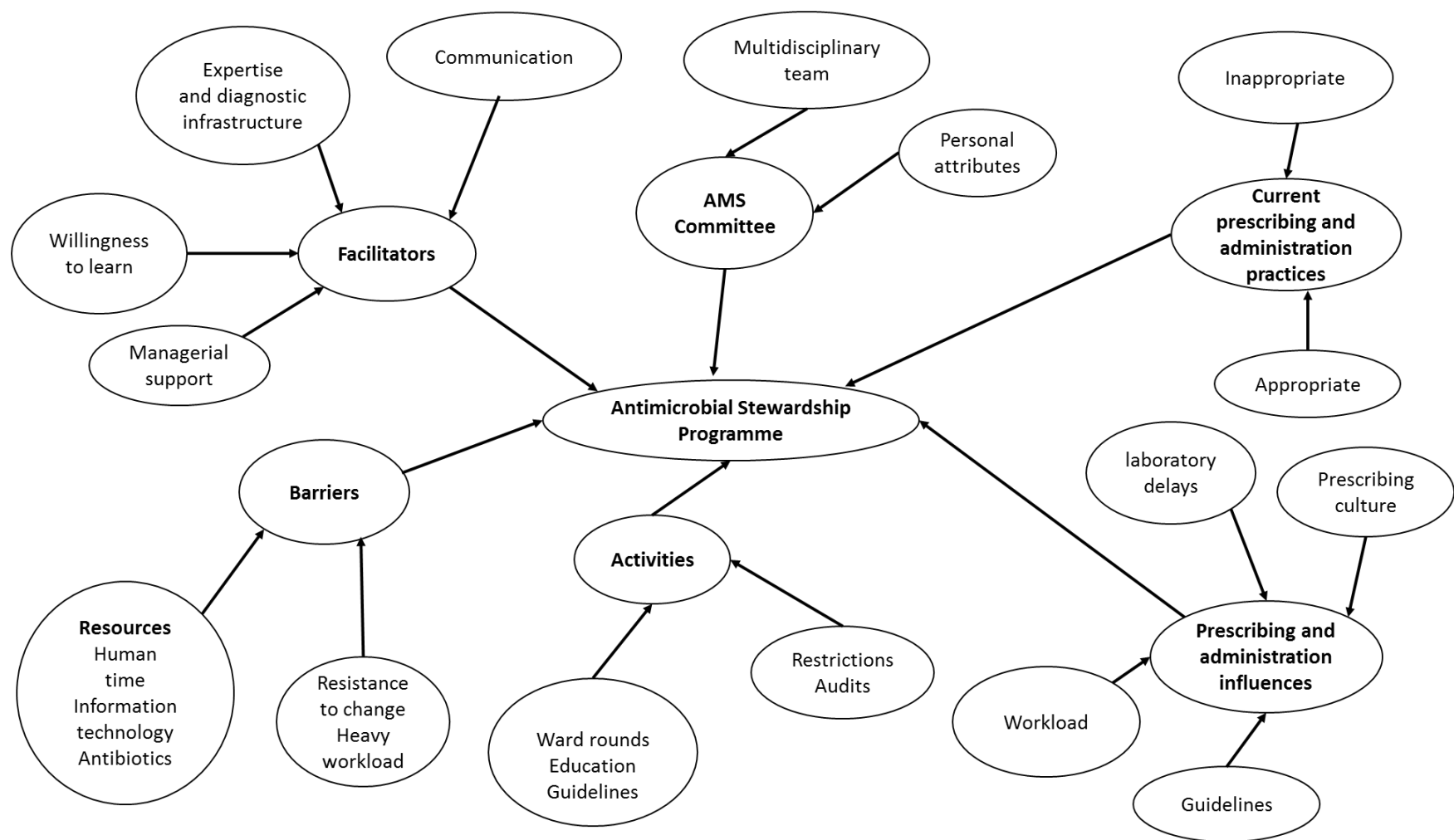


Figure 1: Summary Flow Diagram of the Interrelationship among Emerging Themes

4 CHAPTER 4: DISCUSSION

4.1 Introduction

In this chapter, the key findings of my study are discussed in relation to the literature. This is followed by a discussion of the strengths and limitations of the study and thereafter recommendations and conclusion will follow in Chapter 5.

This study set out to explore the perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme in a tertiary hospital in Gauteng province. This was specifically done using an exploratory qualitative study to obtain an in-depth understanding of the perceived facilitators and barriers to the establishment of this programme at the participating tertiary hospital. Many studies of this nature are mostly quantitative and have focused on the effectiveness of an already existing antimicrobial stewardship programme, with limited qualitative studies existing that provide insights into what it takes to establish these stewardship programmes, who should form part of their team, what interventions should they implement, as well as how they are accepted by health professionals affected by them. To my knowledge, this is the first study conducted in a public sector hospital in the Gauteng province of South Africa.

In addition, most of the available studies on antimicrobial stewardship focused on doctors and pharmacists, and not so much on other cadres of health care workers that might be affected by the implementation of this programme. By including different cadres of health professionals, my study identified some strategic areas that could be targeted to facilitate the implementation of the antimicrobial stewardship programme in the participating tertiary hospital and could be replicated in other similar settings.

4.2 Summary and Interpretation of Study Findings

4.2.1 Antimicrobial administration and prescribing practices

Antimicrobial administration and prescribing practices

My study found that antibiotic administration was the responsibility of professional nurses in this hospital, this was expected as it is the norm in most health care facilities. However, in some low-resource settings nurses not only administer antibiotics but they also prescribe them such as in primary health care facilities and this is the case with antiretroviral treatment in South Africa (96). One unexpected finding was that nurses stopped antibiotics without consulting doctors when they thought that patients had received a sufficient number of days of antibiotics. This was mostly done in situations when the prescription charts were full and the doctors did not indicate whether the antibiotic should be continued. This practice is indicative of poor communication between nurses and doctors in this facility. This and other unexpected findings in the administration of antibiotics raise the question of whether nurses in this facility are aware of the serious consequences of these practices and could be indicative of a lack of supervision and insight.

Antibiotic prescribing practices

Consistent with many other studies, my study identified that there is a hierarchical nature of antibiotic prescribing in the participating facility in which consultants oversee antibiotic prescriptions written by junior doctors. This was expected because this facility is a teaching hospital with various ranks of doctors. This hierarchy of prescribing was also described by Broom et al (45) and they found that when the consultant's advice differed from that given by the ASP team, the junior doctors followed their consultants' advice. The kinds of inappropriate antibiotic prescribing practices demonstrated in my study were much the same as those reported in other studies such as by Grebetekle et al and Chunnillal et al (47, 51).

Workaround behaviours in the prescribing and administration of antibiotics

Workaround behaviours are behaviours that are created in order to bypass an evident or perceived workflow block and a number of these behaviours have been described in health care settings (97). This study revealed several workaround behaviours taking place in this facility

related to the prescription and administration of antibiotics. The most notable ones were the deliberate disregard of the prescribed route of administration of an antibiotic by some nurses who reported that sometimes an oral preparation of an antibiotic was administered instead of an intra-venous one that was prescribed, the administration of double the prescribed dose of an antibiotic at once to avoid having to give another dose later, the hiding of restricted antibiotics in the ward and reporting to the pharmacy that they are finished and the prescription of broad-spectrum antibiotics by doctors to avoid having to do a full septic workup on their patients. Workaround behaviors have been described in many industries and they occur for various reasons such as when processes seem too slow or when there are constraints that make it difficult for one to perform their duties properly, when personal goals are not aligned to the facility's goals or when individuals are willing to bypass the processes that are mandated by an institution's guidelines or by the nature of their profession (98). In this study, it appears that the workaround behaviours were instituted to overcome slow processes such as the process of manual submission of prescriptions and collection of antibiotics from the pharmacy in an attempt to ease the heavy workload of nurses and doctors amidst other things. Mula et al (99) have described workaround behavior in relation to the administration of antibiotics in a qualitative study conducted in Malawi and although their study's focus was slightly different, they found that irregularities in the administration of antibiotics by nurses were attributed to trying to save time due to staff shortages. Similar to my study, they found that nurses take shortcuts and follow unauthorized procedures when administering antibiotics (100). Similarly, another review of medication administration errors showed that various systems factors such as the availability of nursing staff, medication and policies can affect the rates of these errors (101). These errors can be a barrier to the success of an ASP as they can promote the emergence of antimicrobial resistance.

