DEVELOPMENT OF A FRAMEWORK FOR A PROPOSED ANTIMICROBIAL USAGE REPORTING TOOL FOR PUBLIC SECTOR HOSPITALS

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DEVELOPMENT OF A FRAMEWORK FOR A PROPOSED ANTIMICROBIAL USAGE REPORTING TOOL FOR PUBLIC SECTOR HOSPITALS

By

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DECLARATION

I, Yumna Ramjan, 213398826, hereby declare that the dissertation for the Master of Pharmacy (Research) to be awarded is my own work and that it has not previously been submitted for assessment or completion of any postgraduate qualification to another University or for another qualification.

Yumna Ramjan (Signature)

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LIST OF ABBREVIATIONS

ACSQHC	Australian Commission on Safety and Quality in Health Care
AMC	Antimicrobial Consumption
AMS	Antimicrobial Stewardship
AMR	Antimicrobial Resistance
AMRU	Antimicrobial Resistance Reference Unit
APA	American Psychological Association
AU	Antibiotic Use
AUR	Antibiotic Use and Resistance
ATC	Anatomical Therapeutic Chemical
BCMA	Bar-coded medication administration
BRICS	Brazil, Russia, India, China, South Africa
CAGR	Compound annual growth rate
CDC	Centers for Diseases Control and Prevention
CPD	Continuing Professional Development
DDD	Defined Daily Dose
DA	Doses Administered
DAMSC	District Antimicrobial Stewardship Committee
df	Degree of freedom
DHIS	District Health Information System
DOT	Days of Therapy
ECDoH	Eastern Cape Department of Health
eMAR	Electronic Medication Administration Records
EML	Essential Medicines List
E-Prescribing	Electronic Prescribing
EPI	Expanded Programme on Immunisation
FPGSC	Faculty Postgraduate Studies Committee (FPGSC)
GFR	Glomerular Filtration Rate
GLASS	The Global Antimicrobial Resistance Surveillance System
haDDD	Hospital-adjusted Defined Daily Dose
HAMSC	Hospital Antimicrobial Stewardship Committee
HIV	Human Immunodeficiency Virus

I	Involved
ICU	Intensive Care Unit
IDS	Infectious Disease Specialist
IDSA	Infectious Disease Society of America
IMS	Intercontinental Marketing Services
IPC	Infection Prevention and Control
IT	Information technology
IV	Intravenous
LOS	Length of stay
LOT	Length of Therapy
M	Medical
MAC	Ministerial Advisory Committee
MAT	Moving annual total
MP	Medical Prescriber
NAUSP	National Antimicrobial Utilisation Surveillance Programme
nDDD	Neonatal Defined Daily Dose
NDoH	National Department of Health
NI	Not involved
NM	Non-medical
NICD	National Institute for Communicable Diseases
NSAF	National Antibiotic Surveillance Forum
NTBLC	National Tuberculosis and Leprosy Control Programme
OBD	Occupied Bed Days
OR	Odds Ratio
p	Probability value
PAMSC	Provincial AMS Committee
PDD	Prescribed Daily Dose
PTC	Pharmacy and Therapeutics Committee
RDD	Recommended Daily Dose
REC-H	Research Ethics Committee-Human
SAAR	Standardised Antimicrobial Administration Ratio
SASCM	South African Society for Clinical Microbiology
SHEA	Society for Healthcare Epidemiology of America
STD	Sexually Transmitted Disease

STG	Standard Treatment Guidelines
TB	Tuberculosis
UK	United Kingdom
USA	United States of America
USC	Unit for Statistical Consultation
WHO	World Health Organization

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ABSTRACT

Background: The inappropriate and unnecessary use of antimicrobials has increased the need to monitor antimicrobial usage so as to identify inappropriate use. In order to support the antimicrobial stewardship (AMS) programme, it is important to quantify the usage of antimicrobials and this can be achieved by promoting the use of AMS utilisation metrics. They are used to measure the progress and efficacy of an AMS programme (Brotherton, 2018).

Primary Aim of Research: The primary aim of the research was to develop a framework for a proposed antimicrobial usage reporting tool, which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in the South African public sector hospital setting.

Methodology: The study was divided into three phases: a preliminary phase, a developmental phase and a post-developmental phase. The preliminary phase focused on obtaining a comprehensive understanding of the type and nature of the AMS utilisation metrics and subsequently identifying the views on the usage, usefulness and clinical relevance of those AMS utilisation metrics using a quantitative questionnaire, which was conducted among infectious disease specialists, pharmacists, medical prescribers, i.e. prescribers who were not specialists and clinical pathologists employed at tertiary level, public sector hospitals in the Eastern Cape province of South Africa. Consequently, a qualitative semi-structured interview was conducted among healthcare professionals who were involved in the daily implementation of AMS in the workplace. Results obtained from the quantitative component and qualitative component were integrated in order to develop a framework for a proposed antimicrobial usage reporting tool.

Results: The Defined Daily Dose (DDD), Prescribed Daily Dose (PDD) and Days of Therapy (DOT) were identified as the most common AMS metrics (Grau et al., 2013). However, the DDD was the only AMS metric currently recommended by the South African National Department of Health (South African National Department of Health, 2017a) and it was the only AMS metric currently being utilised at two of the

five research sites in the Eastern Cape province of South Africa. It was identified that data pertaining to antimicrobial usage was available and was being extracted from Rx Solution®. However, the programme did not have the ability of automatically producing the reports, hence, emphasising on the need for an antimicrobial usage reporting tool for South African public sector hospitals. Therefore, the framework for the proposed antimicrobial usage reporting tool would integrate antimicrobial stock management data with the following AMS utilisation metrics: DDD, DOT and PDD, were considered for inclusion in the proposed antimicrobial usage reporting tool.

Conclusion: The qualitative findings obtained during the post-developmental phase, therefore, established that although an electronic platform for the purpose of monitoring antimicrobial usage for the South African public sector hospitals was required, there would be many challenges obstructing the implementation of the proposed antimicrobial usage reporting tool.

Keywords: Antimicrobial Stewardship, antimicrobial utilisation metrics, reporting tool, antimicrobial usage

CHAPTER 1
INTRODUCTION

1.1 Introduction

Antimicrobial stewardship (AMS) is a coordinated programme implemented by healthcare professionals and aims to improve the usage of antimicrobials for the best outcome of a patient while limiting toxicity and resistance (South African National Department of Health, 2016). AMS requires an inter-professional approach and is supported at the national and provincial level in South Africa (South African National Department of Health, 2016). AMS programmes are typically led by an infectious disease specialist but also incorporate the expertise of nurses, clinical microbiologists and pharmacists (MacDougall & Polk, 2005).

During the last century, the morbidity and mortality rates caused by infectious diseases have decreased substantially, the main reasons being, the introduction of antimicrobial treatment as well as infection prevention and control practices (IPC), such as hygiene measures. However, the rate at which resistant microorganisms are occurring is increasing alarmingly and the most commonly used antimicrobials are no longer effective against the resistant microorganisms (Stanic Benic et al., 2018). One factor seen to be contributing to antimicrobial resistance is the misuse and overuse of antimicrobials (Bennett, Schulz, Boyd, & Newland, 2018). Therefore, it is important to make responsible use of the currently available antimicrobials so as to prevent the spread of infectious diseases and maintain the efficacy of antimicrobials (Stanic Benic et al., 2018).

The quantification of antimicrobial usage has been considered to be a key strategy to implement in an AMS programme as it is believed that measuring antimicrobial usage is the first step which could control and improve usage (Stanic Benic et al., 2018). It has been identified from the literature that standardised and validated metrics are required in order to determine the effectiveness of an AMS programme (Bennett et al., 2018). Many AMS metrics have been identified throughout the literature, however, there is no existing standard, ideal and reliable AMS metric utilised in the

evaluation of an AMS programme and which could reflect the true quality of antimicrobial prescribing (Bennett et al., 2018; Fridkin & Srinivasan, 2014). The different AMS metrics identified throughout the literature will be discussed in more details in Section 2.6.

1.2 Problem Statement

Although the rate of antimicrobial resistance has increased drastically, classes of antimicrobials have not been discovered since 1963 (Aminov, 2017). Increasing use of antimicrobials has resulted in multi-drug-resistant organisms, which no longer respond to the older classes of antimicrobials (Coates, Halls, & Hu, 2011). According to the Antimicrobial Resistance National Strategy Framework of South Africa, treating infectious diseases caused by resistant pathogens is economically problematic (South African National Department of Health, 2014). These infections lead to extended hospitalisations and more visits to the general practitioner, and may even result in death (Alliance for the Prudent use of Antibiotics, 2014). In order to minimise the development of antimicrobial resistance, it is important to reduce the inappropriate use of antimicrobials. This can be partially achieved by monitoring the use of antimicrobials. In the South African public healthcare setting, data pertaining to antimicrobial usage is available and is being extracted from Rx Solution® but specific AMS metrics reports required by AMS practitioners for monitoring purposes are time consuming to produce and not readily available in one consolidated database. Therefore, the current research aimed to develop a framework for a proposed antimicrobial usage reporting tool, which would be utilised by AMS practitioners in a tertiary level public sector hospital setting.

1.3 Research Aim

The primary aim of the research was to develop a framework for a proposed antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in a tertiary level, public sector hospital setting.

1.4 Research Objectives

In order to fulfill the aim of the research, the following research objectives were to:

- Identify the most commonly used Antimicrobial Stewardship (AMS) metrics, which focus on antimicrobial utilisation according to the published literature.
- Describe practitioners' views on the usage, usefulness and clinical relevance of the AMS metrics, in the South African public healthcare setting.
- Develop a framework of AMS metrics to be included in the antimicrobial usage reporting tool.
- Explore the applicability and practicality of the proposed antimicrobial usage reporting tool prior to implementation, from the perspectives of the members of an AMS team.

1.5 Brief Summary of Methodology

The research design of the study adopted an explanatory sequential mixed methods approach: a quantitative methodology followed by a qualitative methodology was employed (Creswell, 2014). The research design is classified as an explanatory sequential mixed method as the researcher first conducted a quantitative research, followed by a qualitative research. The results obtained from the quantitative research were analysed and further enriched using a qualitative research (Creswell, 2014).

The study was divided into three phases – a preliminary phase, a developmental phase and a post-developmental phase (Figure 1.1).

The preliminary phase consisted of three components: an in-depth literature review, followed by a quantitative component and a qualitative component. The purpose of the preliminary phase was to identify the most commonly used AMS metrics according to the published literature. A questionnaire was developed in order to collect quantitative data. It was subsequently used to identify the views on the usage, usefulness and clinical relevance of those AMS metrics in the South African setting

(Appendix A). Furthermore, a qualitative component was conducted in order to obtain a comprehensive understanding of the quantitative responses.

Various journal articles and textbooks were consulted in order to gain a thorough understanding of the type and nature of the AMS utilisation metrics. A quantitative questionnaire was then conducted among infectious disease specialists, pharmacists, medical prescribers, i.e. medical prescribers who were not specialists and clinical pathologists, employed at tertiary level, public sector hospitals in Port Elizabeth and East London, in the Eastern Cape province of South Africa. The questionnaire allowed the researcher to determine the views of the practitioners on the usage, usefulness and clinical relevance of different AMS utilisation metrics (Appendix A). The quantitative data was further deepened using qualitative data, which was in the form of semi-structured interviews with open-ended questions. The respondents who were invited to participate in the semi-structured interviews, were healthcare professionals involved in the implementation of AMS on a daily basis in the workplace. The qualitative data allowed the researcher to obtain more clarity related to the role of the respondents in terms of monitoring antimicrobial usage, i.e. quantification of antimicrobials using AMS metrics, at the research sites. It also allowed the researcher to determine the type and source of data used by the respondents in order to calculate the relevant AMS metric reports. It then helped the researcher to identify any challenges related to the compilation of the AMS metric reports and also helped to identify which data was useful to develop the framework for the proposed antimicrobial usage reporting tool.

The purpose of the developmental phase was to integrate quantitative and qualitative data obtained during the preliminary phase with the aim of developing a framework of AMS metrics to be included into the antimicrobial usage reporting tool.

The purpose of the post-developmental phase was to obtain feedback on the applicability and practicality of the framework for the proposed antimicrobial usage reporting tool. Feedback was obtained from the respondents who participated in the preliminary phase, in the form of qualitative data during a second round of semi-structured interviews.

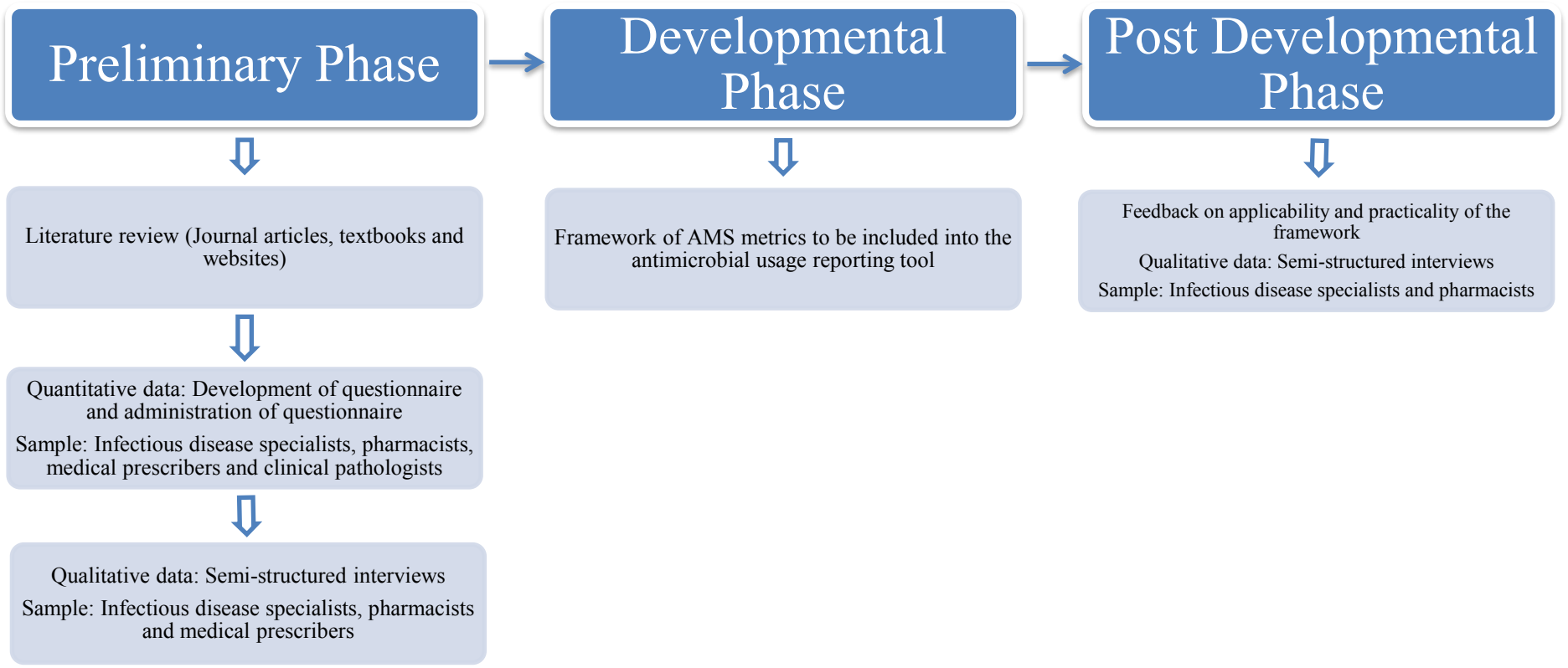

Figure 1.1. Overview of the explanatory sequential mixed method design illustrating the three phases of the study – the preliminary phase followed by the developmental phase and post-developmental phase

1.6 Layout of Dissertation

Chapter One provided an overview of the context research of the study and a summary of the research design. It also stipulated the problem statement, aim and objectives of the study.

Chapter Two will present an overview on antimicrobial resistance and the need for antimicrobial stewardship (AMS) programmes. The development of AMS, both on an international level and national level (South Africa) will also be focused on. An in-depth review of antimicrobial surveillance focusing on AMS utilisation metrics will also be presented.

Chapter Three will focus on a detailed description of the data collection process of the study, i.e. the data collection process for the quantitative and qualitative data obtained during the preliminary phase. Details related to the developmental phase and the process how qualitative data will be collected during the post-developmental phase will also be presented.

Chapter Four will present the results obtained during the preliminary phase of the study, i.e. quantitative and qualitative data. Results obtained during the developmental and post-developmental phases will also be presented. Chapter Five will link the results obtained during the three phases of the study, to the aim and objectives of the study, while Chapter Six will present a conclusion, recommendations, and possible future areas of research linked to the findings of the study.

1.7 Referencing Style

The researcher used a referencing software, EndNote®, which was integrated with Microsoft Word®. The referencing style used by the researcher was the American Psychological Association (APA) style.

1.8 Key Concepts

Below is a list of the key concepts and definitions that will be used throughout the study.

Antimicrobial Stewardship (AMS): Antimicrobial stewardship (AMS) is a coordinated programme implemented by health care professionals and aims to optimise the use of antimicrobials for the best outcome of a patient while limiting toxicity and resistance (South African National Department of Health, 2016).

Antimicrobial utilisation metric: An aggregate or average amount of antimicrobials being consumed at the level of the patient, a hospital unit or service, or an entire institution (Morris, 2014, p. 102).

Defined Daily Dose (DDD): Assumed average maintenance dose per day for a drug used for its main indication in adults (WHO Collaborating Centre for Drug Statistics Methodology, 2016a)

Days of Therapy (DOT): Number of days that a patient receives an antimicrobial, irrespective of the dose given (Grau et al., 2013)

Prescribed Daily Dose (PDD): "The average dose prescribed per day according to a representative sample of prescriptions at a hospital" (Grau et al., 2013)

Rx Solution®: It is a software programme used in public health facilities, by eight of the nine provinces in South Africa, including the Eastern Cape to manage pharmaceutical supplies, from procurement to dispensing. It also assists in stock management, prevention of stock-outs, minimising expired stock, and dispensing medication to patients (System for Improved Access to Pharmaceuticals and Services Program, 2017).

CHAPTER 2
LITERATURE REVIEW

2.1 Antimicrobial Resistance and the Need for Antimicrobial Stewardship (AMS) Programmes

The inappropriate and unnecessary usage of antimicrobials during the 21st century has contributed to antimicrobial resistance (Momattin, Al-Ali, Mohammed, & Al-Tawfiq, 2018). Other than the increase in use of antimicrobials, antimicrobial resistance can be caused by other several reasons, for instance, the lack of infection control practices in the hospital environment (White, 2005). Despite not being the most important factor contributing to resistance, antimicrobial usage is a factor which be modified in order to combat resistance (File, Srinivasan, & Bartlett, 2014). The issue of 'antimicrobial resistance' is recognised as a global health crisis (Bennett et al., 2018). It is complex and it needs to be addressed across its multiple dimensions (Wernli et al., 2017).

Antimicrobial resistance can either be microbiological or clinical in nature. Microbiological resistance is the ability of the microorganism to develop resistance mechanisms against the antimicrobial whereas clinical resistance is linked to treatment failure (MacGowan & Macnaughton, 2017). Thus, an increase in resistance cause prescribers to opt for broader-spectrum antimicrobials, which eventually contributes to a higher incidence of multi-drug resistant pathogens (Jacob & Gaynes, 2010).

As a result of an exacerbating curb in antimicrobial resistance, the Infectious Disease Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) introduced a formal antimicrobial stewardship (AMS) programme in 2007. According to the IDSA and SHEA, AMS aims at "optimising therapeutic outcomes of a patient whilst minimising adverse effects such as toxicity, emergence of resistance and risk of *Clostridium difficile* infections associated with an antimicrobial" (Dellit et al., 2007; Goff et al., 2017; Momattin et al., 2018).

2.2 AMS at the International Level

2.2.1 World Health Organization (WHO)

The primary goal of an AMS programme is to ensure the appropriateness of therapy for patients and this can be determined by applying the "4 D's of optimal antimicrobial therapy": right Drug, right Dose, De-escalation of treatment and right Duration of treatment (Doron & Davidson, 2011; Joseph & Rodvold, 2008). Other goals include improving the usage of antimicrobials and decreasing the rate of antimicrobial resistance, which can be achieved by preventing their overuse, misuse and abuse (Doron & Davidson, 2011).

In 2015, the World Health Organization (WHO) developed a document on global actions to be taken against antimicrobial resistance (World Health Organization, 2015a). Antimicrobial resistance cannot be completely eradicated but the WHO has set up a goal to ensure that infectious diseases are successfully treated and prevented. In an attempt to achieve this goal, five objectives were introduced and they are: i) To educate and provide training on antimicrobial resistance, ii) to increase antimicrobial surveillance and research, iii) to improve infection prevention and control (IPC) practices, iv) to optimise the usage of antimicrobials, and v) to economically contribute to the development of new antimicrobials, diagnostic tools and vaccines (World Health Organization, 2015a).

The Global Antimicrobial Resistance Surveillance System (GLASS) was simultaneously implemented so as to support the Global Action Plan on Antimicrobial Resistance. The aim of GLASS consists of integrating patient, laboratory and epidemiological surveillance data at a national level, with the aim of understanding the extent and consequence of antimicrobial resistance on the population. The rates of antimicrobial resistance would be calculated from aggregrate data collected from respective surveillance sites and would be submitted to the WHO. The rates of antimicrobial resistance can be submitted, stored, shared and retrieved onto a web-based interface tool (World Health Organization, 2015b).

2.2.2 United States of America (USA)

In 2007, the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) introduced AMS as a clinical activity and they developed guidelines for the implementation of AMS programmes. The following strategies comprise of the foundation for an AMS programme and they must be implemented in order to improve the usage of antimicrobials:

1. **Prospective audit with intervention and feedback:** reviewing the appropriateness of antimicrobial therapy for each patient based on clinical outcomes, antimicrobial utilisation, costs, resistance, patient safety and process metrics, and therefore, making recommendations as required (Griffith, Postelnick, & Scheetz, 2012; Morrill, Caffrey, Gaitanis, & LaPlante, 2016).

2. **Formulary restriction and preauthorisation** (Barlam et al., 2016; Goff et al., 2017).

Other elements were also recommended as part of an AMS programme and they will be discussed further. Educational AMS activities are the basis to create awareness about reducing the inappropriate usage of antimicrobials. Improving the prescribing of antimicrobials is a fundamental element of an AMS programme and it can be achieved through the development of evidence-based guidelines for infectious diseases (Barlam et al., 2016). Antimicrobial cycling, also known as "the substitution of a class of antimicrobial with a different class that exhibits similar spectrum of activity against a certain microorganism", has been proposed towards the implementation of an AMS programme. However, it is a difficult and labour-intensive approach and there is insufficient evidence proving that antimicrobial cycling contributes to improvement in antimicrobial usage. The practice of intravenous (IV) to oral switch is considered a compulsory activity to reinforce as it reduces the length of hospitalisation and costs associated with hospitalisation (Barlam et al., 2016). Furthermore, antimicrobial order forms, combination treatment, rationalising or de-escalation of antimicrobial treatment and optimisation of the antimicrobial dose must also be emphasised on (Barlam et al., 2016; Goff et al., 2017).

The concept of AMS is also being supported by the ex-president of the United States of America (USA), Barack Obama, as in 2014, he issued a "National Action Plan for Combating Antibiotic-resistant Bacteria", with the aim of slowing the occurrence of resistant organisms and preventing the spread of infectious diseases (The White House, 2015). The National Action Plan supports the 'One-Health' approach and the Centers for Diseases Control and Prevention (CDC) defines the 'One-Health' approach as "a collaborative, multisectoral and trans-disciplinary approach – working at the local, regional, national and global levels – with the goal of achieving optimal health outcomes recognising the interconnection between people, animals, plants and their shared environment" (Centers for Disease Control and Prevention, 2017b). By 2020, the National Action Plan is aiming at introducing AMS programmes in all acute hospital settings in the USA (The White House, 2015).

In addition, the National Action Plan is aiming to fulfill the following objectives: i) to develop rapid and innovative diagnostic tests for the identification of resistant microorganisms, ii) to promote research for the development for new antibiotics, other therapeutics and vaccines and iii) to work in partnership with other countries for the prevention, monitoring and control of antimicrobial resistance (The White House, 2015).

2.2.3 United Kingdom (UK)

Due to a rise in the occurrence of resistant microorganisms and *Clostridium difficile* infections, AMS was implemented in the United Kingdom in the early 2000s. The Department of Health in the United Kingdom (UK) had endorsed the initiative of AMS by proving funding to hospitals within the country. The hospitals were able to develop guidelines for infectious diseases, introduce antimicrobial ward rounds, conduct antimicrobial surveillance and audits and increase awareness about antimicrobial resistance, which had led to an overall reduction in infectious diseases (Goff et al., 2017).

In an effort to combat the problem of antimicrobial resistance, the UK's Department of Health explored seven fields as follows:

- Improving infection prevention and control practices.
- Optimising prescribing practice.
- Improving professional education, training and public engagement.
- Developing new drugs, treatments and diagnostics.
- Better access to and use of surveillance data.
- Better identification and prioritisation of AMR research needs.
- Strengthened international collaboration.

Improving infection prevention and control practices (IPC) was the first strategy that the UK focused on to combat resistance. The development of AMS programmes and integrated surveillance data on antimicrobial usage, bacterial resistance, epidemiology of bacterial infections and clinical outcomes would further reduce the rate of antimicrobial resistance. An AMS programme aims to preserve the efficacy of the currently available antimicrobials, however, it is the role of the AMS practitioners to differentiate between a viral and bacterial infection (Department of Health, 2013).

In partnership with the pharmaceutical industry, research councils and the academia, governmental and non-governmental organisations must promote research for the development of new antimicrobials. Since healthcare professionals are the primary educators of patients, they must have a sound understanding of antimicrobial resistance and stewardship. AMS practitioners are required to attend continuing professional development (CPD) programmes on AMS in order to remain currently informed on the number of resistant infectious diseases cases, emergence of new resistant microorganisms and prescribing patterns (Department of Health, 2013).

In 2015, an antimicrobial stewardship toolkit also known as the "Start Smart – Then Focus" was developed for British hospitals (Figure 2.1). It is recommended that British hospitals implementing AMS programmes, follow the *Start Smart – Then Focus* approach, which is further illustrated in Figure 2.1 (Public Health England, 2015).

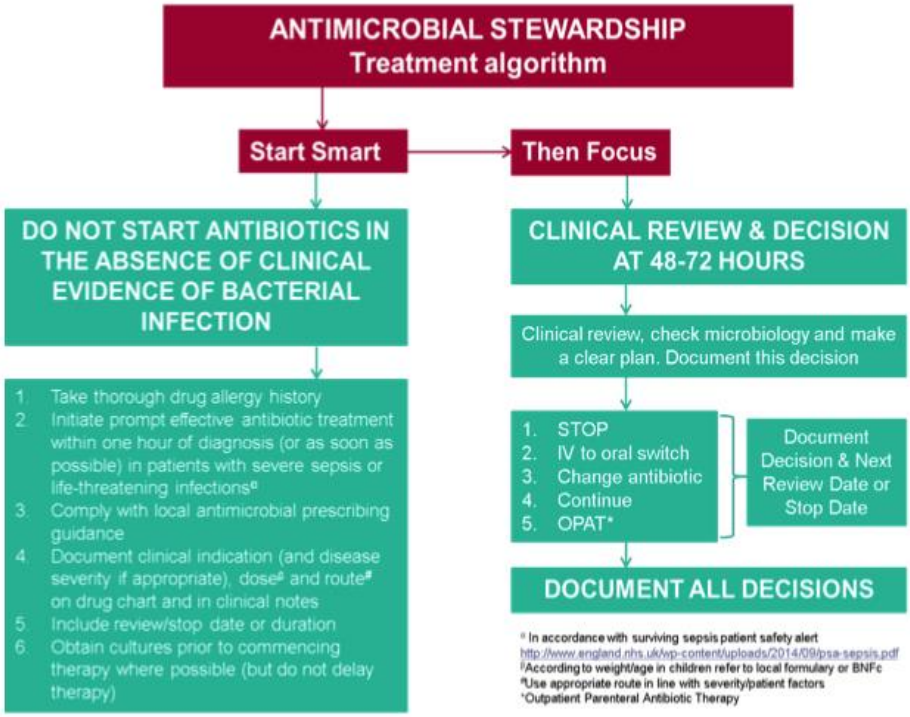

Figure 2.1. Antimicrobial Stewardship (AMS) – Treatment algorithm (Public Health England, 2015, p. 7)

The "Start Smart – Then Focus" toolkit reinforces to establish an AMS team and a ward-focused AMS team. The AMS team must at least be made up of an infectious disease specialist, a pharmacist trained in infectious diseases, a physician, a microbiologist, a surgeon, an anesthetist, a pediatrician and a nurse. The AMS team must continuously update and adhere to evidence-based guidelines and remain responsible to perform frequent quality assurance auditing so as ensure that AMS practices meet the required standards. The ward-focused AMS team must consist of an antimicrobial pharmacist, a microbiologist and an infectious disease specialist. The members are liable to review the antimicrobial therapy for each patient in the ward and give a constant progress report to the AMS team (Public Health England, 2015).

2.2.4 Australia

The first Australian antimicrobial resistance strategy guideline was implemented in 2015. In response to address the issue of antimicrobial resistance, the Australian

Government also follows the 'One Health' approach, which is aligned with the WHO's Global Action Plan on antimicrobial resistance (2015).

In favour of decreasing the rate of antimicrobial resistance, it is important for the public to understand the concept of 'antimicrobial resistance'. Increasing awareness and education on antimicrobial resistance are the first required efforts to confront this serious issue. To convey an effective message about antimicrobial resistance, the Australian Government supports the following initiatives: i) to increase awareness of the consumer on the concept of antimicrobial resistance and rationale of appropriate antimicrobial usage, ii) to develop guidelines on appropriate antimicrobial prescribing for healthcare and veterinary professionals and iii) to hold regular workshops on antimicrobial resistance and stewardship for healthcare professionals and to increase communication between healthcare professionals (Australian Government, 2015).

Since an AMS programme does not exist in every Australian healthcare institution, other resources such as evidence-based guidelines must be developed in support of implementing AMS. Furthermore, to understand the cause of antimicrobial resistance, surveillance of antimicrobial usage is a fundamental strategy to implement.

Infection prevention and control (IPC) practices are aiming to control the spread of infectious diseases through disinfection, hand hygiene and vaccination programmes, which would eventually result in a reduction in the usage of antimicrobials or absolutely no need for antimicrobials. The Australian Government is also promoting research activities, which include making appropriate use of the available resources in an endeavor to develop new technologies against the prevention and detection of antimicrobial resistance (Australian Government, 2015).

Antimicrobial resistance is an international concern. The Australian Government believes that for AMS to be optimally beneficial, collaboration between countries is important. The Western Pacific Regional Office of the WHO is collaborating with Australia and they are supporting activities such as monitoring and reporting of antimicrobial resistance in the Asia-Pacific region. Some countries are already taking the lead in terms of antimicrobial surveillance. In partnership with those countries, Australia is investigating new prospects on how to address the global and complex

issue of antimicrobial resistance. Furthermore, the country is looking forward to contribute more funds towards the development of new antimicrobials, diagnostic tests and vaccines and its focus is to combat drug-resistant tuberculosis. Therefore, to support its activities, various stakeholders across Australia and state and territory government are also contributing towards improving antimicrobial usage (Australian Government, 2015).