4.2.2 Factors influencing antimicrobial prescribing practices

My study demonstrated that pressure from patients was uncommon in this hospital, and some participants believed that this was likely to be common in the private health care sector. Gebreteckle et al (47) had a similar finding and attributed it to the fact that private sector patients are likely to be more literate, and of a better socioeconomic status whereas patients in the public health sector tend to accept whatever they get without making demands. Conversely, other studies in high and LMICs found this to be a significant influencing factor in antibiotic

prescribing (21, 33, 81). Other drivers of antibiotic prescribing practices identified in my study namely, lack of knowledge, insufficient time, laboratory delays, unavailability of guidelines, heavy workload and mimicking colleagues were aligned with the findings of other studies (36, 61). Charani et al (61) found that senior clinicians overruled guidelines and policies because they relied more on their clinical experience but in my study, clinical experience was only mentioned by one consultant with 19 years of work experience as a consultant. This could be explained by the fact that the majority of the prescribers in my study did not have many years of experience, two out of the three consultants interviewed had been working as consultants for less than a year. This could indicate the need to involve senior consultants in the formulation of guidelines to avoid non-compliance from them. Mattick et al found that junior doctors did not get support from seniors when prescribing antibiotics, this was not reported as a problem by the registrars and interns in my study (63).

4.2.3 Perceptions on the establishment of a stewardship programme

The support for the establishment of an ASP by all three staff categories demonstrated in my study differed from the findings by Sutthiruk et al (102) in which the receptiveness of antibiotic stewardship interventions was not fully supported by every cadre of health professionals. In their study, doctors were less supportive than nurses and pharmacists of AMS interventions. This difference could indicate that in my study setting, the doctors are more open to receiving outside support in managing their patients compared to Sutthiruk et al. However, similar to my study findings, these authors found that if communicated in a collegial and friendly manner, recommendations from the AMS team may be better accepted (102).

4.2.4 Perceptions on the composition of an antimicrobial stewardship committee

With regard to the composition of the AMS committee, my study participants expressed that it should consist of a multidisciplinary team with infectious diseases specialists, microbiologists, pharmacists, IPC practitioners and hospital management as the main stakeholders. This is in alignment with the recommendations provided by the Guidelines for the Prevention and Containment of AMR in South African Hospitals and the Guidelines on Implementation of the AMR Strategy in South Africa as well as International Guidelines from the Infectious Diseases Society of America (IDSA) (43, 67, 103, 104). Contrary to the IDSA recommendations, the participants in my study did not recommend the inclusion of an information systems specialist because there was not any electronic data system in place in the participating hospital (71).

In my study, it was noted that except for one pharmacist who was undergoing training, the pharmacists in this hospital have not been trained on antimicrobial stewardship or infectious diseases. This is a concerning finding as one of the core elements of a hospital's ASP according to the Center for Disease Control and Prevention (CDC) is the inclusion of pharmacy expertise in the AMS committee. While the number of pharmacists that are specialized in antibiotic stewardship is rising in the United Kingdom (105), this is not the case in low- and middle-income countries. The use of non-specialized pharmacists in antibiotic stewardship initiatives has been successful in a private sector study in South Africa but the question remains whether this would have the same impact in the public sector which has a significantly higher patient load (106).

Some participants in my study felt strongly that all health care workers should be part of the committee including non-clinical workers such as porters and administrative staff with the rationale that antimicrobial resistance should be combatted by everyone. This is not reflected in the literature and is not recommended by IDSA. While it is true that the interventions instituted by an ASP should target everyone, the members of the committee and AMS team need to have specific skills and knowledge to create the programme and implement the activities, therefore is limited to a small subset of individuals. One of the core requirements for an ASP is that the members of the AMS team are trained regularly and this would not be feasible if the team consists of all staff members as suggested by the participants in my study (107).

4.2.5 Perceptions about the activities to be carried out by the antimicrobial stewardship programme

Formulary restriction and preauthorization

Pre-authorization of restricted antibiotics is a core AMS strategy and in fact, some centers have introduced the re-authorization of restricted antibiotics at day 3 of therapy in addition to pre-authorization which is more effective compared to pre-authorization on its own (108). In relation to the pre-authorization of restricted antibiotics, a concern was raised in my study over the availability of consultants after hours to sign motivation forms for the pre-authorization of antibiotics. Computerized pre-authorization has been found to be effective in reducing the use

of broad-spectrum antibiotics and can be used to address the problem of obtaining pre-authorizations from consultants as it does not require them to be on sight in order to authorize (109). Reed and colleagues have described the successful implementation of formulary restriction and pre-authorization in a university hospital in Ohio in which remote pre-authorization was carried out but this requires good internet access and electronic record keeping which is often a challenge in our study setting (110). In their study, there was no need for pre-authorization to access antibiotics after hours and they still had a significant reduction in the inappropriate antibiotic use (110).

Another interesting finding from my study was that some professional nurses and doctors did not think that pharmacists were in a position to be involved in the restriction of antibiotic access due to their lack of interaction with in-patients in the hospital. This highlights the fact that there is a need for pharmacists to be more visible in the wards, to participate in ward rounds and be more involved in direct patient care. This involvement could improve their ability to exercise their role in antibiotic stewardship. As already described in the literature review, pharmacists are reported to be one of the core members of the AMS committee and have an important role to play.

Prospective audits with intervention and feedback

PAF is also a core strategy for ASPs and has been successfully used to reduce inappropriate antibiotic use (31). My study findings indicated that nurses were supportive of PAF, and they felt that it would curb the problem of antibiotic prescriptions not being reviewed by doctors. On the contrary, some doctors were concerned about potential conflicts arising between the people conducting the audits and the clinicians. Broom et al have described conflicts between senior consultants and microbiology and ID specialists when they disagreed with the antibiotic advice they gave (60). Broom et al also found that treating consultants were resistant to unsolicited external interference in the management of their patients and made a distinction between laboratory-based and bedside medicine, the former being the microbiologists and the latter the ID specialists (60).

Education

Educational activities were highly requested by the health professionals in my study and these ranged from lectures, bedside teaching to educational documents and posters. This is not a new

finding in South African studies (57, 66). Mattick and colleagues identified that junior doctors preferred ward-based teaching as an educational intervention over formal education methods like lectures (63). Wasserman et al (58) found that in a sample of medical students from three South African universities although there was some heterogeneity, problem based learning and registrar based learning on ward rounds were perceived as the least useful modalities of education on antibiotic prescribing while bedside tutorials and consultant- led ward rounds were found to be more useful. One study that focused on antibiotic use amongst junior doctors reported that sometimes seniors were reluctant to provide teaching rounds and they missed teaching opportunities, this is an important issue to take into account when planning educational activities (107).

Guidelines

Hospital guidelines for antibiotic prescribing were recommended by the participants in my study. This was an expected finding as guideline provision is a well described supplemental strategy for ASPs which is also advocated for in the national AMR strategic plan (84). IDSA recommends that the guidelines should be created by a multidisciplinary team taking into account the local microbiological resistance patterns (71).

Antibiotic prescription charts

Using a specific antibiotic prescription chart is an intervention that allows for better adherence with appropriate antibiotic use. In my study, it was raised that these charts were tedious and time consuming to complete. The successful use of a dedicated antibiotic prescription chart in a South African hospital was reported by Boyles et al and the chart has been adopted for use in all health care facilities in South Africa as part of their antimicrobial stewardship programmes (32).

4.2.6 Perceived barriers and facilitators to the establishment of an antimicrobial stewardship programme

A delay in obtaining microbiological laboratory results has been described as a barrier to antimicrobial stewardship in this study as well as in the Ethiopian study (47). Interestingly, this was noted as a barrier to AMS by the study participants despite the hospital having a laboratory located within its premises. Similar to the findings of other studies, this study showed that the post prescriptive audits with feedback could potentially be a source of conflict if

communication with the attending clinicians is not handled carefully. Black et al (81) described that resistance by clinicians to accept antibiotic prescribing recommendations from other health professionals was a barrier to ASP implementation in their study. Like in our study they found that the manner in which the recommendations are delivered is important with a need for respect, friendliness and collegiality to avoid conflict (81).

Antibiotic consumption and expenditure as well as the length of hospital stay is a commonly used outcome measure for ASPs and the lack of computerized systems to measure this in my study setting was identified as a barrier to assessing the effectiveness of the ASP. Similar to my study, Baraka et al (111) found that the lack of time and personnel was perceived as a barrier to ASP implementation. In my study, a shortage of doctors and nurses affected the antibiotic prescribing and administration practices resulting in prolonged scripts. In addition, I also found that the lack of hospital guidelines was a major barrier to the implementation of an ASP similar to Baraka et al (111). Furthermore, Baraka et al (111) identified that the lack of financial resources was a barrier to ASP implementation but interestingly, in my study, the participants were not informed of the financial resources that the hospital possesses.

My study was limited to the Department of Internal Medicine where there is usually continuity of care between patients and clinicians, therefore a lack of continuity of care was not identified as a barrier to ASP implementation. The availability of experts in the hospital as well as a robust infectious diseases unit was seen as favorable for an ASP in my study and is similar to the findings by Black and colleagues (81). However, the shortage of staff and subsequent work overload was seen as a significant barrier to ASP implementation. The prior exposure of medical registrars to ASPs in other health facilities is a possible facilitator to the implementation of an ASP in this hospital as registrars form a significant proportion of antibiotic prescribers and this exposure appears to have made them more accepting of ASP interventions. There was a perception that health professionals in this hospital are resistant to change, and this was seen as a potential barrier to ASP implementation in my study. This was similar to the findings from a survey by Pope et al in which 27% of respondents expressed that opposition by prescribers was a barrier to ASP establishment (112). An ASP would need to introduce changes and if there is non-compliance to those changes, the ASP would not be successful. This was demonstrated in a study in which surgeons were non-compliant to ASP recommendations (79).

My study demonstrated that ineffective communication was a potential barrier to the implementation of the ASP. Effective communication between stakeholders is vital for AMS because many disciplines have an input in the running of the ASP. Some important communication channels include those between the AMS committee and the heads of departments to keep them abreast of new developments as well as between the different disciplines involved in AMS such as infection control and microbiology or pharmacy and the clinicians. My study highlighted that difficulties in communication between pharmacists and doctors were a barrier to ASP effectiveness as doctors did not write their contact details on prescription charts and therefore could not be reached when pharmacists needed clarification on prescriptions. Furthermore, the physical distance between the pharmacy and the wards was also identified as a reason for the poor communication which hampered the submission of any additional documents required by the pharmacy for restricted antibiotics. This differed from the findings by Black and colleagues (81) who described that in their study setting, pharmacists and nurses did not communicate with doctors because they lacked the confidence to discuss antibiotic prescriptions with them. Efforts should be made to ensure that communication is possible whenever needed. Pakyz et al also identified that the use of effective communication is required for the success of an ASP (89).

Another barrier identified in my study is the use of a paper-based system for patient records, prescribing antibiotics and pharmacy records. Having an electronic system linking the laboratory data, pharmacy data and patient records was perceived as a facilitator for the ASP implementation and this has been demonstrated in the literature. The paper-based system can result in a number of problems that could be avoided if electronic systems are used (74). Measurement and reporting of antibiotic consumption is one of the recommended core components of an ASP, but without electronic record keeping, this is very difficult to do (73). The lack of technological infrastructure in the pharmacy to measure the defined daily doses (DDDs) of antibiotics which is the international technical unit of measurement of antibiotic consumption was also identified as a barrier to ASPs in my study because it meant that the AMS committee would be unable to use DDDs as an outcome measure of their activities.

4.2.7 Power dynamics in the AMS platform

Throughout this study, some power dynamics were raised through the responses of the study participants which greatly influenced the way that ASP activities were implemented. First, the relationship between the senior doctors and the junior doctors was portrayed as one that the

senior doctors hold the power to support or oppose the decisions taken by the junior doctors hence they were more likely to make decisions that would please their seniors. Second, the use of unfamiliar abbreviations and medical jargon by doctors in requesting antibiotics from the pharmacy was a display of power as the doctors were trying to bypass the restrictions by using this. Another exercise of power was noted in the acts of nurses who decided how and when they administer antibiotics. These power dynamics are important to understand as these stakeholders can exercise their power to facilitate or hinder the implementation of ASP activities.

4.3 Strengths and Limitations

4.3.1 Strengths

A strength of this study is that the views of a variety of cadres of health professionals were explored providing a comprehensive overview of the issues around antibiotic stewardship in this facility. This differs from most other studies that focused on each group separately. Another strength is that a qualitative methodology was used which allowed for probing questions to be asked to get more depth in the responses that may have not been possible in a quantitative study.

4.3.2 Limitations

One of the limitations of this study was that as I am a full-time medical doctor working in the same hospital where I conducted the interviews and I had a pre-existing relationship with some of the study participants. This could have influenced their responses and introduced some bias despite my conscious efforts to avoid it. Furthermore, as this study is a Masters' thesis, the limited funding did not allow for the hiring of another experienced qualitative interviewer to assist me with conducting the interviews which could have enabled me to increase the sample size.

With the exception of pharmacists, only staff from the medical department were interviewed as a result, their views may be very different from those of health professionals in other departments and the findings cannot be generalized. Interns had only been working in the department for three months and therefore had limited experience with antibiotic prescribing which could have influenced their perceptions. Key respondents such as hospital management, the CEO and those that are actively involved in establishing the ASP such as the committee

chairperson were also not included in this study and could have contributed more insight into the barriers and facilitators to the ASP programme. Similar studies of this nature should include these key respondents. The small sample size is also a limitation to this study although in qualitative research there is no recommended sample size. In qualitative research sample size is important, in determining an adequate sample size one has to consider the quality of the information being collected and the purpose of the study (113). Normally one relies on reaching the point of data saturation to determine data sufficiency but this has limitations. There is no quantitative component in my study which could have strengthened the study by providing a more objective way of measuring the significance of the study findings and identifying relationships between variables. Furthermore, potentially identifying information such as the sub-specialty, gender and age of the study participants was omitted in order to maintain anonymity of the respondents but this could have provided additional insight into the views of the participants.

5 CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1 Study Conclusion

This study was able to explore the perceptions of health care professionals on the establishment of an antibiotic stewardship programme in a setting where a study of its nature had never been conducted before. By analyzing the antibiotic prescribing and administration practices among different cadres of health professionals as well as what drives them, this study brought to light potential facilitators and barriers to establishing an antimicrobial stewardship programme in this health care facility. Barriers included staff shortages, poor communication, drug shortages, lack of tailored antibiotic guidelines, a lack of knowledge and a lack of technological advancements such as electronic prescribing and records. Being cognizant of these barriers and facilitators allows for better planning so that the ASP is more likely to have the desired outcomes. Solutions for addressing antimicrobial resistance that have been successful in high-income countries may not always work when implemented in lower-income settings and this study has provided some insight for the development of tailored solutions that will meet the needs of its unique setting.

5.2 Recommendations

Based on my study findings, I have put together the following recommendations to be considered in the ongoing establishment of the ASP in this health facility which is currently in process. These recommendations are sub-divided into three levels namely, individual, organizational and policy level.