2.2.4.1 National Antimicrobial Utilisation Surveillance Programme (NAUSP)

The National Antimicrobial Utilisation Surveillance Programme (NAUSP) is a programme funded by the Australian Government in collaboration with the Australian Commission on Safety and Quality in Health Care (ACSQHC) (Government of South Australia, 2012). The NAUSP reports on the usage of antimicrobial for adults in Australian acute care inpatient settings. The healthcare facilities submit their monthly total antimicrobial usage data and bed occupancy data via the NAUSP portal. The total usage is then expressed as DDD per 1000 occupied bed days (OBDs) (Government of South Australia, 2017).

2.2.5 AMS in developing countries – Botswana, Nigeria and Colombia

Brazil, Russia, India, China and South Africa, also known as the BRICS nations, are among the five countries with the greatest usage of antibiotics (Taneja & Kaur, 2017). In many African countries such as Botswana and Nigeria, the high rate of poverty and Human Immunodeficiency virus (HIV), and antimicrobials being freely available as over the counter medications are factors contributing to the unnecessary usage of antimicrobials (IFLScience, 2017; Massele et al., 2016). Botswana is currently engaged in some AMS activities such as the development of antimicrobial guidelines but they are not always adhered to. Developing African countries do not possess good laboratory facilities, therefore, limiting the practice of antimicrobial susceptibility testing. Antimicrobials are available at high costs, therefore, causing patient to be non-compliant with treatment (Massele et al., 2016).

In many African countries, the burden of antimicrobial resistance is not well explored due to a lack of national surveillance systems (IFLScience, 2017). It is, therefore, relatively impossible to identify new resistance patterns to combat antimicrobial resistance. Though, it may be interesting to note that the National Tuberculosis and Leprosy Control Programme (NTBLCP) in Nigeria has been collecting data on resistance patterns of Tuberculosis (TB). In Nigeria, antimicrobials are often out-of-stock or too expensive causing patients to opt for counterfeit medicines (Nasir, Babyo, Emeribe, & Sani, 2015). Due to a limited avaibility and use of diagnostic tests, patients are often prescribed antimicrobials for self-limiting infections. For many infectious diseases occurring in Nigeria, cephalosporins and fluoroquinolones are the only last and affordable antimicrobials used for the serious and life-threatening infections (Nigeria Health, 2015).

Even though Colombia is a resource-limited country, it has made progress in terms of antimicrobial surveillance. The Colombian Nosocomial Resistance Study Group generates antimicrobial consumption reports on a bi-annual term basis for 31 public and private hospitals in Colombia. It has been reported that, AMS being implemented in a Colombian hospital, has increased appropriate antimicrobial usage and decreased antimicrobial resistance. Furthermore, Colombia supports a multidisciplinary approach towards AMS, with the exception of pharmacists, who are not involved in the AMS programme (Goff et al., 2017).

The situation in India is becoming alarming as Gram-negative microorganisms are not only resistant to the third generation cephalosporins, aminoglycosides, fluoroquinolones but, also to the carbapenems. As a result, Indian medical practitioners are prescribing the last resort antibiotics such as colistin, tigecycline and fosfomycin (Taneja & Kaur, 2017).

2.3 AMS Developments in the South African Setting

As discussed in section 2.2.5, South Africa, being part of the BRICS nations, contributes the most to the overall increase in antimicrobial usage (Mendelson & Matsoso, 2015). Netcare, being the largest private hospital network in South Africa,

responded to the threat presented by carbapenemase-producing enterobacteria by implementing AMS programmes in its hospitals since 2010 (Huttner, Harbarth, & Nathwani, 2014).

In 2014, South Africa was the first country in Africa, which published a framework as a guide to control antimicrobial resistance, and it was published by the South African Department of Health (IFLScience, 2017). The three goals of the Antimicrobial Resistance (AMR) National Strategy Framework include: antimicrobial surveillance and reporting, antimicrobial stewardship and infection prevention and control (IPC) practices (Mendelson & Matsoso, 2015; South African National Department of Health, 2014).

The South African National Department of Health has advised on the implementation of a multi-disciplinary intersectoral Ministerial Advisory Committee (MAC), who would be in charge of national antimicrobial surveillance and reporting of antimicrobial resistance (South African National Department of Health, 2014). However, there is a lack of in-depth antimicrobial surveillance reports due to no linkage between laboratory and clinical information in South Africa (Mendelson & Matsoso, 2015). Furthermore, MAC would provide guidance on the rationale prescribing of antimicrobials based on resistance patterns and appropriate guidelines available (South African National Department of Health, 2014). Though, it is only possible to identify the resistance patterns in a hospital setting and not in the community, since laboratory and clinical data are not linked (Mendelson & Matsoso, 2015). The MAC-AMR would also be responsible to ensure that healthcare institutions implement a minimum set of activities pertaining to AMS and they would encourage the minister to conduct public health talks on antimicrobial resistance. Antimicrobials, vaccines and diagnostic tests would be readily available and accessible to the public. A key aspect to promote rational prescribing is to develop national antibiotic stewardship prescribing guidelines, which are aligned with the Essential Medicines List (EML) and Standard Treatment Guidelines (STGs) (Mendelson & Matsoso, 2015; Schellack et al., 2017; South African National Department of Health, 2014, 2017a). The South African National Department of Health is also aiming to improve the monitoring system of antimicrobial usage with the aim of detecting resistance at an early stage. Infection prevention and control

(IPC) practices and promoting the appropriate usage of antimicrobials also form part of the AMS strategies (Mendelson & Matsoso, 2015; South African National Department of Health, 2014).

However, the strategies discussed above cannot be implemented on their own. Education, communication and promoting research would also contribute towards the implementation of those strategies. The strategic objectives and strategies enablers are illustrated in Figure 2.2.

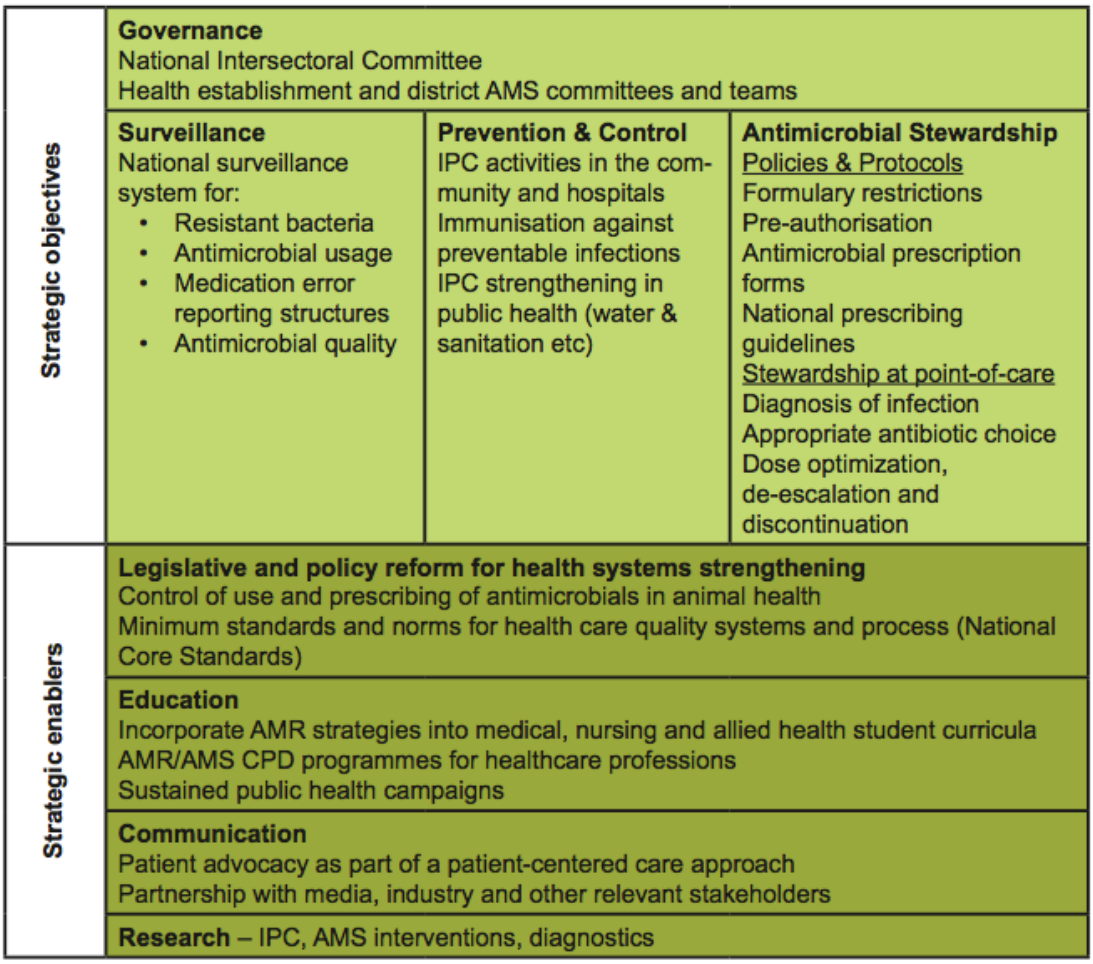

Figure 2.2. The South African AMR Strategy Framework with the strategic objectives and key enablers (South African National Department of Health, 2014, p. 11)

In 2017, the South African Government devised a guide on the implementation of antimicrobial stewardship (AMS) in South Africa in an attempt to implement AMS in the public sector hospitals. South Africa also forms part of the countries that follows the 'One Health Approach' towards AMS and it is one of the strategic objectives

discussed in the strategy framework for antimicrobial resistance. In South Africa, there are programmes, which are already focusing on the monitoring of HIV, TB and malaria. However, the AMR and implementation guidelines on AMS would focus on antibiotic and antifungal resistance. At the national level, AMR is regulated by the MAC-AMR, who has certain responsibilities towards the implementation of AMS (South African National Department of Health, 2017a).

At the provincial level, AMS is governed by a Provincial AMS Committee (PAMSC). The chairperson of the PAMSC would be responsible to ensure that decisions taken within the committee are aligned with the policies of the province, the relevant National Drugs Policy and the AMR Strategy Framework. It would undertake the responsibility of recommending a culture test for interventions whilst supporting a multidisciplinary opinion towards a decision taken against an AMS intervention (South African National Department of Health, 2017a).

The PAMSC would undertake the responsibility of the monitoring and surveillance of antimicrobial resistance and usage and would provide a bi-annual progress report to the MAC-AMR. It would provide support to public sector hospitals by guiding their AMS activities, by providing accessibility to tools for the monitoring of AMS and by providing funding for the implementation of AMS (South African National Department of Health, 2017a).

The District AMS Committee (DAMSC) would be responsible for the monitoring and surveillance of antimicrobial and it would report to the PAMSC. It would organise educational AMS activities and institutional training with the aim of changing the perception of healthcare professionals concerning the appropriate usage of antimicrobials and ensuring adherence to STGs for infectious diseases (South African National Department of Health, 2017a).

The Hospital Antimicrobial Stewardship Committee (HAMSC) would also provide bi-annual progress reports to the PAMSC. The goal of the HAMSC would be to reinforce activities, such as, infection and control practices (IPCs) and expanded programme on immunisation (EPI) with the objective of reducing infections in the population. For the public to change their insights on appropriate antimicrobial usage,

education is of utmost importance and it would be the responsibility of the HAMSC to fulfill its role as the educators of patients and healthcare professionals (South African National Department of Health, 2017a).

The HAMSC intends on retrieving antimicrobial usage data from pharmacy dispensing systems and express the usage in Defined Daily Doses (DDD) per hundred patient days as supported by the WHO. It would also be accountable for the monitoring of all existing AMS activities as well as reporting to members of an AMS team on the progress of AMS interventions (South African National Department of Health, 2017a).

2.3.1 The Use of Rx Solution® for Monitoring and Surveillance

Rx Solution® is a software programme used in public healthcare facilities, in eight of the nine provinces in South Africa, including the Eastern Cape, to manage pharmaceutical supplies, from procurement to dispensing. It also assists in stock management, prevention of stock-outs, minimising expired stock, and dispensing medication to patients (System for Improved Access to Pharmaceuticals and Services Program, 2017).

District and provincial hospitals in the North-West province of South Africa were involved in a drug utilisation study. The primary aim of the study was to evaluate the use of the dispensing data, extracted from Rx Solution®, in order to monitor antimicrobial consumption and prescribing practices in out-patients. Defined Daily Doses (DDD) were calculated for a time period of approximately two years. However, Rx Solution®, was not assessed in terms of its ability to extract and collect data for the purpose of AMS monitoring for the South African public healthcare sector. The findings of the study concluded that, data extracted from Rx Solution® could be used to the purpose of surveillance studies (Berrada, Mphaka, & Van Loggerenberg, 2016). The recommendations made based on the findings of study identified Rx Solution® as a useful stock management tool. However, it was noted that the dispensing programme did not have the ability of capturing certain relevant information, such as age and diagnosis. It was highlighted that information related to diagnosis could not be recorded on the dispensing component of Rx Solution® and

therefore, it was not always possible to assess appropriateness of therapy (Berrada et al., 2016).

The study concluded that Rx Solution® must be implemented in all hospital facilities in South Africa. It was emphasised that the dispensing programme could be improved and ICD-10 codes, also known as diagnosis codes, could be recorded in the dispensing programme so as to support AMS decision making (Berrada et al., 2016).

2.4 Role Players in Antimicrobial Stewardship

In order for an antimicrobial stewardship (AMS) team to function efficiently, it is important for a multidisciplinary team to be established. An antimicrobial stewardship team must ideally consist of an infectious disease specialist (IDS), a pharmacist, a clinical microbiologist, hospital epidemiologists, infection preventionists and nurses (Goff et al., 2017; Griffith et al., 2012). The roles of the different members of an AMS team will be further explained below.

2.4.1 Role of the Infectious Disease Specialist (IDS), Nurses and Clinical Microbiologist

Guidelines available on AMS have put emphasis on the importance of a multidisciplinary approach towards AMS (Monsees, Goldman, & Popejoy, 2017). Infectious disease specialists (IDS) are physicians who have been specialised in infectious diseases. They are trained in selecting the appropriate antimicrobials with the correct dose and duration. It is easy to prescribe antimicrobials, but for its optimal prescribing, it is important that patients are correctly diagnosed (Nahass, 2014). The role of an IDS in an AMS team must, therefore, be emphasised on, as they understand the consequences associated with inappropriate antimicrobial prescribing due to incorrect diagnosis (Cooper & Duguid, 2011; Nahass, 2014). Studies have shown that these interventions can make a significant impact on a patient's health by reducing the length of hospital stay, decreasing mortality rate and reducing resistance patterns of pathogens, leading to an overall reduction of antimicrobial usage and cost (Pulcini, Botelho-Nevers, Dyar, & Harbarth, 2014).

It is evident that nurses play different roles in terms of obtaining appropriate cultures prior to the start of antimicrobials, administering and monitoring of antimicrobial treatment, however, the influence of their contribution in an AMS programme is unspecified (Monsees et al., 2017). It has been identified from the literature that although nurses are often prescribers of antimicrobials, they only receive a minimum of less than ten hours of antimicrobial training in their courses. In consequence, nurses tend to have a knowledge gap in antimicrobials (Monsees et al., 2017). In summary, nurses are the primary educators of patients. They also closely monitor patient's safety and compliance to antimicrobial treatment, thus, concluding that nurses should be considered as important members of an AMS team (Edwards, Drumright, Kiernan, & Holmes, 2011; Monsees et al., 2017). Moreover, the clinical microbiologists are responsible in culturing lab cultures and identifying resistance patterns. The reports obtained from the lab cultures allow the infectious disease specialists to select the optimal antimicrobial prior to starting therapy (Ferguson, 2011).

2.4.2 Role of the Pharmacist

An emerging role for pharmacists in an AMS program includes monitoring and surveillance of antimicrobial usage, by frequently reviewing prescriptions (Ashiru-Oredope, Fleming, & Ladenheim, 2015; Li et al., 2017). The key responsibilities of pharmacists in an AMS programme, are, to develop antimicrobial usage guidelines, participate in ward rounds and educate healthcare professionals on antimicrobial resistance (Duguid & Kong, 2011). AMS pharmacists are responsible to review lab culture test results before a medical prescriber or infectious disease specialist prescribes an antimicrobial. In addition, the pharmacists are liable to monitor intravenous antimicrobials, which have been administered for more than 72 hours and encourage IV to oral switch as soon as a patient is clinically stable (Li et al., 2017). Pharmacists may be untrained in infectious diseases, however, this does not prevent them from taking a role in the AMS team (Cosgrove et al., 2014).

The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) guidelines encourage the training of pharmacists in infectious diseases (Heil, Kuti, Bearden, & Gallagher, 2016). Despite being

considered a core member of an AMS team, there is a lack of adequately trained infectious disease pharmacists in the South African public healthcare sector (Heil et al., 2016; South African National Department of Health, 2015). The pharmacist's role in an AMS team must be promoted as their knowledge on the pharmacology of the various antimicrobials allow them to help with the safe and effective use of medications, reducing patients' risk for adverse drug reactions (Kim, Craft, & Katzman, 2015). Studies have shown that the inclusion of a pharmacist in an AMS programme has contributed to a decrease in inappropriate usage of antimicrobials in South Africa (Li et al., 2017).

2.5 Antimicrobial Monitoring and Surveillance

Antimicrobials are still inappropriately prescribed, misused and overused (Broom, Broom, Kirby, Plage, & Adams, 2015). The overconsumption of antimicrobials has led to resistance which is now becoming a threat (Morris, 2014). The efficacy of antimicrobials against resistant strains of microorganisms is now compromised, leading to an increase in the rate of morbidity and mortality globally (Llor & Bjerrum, 2014; Ventola, 2015). As a result, it has become the ultimate goal to preserve the effectiveness of antimicrobials (Wernli et al., 2017).

The assumption that inappropriate and unnecessary use of antimicrobials is contributing to resistance, has increased the need to monitor antimicrobial usage, which can be monitored at the patient-level and population-level (Duguid, Ferguson, McNeil, & Wilkinson, 2011; Fridkin & Srinivasan, 2014). Monitoring the antimicrobial usage at the patient-level is most accurate but is generally more intensive (Duguid et al., 2011). Information obtained from surveillance studies are of utmost importance as it has allowed AMS practitioners to understand the relationship between excessive antimicrobial usage and the emergence of resistant microorganisms (Gravatt & Pakyz, 2013; McNeil, Cruickshank, & Duguid, 2010).

2.5.1 Monitoring and Surveillance in South Africa

Since 2011, South Africa has participated in National AMR surveillance activities.

The National Antibiotic Surveillance Forum (NSAF), currently known as the South African Society for Clinical Microbiology (SASCM), has been reporting antimicrobial usage data from microbiology laboratories affiliated to national academic hospitals. However, those reports do not encompass and reflect the true antimicrobial usage of the general population (Duse, 2011).

In addition, the STI Reference Centre of the National Institute for Communicable Diseases (NICD), in collaboration with the National Department of Health (NDoH), is performing antimicrobial surveillance of sexually transmitted diseases (STDs). In 2010, the Antimicrobial Resistance Reference Unit (AMRU) of the NICD introduced a laboratory-based surveillance system for hospital-acquired infections associated *Staphylococcus aureus* and *Klebsiella pneumonia* (Bamford et al., 2011).

Data collection on antimicrobial usage for the public healthcare sectors differs from the private healthcare sectors. Private healthcare sectors data are obtained from the Intercontinental Marketing Services (IMS) health, which collects data from various sources, such as medical sales, prescriptions, medical claims, electronic medical records and social media, while the public healthcare sectors obtain their data from tenders and wholesale, which only consist of quantities forecasted for use, hence, being a misleading reflection of usage (Schellack et al., 2017). Although the South African National Department of Health emphasises on the use of DDD as a metric to measure antimicrobial usage, this type of monitoring is not consistently being carried out by healthcare facilities (Schellack et al., 2017; South African National Department of Health, 2017a).

2.6 Antimicrobial Stewardship (AMS) Metrics

One of the main aims of an AMS programme is to reduce the inappropriate usage and identify the overconsumption of antimicrobials in a healthcare setting (Brotherton, 2018). This aim can be partly achieved by quantifying the antimicrobial usage, which is usually expressed as a rate with a utilisation metric as the numerator and a measurement of person time at risk for antimicrobial exposure as the denominator (Brotherton, 2018).

Sir William Thomson (Lord Kelvin), a physicist from the nineteenth-century said, 'If you cannot measure it, you cannot improve it' (Davey, Wilcox, Irving, & Thwaites, 2015). A standard and reliable metric needs to be approved by all institutions and countries in order to report antimicrobial usage, as it is fundamental to understand the emergence of antimicrobial resistance (Schellack et al., 2017).

According to Morris (2014), an antimicrobial utilisation metric reflects "an aggregate or average amount of antimicrobials being consumed at the level of the patient, a hospital unit or service, or an entire institution" (Morris, 2014, p. 102). The antimicrobial stewardship (AMS) metrics consist of four main categories, based on: patient outcomes, unintended consequences, antimicrobial utilisation, costs and process measures and they can be employed to measure antimicrobial usage (Dodds, Kaye, DePestel, & Hermsen, 2014; Morris, 2014). The four categories of AMS metrics, as described above, must be reported as a care bundle, with the objective of supporting an AMS programme (Dodds et al., 2014).

The study will focus on the antimicrobial utilisation metrics. They may not be accurate measures and only provide an overview of antimicrobial usage, but they remain the commonly used AMS metrics, since data pertaining to usage are the easiest to obtain (Dodds et al., 2014). The AMS utilisation metrics cannot be used independently of each other to measure antimicrobial usage and they must not be used as an alternative to one another. Instead, they should be used together to complement each other (Almirante, Garnacho-Montero, Pachón, Pascual, & Rodríguez-Baño, 2013). However, the other categories of AMS metrics only qualitatively measure the impact of AMS interventions and data pertaining to the other metrics are subjectively interpreted (Almirante et al., 2013; Hackethal, 2014).

Reports of the relevant AMS utilisation metrics help to measure the effectiveness and outcomes of AMS interventions and not the appropriateness of treatment. AMS metric reports have contributed to the improved usage of antimicrobials and have therefore, helped to minimise the rate of resistance (Bennett et al., 2018; Curtis, 2010; McNeil, 2015). Antimicrobial usage data are also utilised by healthcare professionals for the purpose of investigating and understanding the prevalence of certain microorganisms occurring in each ward. However, it is also important to note that

antimicrobial usage data on its own are not enough in order to prevent antimicrobial resistance (Ruef, 2006).

The most common measurements units are the Defined Daily Dose (DDD), Prescribed Daily Dose (PDD) and Days of Therapy (DOT) (Grau et al., 2013).

Table 2.1 is a summary of the most commonly encountered AMS metrics. A detailed review and description of the AMS metrics will be given below.

Table 2.1 *The most commonly used AMS utilisation metrics and their definitions*

Antimicrobial Stewardship (AMS) metrics	Definition
Defined Daily Dose (DDD)	The assumed average maintenance dose per day for a drug used for its main indication in adults (WHO Collaborating Centre for Drug Statistics Methodology, 2016a)
Days of Therapy (DOT)	Number of days that a patient receives an antimicrobial, irrespective of the dose given (Grau et al., 2013)
Prescribed Daily Dose (PDD)	The average dose prescribed per day according to a representative sample of prescriptions of a hospital or ward (Grau et al., 2013, p. 18)
Length of Therapy (LOT)	The number of days a patient receives an antimicrobial, irrespective of the number of agents administered (DUKE Antimicrobial Stewardship Outreach Network, 2016)
Exposure days	Number of days a patient is exposed to an antimicrobial (Morris, 2014)
Costs of Antimicrobial	Individual cost of antimicrobial (per unit or pack size)
Grams of Antimicrobial	Overall mass of antimicrobial consumed by a patient (Morris, 2014)
IV to oral switch	Ratio of IV to oral – expressed in DDD, DOT and/or PDD (Dik et al., 2016)

2.6.1 Defined Daily Dose (DDD)

Referring to Table 2.1, according to the World Health Organization (WHO) and the Anatomical Therapeutic Chemical (ATC) classification system, the Defined Daily Dose (DDD) is considered to be the most common and standard metric for reporting antimicrobial usage, which can be defined as the "assumed average maintenance dose per day for a drug used for its main indication in adults" (WHO Collaborating Centre for Drug Statistics Methodology, 2016a). The South African National Department of

Health also emphasises on the use of DDD for monitoring antimicrobial usage (South African National Department of Health, 2017a). Only one DDD is assigned to drugs that have an ATC code and it represents a global dosage irrespective of genetic polymorphism (WHO Collaborating Centre for Drug Statistics Methodology, 2016b). Although it is the most common metric used, it only provides a rough estimate of antimicrobial usage (WHO Collaborating Centre for Drug Statistics Methodology, 2016a).

The DDD is a measurement unit established by the WHO, therefore, facilitating comparison within a hospital or between hospitals. The DDD may be a dose that is not often prescribed and it can be an average of two or more commonly prescribed doses (WHO Collaborating Centre for Drug Statistics Methodology, 2016a). The DDD is calculated based on pharmacy sales or dispensing data (Mertz, 2011). However, the DDD value may be misinterpreted if the antimicrobial usage is measured using pharmacy purchasing or ordering data, instead of pharmacy dispensing data (Reddy, Jacob, Varkey, & Gaynes, 2015).

2.6.1.1 Limitations on DDD

DDD underestimates the usage of antimicrobials in paediatrics, obese patients or a patient with renal failure, since dosing is according to body weight of a patient (Grau et al., 2013; Liem, Heerdink, Egberts, & Rademaker, 2010; Morris, 2014). Furthermore, a DDD value is not allocated to every antimicrobial available the market (Monnet, 2007). The WHO DDD cannot also be applied to the paediatric population as many antimicrobials are not approved for use in this population (Liem et al., 2010; Septimus, 2014). Variations in DDD are not only caused by change in dosages but also by change in dosing frequencies (Zagorski et al., 2002). Therefore, using the DDD as the only metric to support AMS is not ideal as it does not always provide a realistic picture of antimicrobial usage (Stanic Benic et al., 2018).

2.6.1.2 Neonatal DDD (nDDD)

A study conducted by Liem and colleagues (2010), proposed to develop neonatal DDDs (nDDDs), for the most common antimicrobials used in this special population

group. Since the variation in body weight in neonates (aged <1 month) is less than the variation in body weight in paediatrics, the DDD methodology is more applicable to neonates. An average weight of 2 kg was considered when the nDDD was developed (Gravatt & Pakyz, 2013; Liem et al., 2010). For the nDDD to be utilised for benchmarking purposes, data pertaining to usage must be available at the patient level. Though, it is important to note that this metric has not yet been internationally approved (Gravatt & Pakyz, 2013; Liem et al., 2010).

2.6.1.3 Hospital-adjusted Defined Daily Doses (haDDDs)

Higher doses of antimicrobials are often recommended for certain clinical conditions, hence, the high consumption of antimicrobials does not always correspond to inappropriate usage (Department of Health, 2017). In hospitalised patients, the DDD may not always be representative of the Recommended Daily Dose (RDD) or the Prescribed Daily Dose (PDD) (Gravatt & Pakyz, 2013; Haug & Reikvam, 2013). As a result, DDD may not be appropriate to measure antimicrobial usage at the patient-level (Australian Commission on Safety and Quality in Health Care, 2016). Higher doses are often used in patients receiving intravenous treatment, therefore, leading to an underestimate in antimicrobial usage (Australian Commission on Safety and Quality in Health Care, 2016; Haug & Reikvam, 2013).

For hospitalised patients, the WHO DDDs has been adjusted to the hospital-adjusted Defined Daily Doses (haDDDs) (Haug & Reikvam, 2013). The haDDD is an estimation of the therapeutic maintenance dose of an antimicrobial for an adult with no renal impairment and this value is in line with the doses recommended in guidelines (Elseviers et al., 2016; Haug, 2014). For the antibiotics having several indications, the haDDD value is estimated between the dose required for severe infections and the dose required for moderately severe infections. However, Haug and Reikvam (2013) concluded that the rates of antimicrobial usage were relatively similar whether the WHO DDDs or the haDDDs were used as numerators (Haug & Reikvam, 2013).

2.6.2 Volume of Antimicrobial Therapy

Volume of antimicrobials refers to the following units: grams, kilograms, litres and number of packages or tablets (WHO Collaborating Centre for Drug Statistics Methodology, 2016b). The volume of antimicrobials is usually obtained from aggregrate pharmacy dispensing records and it can be used to calculate a rough value of DDD as an estimation of antimicrobial usage (Polk, Fox, Mahoney, Letcavage, & MacDougall, 2007).

DDD can be calculated using the formula below:

$$DDD = \frac{\text{Total grams used}}{\text{WHO DDD}}$$

(Government of South Australia, 2017)

Despite being a simple and easy data to obtain, the differences in drug potency may be a challenge to account for while measuring the usage (Jacob & Gaynes, 2010). Furthermore, DDD can be used as an estimate of DOT, but, if the administered dose is not equivalent to the WHO-DDD dose, the actual number of days that a patient would receive an antimicrobial cannot be deduced (Bansal et al., 2014; Momattin et al., 2018; Morris, 2014).

In addition to pharmacy dispensing records, DDD can also be compiled from electronic medication administration records (eMAR) data (B. R. Dalton, Sabuda, Bresee, & Conly, 2015). A study conducted by Dalton B. R. and colleagues (2015) concluded that, DDD values measured using pharmacy dispensing records differed from DDD values measured from nursing administration records, also known as the eMAR. The observed variation between the DDD values obtained from the two different sources can be explained by the fact that antimicrobial orders may change from the time of dispensing to the time of administration. Therefore, the study concluded that nursing administration records provided more accurate and reliable data for compiling DDD surveillance reports (B. R. Dalton et al., 2015).

2.6.2.1 The AMC tool: the antimicrobial consumption tool

In April 2015, the WHO developed a new version for an antimicrobial consumption (AMC) tool. The AMC tool uses the ATC classification system. In addition, the tool has the capacity of converting number of packages or vials used to DDDs. The DDD is normally expressed per 1000 inhabitants per day or per 100 bed-days (Muller, 2015).

2.6.3 Days of Therapy (DOT)

Referring to Table 2.1, Days of Therapy (DOT) represents the number of days that a patient receives an antimicrobial, irrespective of the dose, quantity and number of administrations given and it is supported by the CDC (Grau et al., 2013; Wong, 2018). It is an AMS metric that is currently used as a standard in the USA, which is more accurate and of greater clinical significance than the DDD, but it may not always reflect the true antimicrobial exposure of a patient (Bennett et al., 2018; Grau et al., 2013; Ibrahim & Polk, 2014; Kubin, Haomia, Alba, & Furuya, 2012; Morris, 2014). In order to improve the accuracy of this AMS metric, many hospitals in the USA measure the DOT from their respective billing and dispensing data as well as from their eMAR data (Brotherton, 2018; Ibrahim & Polk, 2014). However, the use of DOT may be restrictive in measuring the usage of antimicrobials when two antimicrobials are used concomitantly for a certain number of days, which leads to a double DOT (Wong, 2018). Where two antimicrobials are prescribed together, DOT metric reports would not necessarily correspond to appropriate duration of treatment (Brotherton, 2018). Consequently, DDD would be a better measurement unit to express antimicrobial usage in patients receiving combination treatment or surgical prophylaxis of antimicrobials (Momattin et al., 2018).