5.2.1 Individual level recommendations

Use of collegial communication strategies

A collegial and non-accusatory communication style should be used when AMS members address the hospital staff or give advice on antibiotic use to increase the likelihood of uptake of the recommendations. In order to avoid conflicts and to respect the existing hierarchy of prescribing, I recommend discussing the cases with the consultant in charge of the patient first before making any changes to prescriptions and instead of only addressing the registrars and

interns. This will hopefully result in the cascading of correct practices from the top to the bottom.

5.2.2 Organizational level

Create a platform for regular stakeholder communication

Frequent and open communication among pharmacists, doctors and nurses should be encouraged by scheduling regular meetings between these stakeholders every week to discuss issues related to antibiotic use. These meetings should be in addition to the monthly AMS committee meeting. The hospital management should provide protected time for the different stakeholders to attend these meetings.

Addressing staff shortages

Staff shortages can be addressed by investing in the training of different cadres of staff to shift certain low-risk tasks from the most overloaded staff cadres such as doctors and professional nurses freeing some time for them to focus more on their antibiotic prescribing and administration practices. Furthermore, up-skilling of pharmacists, nurses and doctors for them to be certified to conduct AMS activities such as educational sessions, therefore reducing the burden on the few ID specialists. The possibility of hiring infectious diseases specialists and trained clinical pharmacists from the private sector on a temporary basis to assist the limited experts in running the programme while other staff members are undergoing training should be explored. In the long term, employment of more staff including infectious diseases specialists, clinical pharmacists trained in AMS and professional nurses would benefit the programme given the challenges described.

Tailored antibiotic guidelines

Creating facility-specific antibiotic guidelines and making them freely available is likely to prompt appropriate prescribing. At the time of data collection for this study, facility-specific antibiotic guidelines were in the process of being developed but had not been finalized. Subsequently, antibiotic guidelines based on the antibiotic resistance profiles of the different clinical areas were released by the AMS team. The guidelines should be disseminated on different platforms including the creation of a mobile application.

Staff education on antibiotic stewardship

I recommend that the hospital should aim to educate all hospital staff not just doctors, nurses and pharmacists on antibiotic stewardship. The lack of knowledge was a significant barrier to appropriate antibiotic prescribing, administration and dispensing in my study. Educational material should be tailored to the target audience, I recommend the use of various methods of education not only targeting the three cadres of health professionals we studied but all hospital staff. Some educational formats to be considered are formal lectures, practical learning around patients on ward rounds, and through documents and facility-based guidelines. The education of nurses on the health and ethical implication of the workaround behavior should also be included in the sessions.

Address the antibiotic administration practices

In addition to auditing antibiotic prescriptions for appropriateness, unannounced audits of antibiotic administration practices should be carried out on a regular basis and feedback should be provided to the nurses involved. Introduction of checklists such as the five rights of medication administration namely right patient, right drug, right dose, right route and right time should be put in place. This can assist in avoiding errors in antibiotic administration.

Leadership support

Hospital leadership should openly take ownership and support the ASP by providing all resources required, reporting the ASP activities and outcomes in hospital board meetings. A representative from the hospital management should attend all the committee meetings and escalate issues that arise to higher levels of management.

Implementation of computer-based infrastructure

Introducing a computerized system linking the laboratory, pharmacy and wards and electronic prescribing will likely overcome the challenge of reaching doctors from the pharmacy and in getting laboratory results. Introducing electronic prescribing would allow the pharmacists to access the prescriptions automatically and would eliminate the difficulties of physically going to and from the pharmacy when prescriptions are questioned by the pharmacists. This would also avoid delays in the submission of prescriptions to the pharmacists as it would reach the pharmacy in real time after it has been written and patients would not miss doses of antibiotics. Computerized systems in pharmacy will also assist in the calculation of DDDs that can be used

to assess the effects of the ASP and to be able to detect when antibiotic stocks are running out to allow for new stock to be ordered therefore avoiding stock-outs. Furthermore, allowing for computerized authorization of restricted antibiotics can overcome the need for signatures which has been anticipated to be a barrier for AMS.

Improve the turnaround time of microbiological results

This can be achieved by introducing a fast-tracking system that prioritizes the processing of specimens from certain high-risk wards that can be identified by the AMS team. Furthermore, the microbiology laboratory can introduce rapid diagnostic testing (RDT) strategies that allow for results to be obtained quicker allowing for unnecessary antibiotics to be stopped earlier and the directed therapy to be initiated earlier. This would ensure that empiric therapy could be directed and increase the reliance on microbiological guided prescribing. The use of RDTs has been recommended by IDSA as well (67).

5.2.3 Policy level

Include antibiotic stewardship in university curricula

The curriculum for undergraduate degrees in medicine, pharmacy and nursing should emphasize greatly on antibiotic stewardship. This would allow for a strong foundation to be in place for these future health professionals to refer to when they enter the clinical field.

5.3 Areas for Future Research

It would be useful to further explore the workaround behaviors with regards to antibiotic dispensing that were identified in this study in order to provide tailored solutions to this potentially serious problem. Furthermore, research focusing on a broader population including all the hospital departments and key informants such as hospital management is needed for the antimicrobial stewardship team to be able to refer to when implementing the programme in other hospital departments.

6 REFERENCES

1. National Department of Health South Africa. ANTIMICROBIAL RESISTANCE NATIONAL STRATEGY FRAMEWORK 2014 – 2024 In: Health NDo, editor. South Africa: Government Printer Pretoria; 2014.
2. Shiel W. Medical definition of antibiotic 2019 [cited 2019 27 October]. Available from: <https://www.medicinenet.com/script/main/art.asp?articlekey=8121>.
3. Drew RH. Antimicrobial stewardship programs: how to start and steer a successful program. *Journal of Managed Care Pharmacy : JMCP*. 2009 Mar;15(2 Suppl):S18-23. PubMed PMID: 19236137. Epub 2009/04/10. eng.
4. Pharmacists ACoC. ABOUT CLINICAL PHARMACISTS: American College of Clinical Pharmacists; 2020 [cited 2020 21 October 2020]. Available from: <https://www.accp.com/about/clinicalpharmacists.aspx>.
5. Cizman M. The use and resistance to antibiotics in the community 2003. 297-307 p.
6. WHO. The evolving threat of antimicrobial resistance: options for action: Geneva: World Health Organization; 2012.
7. Jim ON. Review on Antimicrobial resistance. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations*. 2014. *Rev Antimicrob Resist*. 2014;20:1-16.
8. Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N, et al. Antibiotic resistance -the need for global solutions. *The Lancet Infectious Diseases*. 2013;13(12):1057-98.
9. O'Neill J. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations: The Review on Antimicrobial Resistance: December 2014. Report No.
10. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clinical Infectious Diseases : an official publication of the Infectious Diseases Society of America*. 2006 Jan 15;42 Suppl 2:S82-9. PubMed PMID: 16355321. Epub 2005/12/16. eng.
11. WHO. Antimicrobial resistance: global report on surveillance: World Health Organization; 2014.
12. Goldenberg SD, Volpé H, French GL. Clinical negligence, litigation and healthcare-associated infections. *The Journal of hospital infection*. 2012 Jul;81(3):156-62. PubMed PMID: 22658237. Epub 2012/06/05. eng.
13. Maragakis LL, Perencevich EN, Cosgrove SE. Clinical and economic burden of antimicrobial resistance. *Expert review of anti-infective therapy*. 2008 Oct;6(5):751-63. PubMed PMID: 18847410. Epub 2008/10/14. eng.
14. Le J, Dam Q, Tran T, Nguyen A, Adler-Shohet F, Kim S, et al. Epidemiology and hospital readmission associated with complications of *Staphylococcus aureus* bacteremia in pediatrics over a 25-year period. *Epidemiology & Infection*. 2017;145(12):2631-9.
15. WHO. Global action plan on antimicrobial resistance. 2015 [cited 2020 09 November]. Available from: <https://www.who.int/publications/i/item/global-action-plan-on-antimicrobial-resistance>.
16. Ekwanzala MD, Dewar JB, Kamika I, Momba MNB. Comparative genomics of vancomycin-resistant *Enterococcus* spp. revealed common resistome determinants from hospital wastewater to aquatic environments. *The Science of the total environment*. 2020 Jun 1;719:137275. PubMed PMID: 32109727. Epub 2020/02/29. eng.
17. WHO. Antimicrobial Resistance 2020 [cited 2020 28/09/2020]. Available from: <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.
18. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-

- analysis. *BMJ (Clinical research ed)*. 2010 May 18;340:c2096. PubMed PMID: 20483949. Epub 2010/05/21. eng.
19. Nordmann P, Dortet L, Poirel L. Carbapenem resistance in Enterobacteriaceae: here is the storm! *Trends in Molecular Medicine*. 2012 May;18(5):263-72. PubMed PMID: 22480775. Epub 2012/04/07. eng.
 20. Pulcini C, Cua E, Lieutier F, Landraud L, Dellamonica P, Roger PM. Antibiotic misuse: a prospective clinical audit in a French university hospital. *European journal of clinical microbiology & infectious diseases*. 2007;26(4):277-80.
 21. Thriemer K, Katuala Y, Batoko B, Alworonga J-P, Devlieger H, Van Geet C, et al. Antibiotic prescribing in DR Congo: a knowledge, attitude and practice survey among medical doctors and students. *PloS one*. 2013;8(2):e55495.
 22. Om C, Vlieghe E, McLaughlin JC, Daily F, McLaws ML. Antibiotic prescribing practices: A national survey of Cambodian physicians. *Am J Infect Control*. 2016 Oct 1;44(10):1144-8. PubMed PMID: 27324610. Epub 2016/06/22. eng.
 23. Center for Disease Dynamics EP. State of the World's Antibiotics 2015 Washington: CDDEP; 2015 [cited 2020 09 November]. Available from: https://cddep.org/wp-content/uploads/2017/06/swa_edits_9.16.pdf.
 24. Adorka M, Dikokole M, Mitonga KH, Allen K. Healthcare providers' attitudes and perceptions in infection diagnosis and antibiotic prescribing in public health institutions in Lesotho: a cross sectional survey. *African health sciences*. 2013 Jun;13(2):344-50. PubMed PMID: 24235934. Pubmed Central PMCID: PMC3824475. Epub 2013/11/16. eng.
 25. Chaw P, Höpner J, Mikolajczyk R. The knowledge, attitude and practice of health practitioners towards antibiotic prescribing and resistance in developing countries—A systematic review. *Journal of Clinical Pharmacy and Therapeutics*. 2018.
 26. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. *The Lancet Infectious Diseases*. 2014 Aug;14(8):742-50. PubMed PMID: 25022435. Epub 2014/07/16. eng.
 27. Essack SY, Desta AT, Abotsi RE, Agoba EE. Antimicrobial resistance in the WHO African region: current status and roadmap for action. *Journal of Public Health*. 2016;39(1):8-13.
 28. Shallcross LJ, Davies SC. The World Health Assembly resolution on antimicrobial resistance. *Journal of antimicrobial chemotherapy*. 2014;69(11):2883-5.
 29. WHO. United Nations high-level meeting on antimicrobial resistance New York, USA2016 [cited 2020 30/09/2020]. Available from: <https://www.who.int/antimicrobial-resistance/events/UNGA-meeting-amr-sept2016/en/>.
 30. WHO. Antimicrobial resistance library of national action plans: WHO; 2020 [cited 2020 04/10/2020]. Available from: <https://www.who.int/antimicrobial-resistance/national-action-plans/library/en/>.
 31. Willis ZI, Gillon J, Xu M, Slaughter JC, Di Pentima MC. Reducing Antimicrobial Use in an Academic Pediatric Institution: Evaluation of the Effectiveness of a Prospective Audit With Real-Time Feedback. *Journal of the Pediatric Infectious Diseases Society*. 2017 Nov 24;6(4):339-45. PubMed PMID: 28339590. Pubmed Central PMCID: PMC5907874. Epub 2016/01/01. eng.
 32. Boyles TH, Whitelaw A, Bamford C, Moodley M, Bonorchis K, Morris V, et al. Antibiotic stewardship ward rounds and a dedicated prescription chart reduce antibiotic consumption and pharmacy costs without affecting inpatient mortality or re-admission rates. *PLoS One*. 2013;8(12):e79747.

33. García C, Llamocca LP, García K, Jiménez A, Samalvides F, Gotuzzo E, et al. Knowledge, attitudes and practice survey about antimicrobial resistance and prescribing among physicians in a hospital setting in Lima, Peru. *BMC clinical pharmacology*. 2011;11(1):18.
34. Rüttimann S, Keck B, Hartmeier C, Maetzel A, Bucher HC. Long-Term Antibiotic Cost Savings from a Comprehensive Intervention Program in a Medical Department of a University-Affiliated Teaching Hospital. *Clinical Infectious Diseases*. 2004;38(3):348-56.
35. Ohl CA, Dodds Ashley ES. Antimicrobial Stewardship Programs in Community Hospitals: The Evidence Base and Case Studies. *Clinical Infectious Diseases*. 2011;53(suppl_1):S23-S8.
36. Sikkens JJ, van Agtmael MA, Peters EJG, Lettinga KD, van der Kuip M, Vandenbroucke-Grauls CMJE, et al. Behavioral approach to appropriate antimicrobial prescribing in hospitals: the Dutch unique method for antimicrobial stewardship (DUMAS) participatory intervention study. *JAMA internal medicine*. 2017;177(8):1130-8.
37. Newland JG, Gerber JS, Weissman SJ, Shah SS, Turgeon C, Hedican EB, et al. Prevalence and characteristics of antimicrobial stewardship programs at freestanding children's hospitals in the United States. *Infection Control & Hospital Epidemiology*. 2014;35(3):265-71.
38. Johannsson B, Beekmann SE, Srinivasan A, Hersh AL, Laxminarayan R, Polgreen PM. Improving antimicrobial stewardship: the evolution of programmatic strategies and barriers. *Infection control and hospital epidemiology*. 2011 Apr;32(4):367-74. PubMed PMID: 21460488. Epub 2011/04/05. eng.
39. Brink AJ, Messina AP, Feldman C, Richards GA, Becker PJ, Goff DA, et al. Antimicrobial stewardship across 47 South African hospitals: an implementation study. *The Lancet Infectious Diseases*. 2016 2016/09/01;16(9):1017-25.
40. Chetty S, Reddy M, Ramsamy Y, Naidoo A, Essack S. Antimicrobial stewardship in South Africa: a scoping review of the published literature. *JAC-Antimicrobial Resistance*. 2019;1(3).
41. SAASP. South African Antibiotic Stewardship Programme (SAASP) South Africa 2020 [cited 2020 19 September]. Available from: <https://www.fidssa.co.za/SAASP>.
42. Schellack N, Benjamin D, Brink A, Duse A, Faure K, Goff D, et al. A situational analysis of current antimicrobial governance, regulation, and utilization in South Africa. *International Journal of Infectious Diseases*. 2017 2017/11/01;64:100-6.
43. NDOH. Guidelines for the Prevention and containment of AMR in South African Hospitals. In: Health NDo, editor. South Africa: Department of Health; 2018.
44. CDC. Measuring outpatient antibiotic prescribing 2017 [cited 2020 09 November]. Available from: <https://www.cdc.gov/antibiotic-use/community/programs-measurement/measuring-antibiotic-prescribing.html>.
45. Broom JK, Broom AF, Kirby ER, Gibson AF, Post JJ. Clinical and social barriers to antimicrobial stewardship in pulmonary medicine: a qualitative study. *American journal of infection control*. 2017;45(8):911-6.
46. Braykov NP, Morgan DJ, Schweizer ML, Uslan DZ, Kelesidis T, Weisenberg SA, et al. Assessment of empirical antibiotic therapy optimisation in six hospitals: an observational cohort study. *The Lancet Infectious Diseases*. 2014 2014/12/01;14(12):1220-7.
47. Gebretekle GB, Mariam DH, Abebe W, Amogne W, Tenna A, Fenta TG, et al. Opportunities and barriers to implementing antibiotic stewardship in low and middle-income countries: Lessons from a mixed-methods study in a tertiary care hospital in Ethiopia. *PloS one*. 2018;13(12):e0208447.
48. Sharma M, Eriksson B, Marrone G, Dhaneria S, Lundborg CS. Antibiotic prescribing in two private sector hospitals; one teaching and one non-teaching: a cross-sectional study in Ujjain, India. *BMC infectious diseases*. 2012;12(1):155.