For patients who are being administered a drug with a long half-life or patients with renal failure, DOT is less accurate as antimicrobials are not administered every day during the duration of treatment (Gravatt & Pakyz, 2013; Kubin et al., 2012). In those instances, exposure days are more accurate to use and represent the number of days a patient is exposed to an antimicrobial (Morris, 2014). Even though little is known about the application of exposure days as a measure of antimicrobial usage, Kubin

and colleagues (2012) investigated how the traditional method of calculating the DOT calculation was different to other methods of calculating the DOT with the inclusion of exposure days in the calculations. Ultimately, the findings of the study concluded that there were no significant differences in the different types of DOT calculations and the inclusion of "exposure days" in the DOT calculations was not necessary (Kubin et al., 2012).

Contrasted with the DDD, no limitations were observed when using DOT as a measurement unit for paediatrics (Gravatt & Pakyz, 2013). Regardless of no limitations being observed by Gravatt & Pakyz (2013), Rose, Coulter, Chan, Hossain, and Di Pentima (2014) do not describe DOT as the most accurate measure of antimicrobial usage in children. Rose et al. (2014) concluded that the dosing of antimicrobials in children depends on the age and clinical condition of the patient. Thus, DOT would not be equal to the same quantity of antimicrobial exposure when comparing data across different age groups (Rose et al., 2014).

It is challenging to determine the number of days of treatment if data at the patient-level is not electronically available (Monnet, 2007; Reddy et al., 2015; Septimus, 2014). Instead of giving an overview of the number of days a patient is receiving treatment, DOT would indicate the number of individual drugs administered daily, therefore, providing no significant information (Polk, Hohmann, Medvedev, & Ibrahim, 2011). Therefore, to supplement the DOT, an alternative AMS metric, called the Length of Therapy (LOT), has been proposed in some studies (Polk et al., 2011). This AMS metric will be discussed in section 2.6.4.

2.6.3.1 Antibiotic use (AU) Days of Therapy (DOT)

The Centers for Disease and Control Prevention (CDC) has developed the "Antibiotic Use and Resistance (AUR) Module" for reporting antimicrobial usage (Centers for Disease Control and Prevention, 2017a). An increase in dispensing errors cause pharmacy dispensing records to be inaccurate and sometimes incomplete to measure antimicrobial usage (Agrawal, 2009). In an attempt to prevent medication errors, the CDC has developed a modified version of DOTs by quantifying bar-coded medication administration (BCMA), also known as eMAR and it involves the electronic

recording of the unit dose of antibiotic administered to a patient (Agrawal, 2009; Centers for Disease Control and Prevention, 2017a). However, the use of BCMA does not record doses adjustments for patients with decreased or impaired renal function (Scheetz et al., 2016).

2.6.4 Length of Therapy (LOT)

Compared to DOT, LOT reflects the true duration of treatment and it can be defined as "the number of days a patient receives an antimicrobial, irrespective of the number of agents administered" (DUKE Antimicrobial Stewardship Outreach Network, 2016; Polk et al., 2011). LOT is a dose-independent metric and can used in pediatrics to measure the antimicrobial usage (Ibrahim & Polk, 2014). It can be used to assess de-escalation of antimicrobial therapy and the subsequent duration of therapy (Bennett et al., 2018). As discussed in section 2.6.3, two different antimicrobials being administered on the same day would be equivalent to two DOT but equivalent to one LOT. This AMS metric may be more useful in identifying unusual duration of treatment (Polk et al., 2011). However, in patients with renal dysfunction, LOT comprises of the days between the administered doses, thus, resulting in an overestimate of antimicrobial usage (Bennett et al., 2018).

2.6.4.1 DOT/LOT ratio

The DOT/LOT ratio is a measure, which has been formulated, in order to identify whether a patient has either been receiving monotherapy or combination antimicrobial treatment. A ratio of less than one suggests that treatment only includes one antimicrobial and a ratio of greater than one indicates combination treatment (Polk et al., 2011). This AMS metric, therefore, estimates the average number of individual antimicrobials received (Ibrahim & Polk, 2014).

2.6.5 Prescribed Daily Dose (PDD)

For hospitalised adult patients with an average glomerular filtration rate (GFR) of more than 90 mL/min per 1.73 m^2, Prescribed Daily Dose (PDD) is another commonly used AMS metric, but it may not represent the real antimicrobial

utilisation as prescriptions are not always dispensed (Curtis, 2010; World Health Organization, 2003). However, studies have shown that, for many antimicrobials, the PDD value differs from the DDD. When comparing with PDD, DDD yields an overestimate of antimicrobial usage (Curtis, 2010; Muller, Monnet, Talon, Henon, & Bertrand, 2006).

Referring to Table 2.1, PDD is defined as "the average dose prescribed per day according to a representative sample of prescriptions at a hospital" (Grau et al., 2013). PDD is a more patient orientated AMS metric. Consequently, it is considered to be more accurate (Dik et al., 2016; Gravatt & Pakyz, 2013). However, it is important to always consider the diagnosis of a patient as the actual prescribed dose of antimicrobials may vary when dosing is based on the severity of an infection (WHO Collaborating Centre for Drug Statistics Methodology, 2016b).

2.6.5.1 PDD - Proxy

PDD measures the antimicrobial usage at the patient-level and data pertaining to PDD would be obtained from computerised pharmacy dispensing records. The PDD-proxy could be used as an alternative metric if the administration of antimicrobials for each patient is not electronically captured. A PDD-proxy is estimated by a mean calculation of the oral and parenteral prescribed doses of a specific antimicrobial on a specific day (Gagliotti et al., 2014).

2.6.5.2 PDD: DDD ratio

The PDD to DDD ratio determines the extent of the difference between the prescribed dose and the DDD value (Gyssenss, 2005). A study conducted by Mousavi et al. (2013), investigated the ratio of PDD to DDD for two antimicrobials only, imipenem and ciprofloxacin. A ratio of greater than one indicated that the prescribed dose of the antimicrobial was more than the defined or recommended daily dose (Mousavi et al., 2013).

2.6.6 Standardised Antimicrobial Administration Ratio (SAAR)

The CDC has developed a new metric, also known as, the Standardised Antimicrobial Administration Ratio (SAAR), with the aim of analysing and obtaining a summarised report of antimicrobial usage (Van Santen et al., 2018). According to the CDC, SAAR is a ratio, which is calculated as the number of actual number of antimicrobial therapy days divided by the number of analytic-predicted antimicrobial days (Bennett et al., 2018; Centers for Disease Control and Prevention, 2017a).

The SAAR is calculated as follows:

$$SAAR = \frac{\text{Observed (O)}\mathit{Antimicrobial\ Use}}{\text{Predicted (P)}\mathit{Antimicrobial\ Use}}$$

(Centers for Disease Control and Prevention, 2017a)

This AMS metric can be used for benchmarking purposes (Bennett et al., 2018). A high SAAR value would indicate excess in antimicrobial usage and a low SAAR value would indicate under-usage of antimicrobial. However, the SAAR value alone cannot be used to measure the appropriateness of antimicrobial usage (Bennett et al., 2018; Centers for Disease Control and Prevention, 2017a).

2.6.7 Recommended Daily Dose (RDD)

The Recommended Daily Dose (RDD) is a standard daily dose adapted to local guidelines and therefore, gives a more precise overview of antimicrobial usage (de With, Bestehorn, Steib-Bauert, & Kern, 2009; Fortin et al., 2014). However, this particular AMS metric varies with the weight of patients (Stanic Benic et al., 2018). When comparing with the RDD, the DDD underestimates the total antimicrobial usage (de With et al., 2009).

2.6.8 Costs of Antimicrobials

Although the cost of antimicrobials could be one of the easiest metrics to measure, measuring cost is not considered as the primary goal of an AMS programme (Dodds et al., 2014; Giusti & Cerutti, 2016; Morris, 2014). Generics would have a great impact on this metric, making it inaccurate when making comparisons between countries (Morris, 2014). This metric only provides an overview of accumulated savings and has no clinical significance (Giusti & Cerutti, 2016). An example of a cost saving situation related to antimicrobials includes intravenous (IV) to oral switch (K. Dalton & Byrne, 2017).

2.6.9 Intravenous (IV) to Oral Switch

Intravenous (IV) to oral switch is considered as an AMS process measure metric (Septimus, 2014). However, the percentage of IV to oral use for agents with both oral and intravenous formulations could possibly be investigated since it indirectly focuses on antimicrobial utilisation and costs (Greater New York Hospital Association, 2011). The percentage of IV to oral agents can be illustrated in DDD, PDD or DOT (Dik et al., 2016). The practice of IV to oral switch directly improves the quality of life of a patient by decreasing the length of hospitalisation and treatment cost, therefore leading to optimal antimicrobial use (Mertz et al., 2009; Thompson, Zahradnik, Brown, Fleming, & Law, 2015). Furthermore, since IV therapy is more likely to cause secondary infections and resistance, it is necessary to promote IV to oral switch as an intervention (Dik et al., 2016).

2.6.10 Doses Administered (DA)

A study done by Rose and colleagues (2014) compared DOT to doses administered (DA) in children. The study found that DA was a more sensitive metric for measuring the antimicrobial usage in children. DA accounts for every dose of antimicrobials administered per patient, independent of dose adjustments based on age, body weight, clinical condition and/ or renal or hepatic impairment. Yet, it would still be a challenge to obtain DA values if information related to the record of antimicrobials is not computerised (Rose et al., 2014).

2.7 Denominator Metric to Report Antimicrobial Usage

Usage is normally reported and expressed as DDD per 100 patient-days for hospitalised patients (DDD/100 patient-days) (South African National Department of Health, 2017a). Patient-days are also sometimes referred as bed-days and the days of admission and discharge are not normally counted in the calculation (Hutchinson et al., 2004; South African National Department of Health, 2017a). Patient-days are normally calculated from the product of the number of admitted patients and the mean length of stay (LOS). If patients are discharged earlier from the hospitals, the mean LOS would decrease and subsequently, patient-days would also decrease. This would result in an overestimation of the total antimicrobial usage (Ibrahim & Polk, 2014).

As a result, the "number of admissions" was proposed as an alternative denominator to report the antimicrobial usage (de With, Maier, Steib-Bauert, Kern, & Kern, 2006; Ibrahim & Polk, 2014). For out-patients, the usage is normally reported as DDD per 1000 inhabitant-days (Momattin et al., 2018).

Usage for the following metrics discussed above namely: DOT, LOT, PDD and RDD, are also reported per 100 patient-days or per number of admissions.

2.8 Metrics Used in South Africa

As reported in section 2.6.1, DDD is the most recommended AMS metric for reporting antimicrobial usage (WHO Collaborating Centre for Drug Statistics Methodology, 2016a). However, in a situational analysis conducted by Schellack and colleagues (2017), it was reported that the following were also used to report antimicrobial usage in South Africa, both in the private and public healthcare sector: i) The total number of antimicrobial units, ii) the total sum of the quantity units per ATC class and iii) the moving annual total (MAT) units, also known as the total value of the sales figures for a product (Schellack et al., 2017).

Furthermore, a comparable AMS metric of antimicrobial consumption across time, the compound annual growth rate (CAGR) of total antimicrobial consumption was calculated using the following formula:

$$CAGR = (SUEnd/SUStart)\ (1/N) - 1$$

Where, SUEnd is the total number of standard units for the last reported year,
SUStart is the total number of standard units for the first reported year,
N is the number of years between the first and the last year of reporting.

(Schellack et al., 2017).

2.9 Summary

It is important to quantify the usage of antimicrobials as a monitoring tool in the AMS programme and this can be achieved by promoting the use of the AMS utilisation metrics reviewed in section 2.6. In summary, the most common antimicrobial stewardship (AMS) metrics, which focus on utilisation are DDD, DOT, PDD (Grau et al., 2013). In addition, the literature identified other useful metrics such as LOT, exposure days and cost. However, there is no evidence to illustrate the most appropriate AMS metric to measure and correlate antimicrobial usage and to show that one metric is superior to the others (Bennett et al., 2018; Giusti & Cerutti, 2016; Rose et al., 2014). Further research are needed to resolve this problem when data at the patient level is not available and a standard denominator also needs to be approved in order to report the usage (Monnet, 2007).

CHAPTER 3
RESEARCH METHODOLOGY

3.1 Introduction

Chapter Three will present the research design and methodology employed for the purpose of this study. The study consisted of three phases: a preliminary phase, a developmental phase and a post-development phase. The three phases of the study will be elaborated and further explained below.

3.2 Research Design

The study followed an explanatory sequential mixed methods approach: quantitative followed by qualitative methodologies were employed (Creswell, 2014). The quantitative component of the study used a non-experimental cross-sectional questionnaire design, where different respondents were studied at a specific point in time and a measurable description of opinions was identified (H. Brink, Van der Walt, & Van Rensburg, 2012; Creswell, 2014). Data was collected in the form of electronic questionnaires, which were cost effective and not time-consuming to complete. Concurrently, a large sample of the population was studied and a broader opinion of facts was obtained (Creswell, 2014). The current research was non-experimental in nature as the researcher did not make any interventions in the study (H. Brink et al., 2012). Results obtained from the quantitative phase of the study built upon and lead to the qualitative phase, which was in the form of semi-structured interviews, in order to provide insight and a greater understanding of the quantitative responses (Creswell, 2014).

3.3 Overview of Study

The study was divided into three phases: i) a preliminary phase, ii) developmental phase and iii) post-developmental phase (Figure 3.1).

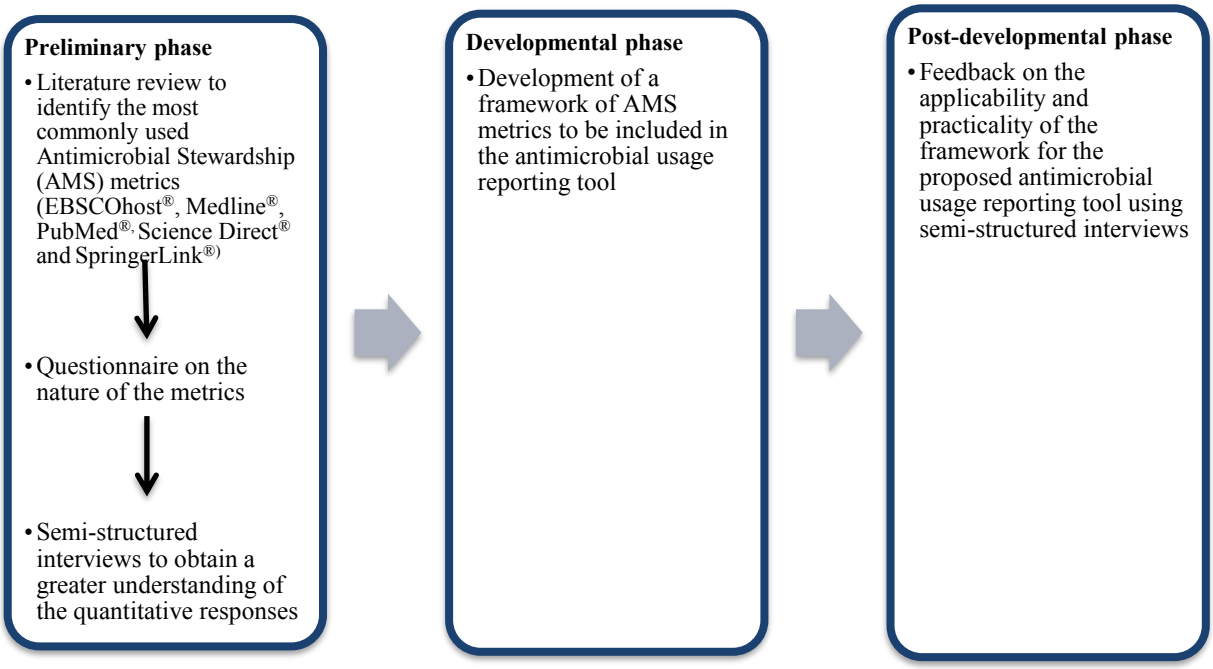

Figure 3.1. Overview of study design

3.3.1 Preliminary Phase

3.3.1.1 Literature review

The aim of this study was to develop a framework for a proposed antimicrobial usage reporting tool, which would be used by AMS practitioners in order to optimise antimicrobial usage in a tertiary level, public sector hospital setting. The resulting framework would integrate antimicrobial stock management data in order to produce the relevant AMS utilisation metric reports. As a result, various search engines, for example EBSCOhost®, Medline®, PubMed®, Science Direct® and SpringerLink®, were consulted in order to conduct an in-depth literature review, extending from 2002 to 2018. Relevant textbooks on antimicrobial stewardship (AMS) were also consulted. The literature review identified the most common utilisation metrics used in AMS monitoring as discussed in section 2.6 and helped to guide the questions to be used in the questionnaire.

3.3.1.2 Quantitative: questionnaire

The questionnaire was electronically distributed, via the software, QuestionPro®, to infectious disease specialists, pharmacists, medical prescribers and clinical pathologists employed at tertiary level, public sector hospitals in Port Elizabeth and East London, in the Eastern Cape province of South Africa, using a convenience stratified sampling technique. The questionnaire determined views of the practitioners on the usage, usefulness and clinical relevance of the AMS metrics. The questionnaire is described in section 3.5.1 (Appendix A).

3.3.1.3 Qualitative: semi-structured interviews

A qualitative component was conducted and consisted of telephonic audio-recorded, semi-structured interviews with open-ended questions. The healthcare professionals, who were involved in the implementation of AMS in the workplace on a daily basis, were invited to participate in the semi-structured interviews using a purposive sampling. A smaller number of respondents were identified based on the quantitative results obtained (Creswell & Plano Clark, 2007).

3.3.2 Developmental Phase – Development of a Framework for a Proposed Antimicrobial Usage Reporting Tool

During the developmental phase, data collected in the preliminary phase guided to the development of a framework of AMS metrics to be included in the proposed antimicrobial usage reporting tool. The framework would integrate antimicrobial stock management data with the relevant AMS utilisation metrics identified in the preliminary phase of the study. The framework for the proposed antimicrobial usage reporting tool will be presented in Chapter Four (Figure 4.15).

3.3.3 Post-Developmental Phase – Feedback on the Framework for the Proposed Antimicrobial Usage Reporting Tool

The framework for the proposed antimicrobial usage reporting tool was electronically disseminated via email to the respondents, who participated in the preliminary phase

of the study, for feedback on its applicability and practicality. Feedback was obtained in the form of qualitative data via telephonic audio-recorded semi-structured interviews. The findings obtained from the semi-structured interviews will be presented in Chapter Four.

3.4 Study Site

The study was conducted in tertiary level, public sector hospitals in Port Elizabeth and East London, in the Eastern Cape province of South Africa and included five hospital research sites. The hospitals were de-identified and renamed as Hospital A, Hospital B, Hospital C, Hospital D and Hospital E (Figure 3.2).

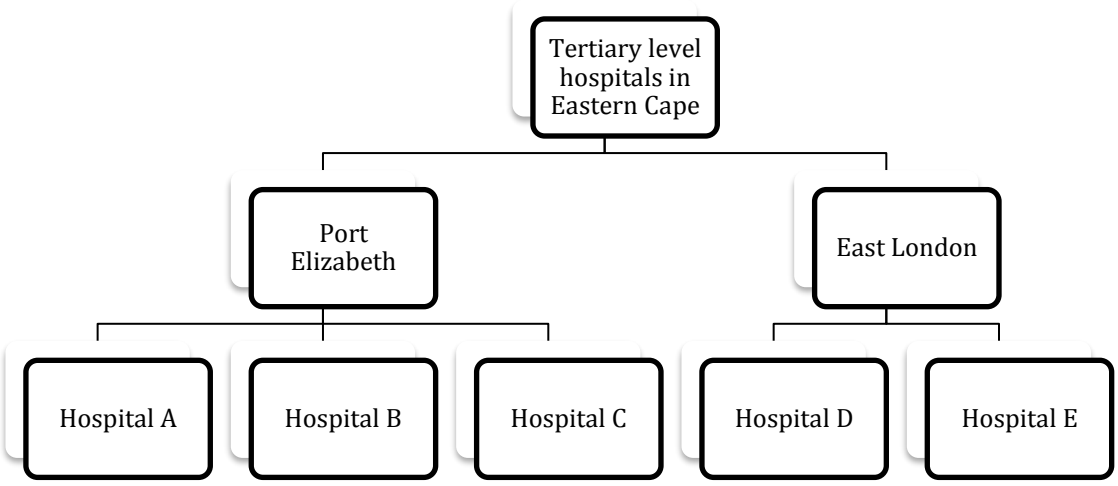

Figure 3.2. Research sites

3.5 Population and Sample Size

3.5.1 Quantitative: Questionnaire – Preliminary Phase

The respondents fulfilled the following inclusion criteria to respond to the questionnaire. The study population consisted of healthcare professionals employed at tertiary level, public sector hospitals, in the Eastern Cape province of South Africa, as described in section 3.4. A convenience sampling method was employed to ensure the

inclusion of respondents from each strata in the population (Daniel, 2012). The study sample included infectious disease specialists, pharmacists, medical prescribers, i.e. prescribers who were not specialists and clinical pathologists involved in provisions of AMS services in the Intensive Care Unit (ICU) and medical wards at the respective research sites. Where an AMS team was not established, the Pharmacy and Therapeutics Committee (PTC) team members were approached since the PTC team acts as an oversight body for antimicrobial prescribing.

3.5.2 Qualitative: Semi-Structured Interviews

3.5.2.1 Preliminary phase

A purposive sampling method was employed and was appropriate for the qualitative component of the study since the respondents were selected based on the criteria, which they met to participate in the study (H. Brink et al., 2012; Creswell, 2014; Daniel, 2012). In order to participate in the semi-structured interview of the preliminary phase, the respondents fulfilled the following inclusion criteria; healthcare professionals, who were involved in the implementation of AMS in the workplace on a daily basis, were invited to participate in the telephonic semi-structured interviews. The sample for the qualitative component of the preliminary phase included eight pharmacists, three infectious disease specialists and three medical prescribers, i.e. prescribers who were not specialists.

3.5.2.2 Post-developmental phase

In the post-developmental phase, a second round of semi-structured interviews was conducted among the respondents who participated in the preliminary phase of the study, for feedback on the applicability and practicality of the proposed framework for the antimicrobial usage reporting tool. The 14 respondents, who participated in the preliminary phase, were invited to participate in the post-developmental phase. However, only nine respondents participated in the semi-structured interview. The sample for the post-developmental phase included six pharmacists and three infectious disease specialists. Five respondents did not consent to participate in the post-developmental phase due to time constraints in their daily routine in the

workplace. Moreover, the post-developmental phase only took place over a period of two weeks, hence, a lower response rate was also due to time constraints posed by the researcher.

3.6 Ethical Approval for this Study

A research proposal was submitted to the Faculty Postgraduate Studies Committee (FPGSC) and Research Ethics Committee-Human (REC-H) at the Nelson Mandela University for approval. The letter of approval from the FPGSC is included in Appendix F (Ethical clearance reference number: H17-HEA-PHA-020).

The principle of the Helsinki Declaration (1964) and Belmont Report (1978) were adopted for purposes of this study (United States, 1978). An online system was used to request approval from Eastern Cape Department of Health (ECDoH), thus a letter was not submitted to the ECDoH. A copy of the approval letter from the ECDoH is included in Appendix G. Permission was also obtained from the Senior Manager: Medical Services or the Chief Executive Officer of the hospital research sites involved (Appendix E). The approval letters from the relevant hospital research sites involved are included in Appendix H to K.

Information pertaining to the study was provided in the preamble email to the questionnaire. In the first section of the electronic questionnaire, the respondents were asked to indicate if they agreed to or not to participate. This was taken as informed consent (Appendix A). To conduct the semi-structured interviews, permission of the selected respondents was obtained through signed informed consent forms (Appendix B). In addition, written information was also given to the respondents prior to participation in the semi-structured interviews (Appendix C). Participation was voluntary and the respondents could withdraw themselves at any point of the study. Sufficient substantial information of the proposed study was provided to the respondents. No respondents identifiers were linked to the collected data so as to ensure confidentiality (H. Brink et al., 2012; Creswell, 2014).

3.7 Data Collection – Quantitative Data

3.7.1 Questionnaire Development

The purpose–designed questionnaire was developed and consisted of two sections. In section A, the respondents were asked to provide demographic information. In subsection one of Section B, eight dichotomous questions, which asked for a 'Yes' or 'No', determined the views of the respondents on the usage of the AMS metrics. Subsections two and three each consisted of seven questions and determined the views of the respondents on the usefulness and clinical relevance of the AMS metrics using a Likert scale of 1 to 4 (Appendix A).

3.7.2 Questionnaire Dissemination – Pilot Phase

Prior to the start of the quantitative data collection process, the questionnaire was piloted among six healthcare professionals not employed at the research sites. The questionnaire was piloted for the purpose of increasing validity and to determine whether the questions being asked were not misleading and gave the required information. The purpose-designed questionnaire was electronically disseminated to five pharmacists and one medical prescriber, using the software, QuestionPro®. Five out of six respondents completed the questionnaire, resulting in a response rate of 83%. One of the respondents did not complete the questionnaire. The respondents included four pharmacists and one medical prescriber and four out of five respondents were involved in an AMS team. The respondents took an average time of 8.54 ± 9.07 minutes to complete the questionnaire.

The respondents did not experience any software related problems while answering the questionnaire. No respondent found the questions to be misleading. However, one respondent commented that the meaning of DDD was not well understood and it was necessary to keep referring to the definition of the acronyms while answering the questions. No amendments were made to the questionnaire. It was then disseminated to the study sample as described in section 3.5.1.

3.7.3 Questionnaire Dissemination – Preliminary Phase

Following the pilot phase of the study, the questionnaire was electronically disseminated, via the software, QuestionPro® over a period of eight weeks, to the respondents as described in section 3.5.1.

Forty AMS practitioners involved in provisions of AMS services in the ICU and medical wards at the five hospital research sites were invited to respond to the questionnaire. Twenty-eight (n=28) responses were obtained resulting in a response rate of 70%. The findings of the quantitative data will be presented in Chapter Four. Where an AMS team was not established, the Pharmacy and Therapeutics Committee (PTC) team members were approached since the PTC team acts as an oversight body for antimicrobial prescribing.

3.8 Data Collection – Qualitative Data

3.8.1 Development of Questions for Semi-Structured Interview

Based on the responses obtained from the questionnaire, questions to be used during the semi-structured interviews of the preliminary phase were designed. Raw qualitative data was collected in the form of telephonic audio recordings and hand written notes. The questions focused on the AMS metrics so that a comprehensive understanding of the questionnaire responses could be obtained. It allowed the researcher to explore the role of the different respondents in terms of monitoring antimicrobial usage at the research sites. It also allowed the researcher to determine the type and source of data utilised by the respondents in order to calculate the AMS metric reports. It helped to identify the challenges faced by the AMS practitioners in extracting consumption data from Rx Solution® in order to produce the relevant AMS metric reports. Finally, the usefulness of implementing a computer based software for the purpose of AMS monitoring in the South African public sector hospitals was also explored. The findings obtained during the semi-structured interviews assisted in the development of the framework of AMS metrics to be included in the proposed antimicrobial usage reporting tool.

The questions used during the semi-structured interviews of the preliminary phase included the following, but were not limited to:

1. Are you currently involved in antimicrobial stewardship activities? If yes, what are the types of activities? What is your role in terms of monitoring antimicrobial usage?
2. Is the hospital you are currently working at involved in monitoring antimicrobial usage?

   If yes, what are the current systems in place to monitor the antimicrobial usage in the hospital? E.g. Does the AMS team meets every week, who does what, does the pharmacist goes to the ward, etc. It should not necessarily be in the ward but it could be with stock.
3. Do you think sufficient emphasis is being placed on monitoring antimicrobial usage at the hospital?
4. Have you undergone any type of AMS training? If yes, what type of AMS training did you undergo? Was it formal or informal?
5. Do you use the most commonly encountered antimicrobial stewardship metrics like the Defined Daily Dose (DDD) or the Prescribed Daily Dose (PDD) to monitor antimicrobial usage?

   If yes, which one of them do you use? If yes, how effective and useful are those metrics?

   If no, why are they not effective and useful?
6. If you use those AMS metrics mentioned above, how do you extract the required data in order to calculate the metrics? Where is the data extracted from? And what data is extracted for each metrics? What do you use the extracted data for? Do you use them to calculate metrics?
7. Have you ever used Rx Solution® to extract antimicrobial usage data? If yes, what data do you extract from Rx Solution®? How useful do you find Rx Solution? How do you feel about this method?
8. If you do not use Rx Solution®, what do you use? How do you feel about this method? If no, what are the methods that you use to obtain the required data?
9. Do you think that a computer based software will be useful for public sector hospitals to monitor the antimicrobial usage? Would you prefer the software linked to Rx Solution® or separate?

3.8.2 Semi-Structured Interview – Pilot Phase

Prior to the start of the qualitative data collection process, the semi-structured interview was piloted between two pharmacists not employed at the research sites. The respondents took an average time of 10.1 ± 1.32 minutes to complete the questionnaire. No amendments were made to the questions.

3.8.3 Semi-Structured Interview – Preliminary Phase

Sixteen respondents, including pharmacists, infectious disease specialists and medical prescribers, i.e. prescribers who were not specialists, involved in the implementation of AMS on a daily basis, at the five hospital research sites were invited to participate in a semi-structured interview. Fourteen respondents agreed to partake in the semi-structured interviews, resulting in a response rate of 87.5%. The semi-structured interviews took place over a period of eight weeks. The findings of the semi-structured interviews, i.e. qualitative data, will be presented in Chapter Four.

3.8.4 Semi-Structured Interview – Post-Developmental Phase

In the post-developmental phase, a second round of semi-structured interviews was conducted for feedback on the applicability and practicality of the framework for the proposed antimicrobial usage reporting tool. Out of fourteen respondents, only nine respondents agreed to participate in the semi-structured interview, resulting in a response rate of 64.3%. The data derived from the semi-structured interviews as in the form of audio recordings and hand written notes. The post-developmental phase took place over a period of two weeks.

The proposed questions to be used during the semi-structured interview of the post-developmental phase included the following, but were not limited to:

1. The purpose of this study was to develop a framework for a proposed antimicrobial usage reporting tool for South African public sector hospitals. What is your overall impression about this framework?

2. Do you feel that the framework for the proposed antimicrobial usage reporting tool could fulfill the requirements for effective AMS monitoring?
3. How practical, applicable and beneficial do you think the framework for the proposed antimicrobial usage reporting tool is to the South African setting?
4. How feasible do you find the implementation of the framework for the proposed antimicrobial usage reporting tool?
5. What challenges do you expect to be faced in implementing the framework for the proposed antimicrobial usage reporting tool? E.g. cost, training of AMS practitioners.
6. How would you improve the framework? Do you have any suggestions or additional comments?