49. Dooling KL, Kandeel A, Hicks LA, El-Shoubary W, Fawzi K, Kandeel Y, et al. Understanding antibiotic use in Minya District, Egypt: physician and pharmacist prescribing and the factors influencing their practices. *Antibiotics*. 2014;3(2):233-43.
50. Chaw PS, Schlinkmann KM, Raupach-Rosin H, Karch A, Pletz MW, Huebner J, et al. Knowledge, attitude and practice of Gambian health practitioners towards antibiotic prescribing and microbiological testing: a cross-sectional survey. *Transactions of The Royal Society of Tropical Medicine and Hygiene*. 2017;111(3):117-24.
51. Chunnillall D, Peer A, Naidoo I, Essack S. An evaluation of antibiotic prescribing patterns in adult intensive care units in a private hospital in KwaZulu-Natal. *Southern African Journal of Infectious Diseases*. 2015;30(1):17-22.
52. Gasson J, Blockman M, Willems B. Antibiotic prescribing practice and adherence to guidelines in primary care in the Cape Town Metro District, South Africa. *South African medical journal*. 2018;108(4):304-10.
53. Mabila N, Schellack N, Gous A. Antibiotic prescribing patterns among healthcare professionals at Van Velden Memorial Hospital in Tzaneen, Limpopo Province, South Africa:: health. *African Journal for Physical Activity and Health Sciences (AJPHEs)*. 2016;22(1-1):79-97.
54. Messina A, Brink A, Richards G, Van Vuuren S. Opportunities to optimise colistin stewardship in hospitalised patients in South Africa: Results of a multisite utilisation audit. *South African Medical Journal*. 2018;108(1):28-32.
55. Mthethwa S, Matjila S. Antibiotic prescribing practices of dentists at Medunsa Oral Health Centre. *South African Dental Journal*. 2018;73(8):520-6.
56. van der Sandt N, Schellack N, Mabope LA, Mawela MP, Kruger D, Godman B. Surgical antimicrobial prophylaxis among pediatric patients in South Africa comparing two healthcare settings. *The Pediatric infectious disease journal*. 2019;38(2):122-6.
57. Minen MT, Duquaine D, Marx MA, Weiss D. A survey of knowledge, attitudes, and beliefs of medical students concerning antimicrobial use and resistance. *Microbial Drug Resistance*. 2010;16(4):285-9.
58. Wasserman S, Potgieter S, Shoul E, Constant D, Stewart A, Mendelson M, et al. South African medical students' perceptions and knowledge about antibiotic resistance and appropriate prescribing: Are we providing adequate training to future prescribers? *South African Medical Journal*. 2017;107(5):405-10.
59. Skodvin B, Aase K, Charani E, Holmes A, Smith I. An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors. *Antimicrobial Resistance and Infection control*. 2015;4(1):24.
60. Broom J, Broom A, Plage S, Adams K, Post J. Barriers to uptake of antimicrobial advice in a UK hospital: a qualitative study. *Journal of Hospital Infection*. 2016;93(4):418-22.
61. Charani E, Castro-Sanchez E, Sevdalis N, Kyratsis Y, Drumright L, Shah N, et al. Understanding the determinants of antimicrobial prescribing within hospitals: the role of "prescribing etiquette". *Clinical Infectious Diseases*. 2013;57(2):188-96.
62. De Souza V, MacFarlane A, Murphy AW, Hanahoe B, Barber A, Cormican M. A qualitative study of factors influencing antimicrobial prescribing by non-consultant hospital doctors. *Journal of Antimicrobial Chemotherapy*. 2006;58(4):840-3.
63. Mattick K, Kelly N, Rees C. A window into the lives of junior doctors: narrative interviews exploring antimicrobial prescribing experiences. *Journal of Antimicrobial Chemotherapy*. 2014;69(8):2274-83.
64. Radyowijati A, Haak H. Improving antibiotic use in low-income countries: an overview of evidence on determinants. *Social Science & Medicine*. 2003 2003/08/01;57(4):733-44.

65. Farley E, Stewart A, Davies M, Govind M, Van den Bergh D, Boyles T. Antibiotic use and resistance: Knowledge, attitudes and perceptions among primary care prescribers in South Africa. *SAMJ: South African Medical Journal*. 2018;108(9):763-71.
66. Burger M, Fourie J, Loots D, Mnisi T, Schellack N, Bezuidenhout S, et al. Knowledge and perceptions of antimicrobial stewardship concepts among final year pharmacy students in pharmacy schools across South Africa. *Southern African Journal of Infectious Diseases*. 2016;31(3):84-90.
67. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clinical Infectious Diseases*. 2016;62(10):e51-e77.
68. Clinical Pharmacist Vs. Hospital Pharmacist 2020 [cited 2020 29 September]. Available from: https://study.com/articles/clinical_pharmacist_vs_hospital_pharmacist.html.
69. Bronkhorst E, Schellack N, Gous A, Pretorius JP. The need for pharmaceutical care in an intensive care unit at a teaching hospital in South Africa. *Southern African Journal of Critical Care*. 2014;30(2):41-4.
70. Rout J, Brysiewicz P. Exploring the role of the ICU nurse in the antimicrobial stewardship team at a private hospital in KwaZulu-Natal, South Africa. *Southern African Journal of Critical Care*. 2017;33(2):46-50.
71. Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. *Clinical Infectious Diseases*. 2007;44(2):159-77.
72. Parente DM, Morton J. Role of the Pharmacist in Antimicrobial Stewardship. *The Medical clinics of North America*. 2018 Sep;102(5):929-36. PubMed PMID: 30126581. Epub 2018/08/22. eng.
73. CDC. The Core Elements of Hospital Antibiotic Stewardship Programs: 2019. In: Services DoHaH, editor. Atlanta, GA: US CDC2019.
74. Bouza E, Munoz P, Burillo A. Role of the Clinical Microbiology Laboratory in Antimicrobial Stewardship. *The Medical clinics of North America*. 2018 Sep;102(5):883-98. PubMed PMID: 30126578. Epub 2018/08/22. eng.
75. Gillespie E, Rodrigues A, Wright L, Williams N, Stuart RL. Improving antibiotic stewardship by involving nurses. *Am J Infect Control*. 2013 Apr;41(4):365-7. PubMed PMID: 23069737. Epub 2012/10/17. eng.
76. Venugopalan V, Trustman N, Manning N, Hashem N, Berkowitz L, Hidayat L. Administration of a survey to evaluate the attitudes of house staff physicians towards antimicrobial resistance and the antimicrobial stewardship programme at a community teaching hospital. *Journal of global antimicrobial resistance*. 2016;4:21-7.
77. Day SR, Smith D, Harris K, Cox HL, Mathers AJ, editors. An infectious diseases physician-led antimicrobial stewardship program at a small community hospital associated with improved susceptibility patterns and cost-savings after the first year. *Open forum infectious diseases*; 2015: Oxford University Press.
78. Du Toit B. The role of the critical care nurse in the implementation of an antimicrobial stewardship programme in a resource-limited country: Stellenbosch: Stellenbosch University; 2015.
79. Duane TM, Zuo JX, Wolfe LG, Bearman G, Edmond MB, Lee K, et al. Surgeons do not listen: evaluation of compliance with antimicrobial stewardship program recommendations. *The American Surgeon*. 2013 Dec;79(12):1269-72. PubMed PMID: 24351354. Epub 2013/12/20. eng.

80. Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev*. 2013;4(4).
81. Black EK, MacDonald L, Neville HL, Abbass K, Slayter K, Johnston L, et al. Health Care Providers' Perceptions of Antimicrobial Use and Stewardship at Acute Care Hospitals in Nova Scotia. *The Canadian Journal of Hospital Pharmacy*. 2019 Jul-Aug;72(4):263-70. PubMed PMID: 31452537. Pubmed Central PMCID: PMC6699866. Epub 2019/08/28. eng.
82. Mehta JM, Haynes K, Wileyto EP, Gerber JS, Timko DR, Morgan SC, et al. Comparison of prior authorization and prospective audit with feedback for antimicrobial stewardship. *Infection Control and Hospital Epidemiology*. 2014 Sep;35(9):1092-9. PubMed PMID: 25111916. Pubmed Central PMCID: PMC4198070. Epub 2014/08/12. eng.
83. Essack SY, Connolly C, Sturm AW. Antibiotic use and resistance in public-sector hospitals in KwaZulu-Natal. *South African Medical Journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2005 Nov;95(11):865-70. PubMed PMID: 16344884. Epub 2005/12/14. eng.
84. Departments of Health and Agriculture FaFftRoSA. AMR National action plan 2018-2024. In: Departments of Health and Agriculture FaFftRoSA, editor. South Africa2018.
85. Boyles T, Naicker V, Rawoot N, Raubenheimer P, Eick B, Mendelson M. Sustained reduction in antibiotic consumption in a South African public sector hospital: Four-year outcomes from the Groote Schuur Hospital antibiotic stewardship programme. *South African Medical Journal*. 2017;107(2):115-8.
86. Brink AJ, Messina AP, Feldman C, Richards GA, van den Bergh D, Alliance NASS. From guidelines to practice: a pharmacist-driven prospective audit and feedback improvement model for peri-operative antibiotic prophylaxis in 34 South African hospitals. *Journal of Antimicrobial Chemotherapy*. 2017;72(4):1227-34.
87. May C. Towards a general theory of implementation. *Implementation Science*. 2013;8(1):18.
88. Health Do. Guidelines for the Prevention and Containment of Antimicrobial Resistance in South African Hospitals. In: Health Do, editor. South Africa2018.
89. Pakyz AL, Moczygemba LR, VanderWielen LM, Edmond MB, Stevens MP, Kuzel AJ. Facilitators and barriers to implementing antimicrobial stewardship strategies: results from a qualitative study. *American journal of infection control*. 2014;42(10):S257-S63.
90. James R, Luu S, Avent M, Marshall C, Thursky K, Busing K. A mixed methods study of the barriers and enablers in implementing antimicrobial stewardship programmes in Australian regional and rural hospitals. *Journal of Antimicrobial Chemotherapy*. 2015;70(9):2665-70.
91. Cox J, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas M, et al. Antibiotic stewardship in low-and middle-income countries: the same but different? *Clinical Microbiology and Infection*. 2017.
92. Sunenshine RH, Liedtke LA, Jernigan DB, Strausbaugh LJ, Network IDSoAEI. Role of infectious diseases consultants in management of antimicrobial use in hospitals. *Clinical infectious diseases*. 2004;38(7):934-8.
93. NDOH. ANTIMICROBIAL RESISTANCE BACKGROUND DOCUMENT South Africa: NDOH; [cited 2020 09 November]. Available from: <http://www.health.gov.za/index.php/component/phocadownload/category/199-antimicrobial-resistance>.
94. Katzenellenbogen J, Joubert G, Karim SA. *Epidemiology: a manual for South Africa*: Oxford University Press Southern Africa; 1997.
95. Suri H. Purposeful sampling in qualitative research synthesis. *Qualitative research journal*. 2011;11(2):63-75.

96. Nyasulu J, Muchiri E, Mazwi S, Ratshefola M. NIMART rollout to primary healthcare facilities increases access to antiretrovirals in Johannesburg: An interrupted time series analysis. *South African Medical Journal*. 2013;103(4):232-6.
97. Debono DS, Greenfield D, Travaglia JF, Long JC, Black D, Johnson J, et al. Nurses' workarounds in acute healthcare settings: a scoping review. *BMC health services research*. 2013;13:175-. PubMed PMID: 23663305. eng.
98. Alter S. Theory of Workarounds. *Communications of the Association for Information Systems*. 2014 01/01;34.
99. Mula CT, Solomon V, Muula AS. The examination of nurses' adherence to the 'five rights' of antibiotic administration and factors influencing their practices: a mixed methods case study at a tertiary hospital, Malawi. *Malawi medical journal : the journal of Medical Association of Malawi*. 2019 Jun;31(2):126-32. PubMed PMID: 31452845. Pubmed Central PMCID: PMC6698626. Epub 2019/08/28. eng.
100. Mula CT, Human N, Middleton L. An exploration of workarounds and their perceived impact on antibiotic stewardship in the adult medical wards of a referral hospital in Malawi: a qualitative study. *BMC Health Serv Res*. 2019 Jan 23;19(1):64. PubMed PMID: 30674316. Pubmed Central PMCID: PMC6345002. Epub 2019/01/25. eng.
101. McBride-Henry K, Foureur M. Medication administration errors: understanding the issues. *The Australian journal of advanced nursing : a quarterly publication of the Royal Australian Nursing Federation*. 2006 Mar-May;23(3):33-41. PubMed PMID: 16568877. Epub 2006/03/30. eng.
102. Sutthiruk N, Considine J, Hutchinson A, Driscoll A, Malathum K, Botti M. Thai clinicians' attitudes toward antimicrobial stewardship programs. *Am J Infect Control*. 2018 Apr;46(4):425-30. PubMed PMID: 29132695. Epub 2017/11/15. eng.
103. Goff DA, Kullar R, Bauer KA, File Jr TM. Eight habits of highly effective antimicrobial stewardship programs to meet the joint commission standards for hospitals. *Clinical Infectious Diseases*. 2017;64(8):1134-9.
104. National Department of Health. ANTIMICROBIAL RESISTANCE NATIONAL STRATEGY FRAMEWORK 2014-2024. In: Health NDo, editor. South Africa: NDOH; 2014.
105. Hand K. Antibiotic pharmacists in the ascendancy. *Journal of Antimicrobial Chemotherapy*. 2007;60(suppl_1):i73-i6.
106. Messina AP, van den Bergh D, Goff DA. Antimicrobial Stewardship with Pharmacist Intervention Improves Timeliness of Antimicrobials Across Thirty-three Hospitals in South Africa. *Infect Dis Ther*. 2015;4(Suppl 1):5-14. PubMed PMID: 26362291. Epub 09/11. eng.
107. Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA, et al. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. *Clinical Microbiology and Infection*. 2019;25(1):20-5.
108. Eljaaly K, Elarabi S, Alshehri S, Nix DE. Impact of requiring re-authorization of restricted antibiotics on day 3 of therapy. *The Journal of Antimicrobial Chemotherapy*. 2018 Feb 1;73(2):527-30. PubMed PMID: 29077862. Epub 2017/10/28. eng.
109. Horikoshi Y, Higuchi H, Suwa J, Isogai M, Shoji T, Ito K. Impact of computerized pre-authorization of broad spectrum antibiotics in *Pseudomonas aeruginosa* at a children's hospital in Japan. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2016 Aug;22(8):532-5. PubMed PMID: 27263807. Epub 2016/06/07. eng.
110. Reed EE, Stevenson KB, West JE, Bauer KA, Goff DA. Impact of formulary restriction with prior authorization by an antimicrobial stewardship program. *Virulence*. 2013;4(2):158-62.
111. Baraka MA, Alsultan H, Alsalman T, Alaithan H, Islam MA, Alasseri AA. Health care providers' perceptions regarding antimicrobial stewardship programs (AMS) implementation-facilitators and challenges: a cross-sectional study in the Eastern province of Saudi Arabia.