3.9 Data Analysis

Quantitative data analysis differs from qualitative data analysis. The process of data analysis for quantitative and qualitative data will be explained below.

3.9.1 Quantitative: Questionnaire – Preliminary Phase

Data obtained from the questionnaires was captured on a Microsoft Excel® spreadsheet in a frequency count table for analysis using a descriptive statistical analysis approach (H. Brink et al., 2012). Descriptive statistics constitute "a mathematical summarisation of the data where a large number of observed values are mathematically converted to a few numbers" (Given, 2008: 210). A visual description of the frequency counts was illustrated as bar charts. The Fisher's exact test and odds ratios (OR) statistical methods were also employed during the data analysis process. A statistician at the Unit for Statistical Consultation (USC) at the Nelson Mandela University provided guidance on the statistical analysis methods to be used.

3.9.2 Qualitative: Semi-Structured Interviews – Preliminary Phase and Post-Developmental Phase

In the preliminary phase and post-developmental phase, qualitative data was collected from semi-structured interviews in the form of telephonic audio recordings and hand-written notes. The audio recordings were transcribed verbatim and proofread. However, before starting the process of qualitative data analysis, the audio recordings were listened to and the transcripts were read several times for the researcher to become acquainted to the data. So as to ensure confidentiality, the study respondents were de-identified and renamed as P1, P2, etc. or IDS1, IDS2, etc. or MP1, MP2, etc. In order to facilitate the process of qualitative data analysis, it was important to organise the transcribed data into categories. This process is called "coding" and was done using the coding software analysis programme, "Atlas.ti® (version 8.2.1)" (H. Brink et al., 2012; Creswell, 2014). The qualitative data was then coded and organised into themes. All direct quotations from the transcripts will be presented in italics font followed by the respondent's unique identifier in brackets. In Chapter Five, network maps, which consisted of the relevant quotations, were also used to illustrate and discuss the qualitative data. An independent co-coder analysed the same qualitative data and crosschecked the codes with the one obtained from the researcher in order to ensure dependability. The researcher and the independent coder agreed upon a list of themes generated. The findings of the qualitative data: preliminary phase and post-developmental phase will be presented in Chapter Four.

3.10 Validity and Reliability

Validity is a process where a researcher would verify that the findings of the study are accurate whereas reliability is a process where a researcher would show that his/her findings can be reproduced under the same conditions but on different occasions (Bloor & Wood, 2006). Validity and reliability are interpreted differently in terms of quantitative and qualitative methodologies.

3.10.1 Quantitative: Questionnaire – Preliminary Phase

Validity was tested during the pilot study, where the questionnaire was electronically distributed, via the software, QuestionPro® to six healthcare professionals not employed at the research sites. The pilot study determined if the questions being asked were not misleading and gave the required information (H. Brink et al., 2012; Creswell, 2014). The Cronbach's alpha test was also performed in order to assess for the internal reliability of the responses obtained. The results obtained from the Cronbach's alpha tests will be presented in Chapter Four.

3.10.2 Qualitative: Semi-Structured Interviews – Preliminary Phase and Post-Developmental Phase

Instead of using validity, a qualitative researcher uses Lincoln and Guba's model of trustworthiness (Creswell, 2014). The terms that address trustworthiness are 'dependability', 'credibility', 'confirmability' and 'transferability' and they were evaluated during the preliminary and post-developmental phase (H. Brink et al., 2012). Dependability was determined using a stepwise replication, where a co-coder analysed the same data and crosschecked the codes with the one obtained from the researcher (H. Brink et al., 2012; Creswell, 2014; Guba, 1981). To achieve credibility and to verify for accuracy and consistency in the findings, each respondent verified the transcripts and the interpretation of the transcripts from their interviews. Confirmability was achieved by developing an audit trail in order to ensure that the findings, conclusions and recommendations of the study were consistent with the interpreted data of the researcher throughout the methodology (H. Brink et al., 2012; Jensen, 2012). The audit trail consisted of raw data, personal written notes, summaries and coded information (H. Brink et al., 2012; Jensen, 2012). To achieve transferability, interviews took place to saturation, until no new data emerged (H. Brink et al., 2012; Creswell, 2014).

CHAPTER 4
RESULTS

4.1 Introduction

Chapter Four will present the results obtained from the data collection process; both the quantitative and qualitative data collected during the preliminary phase of the study will be presented. The results obtained during the preliminary phase of the study allowed the researcher to develop a framework of AMS metrics to be included in the proposed antimicrobial usage reporting tool, i.e. during the developmental phase. The proposed framework was electronically disseminated, via email, to the respondents who participated in the preliminary phase of the study for feedback on applicability and practicality, i.e. during the post-developmental phase. The results obtained from the developmental and the post-developmental phases will also be presented in Chapter Four. A discussion of the three phases, preliminary, developmental and post-developmental phases, linked to the research aim and objectives will be presented in Chapter Five.

4.2 Preliminary Phase

As described in Chapter Three, the questionnaire was developed and distributed to infectious disease specialists, pharmacists, medical prescribers, i.e. medical prescribers who were not specialists and clinical pathologists employed at tertiary level, public sector hospitals in Port Elizabeth and East London, in the Eastern Cape province of South Africa, using a convenience sampling method. The quantitative questionnaire allowed the researcher to identify the views of respondents on the most commonly used AMS utilisation metrics in the South African public healthcare setting. The quantitative data obtained was further enriched by conducting semi-structured interviews with selected experts involved in the implementation of AMS on daily basis in the workplace. The quantitative data will be presented in section 4.2.1 while the qualitative data obtained from the semi-structured interviews will be presented in section 4.2.2.

4.2.1 Questionnaire – Quantitative Data

Forty AMS practitioners employed at the five hospital research sites (Figure 3.2) were invited to respond to the electronically distributed questionnaire, via the software, QuestionPro® (Appendix A). A response rate of 70% (n=28) was obtained. The quantitative data was captured on a Microsoft Excel® spreadsheet for analysis. Frequency count tables and graphical representations were used to illustrate and summarise the quantitative data. The Fisher's exact test and odds ratios (OR) statistical methods were also employed during the data analysis process. The Fisher's exact test is a nonparametric version of the chi-square test and it was used to determine whether two variables were correlated and subsequently used to calculate the p-values. It is most commonly used when the sample size is small or when at least one cell in a cross-tabulation table has an expected frequency of less than five (Bond, 2012; Pett, 2012). The Fisher's exact tests were calculated at a df (degree of freedom) (1) and a statistical significance of 5%. A p-value of less than .05 was considered significant. Where an association was found between the two variables, OR were calculated in order to determine the strength of the association (Motel, 2018). For the Fisher's exact test to be valid, the different options provided in Section B, Question Two and Three were grouped. The options 'extremely useful and useful' were classified as useful and the options 'slightly useful or not useful' were classified as less useful. The options 'extremely clinically relevant or clinically relevant' were classified as clinically relevant and the options 'slightly clinically relevant or not clinically relevant' were classified as less clinically relevant.

Cronbach's alpha was performed in order to test for the internal consistency of the following responses: i) the usage, ii) the usefulness and iii) the clinical relevance of each AMS metric (Appendix A).

4.2.1.1 Demographic profile of the respondents

The demographics details recorded included the following: gender, occupation, involvement in an AMS team and information with respect to AMS training (Appendix A, Section A, Questions 1 to 5).

Gender

The gender and occupation of the respondents are illustrated in Figure 4.1. Overall, the majority of the respondents were females (57.1%; f=16; n=28). When further analysed, it was found that the infectious disease specialists comprised of two males and one female. The pharmacists consisted of two males and eleven females; the medical prescribers consisted of seven males and four females, while the clinical pathologist was a male.

Occupation

The largest group of respondent was pharmacist (46.4%; f=13; n=28) and there was only one clinical pathologist among the respondents (3.6%; f=1; n=28). The medical respondents comprised of three infectious disease specialists (10.7%; f=3; n=28) and 11 medical prescribers (39.3%; f=11; n=28), i.e. the medical prescribers who were not specialists.

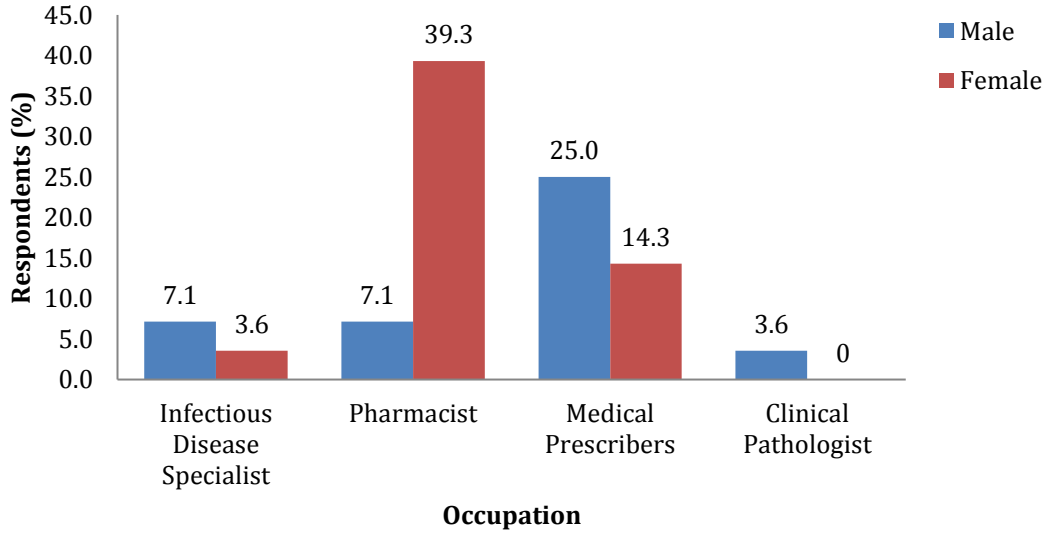

Figure 4.1. Respondent occupations (n=28)

AMS involvement

Twenty-two respondents (78.6%; f=22; n=28) were involved in a formalised AMS team at the hospital research sites (Table 4.1). The respondents were contributing to

AMS services in the ICU and medical wards at the respective research sites. However, two medical prescribers and four pharmacists stated that they were not involved in an AMS team, due to the possible fact that two of the research sites (Hospital A and Hospital B) did not have a formally established AMS team. At Hospital A, the prospective PTC team members had been approached as the AMS committee had not commenced functioning, whilst at Hospital B, the respondents who participated in the study, were involved in informal AMS activities.

Table 4.1 *AMS involvement (n=28)*

YES n (%)	**NO** n (%)
22 (78.6%)	6 (21.4%)

Figure 4.2 gives a detailed illustration of how the different categories of respondents were involved in an AMS team. Of the twenty-two respondents (f=22; n=28) involved in an AMS team, there were three infectious disease specialists (10.7%; f=3; n=28), nine pharmacists (32.1%; f=9; n=28), nine medical prescribers (32.1%; f=9; n=28) and one clinical pathologist (3.6%; f=1; n=28) involved in the AMS teams at the respective research sites.

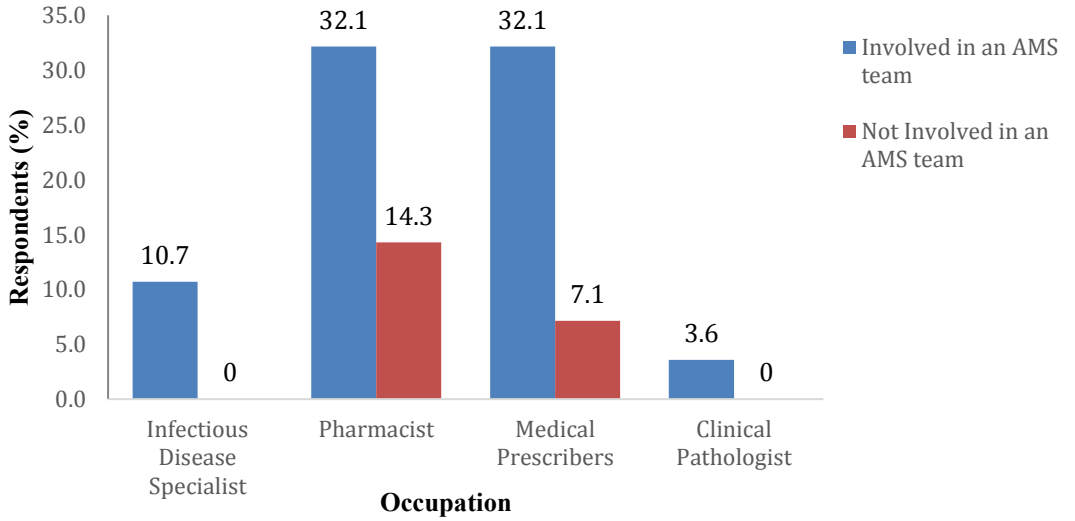

Figure 4.2. AMS involvement of the different categories of respondents (n=28)

AMS training completed

The percentage of respondents who had completed AMS training is illustrated in Table 4.2. The majority of the respondents had undergone AMS training (60.7%; f=17; n=28). Further analysis of the seventeen responses revealed that three infectious disease specialists, eight pharmacists, five medical prescribers and one clinical pathologist had completed AMS training. The type of AMS training included the following: i) short/online course, ii) workshop and iii) university course, with most of the respondents identifying workshops as the most commonly encountered training format (35.7%; f=10; n=28). Of the four respondents who had completed other types of training, one respondent had completed AMS training by attending talks and bedside training and another respondent stated that it was part of the critical care training programme. The other two respondents did not specify the nature of the AMS training.

Table 4.2 *AMS training completed (n=28)*

AMS training	n (%)
Yes	
Short/online course	2 (7.14%)
Workshop	10 (35.7%)
University course	1 (3.57%)
Other	4 (14.3%)
No	11 (39.3%)

Further investigation reported that fifteen respondents involved in an AMS team had completed AMS training whilst seven of the respondents involved in an AMS team were not trained. Thus, it could be concluded that, not all respondents involved in an AMS team were trained. Yet, all the respondents involved in an AMS team were applying AMS principles in the workplace.

4.2.1.2 Perceptions of the respondents regarding the application of the AMS metrics

During the preliminary phase, the questionnaire was used to integrate the usage, usefulness and clinical relevance of the antimicrobial stewardship (AMS) metrics in the workplace as perceived by the different categories of respondents (Figure 4.1).

The respondents were asked the following question regarding the usage of the AMS metrics:

"Have you ever utilised the metrics below to monitor antimicrobial utilisation?" (Appendix A)

Usage

Figure 4.3 represents the usage of the most common AMS metrics. The usage of the AMS metrics was the highest for IV to oral switch (75.0%; f=21; n=28), followed by LOT (71.4%; f=20; n=28) and DDD (64.3%; f=18; n=28). Cost was used by 60.7% (f=17; n=28) and PDD was only used by half (50.0%; f=14; n=28) of the respondents to monitor antimicrobial usage. The AMS metric, exposure days was reported to be used by the least number of respondents (28.6%; f=8; n=28).

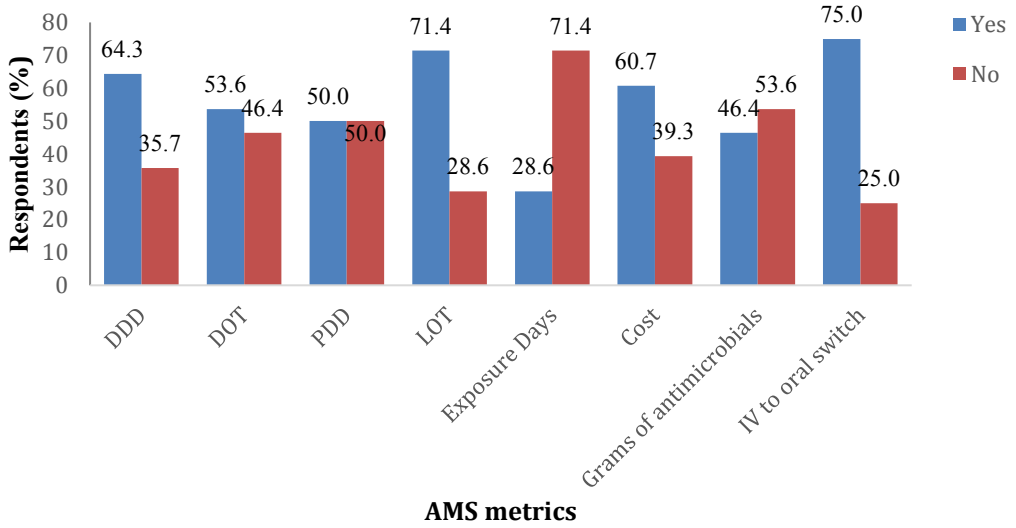

Figure 4.3. Usage of the AMS metrics (n=28)

DDD – Defined Daily Dose; DOT – Days of Therapy; PDD – Prescribed Daily Dose; LOT – Length of Therapy; IV to oral switch – Intravenous to oral switch

The usage of the AMS metrics was then compared between the two groups, namely the medical respondents (M) and non-medical respondents (NM) (Figure 4.4). The 'medical' respondents (M) consisted of infectious disease specialists and medical prescribers and would actively be involved in the prescribing of antimicrobials, while the 'non-medical' respondents (NM) consisted of pharmacists and the clinical pathologist.

Overall, 64.3% (f=9; n=14) of the medical and non-medical respondents used DDD to monitor antimicrobial usage (Figure 4.4). While only half (50%; f=7; n=14) of the medical respondents used DOT, it was observed that 57.1% (f=8; n=14) of the non-medical respondents used this AMS metric. LOT was equally used by the medical and non-medical respondents (71.4%; f=10; n=14). The AMS metric, IV to oral switch, was used by 78.6% (f=11; n=14) of the medical respondents and 71.4% (f=10; n=14) of the non-medical respondents.

It was observed that, although more non-medical respondents than medical respondents used cost, no statistically significant difference in the usage of cost was observed between the two groups (M vs. NM: 64.3% vs. 57.1%; Fisher's exact test p= .70). Exposure days was used by the minority of the medical and non-medical respondents (M vs. NM: 35.7% vs. 21.4%; Fisher's exact test p= .40). Overall, there were no statistically significant differences in the usage of the eight AMS metrics between the medical and non-medical respondents (Fisher's exact test p>.05).

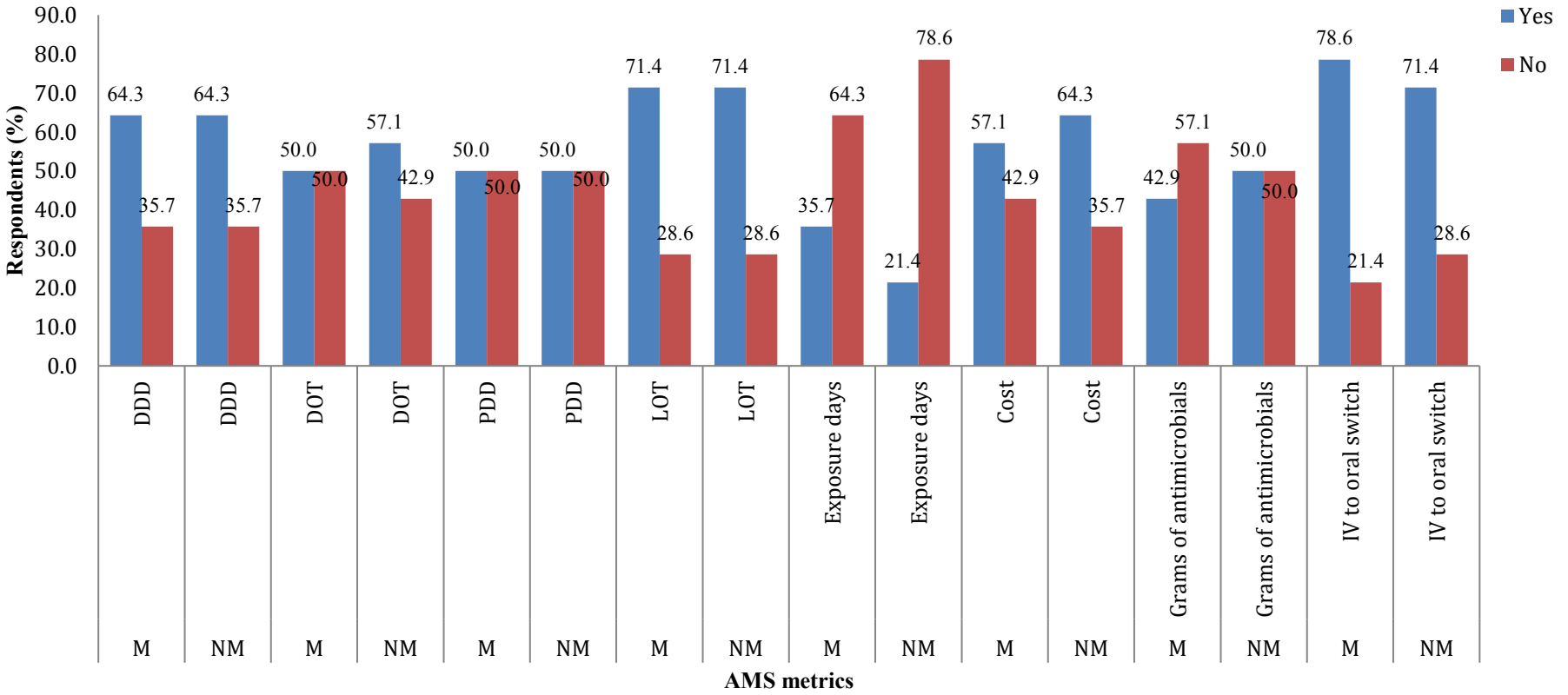

Figure 4.4. Usage of the AMS metrics between the medical (n=14) and non-medical respondents (n=14)

DDD – Defined Daily Dose; M vs. NM: Fisher's exact test =0.00; p = 1.00; DOT – Days of Therapy; M vs. NM: Fisher's exact test = 0.14; p = .70; PDD – Prescribed Daily Dose; M vs. NM: Fisher's exact test =0.00; p = 1.00; LOT – Length of Therapy; M vs. NM: Fisher's exact test =0.00; p = 1.00; Exposure days; M vs. NM: Fisher's exact test =0.70; p = .40; Cost; M vs. NM: Fisher's exact test =0.15; p = .70; Grams of antimicrobials; M vs. NM: Fisher's exact test =0.14; p = .70; IV to oral switch – Intravenous to oral switch; M vs. NM: Fisher's exact test =0.19; p = .66; M – Medical; NM – Non-medical

The usage of the AMS metrics was then compared between the respondents who were involved (I) or not involved (NI) in an AMS team (Figure 4.5). The respondents involved in an AMS team at the research sites were mostly using the following AMS metrics: IV to oral switch (77.3%; f=17; n=22), followed by DDD (72.7%; f=16; n=22) and LOT (72.7%; f=16; n=22). Exposure days (31.8%; f=7; n=22) was used by the least number of respondents involved in an AMS team.

Most of the respondents not involved in an AMS team were equally using DOT, PDD, LOT, grams of antimicrobials and IV to oral switch (66.7%; f=4; n=6). When comparing with the respondents involved in an AMS team, only 33.3% (f=2; n=6) of the respondents not involved in an AMS team were using DDD. Overall, there were no statistically significant differences noted between the two groups (I and NI) regarding the usage of any of the eight AMS metrics (Fisher's exact test $p > .05$).

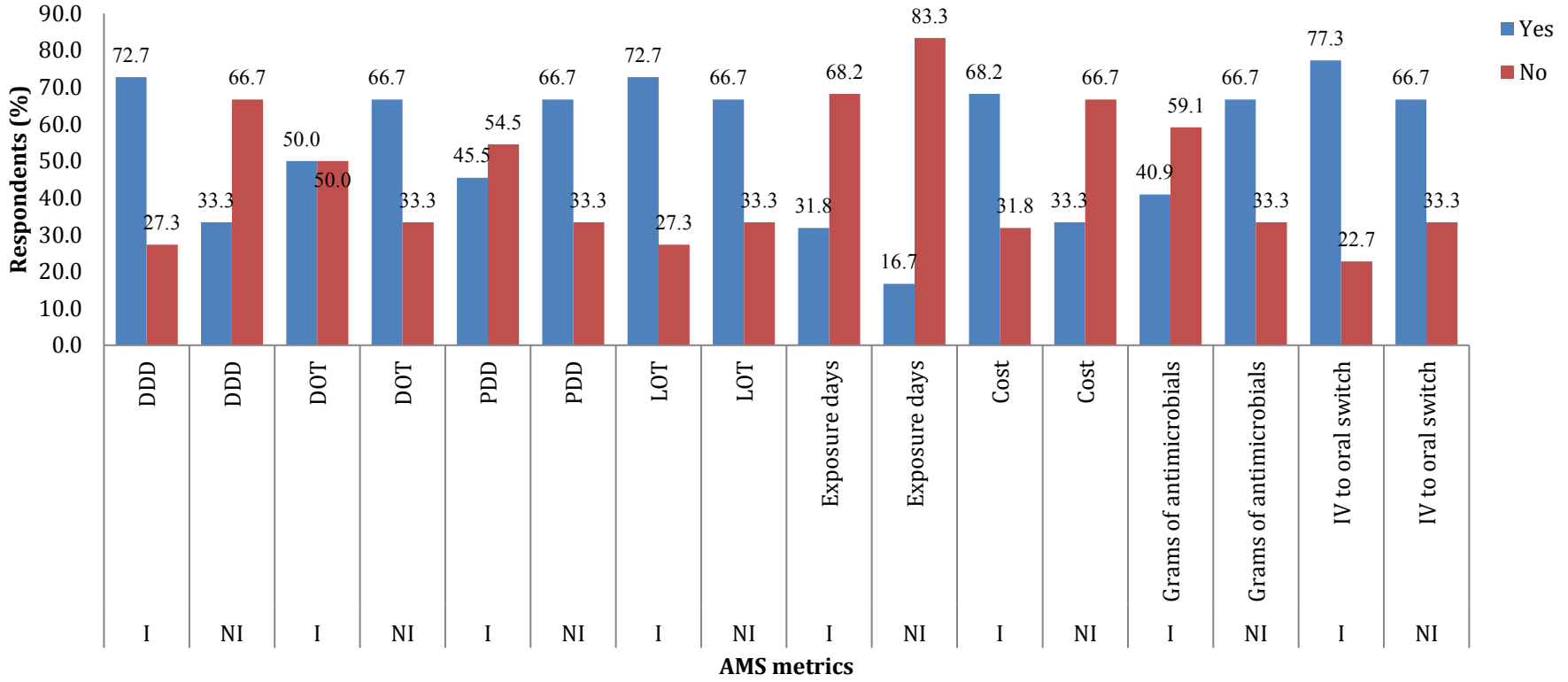

Figure 4.5. Usage of the AMS metrics between the respondents who were involved (n=22) or not involved (n=6) in an AMS team

DDD – Defined Daily Dose; I vs. NI: Fisher's exact test =3.19; p = .07; DOT – Days of Therapy; I vs. NI: Fisher's exact test = 0.53; p = .47; PDD – Prescribed Daily Dose; I vs. NI: Fisher's exact test =0.85; p = .36; LOT – Length of Therapy; I vs. NI: Fisher's exact test =0.085; p = .77; Exposure days; I vs. NI: Fisher's exact test =0.53; p = .47; Cost; I vs. NI: Fisher's exact test =2.40; p = .12; Grams of antimicrobials; I vs. NI: Fisher's exact test =1.26; p = .26; IV to oral switch – Intravenous to oral switch; I vs. NI: Fisher's exact test =0.28; p = .59; I – Involved; NI – Not involved

The usage of the AMS metrics by the respondents who underwent AMS training (A) was then compared to the respondents who did not undergo AMS training (NA) (Figure 4.6). The majority of the respondents (82.4%; f=14; n=17) who underwent AMS training used LOT, cost and IV to oral switch to monitor antimicrobial usage in the workplace. It can be noted that AMS training of the respondents did not influence the usage of exposure days, i.e. the least number of respondents with AMS training used exposure days (29.4%; f=5; n=17).

The majority of the respondents with no AMS training were using IV to oral switch (63.6%; f=7; n=11). It was also observed that the respondents with no AMS training equally used PDD, LOT and grams of antimicrobials (54.5%; f=6; n=11). With the exception of PDD and grams of antimicrobials, it was observed that there were more respondents with AMS training than respondents with no AMS training, who were using the other six AMS metrics.

While the majority of the respondents with AMS training were using cost 82.4% (f=14; n=17), it was observed that this AMS metric was used by the minority of respondents with no AMS training (27.3%; f=3; n=11). A statistically significant difference was observed in the usage of 'cost' between the respondents who underwent AMS training (A) or no AMS training (NA) (Fisher's exact test p= .0036). Furthermore, it was observed from the odds ratio calculations that the odds that a respondent with AMS training uses cost is 10.06 times higher than the odds that a respondent with no AMS training uses cost (OR=10.06).

Overall, there were no statistically significant differences in the usage of the other seven AMS metrics between the following groups of respondents (A and NA) (Fisher's exact test p>.05).

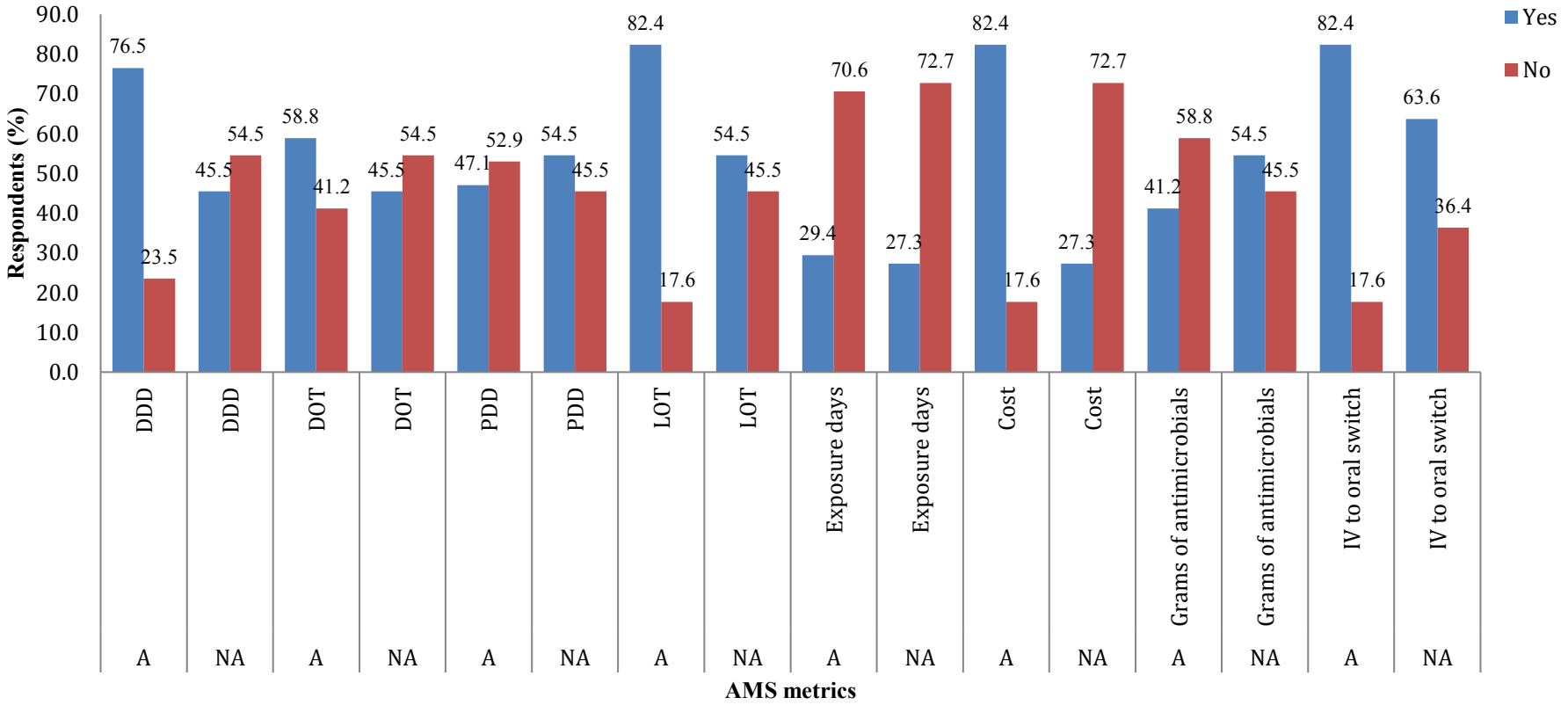

Figure 4.6. Usage of the AMS metrics between the respondents who underwent AMS training (n=17) or did not undergo AMS training (n=11)

DDD – Defined Daily Dose; A vs. NA: Fisher's exact test =2.80; p = .70; DOT – Days of Therapy; A vs. NA: Fisher's exact test = 0.48; p = .49; PDD – Prescribed Daily Dose; A vs. NA: Fisher's exact test =0.15; p = .70; LOT – Length of Therapy; A vs. NA: Fisher's exact test =2.53; p =. 11; Exposure days; A vs. NA: Fisher's exact test =0.015; p = .90; Cost; A vs. NA: Fisher's exact test =8.50; p = .0036; Grams of antimicrobials; A vs. NA: Fisher's exact test =0.48; p = .49; IV to oral switch – Intravenous to oral switch; A vs. NA: Fisher's exact test =1.25; p = .26; A – AMS training; NA – No AMS training

Usefulness

The views on the usefulness of the most common AMS metrics were reported by the respondents (Figure 4.7). The vast majority of the respondents (96.4%; f =27; n=28) felt that IV to oral switch was useful (i.e. extremely useful or useful). Of the respondents, 85.7% (f=24; n=28) found LOT to be useful (i.e. extremely useful or useful). DOT was used by just over half of the respondents (53.6%; f=15; n=28) (Figure 4.3). However, a greater percentage of the respondents (82.1%; f=23; n=28) classified DOT as useful (i.e. extremely useful or useful) (Figure 4.7). It can be observed in Figure 4.3, that even though 64.3% (f=18; n=28) of the respondents used DDD as a measure of antimicrobial usage in the workplace, a larger percentage, 71.4% (f=20; n=28) of the respondents identified the DDD as useful (i.e. extremely useful or useful). Fewer respondents identified the AMS metric, exposure days as useful (i.e. extremely useful or useful) (53.6%; f=15; n=28) (Figure 4.7). Overall, it was observed that there were more respondents who found the AMS metrics useful (i.e. extremely useful or useful) than there were respondents who used the AMS metrics in the clinical setting.

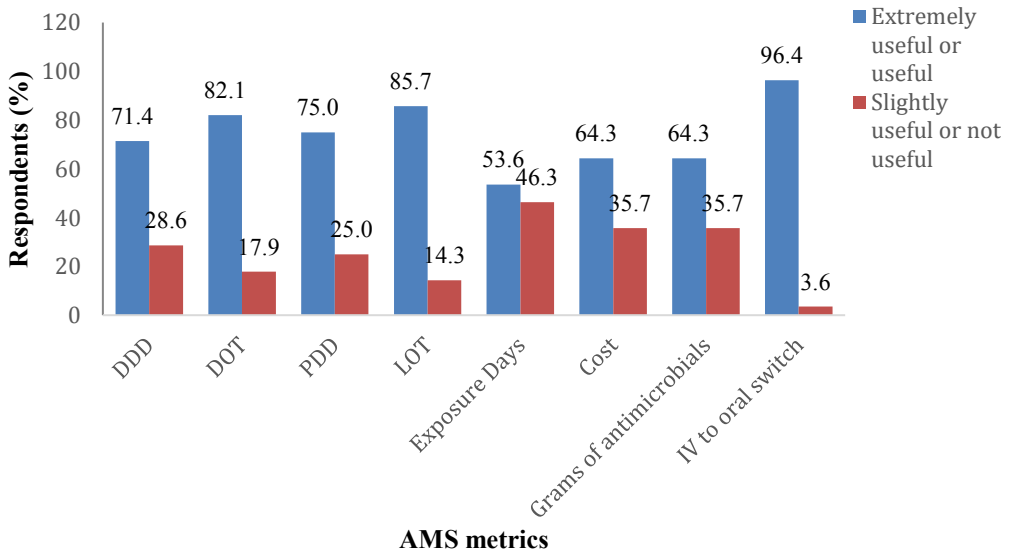

Figure 4.7. Usefulness of the AMS metrics as perceived by the respondents (n=28)

DDD – Defined Daily Dose; DOT – Days of Therapy; PDD – Prescribed Daily Dose; LOT – Length of Therapy; IV to oral switch – Intravenous to oral switch

The usefulness of the AMS metrics was then compared between the medical respondents (M) and non-medical respondents (NM) (Figure 4.8). The following

AMS metrics were found to be useful (i.e. extremely useful or useful) by the most number of medical and non-medical respondents respectively, namely, IV to oral switch (92.9% vs. 100%), LOT (85.7% vs. 85.7%) and DOT (78.6% vs. 85.7%).

All of the non-medical respondents categorised IV to oral switch as useful (i.e. extremely useful or useful) (100%; f=100; n=14). It may be interesting to highlight that cost was classified as a useful (i.e. extremely useful or useful) AMS metric by 78.6% (f=11; n=14) of the non-medical respondents, while only half (50.0%; f=7; n=14) of the medical respondents identified cost as useful (i.e. extremely useful or useful). The AMS metrics, exposure days and grams of antimicrobials were found to be useful AMS metrics (i.e. extremely useful or useful) by 35.7% (f=5; n=14) and 57.1% (f=8; n=14) of the medical respondents while equal number (71.4%; f=10; n=14) of the non-medical respondents identified those AMS metrics as useful (i.e. extremely useful or useful).

With the exception of LOT, it was observed that there were more non-medical respondents than medical respondents who classified the other seven AMS metrics as useful (i.e. extremely useful or useful). As an example, there were more non-medical respondents than medical respondents who considered IV to oral switch (NM vs. M: 100% vs. 92.9%; Fisher's exact test p= .31) and DOT (NM vs. M: 85.7% vs. 78.6%; Fisher's exact test p= .62) as useful AMS metrics (i.e. extremely useful or useful).

It was also noted that 64.3% of the medical respondents who were using DDD (Figure 4.4) also perceived it as useful (i.e. extremely useful or useful). However, no statistically significant differences were found overall in the usefulness of the eight AMS metrics between the medical (M) and non-medical (NM) respondents (Fisher's exact test p >.05).

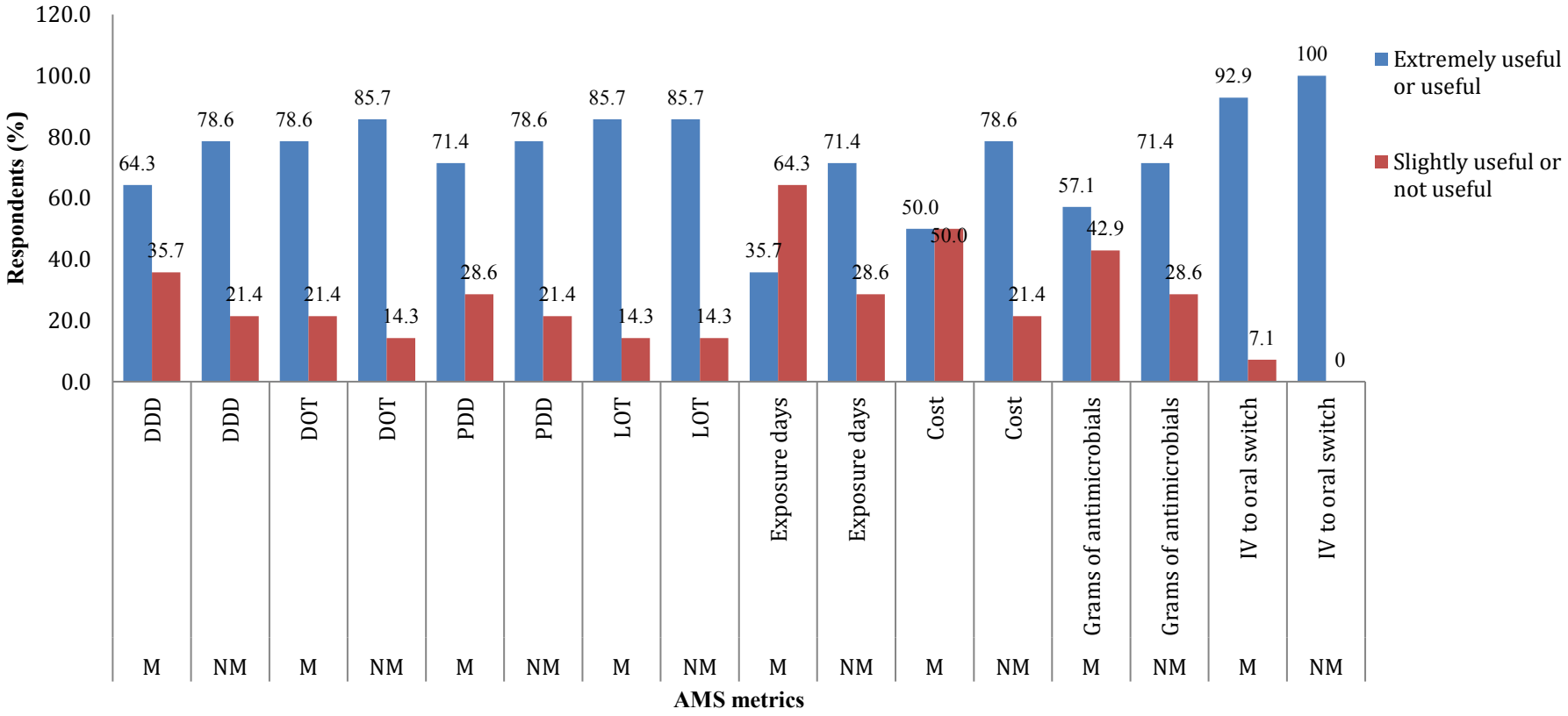

Figure 4.8. Usefulness of the AMS metrics between the medical (n=14) and non-medical respondents (n =14)

DDD – Defined Daily Dose; M vs. NM: Fisher's exact test =0.70; p = .40; DOT – Days of Therapy; M vs. NM: Fisher's exact test = 0.24; p = .62; PDD – Prescribed Daily Dose; M vs. NM: Fisher's exact test =0.19; p = .66; LOT – Length of Therapy; M vs. NM: Fisher's exact test =0.00; p = 1.00; Exposure days; M vs. NM: Fisher's exact test =3.59; p = .06; Cost; M vs. NM: Fisher's exact test =2.49; p = .11; Grams of antimicrobials; M vs. NM: Fisher's exact test =0.62; p = .43; IV to oral switch –Intravenous to oral switch; M vs. NM: Fisher's exact test =1.03; p = .31; M – Medical; NM – Non-medical

The usefulness of the AMS metrics was then compared between the respondents who were involved (I) or not involved (NI) in an AMS team (Figure 4.9). The majority of the respondents involved in an AMS team (95.5%; f=21; n=22) identified IV to oral switch as useful (i.e. extremely useful or useful). DOT and DDD were found to be useful (i.e. extremely useful or useful) by 77.3% (f=17; n=22) and 72.7% (f=16; n=22) of the respondents involved in an AMS team respectively.

It was previously established that six respondents were not involved in a formally established AMS team (Table 4.1). All of those six respondents categorised DOT, PDD, LOT, grams of antimicrobials and IV to oral switch as less useful (i.e. slightly useful or not useful) (100%; f=6; n=6) (Figure 4.9).

A statistically significant difference was only found when the two groups of respondents (I and NI) were asked to comment on the usefulness of the 'grams of antimicrobials' (I vs. NI: 54.5% vs. 100%; Fisher's exact test p= .04). In order to determine the strength of this correlation, the odds ratio (OR) was calculated. The odds that a respondent involved in an AMS team identifies grams of antimicrobials as useful (i.e. extremely useful or useful) is 10.92 times higher than the odds that a respondent who is not involved in AMS team identifies grams of antimicrobials as useful (i.e. extremely useful or useful) (OR=10.92).

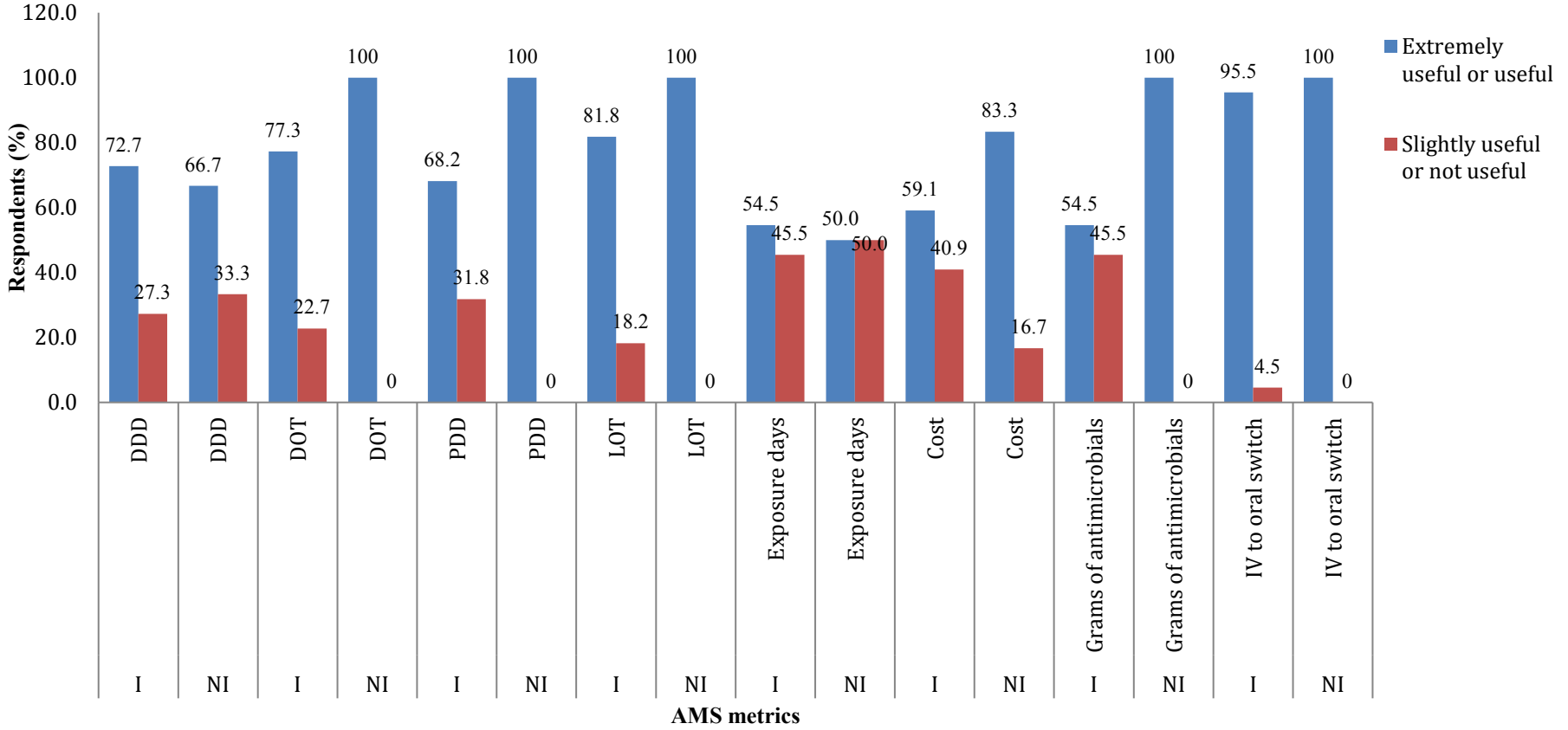

Figure 4.9. Usefulness of the AMS metrics between the respondents who were involved (n=22) or not involved (n=6) in an AMS team

DDD – Defined Daily Dose; I vs. NI: Fisher's exact test =0.085; p = .77; DOT – Days of Therapy; I vs. NI: Fisher's exact test = 1.66; p = .20; PDD – Prescribed Daily Dose; I vs. NI: Fisher's exact test =2.55; p = .11; LOT – Length of Therapy; I vs. NI: Fisher's exact test =1.27; p = .26; Exposure days; I vs. NI: Fisher's exact test =0.039; p = .84; Cost; I vs. NI: Fisher's exact test =1.20; p = .27; Grams of antimicrobials; I vs. NI: Fisher's exact test =4.24; p = .04; IV to oral switch – Intravenous to oral switch; I vs. NI: Fisher's exact test =0.28; p = .59; I – Involved; NI – Not involved

The usefulness of the AMS metrics was then compared between the respondents who underwent AMS training (A) and those who had no AMS training (NA) (Figure 4.10). The most number of respondents who had completed AMS training found the following AMS metrics, IV to oral switch (100%; f=17; n=17), DOT (82.4%; f=14; n=17) and LOT (76.5%; f=13; n=17) to be useful (i.e. extremely useful or useful) while the most number of respondents who had no AMS training found LOT (100%; f=11; n=11), PDD (90.9%; f=10; n=11) and grams of antimicrobials (90.9%; f=10; n=11) to be useful (i.e. extremely useful or useful).

The Fisher's exact test value for testing the null hypothesis between the usefulness of 'grams of antimicrobials' and the two categories of respondents (A and NA) indicated that there was an association between the usefulness of 'grams of antimicrobials' and the respondents who underwent AMS training or no AMS training (Fisher's exact test p= .018). The odds that a respondent with AMS training identifies grams of antimicrobials as useful (i.e. extremely useful or useful) is 7.82 times higher than the odds that a respondent with no AMS training identifies grams of antimicrobials as useful (i.e. extremely useful or useful) (OR=7.82).

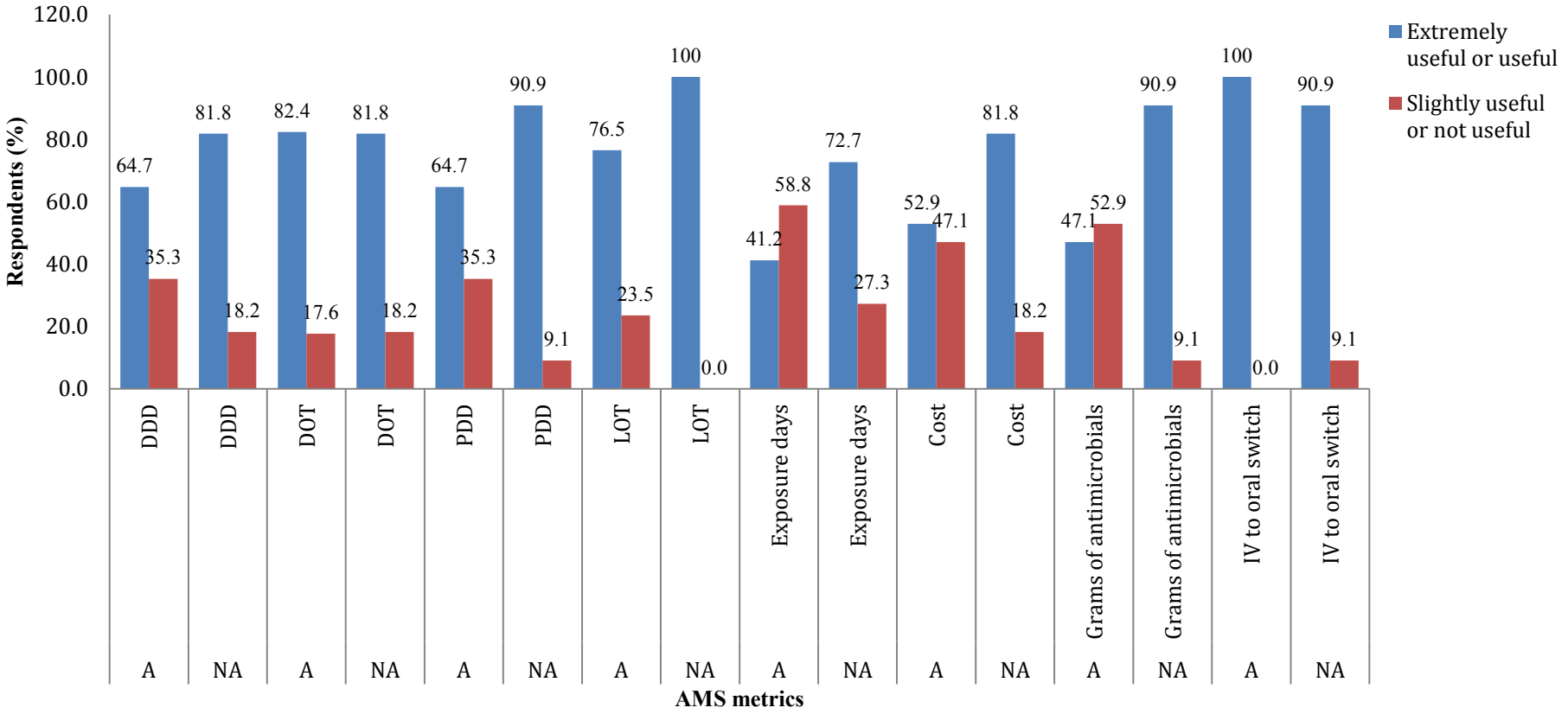

Figure 4.10. Usefulness of the AMS metrics between the respondents who underwent AMS training (n=17) or did not undergo AMS training (n=11)

DDD – Defined Daily Dose; A vs. NA: Fisher's exact test =0.96; p = .30; DOT – Days of Therapy; A vs. NA: Fisher's exact test = 0.0001; p = .97; PDD – Prescribed Daily Dose; A vs. NA: Fisher's exact test =2.45; p = .12; LOT – Length of Therapy; A vs. NA: Fisher's exact test =3.02; p = .08; Exposure days; A vs. NA: Fisher's exact test =2.67; p = .10; Cost; A vs. NA: Fisher's exact test =2.43; p = .12; Grams of antimicrobials; A vs. NA: Fisher's exact test =5.59; p = .0.018; IV to oral switch – Intravenous to oral switch; A vs. NA: Fisher's exact test =1.60; p = .21; A – AMS training; NA – No AMS training

Clinical relevance

The respondents' views on whether the most commonly encountered AMS metrics were clinically relevant were investigated (Figure 4.11). The AMS metrics viewed as clinically relevant (i.e. extremely clinically relevant or clinically relevant) by the most number of respondents, with a percentage of 92.9% (f=26; n=28) was DOT, followed by LOT and IV to oral switch, which were found to be clinically relevant (i.e. extremely clinically relevant or clinically relevant) by equal number of respondents (89.3%; f=25; n=28). Fewer respondents identified exposure days, cost and grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (53.6%; f=15; n=28). Despite being used by 64.3% (f=18; n=28) of the respondents in practice (Figure 4.3), only 60.7% (f=17; n=28) of the respondents perceived DDD to be clinically relevant (i.e. extremely clinically relevant or clinically relevant).

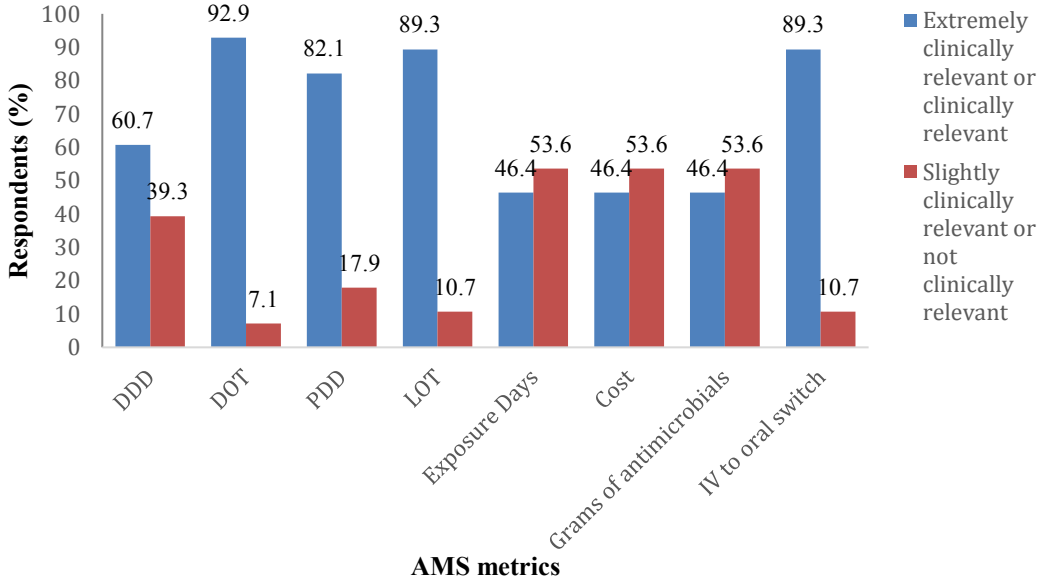

Figure 4.11. Clinical relevance of the AMS metrics as perceived by the respondents (n=28)

DDD – Defined Daily Dose; DOT – Days of Therapy; PDD – Prescribed Daily Dose; LOT – Length of Therapy; IV to oral switch – Intravenous to oral switch

Perceptions of the clinical relevance of the AMS metrics were then compared between the two groups, i.e. between the medical respondents (M) and non-medical respondents (NM) (Figure 4.12). Most of the medical respondents (92.9%; f=13;

n=14) perceived DOT and LOT as clinically relevant AMS metrics (i.e. extremely clinically relevant or clinically relevant). The least number of medical respondents identified grams of antimicrobials (42.9%; f=6; n=14), exposure days (35.7%; f=5; n=14) and cost (35.7%; f=5; n=14) as clinically relevant (i.e. extremely clinically relevant or clinically relevant).

The majority of the non-medical respondents found IV to oral switch and DOT to be clinically relevant (i.e. extremely clinically relevant or clinically relevant) AMS metrics (92.9%; f=13; n=14). The AMS metrics identified as clinically relevant (i.e. extremely clinically relevant or clinically relevant) by the least number of non-medical respondents, were cost (57.1%; f=8; n=14), exposure days (57.1%; f=8; n=14) and grams of antimicrobials (50.0%; f=7; n=14) respectively.

As opposed to the non-medical respondents, the medical respondents did not perceive DDD to be as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (M vs. NM: 57.1% vs. 64.3%; Fisher's exact test p= .70). It was noted that all of the non-medical respondents (64.3%; f=9; n=14) who were using DDD to monitor antimicrobial usage patterns (Figure 4.4) also perceived this AMS metric as clinically relevant (i.e. extremely clinically relevant or clinically relevant). However, overall there were no observed statistically significant differences in the perceptions of the clinical relevance of the eight AMS metrics when medical (M) and non-medical (NM) respondents' views were compared (Fisher's exact test p>.05).

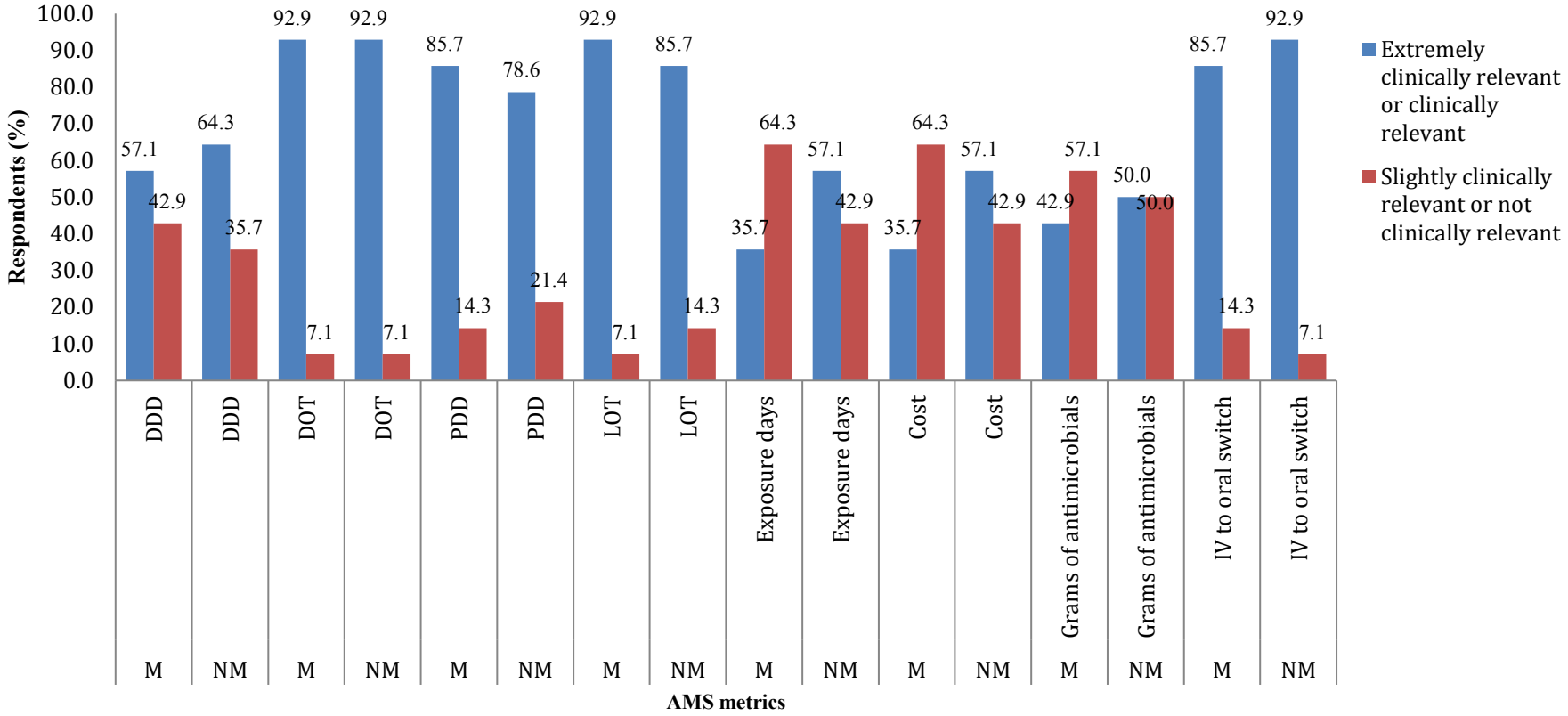

Figure 4.12. Clinical relevance of the AMS metrics between the medical (n=14) and non-medical respondents (n=14)

DDD – Defined Daily Dose; M vs. NM: Fisher's exact test =0.15; p = .70; DOT – Days of Therapy; M vs. NM: Fisher's exact test = 0.00; p = 1.00; PDD – Prescribed Daily Dose; M vs. NM: Fisher's exact test =0.24; p = .62; LOT – Length of Therapy; M vs. NM: Fisher's exact test =0.37; p = .54; Exposure days; M vs. NM: Fisher's exact test =1.29; p = .26; Cost; M vs. NM: Fisher's exact test =1.29; p = .26; Grams of antimicrobials; M vs. NM: Fisher's exact test =0.14; p = .70; IV to oral switch – Intravenous to oral switch; M vs. NM: Fisher's exact test =0.37; p = .54; M – Medical; NM – Non-medical

The perceived clinical relevance of the AMS metrics was compared between the respondents who were involved (I) or not involved in an AMS team (NI) (Figure 4.13). Most of the respondents involved in an AMS team (I) perceived DOT (90.9%; f=20; n=22), IV to oral switch (86.4%; f=19; n=22) and LOT (86.4%; f=19; n=22) as clinically relevant (i.e. extremely clinically relevant or clinically relevant). Grams of antimicrobial was identified as clinically relevant (i.e. extremely clinically relevant or clinically relevant) by the least number of respondents involved in an AMS team (31.8%; f=7; n=22).