Annals of clinical microbiology and antimicrobials. 2019 Sep 24;18(1):26. PubMed PMID: 31551088. Pubmed Central PMCID: PMC6760054. Epub 2019/09/26. eng.

112. Pope SD, Dellit TH, Owens RC, Hooton TM. Results of survey on implementation of Infectious Diseases Society of America and Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Infection Control and Hospital Epidemiology. 2009 Jan;30(1):97-8. PubMed PMID: 19046053. Epub 2008/12/03. eng.

113. Sandelowski M. Sample size in qualitative research. Research in Nursing & Health. 1995;18(2):179-83.

Appendix 1: Plagiarism Declaration



PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Hermenegilda Lucia Caetano Jose Madeira (Student number: 0213182A) am a student registered for the degree of Masters of Public Health in the academic year 2020.

I hereby declare the following:

- ❖ I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- ❖ I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- ❖ I have followed the required conventions in referencing the thoughts and ideas of others.
- ❖ I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature Hermenegilda Madeira Date: 26 October 2020

Appendix 2: Ethics Clearance Certificate



R14/49 Dr H Madeira

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL) CLEARANCE CERTIFICATE NO. M181172

NAME: Dr H Madeira
(Principal Investigator)
DEPARTMENT: School of Public Health
Medical School
University

PROJECT TITLE: Perceptions and attitudes of health professionals on the establishment of an antimicrobial stewardship programme at a tertiary hospital in Gauteng Province

DATE CONSIDERED: 30/11/2018

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr P Ditlopo

APPROVED BY:

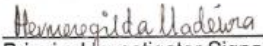

Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 08/03/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report.** When a funder requires annual re-certification, the application date will be one year after the date of the meeting when the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore reports and re-certification will be due early in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature

08/03/2019
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 3: Turnitin Report

0213182a:PERCEPTIONS_AND_ATTITUDES_OF_HEALTH_P..			
ORIGINALITY REPORT			
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Appendix 4: Interview Guide for Professional Nurses and Pharmacists

1. Characteristics of the Respondents

Questions		Response
1.1	In which department do you work in this hospital?	☐ Internal Medicine ☐ Pharmacy
1.2	In which sub-specialty do you work	
1.3	What is your current position in this hospital?	☐ Nurse Specify position _____ ☐ Pharmacist Specify position _____
1.4	How long have you been working in this position for?	_____ years; _____ months
1.5	How long have you been working in your profession for?	_____ years; _____ months
1.6	How long have you been working in this hospital for?	_____ years; _____ months

2. Antimicrobial Prescribing Practices

2.1 What role do you play in antimicrobial management in this hospital?

– Probe on:

- Prescribing, monitoring, restricting, administration and or other

2.2 How would you describe the current use of antibiotics in this hospital?

– Probe on:

- To what extent do you think inappropriate use of antibiotics is a problem in this hospital?
- Which problems are more prevalent or common in this hospital?
- What factors contribute to appropriate/inappropriate use of antibiotics in this hospital?

3. The Establishment of an Antimicrobial Stewardship Programme (ASP)

(Define antimicrobial stewardship)

Provide definition -Antimicrobial stewardship: a multidisciplinary, systematic approach to optimizing the appropriate use of all antimicrobials to improve patient outcome and limit the emergence of resistant pathogens whilst ensuring patient safety

3.1 In your view, what is your understanding of antimicrobial resistance?

3.2 What strategies do you recommend to combat the misuse of antimicrobials in this hospital?

3.3 What are your views regarding the establishment of an antimicrobial stewardship programme (ASP) in this hospital?

– Probe on:

- What should be its roles and responsibilities?
- Which cadres should be part of the committee and why
- What are your views on the capacity of the hospital to implement a successful ASP
- What interventions should be implemented by an ASP in the hospital? (formulary restriction, Prospective Audit With Feedback, other supplementary interventions)

4. In your opinion, what do you think are the existing facilitators to the implementation of an antimicrobial stewardship programme (ASP) in this hospital?

Probe on:

- Contextual factors (e.g. availability of policies & procedures, organizational culture, financial and human resources capacity, organizational structure)
- Process factors (e.g. regular auditing, feedback to prescribers)
- Organizational readiness and commitment to change

5. In your opinion, what do you think are the existing barriers to the implementation of an antimicrobial stewardship programme (ASP) in this hospital?

Probe on:

- Contextual factors (e.g. unavailability of policies & procedures, organizational culture, lack of financial and human resources capacity, organizational structure)
- Process factors (e.g. lack of monitoring, weak communication between multidisciplinary teams)
- Organizational readiness and commitment to change

6. What recommendations can you make to ensure effective implementation of an antimicrobial stewardship programme (ASP) in this hospital?

THANK YOU FOR PARTICIPATING IN THIS INTERVIEW

Appendix 5: Interview guide for consultants, registrars and medical interns

1. Characteristics of the Respondents

Questions		Response
1.1	In which department do you work in this hospital?	☐ Internal Medicine ☐ Pharmacy
1.2	In which sub-specialty do you work	_____
1.3	What is your current position in this hospital?	☐ ☐ Consultant physician ☐ Fellow (postgraduate) physician ☐ ☐ Registrar physician ☐ Intern ☐ Other (specify): _____
1.4	How long have you been working in this position for?	_____ years; _____ months
1.5	How long have you been working in your profession for?	_____ years; _____ months
1.6	How long have you been working in this hospital for?	_____ years; _____ months

2. Antimicrobial Prescribing Practices

2.1 What role do you play in antimicrobial management in this hospital?

– Probe on:

- Prescribing, monitoring, restricting, administration and or other

2.3 If you prescribe antibiotics, what influences your decision to start a patient on an antimicrobial?

– Probe on:

- Decision processes relating to how you decide which antimicrobial is appropriate
- Is decision based on evidence, or experience, or policy, or pressure from patients

2.4 To what extent would you say you have prescribed an antibiotic when you thought it was not needed?

- Provide a brief scenario of a particular incident when an antibiotic was inappropriately prescribed
- Reasons for inappropriate prescription

2.5 How would you describe the current use of antibiotics in this hospital?

- Probe on:
 - To what extent do you think inappropriate use of antibiotics is a problem in this hospital?
 - Which problems are more prevalent or common in this hospital?
 - What factors contribute to appropriate/inappropriate use of antibiotics in this hospital?

3. The Establishment of an Antimicrobial Stewardship Programme (ASP)

Provide definition -Antimicrobial stewardship: a multidisciplinary, systematic approach to optimizing the appropriate use of all antimicrobials to improve patient outcome and limit the emergence of resistant pathogens whilst ensuring patient safety

- In your view, what is your understanding of antimicrobial resistance?
- What strategies do you recommend to combat the misuse of antimicrobials in this hospital?
- What are your views regarding the establishment of an antimicrobial stewardship programme (ASP) in this hospital?
- Probe on:
 - What should be its roles and responsibilities?
 - Which cadres should be part of the committee and why?
 - What are your views on the capacity of the hospital to implement a successful ASP?
 - What interventions should be implemented by an ASP in the hospital? (formulary restriction, Prospective Audit With Feedback, other supplementary interventions)?

4. In your opinion, what do you think are the existing facilitators to the implementation of an antimicrobial stewardship programme (ASP) in this hospital?

Probe on:

- Contextual factors (e.g. availability of policies & procedures, organizational culture, financial and human resources capacity, organizational structure)

- Process factors (e.g. regular auditing, feedback to prescribers)
- Organizational readiness and commitment to change

5. In your opinion, what do you think are the existing barriers to the implementation of an antimicrobial stewardship programme (ASP) in this hospital?

Probe on:

- Contextual factors (e.g. unavailability of policies & procedures, organizational culture, lack of financial and human resources capacity, organizational structure)
- Process factors (e.g. lack of monitoring, weak communication between multidisciplinary teams)
- Organizational readiness and commitment to change

6. What recommendations can you make to ensure effective implementation of an antimicrobial stewardship programme (ASP) in this hospital?

THANK YOU FOR PARTICIPATING IN THIS INTERVIEW