Although 72.7% (f=16; n=22) of the respondents involved in an AMS team classified DDD as useful (i.e. extremely useful or useful), it was noted that only 54.5% (f=12; n=22) of the respondents involved in an AMS team found this AMS metric to be clinically relevant (i.e. extremely clinically relevant or clinically relevant). All of the six respondents (100%; f=6; n=6) who were not involved in an AMS team, classified DOT, PDD, LOT, grams of antimicrobials and IV to oral switch as less clinically relevant (i.e. slightly clinically relevant or not clinically relevant).

There was an observed statistically significant difference, in terms of how the respondents who were involved (I) or not involved (NI) in an AMS team categorised the clinical relevance of ‘grams of antimicrobials’ (Fisher’s exact test p= .003). The odds that a respondent involved in an AMS team identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) is 26.87 times higher than the odds that a respondent who is not involved in an AMS team identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (OR=26.87).

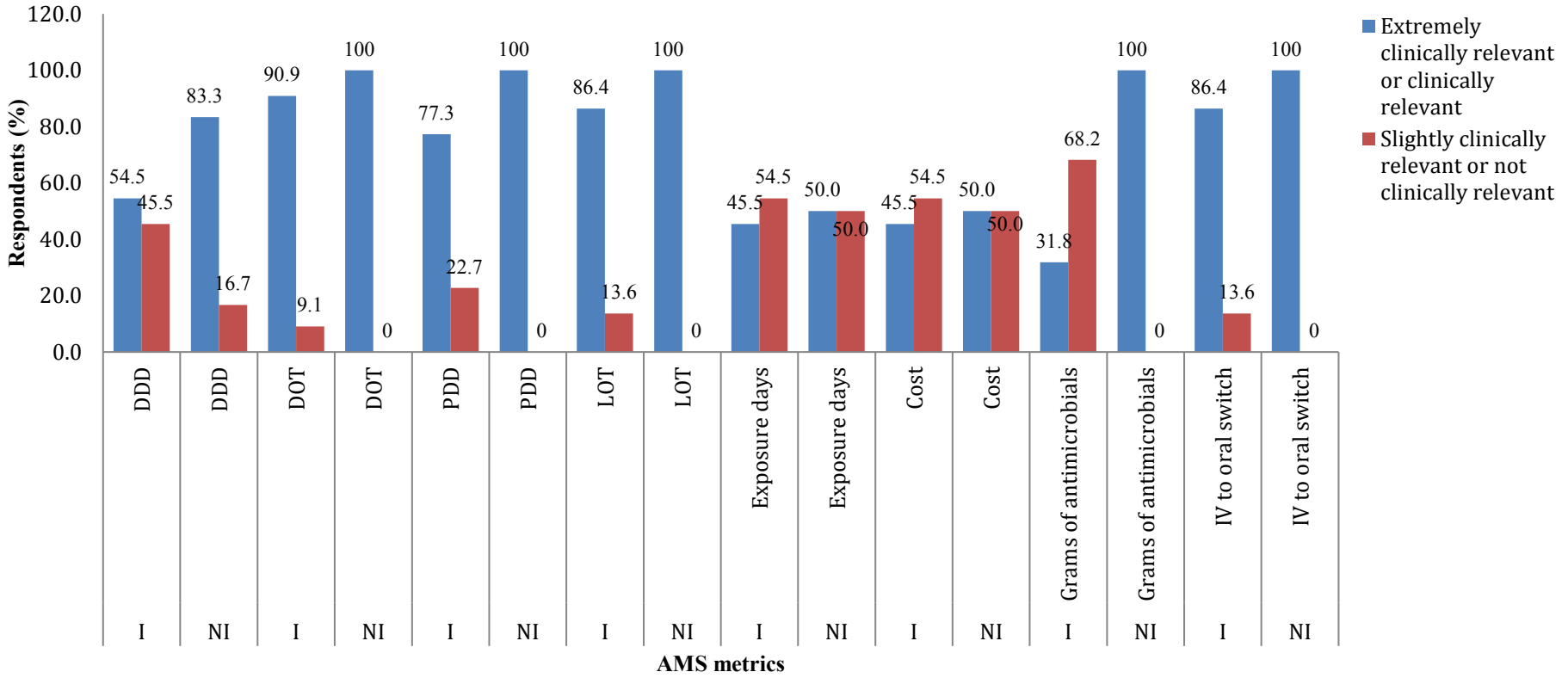

Figure 4.13. Clinical relevance of the AMS metrics between the respondents who were involved (n=22) or not (n=6) involved in an AMS team

DDD – Defined Daily Dose; I vs. NI: Fisher's exact test =1.64; p = .20; DOT – Days of Therapy; I vs. NI: Fisher's exact test = 0.59; p = .44; PDD – Prescribed Daily Dose; I vs. NI: Fisher's exact test =1.66; p = .20; LOT – Length of Therapy; I vs. NI: Fisher's exact test =0.92; p = .34; Exposure days; I vs. NI: Fisher's exact test =0.039; p = .84; Cost; I vs. NI: Fisher's exact test =0.039; p = .84; Grams of antimicrobials; I vs. NI: Fisher's exact test =8.81; p = .0030; IV to oral switch – Intravenous to oral switch; I vs. NI: Fisher's exact test =0.92; p = .34; I – Involved; NI – Not involved

The perceptions of the clinical relevance of the AMS metrics were compared between the respondents who underwent AMS training (A) or no AMS training (NA) (Figure 4.14). While 88.2% (f=15; n=17) of the respondents with AMS training found DOT and IV to oral switch to be clinically relevant (i.e. extremely clinically relevant or clinically relevant), all the respondents (100%; f=11; n=11) who were not trained identified DOT and LOT to be clinically relevant (i.e. extremely clinically relevant or clinically relevant).

The AMS metric, grams of antimicrobials was seen to be clinically relevant (i.e. extremely clinically relevant or clinically relevant) by the minority of the respondents with AMS training (23.5%; f=4; n=17). The odds that a respondent with AMS training identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) is 11.40 times higher than the odds that a respondent with no AMS training identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (OR=11.40).

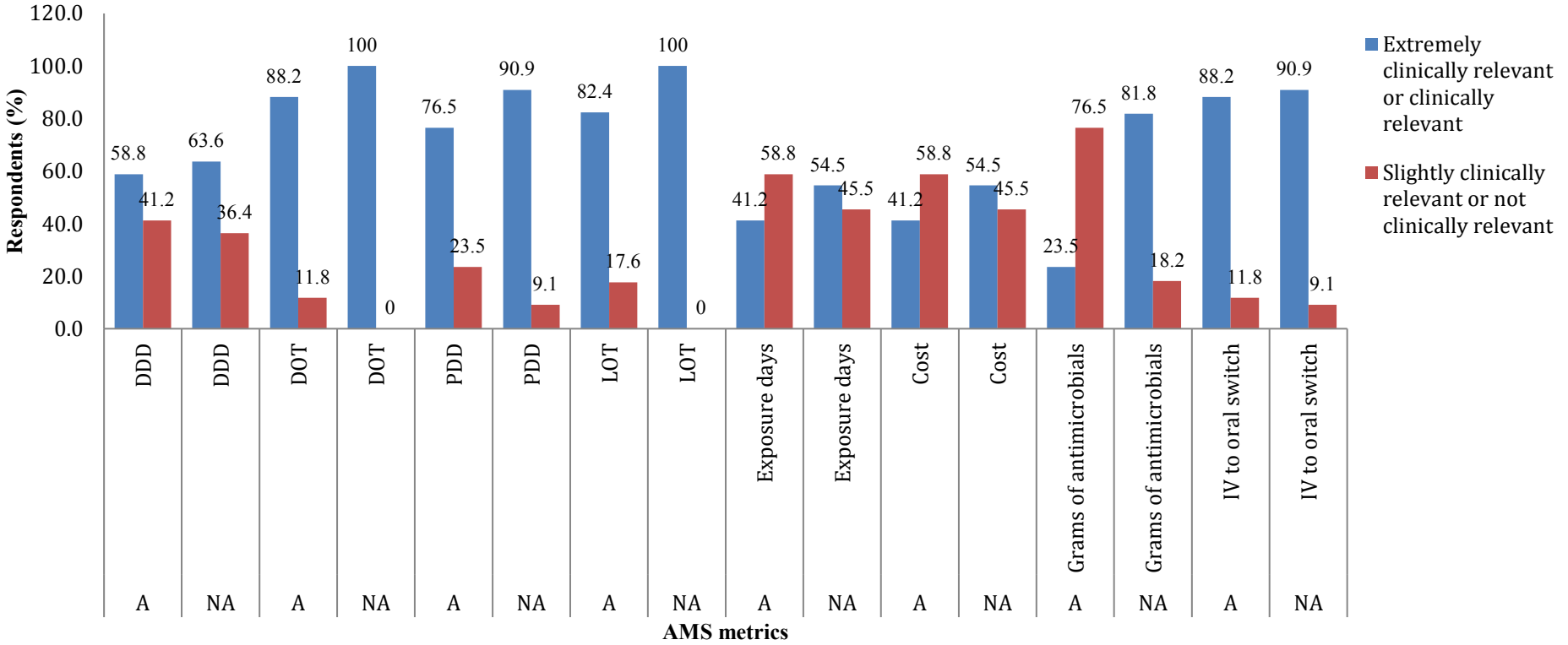

Figure 4.14. Clinical relevance of the AMS metrics between the respondents who underwent AMS training (n=17) or did not undergo AMS training (n=11)

DDD – Defined Daily Dose; A vs. NA: Fisher's exact test =0.065; p = .80; DOT – Days of Therapy; A vs. NA: Fisher's exact test = 1.40; p = .24; PDD – Prescribed Daily Dose; A vs. NA: Fisher's exact test =0.95; p = .33; LOT – Length of Therapy; A vs. NA: Fisher's exact test =2.17; p = .14; Exposure days; A vs. NA: Fisher's exact test =0.48; p = .49; Cost; A vs. NA: Fisher's exact test =0.48; p = .49; Grams of antimicrobials; A vs. NA: Fisher's exact test =9.12; p = .0025; IV to oral switch – Intravenous to oral switch; A vs. NA: Fisher's exact test =0.050; p = .82; A – AMS training; NA – No AMS training

4.2.1.3 Internal reliability of the questionnaire

The reliability of the questionnaire was measured in terms of internal consistency of the following responses: i) Usage, ii) Usefulness and iii) Clinical relevance of the AMS metrics. Cronbach's alpha coefficient was utilised. A Cronbach's alpha coefficient greater than .70 is considered to be coherent enough and, therefore, reliable, with a possible range from 0 to 1 (Johnson, 2018).

The Cronbach's alpha coefficient for the usage and usefulness of the antimicrobial stewardship (AMS) metrics were .804 and .734 respectively, indicating a high strength of consistency in the responses. However, a Cronbach's alpha coefficient of .565 was obtained for the clinical relevance of the AMS metrics, indicating a medium strength of consistency in the responses.

4.2.2 Semi-Structured Interview: Qualitative Data

As described in Chapter Three, the preliminary phase also included the collection of qualitative data. Sixteen healthcare professionals, involved in the daily implementation of AMS at the public sector hospital research sites, were invited to participate in the semi-structured interviews using a purposive sampling method. Fourteen respondents agreed to partake in the semi-structured interviews, resulting in a response rate of 85.7%. The sample included eight pharmacists (P), three infectious disease specialists (IDS) and three medical prescribers (MP). The pharmacists, infectious disease specialists and medical prescribers were de-identified and renamed with the prefix P, IDS and MP respectively in order to preserve respondent anonymity. A number was given as a suffix to identify the number of the respondent. The term 'Prelim.' was also added as a suffix in order to illustrate that the researcher was referring to the preliminary phase. The respondents were identified as follows: e.g. (P1: Prelim.). The hospital research sites were also de-identified and renamed with letters A to E. The transcribed interviews were organised into codes and sub-organised into themes using the qualitative data analysis software programme, Atlas.ti® (version 8.2.1). The identified themes generated from the semi-structured interviews are presented in Table 4.3. All direct quotations from the transcripts will be

presented in italics font followed by the respondent's unique identifier in brackets. The semi-structured interviews were guided by five main questions, namely:

1. Are you currently involved in antimicrobial stewardship activities?
2. Have you undergone any type of AMS training?
3. Do you use the most commonly encountered antimicrobial stewardship metrics like the Defined Daily Dose (DDD) or the Prescribed Daily Dose (PDD) to monitor antimicrobial usage?
4. Have you ever used Rx Solution® to extract antimicrobial usage data?
5. Do you think that computer based software will be useful for public sector hospitals to monitor the antimicrobial usage?

Table 4.3 *Themes identified during analysis of qualitative data derived from semi-structured interviews during the preliminary phase*

Themes
1. Antimicrobial stewardship (AMS)
2. Surveillance
3. Extraction of data
4. Challenges
5. Implementation of an antimicrobial usage reporting tool

4.2.2.1 Theme 1: Antimicrobial stewardship (AMS)

The first theme to be identified focused on antimicrobial stewardship (AMS). The following opening general question was asked to all the respondents:

"Are you currently involved in any antimicrobial stewardship activities?"

The responses to this question allowed the researcher to determine the extent to which the respondents were involved in the implementation of antimicrobial stewardship (AMS) in their daily role as a healthcare professional at the research sites. The majority of the respondents were involved in weekly AMS ward rounds as a primary AMS activity. In addition, the pharmacists were also involved in reviewing the appropriateness of prescribed antimicrobials, with the exception of one pharmacist

(P2), who was also compiling the DDD consumption data of antimicrobials for the different wards of one research site (Hospital C).

"Right now in the outpatient pharmacy, it is not as intense as the in-patients, so whenever we get a script and there is an antibiotic prescribed, we make sure that it's the proper indication, it's the proper antibiotic, the proper dose, the proper frequency. In the out-patient, this is what you do right now." (P1: Prelim.)

"The activities are, that I am part of the antimicrobial stewardship committee, so I attend those meetings and also that I compile data on Defined daily Doses for the different sections in the hospital." (P2: Prelim.)

"We do weekly ward rounds with the antimicrobial team, that's currently what I am doing. I was involved in assessing appropriateness and doing sort of mini projects. I am a Pharm.D student, I am currently not doing my rotations in infectious diseases, so I am not doing that anymore. We're basically doing weekly antimicrobial stewardship rounds." (P3: Prelim.)

"Just ward rounds with medical department." (P4: Prelim.)

"I am influencing how they [doctors] prescribe and advise based on lab results, the sensitivity results. I phone and I advise on alternate therapies." (P6: Prelim.)

"…Our other AMS activities are that we're continuously reviewing scripts and IVOST [Intravenous to Oral Antibiotic Switch Therapy] and all those things, on a daily basis." (P8: Prelim.)

"So we do ward rounds in the paediatric ward and then I am also on the antimicrobial stewardship committee, at the hospital and provincial level." (IDS2: Prelim.)

"…I do antimicrobial stewardship ward rounds…at the moment just at Hospital D in the medicine department." (IDS3: Prelim.)

"Well, we try and conduct antimicrobial stewardship rounds and I will join them from time to time, not on a weekly basis. I do try and attend those and then we've got an antibiotic prescription chart that we try and audit from time to time to see if the indications for the antibiotic are correct, basically looking at dosages, if the chart has been filled completely or not." (MP3: Prelim.)

The medical practitioners, i.e. the infectious disease specialists and medical prescribers, were also involved in other types of AMS activities, such as implementing infection prevention and control (IPC) practices, increasing awareness on AMS as well as evaluating the usage of antimicrobials.

"It is being part of the [AMS] committee member and as well as trying to develop ways of evaluating antibiotic usage and providing feedback, so the role on the [AMS] committee is to support that." (IDS1: Prelim.)

"So I'm on the two hospitals, D and E, sharing antimicrobial stewardship committee at both hospitals. So…involving some of more strategic stuff in the hospitals, antimicrobial prescription charts, looking at antibiotic guidelines, hospital policies, in a more broader spectrum, improving infection control issues and then more directly, I do antimicrobial stewardship ward rounds…at the moment just at Hospital D in the medicine department." (IDS3: Prelim.)

"We have a stewardship type of ward rounds that I attend. Sometimes I advise on de-escalation and principles of stewardship in the hospital." (MP1: Prelim.)

"Quality control, quality improvement, introducing stewardship charts, introducing stewardship ward rounds, awareness protocols, etc." (MP2: Prelim.)

It was noted that the respondents played different roles in terms of the AMS activities. One of the respondents (P4) reflected that the pharmacists are the healthcare professionals dealing with medications and they are expected to be the final persons adhering with AMS principles, i.e. ensuring the appropriateness of antimicrobial treatment before dispensing the antimicrobials to the patient. In fact, it can be concluded from the types of AMS activities described that the pharmacists were

certainly undertaking appropriate roles as AMS practitioners. On the other hand, the medical practitioners were mostly involved in the implementation of AMS strategies, which formed the foundation of the AMS programme.

"I think it [AMS] goes down to the final person who is dealing with the medication process and that's the pharmacist." (P4: Prelim.)

With the objective of exploring and describing the level of AMS knowledge, the respondents were asked to indicate if any type of AMS training had been undertaken. The format of training varied between formal and informal training. The majority of the respondents had undergone AMS training with the exception of two pharmacists and one medical prescriber, who had no AMS training at all. The infectious disease specialists were trained as part of their specialisation.

"Just short courses, specifically how to start an antibiotic, what to use and how often you must need." (P1: Prelim.)

"I've done an antimicrobial stewardship workshop, a three day workshop and an assignment." (P2: Prelim.)

"Yes, we did a course through, I think it was through SAASP [South African Antimicrobial Stewardship Programme]. SAASP organised it, it was about three to four years ago, a three day course." (P3: Prelim.)

*"I have…For my Pharm.D, I have done an infectious disease rotation and I have also done through Medunsa [*Sefako Makgatho Health Sciences University*], a course on stewardship."* (P4: Prelim.)

"I went onto, three years ago, it was a two or three day course on antimicrobial stewardship." (P5: Prelim.)

"Yes, I went to Cape Town, I started the green plan Eastern Cape, we were about six or eight of us. Between two hospitals, we were three, the ID specialist and two clinical pharmacists, together with other people. We went to Cape Town with Marc

Mendelson; there were other people as well for a week, that was about two years ago. We had official lectures but we also went to ICU, we went to the maternity wards as well and we did rounds…so that was the AMS training that we went for." (P8: Prelim.)

"Yes, part of my specialisation was involved in antibiotic stewardship as an infectious disease specialist." (IDS1: Prelim.)

"Yes, it was part of my infectious diseases training… we do AMS, when we are in the microbiology labs, we do our clinical practice but I haven't attended a formal course." (IDS2: Prelim.)

"Yeah, I did my infectious disease specialist. I did do quite a bit of AMS as part of that two years and I subsequently went on together with a team from Eastern Cape, on an intensive five days hand on training on stewardship. That's basically all the formal training that I had." (IDS3: Prelim.)

"It's informal training, we have an infectious disease specialist at the hospital. He does ward rounds with us and we have a lot of academic interactions plus [and] obviously talks and conferences." (MP1: Prelim.)

"Informal training, yes. On the job training as you can call it." (MP2: Prelim.)

With the exception of the infectious disease specialists who had extensive training on AMS as part of their specialisation, it was observed that the level and extent of AMS training varied between the other respondents, i.e. pharmacists and medical prescribers. Although the undergraduate B.Pharm curriculum provides training on infectious diseases and antimicrobials, it was interesting to note that two pharmacists (P6 and P7) stated that they did not undergo any type of formal or informal AMS training. It was also noted that respondent (P6) was involved in AMS activities despite having no formal AMS training. This finding is in line with Cosgrove et al. (2014), who stated that, even though pharmacists may be untrained in infectious diseases, it does not prevent them from taking a role in an AMS team. The other

pharmacists attended formal workshops and courses of short durations while the medical prescribers only had informal training.

4.2.2.2 Theme 2: Surveillance

The surveillance theme reflected the role of the respondents in terms of monitoring antimicrobial usage at the research sites. After having identified the different types of AMS activities that the respondents were involved in, the respondents were asked to further elaborate on their role in terms of monitoring antimicrobial usage. The following opening question was asked to the respondents:

"What is your role in terms of monitoring antimicrobial usage?"

All the respondents did not necessarily monitor antimicrobials by quantifying the usage. The antimicrobial usage was also monitored in terms of appropriateness and epidemiological data. The quotations below illustrate the different ways in which the respondents monitored the antimicrobial usage.

"As a pharmacist, you have to make sure that first of all the doctors follow our standard treatment guidelines, that they follow the proper protocols and also if there is any microbial results, any lab results and that they choose the proper antibiotics, obviously if the normal dosage and frequency is fine." (P1: Prelim.)

"My personal role, unfortunately, I don't necessarily monitor the usage in terms of numbers. We monitor usage in terms of assessing appropriateness of indication, duration, if the duration is going on for too long, so that's the type of monitoring we do. But it's not like DDD. The [pharmacy] manager does that." (P3: Prelim.)

"…so antibiotic stewardship is just one of many functions, so looking at rational medicine use, assessing indication, efficacy, safety, adherence, obviously stewardship falls into that broad domain…" (P4: Prelim.)

"…I get queries at pharmacy where they sometimes get a script that are sent down for antibiotics, with restricted items, and they'll phone me, and we will try and review the indication of the antibiotic with the prescriber…" (IDS3: Prelim.)

"We monitor epidemiological data for our unit, in terms of the number of infections but we are limited in what we can do…" (MP1: Prelim.)

"My role directly is as a consultant in the hospital…so my role is an oversight role. I rarely prescribe the antibiotic myself but I act as an oversight to the prescription practices." (MP2: Prelim.)

"…We try to get a very crude idea of whether the appropriate antibiotics were being used for the appropriate infections that were being cultured…" (MP3: Prelim.)

However, for the purpose of this study, the quantification aspect was focused on. In order to quantify the antimicrobial usage, healthcare institutions are required to use a standard and reliable AMS metric (Schellack et al., 2017). In an attempt to identify the AMS metrics currently being employed in the South African public healthcare setting, the respondents were asked if the most commonly encountered AMS metrics were being used as a measure of antimicrobial usage. According to the published literature, the Defined Daily Dose (DDD), the Days of Therapy (DOT) and the Prescribed Daily Dose (PDD) were identified as the most widely used and recommended AMS metrics (Grau et al., 2013). The semi-structured interviews revealed that the DDD was the only AMS metric being used at two of the five research sites (Hospital C and Hospital D) whilst the other research sites (Hospital A, Hospital B and Hospital E) were not yet involved in that type of data monitoring. The reasons why the stated research sites were not yet involved in quantifying antimicrobial will be further discussed under Theme 4 (Challenges).

It was apparent that the DDD consumption data was utilised to varying degrees by the different respondents practicing at Hospital C.

"…I compile data on Defined Daily Doses for the different sections in the hospital." (P2: Prelim.)

"They do DDDs." (P3: Prelim.)

"Yeah [yes], we do the Defined Daily Doses." (IDS1: Prelim.)

At one of the research sites (Hospital C), the pharmacy manager was responsible for monitoring antimicrobial usage, in terms of antimicrobial consumption data, and the data was then utilised by the infectious disease specialist.

"My personal role, unfortunately, I don't necessarily monitor the usage in terms of numbers. We monitor usage in terms of assessing appropriateness of indication, duration, if the duration is going on for too long, so that's the type of monitoring we do. But it's not like DDD. The [pharmacy] manager does that." (P3: Prelim.)

"Our [pharmacy] manager is actually taking down the DDD and then forwarding that to the infectious disease specialist and that's basically how far we go." (P4: Prelim.)

"…the pharmacy monitors usage data." (MP1: Prelim.)

"Yes, it's [antimicrobial usage] monitored at pharmacy level." (MP2: Prelim.)

"…We also monitor on a larger level what the pharmacy, from both hospitals [silence]… we try and look at the antibiotic consumption data, which they [pharmacists] record…" (IDS3: Prelim.)

Moreover, one of the medical prescribers (MP3) working in the infectious diseases ward was also evaluating the DDD consumption data provided by the pharmacy manager (P2). Information related to the DDD consumption was concurrently being used with the microbiological lab cultures, in order to determine the appropriateness of antimicrobials at Hospital C.

"…but I have done my own sort of things looking at the Defined Daily Doses that the pharmacy manager provides me with on a monthly basis. We've done some charts where we looked at January 2017 to December 2017, we've tracked the use of the

different antibiotics in the hospital and that together looking at how many cultures were done in the labs..." (MP3: Prelim.)

Hospital D was also involved in the compilation of DDD metric reports.

"…And then also there is other means of monitoring usage. Furthermore, we have done [silence]…One of my colleagues has done the DDD consumption data…" (P8: Prelim.)

"…but we're looking at DDDs per 1000 patient-days and try to look at trends over time and look at usages in the different departments…usage of restricted items like carbapenems, colistin etc." (IDS3: Prelim.)

Additionally, one of the respondents (IDS3) mentioned that Hospital E was monitoring antimicrobial usage in terms of investigating the number of units and costs of antimicrobials and it was one of those issues that the AMS practitioners were still working on.

"Yeah but Hospital E is a bit behind. They still looking at units and cost items…" (IDS3: Prelim.)

It can be established that, at one of the research sites (Hospital C), the pharmacy manager was involved in the collation of the DDD whilst the infectious disease specialist was involved in evaluating and providing feedback on the consumption data to the AMS committee members.

"It is being part of the [AMS] committee member and as well as trying to develop ways of evaluating antibiotic usage and providing feedback, so the role on the [AMS] committee is to support that." (IDS1: Prelim.)

When respondent (P7) was asked about the usage of the common AMS metric like the DDD or PDD to monitor antimicrobial usage, it was confirmed that Hospital A was not yet involved in that type of data monitoring.

"No, we haven't started with anything [using AMS metrics to monitor the antimicrobial usage],…" (P7: Prelim.)

The respondents were further asked to elaborate on the reason for selecting the DDD as the only AMS metric to monitor antimicrobial usage. Despite being aware that the DDD has limitations and disadvantages, one of the respondents (IDS1) described this AMS metric as being *"a convenience more than anything"*. Another respondent (P3) stated that when compared to the grams of antimicrobials, the DDD provided more clinically relevant information. The limitations of the DDD will be presented under Theme 4 (Challenges).

"I think it [the DDD] is more sort of clinically orientated than grams of antibiotics or antibiotic expenditure. So it [the DDD] has its disadvantages as well…" (P3: Prelim.)
"It's [The DDD is] just the one that we have chosen because it's [the DDD is] well described. It's one that we are most familiar with and the formulas are readily available for each antibiotic… It's a convenience more than anything." (IDS1: Prelim.)

One respondent (IDS3) also mentioned that the DDD is an AMS metric that was suggested by the National Department of Health (NDoH) and that was the reason why they decided to go forward with the DDD (South African National Department of Health, 2017a). The NDoH is currently enforcing the implementation of AMS in the South African public healthcare setting. However, it is also important to note that the national directive for this implementation phase was only initiated in 2017, while the data collection process for this research project was underway. One of the respondents (P4) emphasised that AMS principles are not always practiced in the South African public sector hospitals and this could be due to the recent implementation of AMS, which is slowly gaining momentum in the public healthcare sector. The slow progress of putting AMS into practice in the public sector hospitals will be discussed under Theme 4 (Challenges).

"I think so, but it's very complex because you need opinion leaders and you need the strong leaders in departments to drive it as well. For example, in our internal medicine department, we have everyone who supports [antimicrobial] stewardship

but if you don't have a strong opinion leader that is driving it in other departments, you fall flat, for example, in surgery no one is driving [antimicrobial] stewardship, so the end result is [antimicrobial] stewardship principles are not always adhered to or practiced, when you don't have a programme that is functioning and which is problematic because only certain areas or sections of the hospital are then rationally used. Then as a public hospital, even if there is stewardship in place, there are still things seeping through…" (P4: Prelim.)

"We are really quite beginners with stewardship, and that was suggested and encouraged from national and the original document, the AMR, the manual that was circulated. That's what we've gone with. I think when we can perfect the DDD, we could also possibly show some of the other metrics." (IDS3: Prelim.)

The respondents involved in the compilation of DDD data at the research sites (Hospital C and Hospital D) and the respondents who worked at the research sites where the DDD was being determined were aware of its usefulness and effectiveness in an AMS programme. The DDD was identified as a useful AMS metric. However, it was emphasised by one of the respondents (P2) that a meaningful interpretation of the DDD consumption data is only possible if the data is collected longitudinally. This fact was also supported by the respondent IDS3.

"In the short term, I don't think that you'll get any information out of it [DDD], but I've been collecting the data now for almost two years and I think you can get a pretty good picture of trends and changes, and prescribing patterns. You see immediately something spikes because something else was out of stock, or you see an overuse of something else. From that point of use, I think it is pretty useful data just as long it is collected long term." (P2: Prelim.)

"I think it [DDD] is useful as an overall marker. Obviously, there are exceptions to it. As long as you can evaluate that further. It's a broad thing that must be focused down on key areas. I think it is useful, but it's not the defined evaluation of prescribing but it gives you a fairly good outcome marker of the programme if you are using correct antibiotic choices within the Defined Daily Dose." (IDS1: Prelim.)

One respondent (MP3) cautioned on the limitations of the DDD metric and explained that a high DDD value would not necessarily correspond to inappropriate usage. Another respondent (IDS3) was aware that the DDD has its disadvantages and could not be used to measure antimicrobial usage in paediatrics. This finding will be discussed under Theme 4 (Challenges).

"We are aware that there are some limitations and I have seen some studies that say that it [DDD] may underestimate or overestimate in some context…it seems that there are no standard for paediatrics due variation of dosing in paeds [paediatrics] according to the weight. In paeds [paediatrics], it's quite a non-representative value. It got some values just for some broad picture and trends…but for some antibiotics, it may underestimate or overestimate usage. Sometimes we are using higher doses than the Defined Daily Dose, so they skew the findings. It is useful over times in terms of trends but I am aware that it does not give you the full picture of antibiotic usage." (IDS3: Prelim.)

"It [the DDD] is very useful information but there is obviously limitations in terms of what it can tell you. It gives you information up to a point, but I think we need far more than just the DDDs. At the end of the day, obviously it will tell you the usage of antibiotics, but the DDDs don't tell you about appropriateness. They just going to be able to tell that we are using more carbapenems or less carbapenems and that can be affected by anything…it could be affected by stock-outages, it could be affected by a whole bunch of things and maybe it might all be appropriate usage. The problem might be that we are using more resistant infections and you have to be using those antibiotics. It does give you a sense of what's going on but it doesn't give you an explanation of why it's happening, so the use is limited." (MP3: Prelim.)

Although one of the respondents (IDS1) described the DDD as not being "the *defined evaluation of prescribing"*, it was highlighted that the DDD has been beneficial in terms of identifying trends in antimicrobial consumption. On the other hand, another respondent (P2) was in agreement that DDD has allowed to identify trends but the need for longitudinal data collection was again stressed.

"You can see trends. You can also see stock outs. That is clearly indicated and when we have changed antibiotic because of the stock out. If there is a small outbreak of a specific issue, at the moment we've got a massive increase in the tigecycline usage related to multi drug resistant acinetobacter infections. C.diff [Clostridium difficile] and vancomycin is one of the other one. We can see an increase in infections that does not necessarily get reflected in the microbiological data, or if we put them together, you can get a better picture. And we have noticed in certain departments, reduction in usage. I think 6 months is a minimum of what you would look at to see where you are." (IDS1: Prelim.)

"We have seen certain trends especially all of a sudden when we get a lack of change in IV to oral and those kind of things, but in general when you look over the two years, there has been very little change,…" (P2: Prelim.)

Even though one of the research sites (Hospital B) was not involved in quantifying antimicrobial usage, one respondent was still knowledgeable about the AMS metrics and the following quotation was given as an explanation as to why the DDD or other AMS metrics would be potentially useful and effective.

"Doctors know 99% of the time what drug they want to use, but they don't know how to use it, that would then tell them what the trends are, what's happening in other places, what is recommended. We've just got printed things e.g. SAMF [South African Medicines Formulary] but we don't know what should be used for this indication right here, right now. Because we all know that 250mg amoxicillin is available but we all know that 250mg amoxicillin is ineffective, right now 1g is effective. It would nice to prove to them why they should be prescribing 1g amoxicillin instead of 250mg, that would be nice evidence based to tell what is the prescribing trends right now and this is what we should be using." (P6: Prelim.)

One respondent was not able to comment on the application of the DDD, as the research site (Hospital A) was not involved in quantifying antimicrobial usage. The respondent (MP1) could not also provide an opinion of the use of the AMS metrics. This will be further elaborated under the challenges experienced (Theme 4).

"I would not know because I don't know about them [AMS metrics]." (P7: Prelim.)

4.2.2.3 Theme 3: Extraction of data

As previously stated, the semi-structured interviews revealed that the DDD was being used at two of the five research sites (Hospital C and Hospital D). The source and nature of the data available for compiling DDD consumption data was explored in the theme of extraction of data. Referring to this process, the respondents were asked several questions, namely: what data was required to calculate the DDD and where did they obtain the required data in order to calculate the DDD.

The respondent (P2) was the only respondent responsible for compiling the DDD consumption data at Hospital C. The detailed process of how the DDD values were obtained was explained during the semi-structured interview.

Interviewer: "Where is the data extracted from?"
Respondent: "From the Rx Solution® [dispensing system]." (P2: Prelim.)

When asked about the details of the actual data that was being extracted from Rx Solution®, the respondents identified that the consumption data of antimicrobials, i.e. dispensed antimicrobials per patient and per ward, was extracted from the dispensing system.

Interviewer: "What do you extract from the system?"
Respondent: "It is consumption data." (P2: Prelim.)

Interviewer: "Do you know what data is extracted from Rx Solution® to be able to calculate the DDD?"
Respondent: "Consumption data." (P4: Prelim.)

"I think the data that she[the pharmacy manager] uses is the [consumption] data that is issued to the wards, not what's administered. It's what is issued, from dispensing data and ward stock issues." (P3: Prelim.)

Other respondents practicing at Hospital C were all in agreement regarding the source and the type of the data obtained. One respondent (P4) also accentuated on the fact that the process of extracting the data from the Rx Solution® and calculating the DDD was a manual process.

"It [consumption data] is on our dispensing system, on Rx Solution®. You have to calculate it manually and put it into a spreadsheet and work it out. The system does not calculate it automatically, you have to extract the data and then calculate it." (P4: Prelim.)

"In the pharmacy, you have Rx Solution® and it both has the ordering as well as the dispensing component to that. On the dispensing component, the data is manually extracted, looking at all the different antibiotic classes, and in-patient versus outpatient, IV and oral, and then that is supplied on a monthly spreadsheet…" (IDS1: Prelim.)

Even though, Hospital D was also involved in the compilation of DDDs, the respondents practicing at the research site (Hospital D) did not know much detail about the process of calculating the DDD as the respondents were not personally involved in the calculation of the DDD.

"It has identified any trends in terms of consumption for that time period, but I don't know more details." (P8: Prelim.)

"It's quite complicated in terms of how the antibiotics go…there is ward stock, pharmacy issue items…It does get extracted from Rx Solution®, and the pharmacist works with the data in Excel® and she tries and adjust it but I don't do all that detail." (IDS3: Prelim.)

In addition, the DDD consumption is usually expressed and reported as a rate per in-patient hospital days (South African National Department of Health, 2017a). At the research site (Hospital C), the relevant information was obtained from the District Health Information System (DHIS), which is the hospital-based database. Additionally, it was confirmed by one of the respondents (P8) practicing at Hospital

D that the number of patient days was certainly obtained from the hospital-based database, which was referred as *"information technology"* by the respondent.

"…We look at the overall consumption which would be in Defined Daily Doses and then we can have a denominator as the in-patient hospital days." (IDS1: Prelim.)

"…which we can then take on the hospital information system, the DHIS, looking at the in-patient bed-days, to look at the denominator…" (IDS1: Prelim.)

"The number of [patient] days we get it from IT [information technology]. There is a stats [statistician] person there who calculate the increase in number of days." (P8: Prelim.)

However, one of the respondents (IDS1) stated they have not been able to find an association between the DDD and the in-patient hospital days.

"…We haven't finalised that reporting component [AMS metric denominator]. At the moment, most of it is just a sum of Defined Daily Doses, so total consumption. The denominator component we are still working on, finalising the best evaluation." (IDS1: Prelim.)

"…What we haven't done is that we haven't been able to connect that [the Defined Daily Dose] yet to the in-patient days. We will have to go back retrospectively and look at the in-patient days and correct it for that…" (IDS1: Prelim.)

When asked to describe the calculation of the AMS metrics, two of the respondents described the process as follows and both respondents were in agreement with each other. The DDD was calculated by dividing the number of grams of a specific antimicrobial dispensed by the WHO DDD value, which is usually obtained from the WHO website.

"I check the DDD from the WHO website, what gram equivalent the DDD is and then I check on the dispensing system basically, how many DDD or how many grams were dispensed and I convert it to that [DDD]." (P2: Prelim.)

"…I know you calculate it [DDD] with the actual grams used and you divide it by the World Health Organization DDD…" (P3: Prelim.)

It was observed that as a result of being Rx Solution® users, the pharmacists were more acquainted with the software and were, therefore, able to provide opinions on the use of Rx Solution®. This is due to the fact that, Rx Solution® is a dispensing programme, which is utilised by the pharmacists for the dispensing of medications. The programme is currently being used in the South African public healthcare sector in eight of the nine provinces, including the Eastern Cape, being the province where the research sites were situated. It may be interesting to note that other provinces also use other programmes and are not limited to Rx Solution®. However, further investigation related to the other programmes utilised was not done.

4.2.2.4 Theme 4: Challenges

It was evident that the respondents experienced several challenges during the process of monitoring the antimicrobial usage. The different types of challenges will be further presented below.

The first challenge identified by one of the pharmacists and two infectious disease specialists pertained to the functionality of Rx Solution®. As previously stated, under Theme 3 (section 4.2.2.3), the consumption data is currently manually extracted from the dispensing programme, Rx Solution®. It was, therefore, established that the DDD consumption reports were tedious to produce. One respondent (IDS3) also described Rx Solution® as being *"not very user friendly in generating data"*.

"It's very time consuming because the reports don't exist on that, it's very difficult actually to get anyone to give decent input into Rx Solution® at the moment. Even though it's an electronic system, it's a manual process of extracting the data. The data is there; it's just getting it out is as tedious as putting it in." (P2: Prelim.)

"…You have to actually manually calculate it and put it into a spreadsheet and work it out. The system [Rx Solution®] does not calculate it [the DDD] automatically, you have to first extract the usage data and then calculate it." (P4: Prelim.)

"…but the problem is that it takes a lot of manual extraction. Unfortunately, there isn't a programme, which you can use that automatically extracts it; you have to manually extract it. So it is very labour intensive." (IDS1: Prelim.)

It can, therefore, be concluded that Rx Solution® appears to have to all the required information to obtain the DDD metric reports. However, the software does not have the capacity for automatically generating reports on the AMS metrics making the programme unsuitable in its current form for the purposes of generating AMS monitoring data.

Another challenge that was identified focused on concerns raised regarding the perceived accuracy of monitoring the antimicrobial usage. As previously stated, the DDD consumption reports were calculated based on dispensed and not administered antimicrobials. Other limitations were described such as the practice of providing frequently prescribed antimicrobials to the wards as ward stock, to be dispensed and administered by nursing staff. The accuracy of antimicrobial consumption data pertaining to ward stock was difficult to track with respect to the actual number of doses administered to patients, raising concerns about inaccurate AMS metrics reports. One of the respondents (P2) highlighted the fact that the pharmacists were able to record the number of units of antimicrobials that were issued to the ward, but not necessarily the number of units administered to patients.

"…But a lot of antibiotics are also ward stock. So those ones are also quite difficult to monitor." (P8: Prelim.)

"I look at the dispensing, but we have certain antibiotics that are ward stock, so we do them under demander transfer so that we have records of everything that goes either at ward stock or dispensed per patient on our dispensing system, so I look at that data. It is not 100% correct because whatever was dispensed for the patient is

not necessarily what's administered to that patient. I don't look at what was actually administered. I look at what was issued." (P2: Prelim.)

One of the respondents (P2) thought of introducing AMS ward rounds, where the total antimicrobial usage could be checked per patient file. The AMS ward rounds would be of value to the AMS practitioners in order to produce more accurate AMS metric reports.

"…because I have been hoping to have antimicrobial stewardship ward rounds in the hospital where we would be able get our total antimicrobial usage, but that has not happened." (P2: Prelim.)

One respondent practicing at Hospital C affirmed that however, the AMS ward rounds that were predominantly taking place only focused on assessing the appropriateness of treatment, i.e. the discussion of patient cases.

"The only thing that I do…I just attend the antimicrobial stewardship rounds on a Friday, where they address to patients and just discuss a case." (P5: Prelim.)

As previously stated, Hospital A was not involved in the compilation of AMS metric reports. When one respondent (P1) practicing at Hospital A was asked if Rx Solution® was ever used to extract antimicrobial usage data at the hospital, it was explained that, even if AMS metrics reports had to be generated, the reports would likely be inaccurate as not every prescription was captured on Rx Solution® before dispensing medications to patients. The respondent explained that, in certain departments, the pharmacists did not have access to computers in order to dispense medications on Rx Solution®.

"…The only problem that we have is not everyone is capturing the scripts on Rx Solution®, so you have a couple of scripts slipping by where people are doing it manually, because in some departments we don't have enough computers…" (P1: Prelim.)

Another respondent practicing at Hospital A confirmed the fact that Rx Solution® was available at the Hospital A. However, the pharmacists were not always making use of the dispensing programme at the research site.

"No, ours [Rx Solution®] is not functional." (P7: Prelim.)

"…Rx solution® is not used properly. They use it [Rx Solution®] today and after three days, they [the pharmacists] don't use it because nobody is watching them or the computers are off. They [the pharmacists] decide to give it [the prescription] out manually." (P7: Prelim.)

Another challenge that was identified was the lack of resources available for AMS monitoring in the area of paediatrics and renally impaired patients. Some respondents expressed their views on the fact that it cannot be applied in certain population groups.

"…or obviously if the patient has any renal impairment, the Defined Daily Dose is going to change." (P1: Prelim.)

"…It is not very accurate for specific populations. You can't use [DDD] for paediatrics or neonates or even renally impaired patients…" (P3: Prelim.)

When respondent (IDS2) was asked about the usage of the common AMS metric like the DDD to monitor antimicrobial usage, it was substantiated that the DDD was not used in the paediatric ward of Hospital D as the DDD values are not applicable for use in children. In fact, another respondent (IDS3) agreed with the statement of respondent (IDS2). The respondent (IDS3) elaborated on the fact that dosing in paediatrics varies according to the body weight. Consequently, the DDD values would show an overestimation of antimicrobial usage in this population group.

"Well, we can't use that [DDD] in children because there aren't Defined Daily Dose for children…so we don't actually have a method of measuring." (IDS2: Prelim.)

"We are aware that there are some limitations and I have seen some studies that say that it may underestimate or overestimate in some context…it seems that there are no standard for paediatrics due variation of dosing in paeds according to the weight. In paeds, it's quite a non-representative value. It got some values just for some broad picture and trends…but for some antibiotics, it may underestimate or overestimate usage. Sometimes we are using higher doses than the Defined Daily Dose, so they skew the findings. It is useful over times in terms of trends but I am aware that it does not give you the full picture of your antibiotic usage." (IDS3: Prelim.)

The respondent (IDS2) was further asked if any other AMS metrics other than the DDD were used in children. However, the only method employed to measure the antimicrobial usage for the paediatric ward was the total of the number of vials and/or grams.

"We haven't quite figured what [AMS metric] we're going to use here at the hospital. There aren't metrics for children, all we can do is measure the usage in the ward." (IDS2: Prelim.)

Although the DDD was identified as a *"useful marker"* in an AMS programme by one of the respondents (IDS1), it was concluded that the DDD cannot be used on its own to evaluate the antimicrobial usage.

Concerns were raised by one respondent regarding the implementation of AMS, and monitoring of antimicrobial usage at one of the research sites (Hospital A), where the lack of leadership by pharmacy management was described as a contributing factor to the lack of AMS activities.

"…Antibiotic stewardship is not practiced here [at the hospital], *Rx solution® is not used properly…"* (P7: Prelim.)

"…It's a lack of leadership here in this pharmacy." (P7: Prelim.)

The lack of adequate training on the specific use of AMS metrics was described by one respondent (P4). As formerly discussed under Theme 2 (section 4.2.2.2), the

majority of the respondents had completed formal AMS training. However, it was apparent that some respondents were not familiar with the AMS metrics.

One respondent (P4) practicing at Hospital C was asked about the usefulness and effectiveness of the DDD. The respondent reported that the DDD consumption data was not really put into practice as required and it was important to train the AMS healthcare practitioners on the use of the AMS metrics before even thinking of generating AMS metric reports.

"I think we haven't actually really applied it [DDD] as we should. I think people need more training on [AMS] metrics, how to use it effectively and how to assess your stewardship or usage and actually use it effectively. It's no point of just generating data but you can't use it." (P4: Prelim.)

Respondent (P2) was asked the reason why the DDD was the only AMS metric used at the hospital. It was reported that respondent (P2) was only familiar with the DDD.

"It was the only one [AMS metric] that I was aware of when I started doing it." (P2: Prelim.)

Another respondent (P7) could not give an opinion on the usefulness and effectiveness of the AMS metrics as the research site (Hospital A) was not involved in quantifying antimicrobial usage with the use of AMS metrics.

"I would not know because I don't know about them [AMS metrics]." (P7: Prelim.)

The respondent (MP1) was unable to provide an opinion on the usage of the most common AMS metrics as he was personally not involved in that kind of surveillance.

Me: "Do you use the most commonly encountered antimicrobial stewardship metrics like the Defined Daily Dose or the Prescribed Daily Dose to monitor antimicrobial usage?"
Respondent: "No, I don't do that kind of epidemiological data collection." (MP1:Prelim.)

Me: "Do you know about those metrics?"
Respondent: "I have heard of them, yes." (MP1:Prelim.)

Me: "Do you know how effective and useful are those metrics?"
Respondent: "I don't know." (MP1:Prelim.)

As previously discussed under Theme 2 (section 4.2.2.2), the National Department of Health had emphasised on the reporting of DDD consumption data (South African National Department of Health, 2017a). It may, thus, be concluded that the AMS practitioners do not appear to possess sufficient knowledge on the application of the AMS metrics. As a result, AMS training, which focuses more on the application of the AMS metrics, should be provided to the AMS practitioners.

It was previously mentioned under Theme 2 (section 4.2.2.2), that AMS principles are not always practiced in the South African public sector hospitals. One of the respondents (IDS1) explained the fact that AMS is not yet considered as an important focus from the hospital's management point of view and this could be a possible reason why AMS was given very little attention in the public sector hospitals.

"We are still in the implementation phase. I think until we provide the data to show the management what the issues are, it's difficult for them to be more involved. I'd like to say, there is a start from the medical manager, but it has not been taken up across the board as an important focus. I think there is still more that can been done from the management point of view to support antimicrobial stewardship." (IDS1: Prelim.)

4.2.2.5 Theme 5: Implementation of an antimicrobial usage reporting tool

As previously explained under Theme 4 (section 4.2.2.4), the respondents described difficulties in extracting consumption data from Rx Solution® in order to produce relevant AMS metric reports for AMS monitoring purposes. It was concluded that the dispensing programme, Rx Solution® does not have the capacity for automatically generating reports on the AMS metrics making the programme unsuitable in its current form for the purposes of generating AMS monitoring data. Therefore, the

respondents were asked to express their views on the usefulness of implementing a computer-based software that would generate AMS metric reports and would be utilised in the monitoring of the antimicrobial usage for the South African public sector hospitals. The majority of the respondents were in agreement that a computerised antimicrobial usage reporting tool was essential for the public sector hospitals. One of the respondents (P4) proposed that a software with built-in AMS metrics would have been a better option instead of having to manually extract the data from Rx Solution®. Another respondent (P6) commented that the antimicrobial usage reporting tool would enable the AMS practitioners to integrate information from the microbiological lab results together with the AMS metric reports in order to identify the trends of antimicrobial usage.

"I think a system where those metrics are built-in in a software would have been much better." (P4: Prelim.)

"Definitely…because you could see then, which antibiotic is being used more in which ward, knowing which specialties are in which wards. So it would make sense and together with the information from the micro lab, you would be able to see what trends are happening, so the two [antimicrobial usage and lab results] converging would make more sense." (P6: Prelim.)

Another respondent (MP1) expressed that an antimicrobial usage reporting tool would only be useful if electronic prescriptions were used. It can be implied that if the option of electronic prescribing was available, an alternate AMS metric, for example the Prescribed Daily Dose (PDD), could have been used and compared with the DDD metric reports.

"Only if the prescribing is done electronically. If you use electronic prescription, then a computer software will be useful." (MP1: Prelim.)

Furthermore, when another respondent (IDS3) was asked about the usefulness of extracting data from Rx Solution®, it was established that with the help of local expertise, one of the research sites (Hospital D) had adapted Rx Solution® to suit their needs. However, it is also important to note that this function was not yet made

available to all the public sector hospitals. Therefore, until function is made available, it would still be a challenge to generate AMS metric reports.

"From what I understand, it's quite difficult. I don't know if it [Rx Solution®] was designed to do that. There are challenges in getting support from the guy that's no longer a contract. There was a period of support and that's now finished. It has been quite of a headache. We had a guy from the UK who was working together with one of the guy that had written Rx Solution®. From what I understand, they wrote an extraction tool programme that helped with the extraction. It does manage to get data out of Rx." (IDS3: Prelim.)

One of the respondent (IDS1) again emphasised on the need to have an electronic system to monitor the antimicrobial usage due to the fact that manual compilation of data was quite time consuming. The respondent (IDS3) also agreed on the usefulness of implementing an antimicrobial usage reporting tool, as it would allow AMS practitioners to identify high usage of antimicrobials and subsequently implement appropriate interventions.

"I think anything that requires manually collected data is bound to fail because people don't have the time." (IDS1: Prelim.)

"Anything that can give us easy data would be great. At the moment, it's still a lot of work and headache. It would be nice to have easy and accessible data in the public sector to try and monitor ours stewardship efforts and try and pick up where the high usage in which departments are and try and have interventions. We want make the feedback loop as easy as possible." (IDS3: Prelim.)

The need for optimal utilisation of an existing database was recognised by one respondent (P4). Since consumption data is currently being extracted from Rx Solution®, the antimicrobial usage reporting tool should ideally be interfaced with Rx Solution®, in such a way that the data could automatically be imported into the antimicrobial usage reporting tool from Rx Solution®.

"... look the data is on Rx, I think the best way is that the software programme is written in such a way that it is interfaced with Rx and you can extrapolate the data from Rx into the new programme..." (P4: Prelim.)

"...Maybe if we can't fix Rx, then there should be an interface that links, that extrapolates the data from Rx solution® and built it in into the software and then calculate it..." (P4: Prelim.)

On the other side, one respondent justified that it would be convenient to link the antimicrobial usage reporting tool to Rx Solution® with the objective of facilitating the transfer of data, but this would be regarded as a technical issue.

"This is a technical issue, whether it's linked or not. To me it doesn't seem to make much difference as long as the information can be extracted and put into a report form. It would make sense to link it, because then that transfer of information could be automatic. If you are using Rx Solution®, then ideally the report system should come off the same thing, unless you are using a completely different system. But if the majority of people are using the one system, it would make sense to link it." (IDS1: Prelim.)

Another respondent (P2) believed that the antimicrobial usage reporting tool should either be linked to Rx Solution® or a different dispensing system should be used.

"Either I think it should be linked to Rx Solution® or we would have to change the dispensing system. I don't believe in having multiple systems running." (P2: Prelim.)

It was earlier stated under Theme 3 (section 4.2.2.3), that the AMS metric denominator, the number of patient days is usually obtained from the DHIS or hospital information system. In addition to being linked to Rx Solution®, one respondent (P8) commented that the antimicrobial usage reporting tool should be also linked to the hospital information system, where the number of patient days would be available. The hospital information system was referred as IT (Information technology) by the respondent.

"Yes, you need IT [information technology] to be involved in order to link that information if you want the consumption data, the DDD, instead of doing it manually." (P8: Prelim.)

The respondent (IDS1) also pointed out that it would be a challenge in getting the AMS practitioners to make optimal use of the antimicrobial usage reporting tool. The implementation of a new programme in the South African public sector hospitals would entail more focused training on the use of the software so that users could optimally utilise the data.

"…But if there would be an automatic programme that would run a spreadsheet that gave us a specific set of indicators that people have agreed on, as part of a stewardship programme…I think the benefit would be that it would be standardised, it would be measurable, it would be useful…but it does require that everyone is using the same system and would generate the same report and using it consistently. I think it's useful in that sense. The problem in getting people to use it and to roll out the system more broadly is more difficult. So I think that's the feel of the electronic system…" (IDS1: Prelim.)

Overall, the implementation of a computer based software to monitor the antimicrobial usage would undeniably be beneficial for the South African public sector hospitals. It would allow AMS practitioners to track the usage of antimicrobials far better than using a manual system. At the same, it will eliminate the time-consuming work that the AMS practitioners have to do and allow them to focus on AMS interventions to improve the usage of antimicrobials.

4.3 Developmental Phase

Since the dispensing programme Rx Solution® was unsuitable in its current form for the purpose of automatically generating AMS metric reports, the need for a proposed antimicrobial usage reporting tool was required for the South African public sector hospitals. During the development phase of the study, the quantitative and qualitative data obtained from the preliminary phase of the study was utilised in the development

of the framework for a proposed antimicrobial usage reporting tool. The framework for the proposed antimicrobial usage reporting tool is presented in Figure 4.15.

It was identified from the qualitative data obtained during the preliminary phase that the dispensing data available on the dispensing component of Rx Solution® is currently manually extracted into a Microsoft Excel® spreadsheet format, and the data is then re-entered manually into another Microsoft Excel® spreadsheet, in order to manually calculate the relevant DDD metric reports.

Ideally, the dispensing data obtained from Rx Solution® should be extracted into a Microsoft Excel® spreadsheet format, as shown in Table A1. The antimicrobial usage reporting tool should be interfaced with Rx Solution®, in such a way that Table A1 could be imported into the antimicrobial usage reporting tool so as to facilitate the calculation of DDD metric reports (Option A). The DDD metric reports would be in the format of Table A1a. Additionally, the number of patient-days is currently obtained from the District Health Information System (DHIS) and it is manually entered into the Microsoft Excel® spreadsheet in order to obtain the DDD per 100 patient days. Therefore, the DHIS could also be linked to the antimicrobial usage reporting tool in such a way that the number of patient-days could be automatically imported into the antimicrobial usage reporting tool. The antimicrobial usage reporting tool could also include an automatic graph generating function, which would be able to collate the DDD values calculated (Table A1a) and generate graphs of DDD per 100 patient days for each antimicrobial agent per month, year and/or ward.

The respondents also described difficulties in tracking the quantities of antimicrobials dispensed as ward stock to the ward, and this limitation was seen to contribute to inaccurate DDD metric reports. Therefore, an electronic medication administration record (eMAR) function could be considered for inclusion into Rx Solution® as it would be easier to track the ward stock and record antimicrobial usage for each patient. The same process of extracting and calculating the DDD from the eMAR data would apply (Table A2) and the DDD consumption data would be in the format of Table A2a. The eMAR function would also enable the AMS team to track the Days of Therapy (DOT) of each antimicrobial dispensed, per patient. The data would be

extracted in the format, as shown in Table B. Option B would, therefore, help to generate DOT metric reports per patient-days for each antimicrobial agent per month, year and/or ward in the format of Table B1a.

The electronic prescribing (E-prescribing) function is another function, which could be considered for addition into Rx Solution®. E-prescribing data would be imported into the antimicrobial usage reporting tool in the format (Table C). Moreover, option C would enable generation of PDD metric reports per patient-days for each antimicrobial agent per month, year and/or ward in the format of Table C1a. The automatic graph generating function would, therefore, be used to generate graphs of DOT and PDD per patient days.

Furthermore, it should be noted that the dispensing component of Rx Solution® is already being utilised by the pharmacists for the issuing of medications per patient and per ward, including antimicrobials. For the eMAR component to function effectively, the eMAR function should be available and utilised in the wards, where the nurses would be able to electronically record the administration of antimicrobial agent for the specific patients. In addition, the medical team could electronically prescribe medications, including antimicrobial agents, through the E-prescribing function. The legality concerning the status of E-prescribing in South Africa will be discussed in Chapter Five. As previously described, both eMAR and E-prescribing data would then be extracted from Rx Solution® into the antimicrobial usage reporting tool and utilised to compile DOT and PDD metric reports respectively. A discussion of the developmental phase will be presented in Chapter Five.

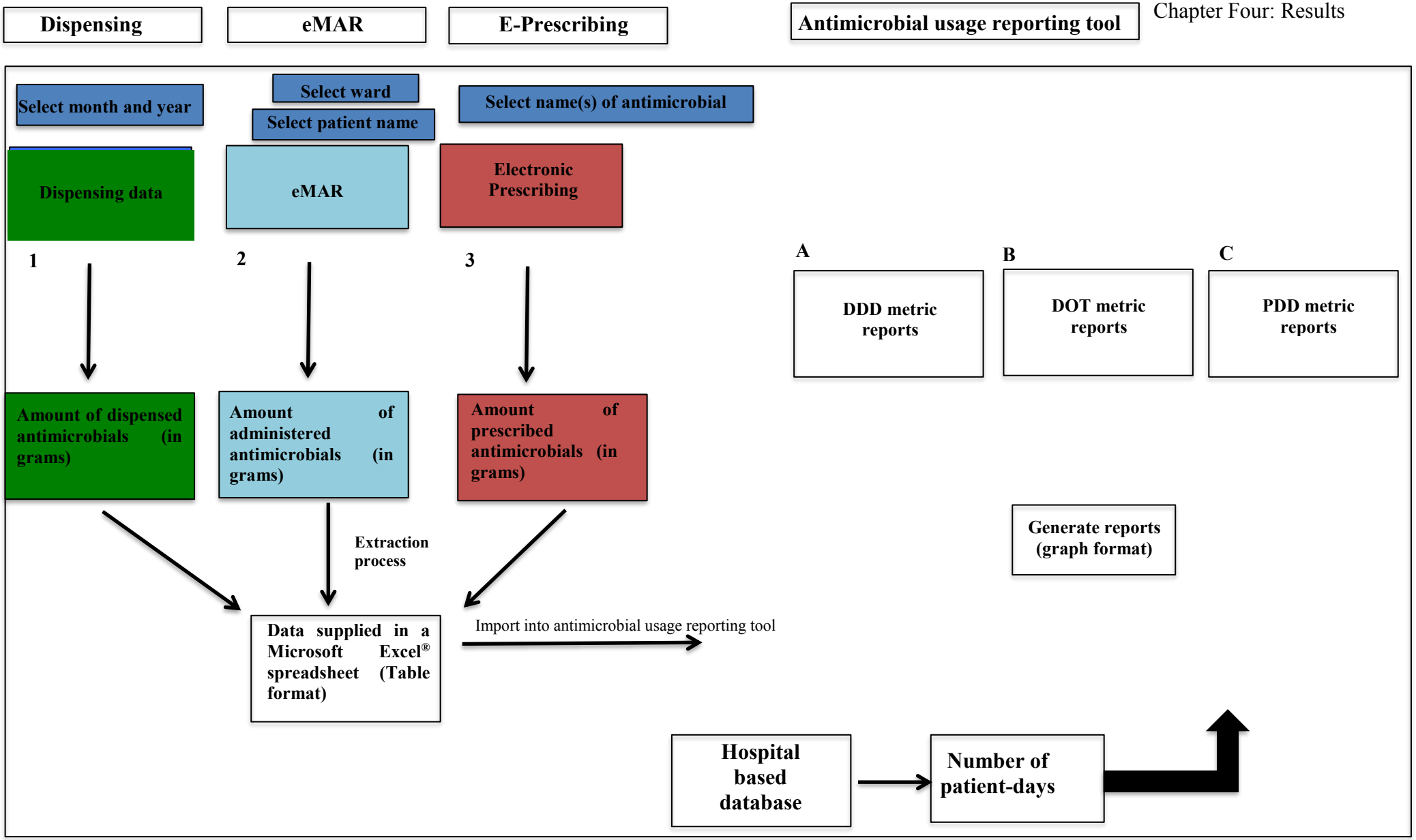

Figure 4.15 Framework for a proposed antimicrobial usage reporting tool for public sector hospitals

The values presented in the following tables are fictitious values, which help to understand how the data would be presented.

A1: Data extracted to calculate the DDD (from dispensing component)

Month/Year/Ward	Antimicrobial agent	ATC code	Route of administration	Number of grams per unit dose	Quantity issued (in grams)
November 2018/ Medical Ward	Amoxicillin 500mg	J01CA04	Oral	0.5	50*[1]
	Amoxicillin 1g	J01CA04	Parenteral	1	100*[2]

*[1]: Includes number of grams dispensed per patient and per ward
*[2]: Includes number of grams dispensed per patient and per ward

A1a: DDD metric reports (obtained from antimicrobial usage reporting tool)

Month/Year/Ward	Antimicrobial agent	Route of administration	Quantity issued (in grams)	WHO DDD*	DDD	DDD/100 patient days
November 2018/ Medical Ward	Amoxicillin 500mg	Oral	50	1 g	50	
	Amoxicillin 1g	Parenteral	100	1g	100	

*Automatically inserted by the antimicrobial usage reporting tool

A2: Data extracted to calculate the DDD (from eMAR component):

Month/Year/Ward	Antimicrobial agent	ATC code	Formulation	Number of grams per unit dose	Quantity administered (in grams)
November 2018/ Medical Ward	Amoxicillin 500mg	J01CA04	Oral	0.5	0.5g x 40 doses = 40g
	Amoxicillin 1g	J01CA04	Parenteral	1	1g x 80 doses = 80g

A2a: DDD metric reports (obtained from antimicrobial usage reporting tool)

Month/Year/Ward	Antimicrobial agent	Formulation	Quantity administered (in grams)	WHO DDD*	DDD	DDD/100 patient days
November 2018/ Medical Ward	Amoxicillin 500mg	Oral	40g	1 g	40	#
	Amoxicillin 1g	Parenteral	80g	1g	80	#

*Automatically inserted by the antimicrobial usage reporting tool

B: Data extracted to calculate the DOT (from eMAR component):

Month/Year/Ward/ Patient details	**Antimicrobial agent**	**Route of administration**	**Date and Time of antimicrobial administration**		
November 2018/ Medical ward/ Patient A	Amikacin 1g IV every 24 hours	Intravenous	01/11/18	02/11/18	03/11/18
				7 am	7 am
	Meropenem 1g IV every 8 hours	Intravenous	3pm 11pm	7am 3pm 11pm	7am 3pm 11pm

Ba: DOT metric reports (obtained from antimicrobial usage reporting tool)

Month/Year/Ward/ Patient details	**Antimicrobial agent**	**Route of administration**	**Date and Time of antimicrobial administration**			**DOT**	**DOT/100 patient days**
November 2018/ Medical ward/ Patient A	Amikacin 1g IV every 24 hours	Intravenous	01/11/18	02/11/18	03/11/18	2DOT	#
				7am	7 am		
	Meropenem 1g IV every 8 hours	Intravenous	3pm 11pm	7am 3pm 11pm	7am 3pm 11pm	3 DOT	#

C: Data extracted to calculate the PDD (from E-prescribing component):

Month/Year/Ward	Antimicrobial agent	Formulation	Number of grams per unit dose	Quantity prescribed (in grams)
November 2018/ Medical Ward	Amoxicillin 500mg	Oral	0.5	0.5g x 50 doses = 25g
	Amoxicillin 1g	Parenteral	1	1g x 50 doses = 50g

Ca: PDD metric reports (obtained from antimicrobial usage reporting tool)

Month/Year/Ward	Antimicrobial agent	Formulation	Quantity prescribed (in grams)	PDD	PDD/100 patient days
November 2018/ Medical Ward	Amoxicillin 500mg	Oral	25g	25	#
	Amoxicillin 1g	Parenteral	50g	50	#

#:Since patient-days is a variable constant, the relevant AMS metric per 100 patient days would be calculated by the antimicrobial usage reporting tool as required.

4.4 Post-Developmental Phase

During the post-developmental phase, the proposed framework was electronically sent out, via email to the respondents who participated in the preliminary phase of the study. The purpose of the post-developmental phase was to explore the applicability and practicality of the proposed antimicrobial usage reporting tool, prior to implementation.

Feedback on applicability and practicality of the framework for the proposed antimicrobial usage reporting tool was obtained during a second round of semi-structured interviews, which was conducted over a period of two weeks. The 14 respondents who participated in the qualitative component of the preliminary phase were invited to participate in the post–developmental phase. However, only nine respondents agreed to participate, resulting in a response rate of 64.3%. Five respondents did not consent to participate in the semi-structured interviews due to time constraints in their daily routine in the workplace. As the post-developmental phase only took place over a period of two weeks, time constraints of the researcher also affected the response rate.

The semi-structured interview was guided by the following main questions:

1. The purpose of this study was to develop a framework for a proposed antimicrobial usage reporting tool for South African public sector hospitals. What is your overall impression about this framework?
2. Do you feel that the framework for the proposed antimicrobial usage reporting tool could fulfill the requirements for effective AMS monitoring?
3. How practical, applicable and beneficial do you think the framework for the proposed antimicrobial usage reporting tool is to the South African setting?
4. How feasible do you find the implementation of the framework for the proposed antimicrobial usage reporting tool?
5. What challenges do you expect to be faced in implementing the framework for the proposed antimicrobial usage reporting tool?

The transcribed interviews were organised into codes and sub-organised into themes using the qualitative data analysis software programme, Atlas.ti® (version 8.2.1). The identified themes generated from the semi-structured interviews are presented in Table 4.4. Out of the 14 respondents who participated in the preliminary phase, nine respondents agreed to participate in the post-developmental phase. Feedback from all 14 respondents could not be obtained due to time constraints of the respondents. The pharmacists (P), infectious disease specialists (IDS) and medical prescribers (MP) were de-identified and renamed with the same prefix P, IDS and MP respectively with the aim of preserving respondent anonymity. The respondents were assigned a number as a suffix. The term 'Post' was also added as a suffix in order to illustrate that the researcher was referring to the post-developmental phase. The respondents were identified as follows: e.g. (P1: Post). All direct quotations from the transcripts will be presented in italics font followed by the respondent's unique identifier in brackets. A discussion of the findings obtained during the post-developmental will be presented in Chapter Five.

Table 4.4 *Themes identified during analysis of qualitative data derived from semi-structured interviews during the post-developmental phase*

Themes
1. Overall impression of the framework for the proposed antimicrobial usage reporting tool
2. Factors related to the implementation of the framework for a proposed antimicrobial usage reporting tool
3. Challenges expected to be faced in the implementation of the framework for a proposed antimicrobial usage reporting tool
4. Practical solutions to be implemented

4.4.1 Theme 1: Overall impression of the framework for the proposed antimicrobial usage reporting tool

The first theme to be identified focused on the overall impression of the framework for the proposed antimicrobial usage reporting tool. The following opening general question was asked to all the respondents:

"The purpose of this study was to develop a framework for a proposed antimicrobial usage reporting tool for South African public sector hospitals. What is your overall impression about this framework?"

One respondent (P1) mentioned the fact that the framework *"is ideal because it includes antibiotic usage at every level in the hospital"* and it takes *"all factors into account"*, therefore, it would provide accurate information on antimicrobial usage data, i.e. the framework considers three different AMS metrics at three different levels: pharmacy level, nursing administration level and prescribing level. Respondent (P2) also reflected that the framework includes all the information required for the purpose of monitoring antimicrobial usage and it would, therefore, be an initial point for implementing AMS interventions. Respondent (P3) and respondent (P4) also agreed that the implementation of the proposed antimicrobial usage reporting tool would be useful throughout the South African public sector hospitals as it takes into consideration three different AMS metrics, while respondent (P7) was of opinion that the implementation of the proposed antimicrobial usage reporting tool would ensure a multidisciplinary approach towards AMS, i.e. the medical prescribers, pharmacists and nurses, would be able to influence the antimicrobial usage.

"The framework takes all factors into account and will give an accurate figure…". (P1: Post)

"I think, it [the framework for the proposed antimicrobial usage reporting tool] sounds good. I think, it includes everything…Otherwise, I'm happy with the framework. I think, it makes sense and it includes all the information that you need." (P2: Post)

"It [The framework for the proposed antimicrobial usage reporting tool] could give the proper information on the antimicrobial usage. I think, that is all it gives; it can give the usage data. Then obviously, there will have to be decision making on that to actually have an impact on the antimicrobial prescribing and usage. I think, the tool is good to actually get that information to work with." (P2: Post)

"I think, it's fantastic that you are doing it. I think, throughout the public sector hospitals, it would be useful..." (P3: Post)

"Definitely, the fact that it [the framework for the proposed antimicrobial usage reporting tool] takes into consideration all three [AMS metrics], I think it would be very useful." (P3: Post)

"…You've covered dispensing data, and then the administration part in the ward, and then the prescribing side. You've managed to cover those three important spheres. I think it can work." (P4: Post)

"I would welcome it [the framework for the proposed antimicrobial usage reporting tool]. Because, I feel, with antimicrobial stewardship, everyone has to get involved in it and by doing it this way, I'm sure everybody will be able to have an impact on the use…" (P7: Post)

The respondent (P4) supported the idea of the framework for the proposed antimicrobial usage reporting tool as the respondent was one of the pharmacists, who stressed on the need of having one integrated system, while respondent (P6) reflected that the proposed antimicrobial usage reporting tool would definitely be an achievement for the South African public sector hospitals.

"I was one of the pharmacists who said that we need one platform. In theory, I like it…" (P4: Post).

"Yes, I can definitely see that it would be a better step in the right direction." (P6: Post)

Additionally, the respondent (IDS1) stated that the proposed antimicrobial usage reporting tool would indeed be beneficial if, from the dispensing point of view, appropriate graphs of the AMS metric reports could be automated from Rx Solution®. However, the respondent was not acquainted with the electronic medication administration records (eMAR) and E-prescribing components, and was, therefore, unable to provide an opinion on incorporating those functions into Rx Solution®, and

subsequently producing the DOT and PDD metric reports. The respondent also reported the uncertainty on the feasibility of including those additional components in the framework. The feasibility of implementing the proposed antimicrobial usage reporting tool will be further discussed under Theme 3 (Challenges expected to be faced in the implementation of the framework for a proposed antimicrobial usage reporting tool). Overall, the respondent agreed that the tool would be able to support AMS decision making for the public sector hospitals.

"First of all, I haven't had experience to the eMAR component or to an electronic prescribing component in the government sector. So how those work and how they would function is not clear to me. But, from a dispensing point view and using the DDDs, I think if it can be automated from the Rx Solution® through into a spreadsheet into appropriate graphs, I think it would be useful more broadly, knowing that there are specific downsides to using DDDs… but I think it would be a useful framework. In terms of the additional ones, the eMAR component and the electronic prescribing, you would have to explain a little bit more to me about how practically that would work to see if there is capability to those systems." (IDS1: Post)

"…I think the broader dispensing data on the DDDs is useful from the first component, it provides you with an overall consumption that does not necessarily pick up patient specific data but it does help down to a ward level, saying that this is how much is being prescribed in these wards. I think, the main goal is that it gives you something more standardised to compare across hospitals, across facilities, within a province or across the country to have a look what at the overall consumption is. So, it's a broader marker…" (IDS1: Post)

"…From what I've read in your proposal, the eMAR and electronic prescribing, that would be a more sophisticated way of having a look at who is prescribing how much. It would be more granular data, but whether or not it would be feasible number one, and what impact it would have is still a little bit unclear to me. From a national and a provincial point of view, the DDD would probably at least fulfill those requirements and to some degree, it may fulfill the requirements as a tool to support antibiotic stewardship decision making at a facility level." (IDS1: Post)

The respondent (IDS2) valued the idea of effecting E-prescribing for the South African public sector hospitals, as it would facilitate the ability to monitor antimicrobial usage.

"I do like the idea of an electronic script so that monitoring can be carried in real-time and subsequent to the event occurring." (IDS2: Post)

The respondent (IDS3) reflected that it is not be feasible to regularly generate AMS metric reports in the South African public sector hospitals. From the AMS perspective, the respondent agreed that an automated tool, with the ability of producing AMS metric reports, would be a good proposal for the public sector hospitals. Moreover, the respondent was of opinion that, the use all three AMS metrics: DDD, DOT and PDD, would provide a better overview of the antimicrobial usage.

"…I think, for your average central hospitals in South Africa, that's asking a bit much to generate that kind of data regularly. I think, if we are looking at something more automated, it's definitely more necessary. I think, overall…obviously, for some of the how that you are wanting to do, but it's a good idea to try and think about what's required and to come up with useful reports from the stewardship perspective." (IDS3: Post)

"Ideally, the more information, the more angles you've got, the better. But, if you really want to be smart about how people are using antibiotics, so DDD, DOT, and PDD…if it's doable, it would probably give us better picture..." (IDS3: Post)

It was, therefore, noted that the majority of the respondents agreed on the idea of implementing the proposed antimicrobial usage reporting tool. However, it must be emphasised that this framework in particular took into consideration antimicrobial usage data from all perspectives, i.e. dispensing, nursing administration and prescribing levels. The applicability and practicality of the framework for the proposed antimicrobial usage reporting will be further explored.

4.4.2 Theme 2: Factors related to the implementation of the framework for the proposed antimicrobial usage reporting tool

The respondents were then asked to comment on the factors related to the implementation of the framework for the proposed antimicrobial usage reporting tool. Before intending to implement the proposed antimicrobial usage reporting tool, it was important to discuss the practicality and applicability of the framework in the South African setting.

As previously stated in section 4.4.1 (Theme 1), the framework for the proposed antimicrobial usage reporting tool took into account three different AMS metrics: DDD, DOT and PDD. Despite being described as ideal by one of the respondents (P1), the respondent also took into consideration the fact that some features included in the framework are currently not realistic and feasible for the South African public sector hospitals. Two respondents were mostly concerned about the optimal use of the eMAR component by the nursing staff. One of the respondents (P3) stated that the nurses do not consistently sign in the patient's file after administration of medication and therefore, questioned whether the nurses would have the capacity of optimally using the eMAR system. Challenges related to the eMAR component and challenges related to the involvement of nurses will be investigated and discussed under Theme 3 (section 4.4.3).

"…Unfortunately, some parameters are not realistic in public sector, for example, nurses quantifying antibiotic usage electronically." (P1: Post)

"My only concern, obviously the electronic of the dispensing side will be easy enough, because that's just out of Rx solution® but the actual usage of the electronic medication administration system done by the nurses, that's what you intended, hey?" (P3: Post)

"We just struggle to get them [the nurses] to sign correctly for an administration of an antibiotic. I was wondering how practical and how they would work it out into their routine for them to actually enter it electronically as well as signing on the charts. I suppose, at the end of the day they could just grab all the charts that they get

with antibiotics and they go and sit in front of the computer and manually enter it. I'm just wondering whether they would have the capacity to do that." (P3: Post)

Furthermore, respondent (P3) emphasised on the fact that the medical team of one ward at Hospital C had recently started the electronic prescription of medications, and therefore, the feasibility of incorporating the E-prescribing component into Rx Solution® in the future was not seen as a problem. Respondent (P2) affirmed that E-prescribing was recently initiated at Hospital C, however, it was not linked to Rx Solution® and all the prescriptions had to be re-captured on the dispensing programme.

"We've got the doctors already sort of starting to prescribe, to electronically prescribing. So, that should not be a problem and that's pretty feasible. It's just the nursing staff doing the Days of Therapy. That would be a problem." (P3: Post)

"…We have started doing it [electronic prescribing] but it's not linked at all [to Rx Solution®]…" (P2: Post)

"We can't even get information out of that system because we have to recapture all these scripts on Rx Solution®, so that we get the information through Rx Solution®." (P2: Post)

Respondent (P2) agreed that interlinking all the three components: dispensing, eMAR and E-prescribing, would be the ultimate goal for the South African public healthcare sector as the proposed antimicrobial usage reporting tool would involve no manual re-entering of data.

"I can't compare it to any other setting, I can only look at what we are doing here, and I think, it is appropriate and I think, it is fairly easy to use, especially if everything is interlinked and there is no manual re-entering of data and those kind of things. The way I understand it, it's the ultimate goal to basically have all these systems all linked. Then I think, yes, it will give the right information, it will work, because the systems are available to actually generate the information…" (P2: Post)

Another respondent (IDS1) reflected that the integration of the eMAR and E-prescribing components in the proposed antimicrobial usage reporting tool might not be feasible and is a step too far at this point in time.

"The question is the functionality of that. I see here, when you are dispensing it, that together with E-prescribing, it requires some sort of electronic way of recording it in the ward. That means, there has to be some electronic system in the ward, one to prescribe and one to dispense…and then would that be a tablet or a computer in the ward? It would have to be mobile, I presume, to be able to take it from bed to bed. That in itself already puts multiple barriers to the role out of this system…" (IDS1: Post)

"…But, from a broader point of view, to put this in district hospitals, to put this into other hospitals, I think, perhaps if that is what's required, perhaps it is a step too far at this point…" (IDS1: Post)

The applicability of the framework for the proposed antimicrobial usage reporting tool in the South African public healthcare setting was investigated. One of the respondents (P1) highlighted that the proposed antimicrobial usage reporting tool would be of utmost benefit for Hospital A, due to its ability to produce reports on antimicrobial usage data.

"…But if done correctly, it would be extremely beneficial having this [antimicrobial usage] data since it is applicable for a fully functional AMS at Hospital A." (P1: Post)

It was stated by one respondent (P6) that, if the proposed antimicrobial usage reporting tool was already put in place in the South African public sector hospitals, it would indeed be beneficial for the healthcare professionals wanting to compile AMS metric reports.

"…But in terms, if it was there and we were using it, I don't see any problem. It will only be a plus from a user point of view…" (P6: Post)

The qualitative data obtained during the preliminary phase of the study identified problems related to the ability of tracking antimicrobials dispensed as ward stock. Respondent (P7) again highlighted the inability of tracking antimicrobials being dispensed as ward stock and agreed that an eMAR system could possibly be integrated with the dispensing programme. The respondent stated that the eMAR component would be an ideal way so as to include the antibiotics being as dispensed as ward stock in the DDD metric reports.

"Definitely, like I said, because of those reasons, because we don't have a 24 hours pharmacy service and we don't have enough pharmacists in the wards…They are not based in the wards all the time to record every item that is issued to a patient. Because that was our biggest concern here, like in the ICU, how do we capture those items, like your carbapenems, colistin…that are issued currently as ward stock to those areas because they needed to make it accessible. How do we actually capture those patients that are on treatment to include it in our DDD audit? When I saw this, I thought that [eMAR] would be an ideal way." (P7: Post)

Moreover, the respondent (P7) stated that the implementation of the proposed antimicrobial usage reporting tool would have to be implemented in a phased way, which would require strategic planning to ensure its successful implementation. The respondent also emphasised on the fact that it would be necessary to clarify the role of the nurses and medical prescribers, as they would also involved in the process of data collection. The respondent (IDS1) also agreed that the framework for the proposed antimicrobial usage reporting tool *"could be certainly rolled out in a phased way."*

"I think, it should be phasic. It's a project on its own and being a project, there is planning involved. It's not just putting a system in an environment because in the environment itself, the systems are not actually structured. We need to ask ourselves what we want and where do we want to go to and we need to work towards getting there. I think, then, there will be a better success." (P7: Post)

"…Then, it's the role clarification of what is expected of the nurses and also the physicians in this new phase, where they are also involved with this whole audit. That is also a big issue…" (P7: Post)

In addition, the respondent (P7) mentioned that the implementation of the proposed antimicrobial usage reporting tool in the South African public healthcare setting would eventually entail better results on antimicrobial consumption data.

"We will get better results [antimicrobial consumption data] compared to what we currently have now…" (P7: Post)

Moreover, the applicability of the framework for the proposed antimicrobial usage reporting tool was discussed by respondent (IDS1). The respondent stated that the tool would certainly be useful, however, it would require consistency among the healthcare professionals, i.e. the same framework for the proposed antimicrobial usage reporting tool would need to be used in all public sector hospitals.

"…If you wanting to do this for public sector hospitals, it would be very useful but it requires that everyone uses the same framework and the same dispensing system. Then you would be able to look at comparing. From the programmatic point, it would be very useful…" (IDS1: Post)

"…I think that would be a reasonable tool to use and would be applicable, but keeping in mind that it would need to be…everyone would have to use the same system…" (IDS1: Post)

Respondent (IDS3) stated that DOT is considered useful to include in the framework for the proposed antimicrobial usage reporting tool as it would be more applicable to the paediatrics. The respondent also discussed that the PDD would be able to complement the DDD, in situations, where high doses of antimicrobials, deviating from the WHO-DDD, are actually prescribed. Hence, the respondent was of opinion that it would generally be ideal if all three AMS metric reports could be generated, with the purpose of obtaining a more accurate overview of the antimicrobial consumption data.

"Yes. Most of the guidelines have recommended using the DDDs per 1000 patient days to try and kind of benchmark and compare in different facilities and different

departments in facilities. I think, that is the main metric that you are using. But, I think it is also useful to have the DOT…" (IDS3: Post)

"…There are some limitations of the DDD, where it sort of overestimates or underestimates in some scenarios. And then, the one key area that you would really thought about it is for paediatrics, they can't use DDDs because of the varying weight doses. So, I imagine DOT might be applicable to a paediatric situation, because we can't at the moment…we don't really know, apart from looking it at total consumption in a paediatric unit, we're not really able to try and get a hand on that consumption, whether it is appropriate. I think, having the DDD plus some other metric, that can give us slightly different perspectives on the antibiotic usage, would be useful…" (IDS3: Post)

"That's [PDD] also useful because they has shown that, where some of the limitations of the DDD, where we are maybe using high doses. So that kind of aligns for that, hey?" (IDS3: Post)

Since respondent (IDS2) was not personally involved in the compilation of AMS metric reports at one of the research sites, the respondent could not comment on the practicality and applicability of the framework for the proposed antimicrobial usage reporting tool.

"As a clinician, I am not involved in directly recording and reporting on antimicrobial usage at our tertiary hospital. I do depend on the pharmacists for this purpose. In paediatrics, we cannot use the DDD to monitor antimicrobial usage. So, I am afraid I will not be able to respond to the questions below because it speaks directly to a monitoring tool." (IDS2: Post)

4.4.3 Theme 3: Challenges expected to be faced in the implementation of the framework for the proposed antimicrobial usage reporting tool

The respondents were asked to express their views on the challenges expected to be faced in the implementation of the framework for the proposed antimicrobial usage

reporting tool. The first challenge, which the respondents identified, was related to training of healthcare professionals on the use of the proposed antimicrobial usage reporting tool. Three respondents (P1, P7 and IDS1) were of opinion that the implementation of the proposed antimicrobial usage reporting tool would demand intense training from the user point of view. Respondent (P1) further stated that training of other healthcare professionals, such as the nurses and medical prescribers, would be the key to the successful implementation of the proposed antimicrobial usage reporting tool.

"...It requires in-service training and time spent by the AMS committee in order for it [the framework for the proposed antimicrobial usage reporting tool] to be implemented..." (P1: Post)

"Definitely training of nurses and doctors,..." (P1: Post)

"My only comment is it would require rigorous training in order to be successful because it involves electronic collection of data, while some sections in the hospital are still working manually." (P1: Post)

"...Then, there is also the training part..." (P7: Post)

"...I think it would require training to use the data from an individual point of view in the hospital." (IDS1: Post)

"...but I think to get people to use it [the proposed antimicrobial usage reporting tool], will probably be one of the biggest challenges." (IDS1: Post)

However, one of the respondents (P3) drew attention on the fact that "*only one person in the pharmacy would need to extract the information"*. Therefore, training of the healthcare professionals was not seen as a challenge by respondent (P3) as only one pharmacist would be responsible to compile the AMS metric reports. However, the nurses and the medical prescribers would require training in order to obtain accurate initial data to produce the relevant reports.

"I think only one person in the pharmacy would need to extract the information. I don't think that would take too much training…" (P3: Post)

Lack of resources was identified as one of the other challenges expected to be faced. The respondent (P1) mentioned that a lack of human resources at Hospital A, especially at a ward level, would be problematic for the proper collection of data. The respondent (P7) highlighted that the dispensing component of Rx Solution® was not consistently being used at one of the research sites (Hospital A), due to a lack of staff at the pharmacy level. Therefore, the consistency of using the proposed antimicrobial usage reporting tool was being questioned by the respondent.

"…Unfortunately, all data is collected electronically, which is unrealistic, especially at ward level and is time consuming when taking public sector manpower into account." (P1: Post)

"Some sections of the data collection is not practical currently, because it is not being done because of time constraints, lack of knowledge and equipment..." (P1: Post)

"…But time and manpower is the biggest constraint, as wards often complain of staff shortages." (P1: Post)

"Challenges would be…One would always be staffing. With staffing, you can put a system and put it in here. But, would it be consistent? For example, what happen is, we have got Rx dispensing here, and we are understaffed. So, if for example when we are adequate, we are using Rx dispensing, but when one or two people are sick, all of a sudden we can't use Rx dispensing because we don't have enough staff…" (P7: Post)

Respondent (IDS3) discussed the fact that, nurses generally struggle to perform their daily routine work in the wards, and therefore, introducing an eMAR system, might result in inconsistency of using this system. It was, therefore, advised by the respondent, to achieve another feasible way of capturing that kind of data, while obtaining compliance from the nurses.

"…Generally, nurses are completely overburdened in the ward. Anybody who is adding to their work… You have to be very careful, whether or not to adhere to that. You need to try and think of some way of using technology to try and make their lives easier as far as possible. By entering it on the screen, whether it's an ipad or something like that, that it can somehow save them some work. You have to be creative on that one. If all you are asking to do is collect data for you, that's for monitoring, you'll probably get low compliance, from a realistic perspective. The nurses are really struggling and they are really short staffed. They are just struggling in getting their work, in getting the observations done. That would add to their work, especially the prescribing sisters, who are the most experienced person in the ward. There is only one or two, who may have to engage in this and find out what possibly might be acceptable, to try and find a way. It has to be super quick and easy, then preferably try and save them some work somehow." (IDS3: Post)

A lack of diligence by the nurses was also reported by one of the respondents (P3). The respondent stated that the nurses do sometimes sign in the patient's file, but the medications have not really been administered. Moreover, the nurses do not always sign in the patient's file and this is considered as missed dose. Therefore, obtaining information for the compilation of DOT metric reports from the patients' files might not be accurate, and could still result in overestimation or underestimation of the antimicrobial usage.

"…My concern with the nurses is actually signing of the Days of Therapy, which is actually antibiotics that are received by the patient. I assume, that at the end of the day the nurses would take all the files with antibiotics and then sitting at the computer and entering it manually, whether they would be administered or not. They just going to find them in the file and then, put them and punch them into the computer. They do that with signing as well, they sign but they haven't actually administer the drug or they don't sign and then there is a missed those dose. They would still enter it into the computer because they would want to cover that up. I know it sounds terrible but it is what happens." (P3: Post)

Respondent (P4) highlighted that the nurses are not concerned about the initiative of AMS, therefore explaining why respondent (P3) identified that the nurses would be

indifferent towards accurate collection of data for the purpose of AMS monitoring, i.e. compilation of AMS metric report.

"Like I said, the only stumble block I see, is on the ward level, the nursing side. Unfortunately, we haven't involved in our antibiotic stewardship initiative, and there is also a lack of enthusiasm and interest from their side…" (P4: Post)

It was, therefore, concluded by one respondent (P4) that the nurses should be made more involved in AMS, with the purpose of educating them and making them more aware about the importance of AMS, and subsequently accurate data collection.

"…I think, that will be your biggest hurdle. I assume, that will become the focus area, getting nurses involved, and making them understand the value in stewardship and obtaining clean data." (P4: Post)

"I just think, getting the nurses involved. You know, not everyone might be interested, but if you can identify someone who can champion the course, that will be of great benefit. You just need someone who will have that ambition. I would focus on education initiatives, focusing on nurses to prove their reporting if this is implemented…" (P4: Post)

Moreover, respondents (P1 and P7) stated that funding would be required for the provision of computers, especially at the ward level.

"…cost of computers at ward level…" (P1: Post)

"…I was thinking now, with budget and all…They will say, oh no, there is no money for computers and printers…" (P7: Post)

Respondent (P2) discussed that the feasibility of implementing the framework for the proposed antimicrobial usage reporting tool would be determined by funding. It was mentioned that the dispensing programme, Rx Solution®, currently has no support, in terms of amending the programme. The respondent also put emphasis on the fact that,

approval from the National Department of Health (NDoH) would be required in order to implement this tool further for the South African public sector hospitals.

"…In order to get a system like that working, it will require funding. Because at this point in time, the system we are using, is free of charge and it has absolutely no support. Rx solution® currently has no one to actually support it anymore. From that point of view, we're not going to have anyone looking at systems and amending systems. So, if there was funding available, I think it should be all-inclusive in that system. If there is funding available, I think it is feasible." (P2: Post)

"…It definitely has to get the standard approval from the Department of health and their support and permission." (P2: Post)

The respondent (P4) was in accordance with respondent (P2), and further elaborated that if initiatives are not enforced in the South African public sector hospitals, then the implementation of this framework would be seen as a hurdle.

"…In practice, I am a little bit concerned with respect to…In government, if things are not enforced, or there are no incentives, things are not done. And if it is not part of the job description and part of the KPA [Key Performance Area] …So, if you want to implement something in the state sector, then you need to incorporate that into the KPA." (P4: Post)

Respondent (P6) also mentioned the uncertainty, whether a software developer is currently appointed to further develop Rx solution®, and this was seen as a challenge in the implementation of the proposed antimicrobial usage reporting tool, while it was previously stated by respondent (P2) that Rx Solution® does not have any current support.

"I think from an Rx point of view, I don't know if there is someone that is paid to develop things or do work for us, software wise, I don't know. I don't know what contracts are with Rx Solution®, if we even pay to have Rx Solution®. So if we had to ask them to develop something or add something, I don't know if there is someone

designated to us to do something like that. That might be a problem. …The only block will be from the software development point of view." (P6: Post)

Furthermore, it was noted that the lack appropriate information technology (IT) support was also seen as a problem. Respondent (P7) stated that there was inadequate computers provided at the pharmacy level and respondent (P2) stated that the computers were old and had to be frequently repaired. Moreover, respondent (P7) mentioned the factor of time constraints being a challenge for the healthcare professionals, i.e. the medical prescribers and nurses would see the incorporation of E-prescribing and eMAR components as an additional and tedious work.

"…Then, we have problems with hardware. Our computers are old and they keep on breaking down, and they are not connected to the printers…" (P2: Post)

"…There isn't enough IT, from the technicians up until to the computers and printers and the labels also, we run out of…" (P7: Post)

"…The doctors will say we are so busy doing other things, we don't have time to do this…and the nurses will say, we need a clerk to load the information on the computer…" (P7: Post)

Respondent (P2) further discussed that the implementation of the proposed antimicrobial usage reporting tool would be a challenge in smaller hospitals, as those hospitals usually do not have IT equipment. Moreover, proper connections of Internet network was also recognised as a challenge.

"…I think, it's going to be a bit of a challenge in smaller institutions. You can implement a system like that in institutions that have got IT support. But, if there is a lack of IT support, you are really going to struggle to implement, especially when you going to look at smaller hospitals, clinics in non-urban areas. You're even going to see that there are a lot of institutions that don't have IT equipment. From that point of view, I think for bigger centers, yes, it is implementable and it would work." (P2: Post)

"…And then, we are also facing challenges with network being down very frequently. It's like we can't access the system many times, especially now recently…" (P2: Post)

Respondent (IDS3) mentioned that obtaining the number of patient-days, in order to obtain a standardised AMS metric, would also involve challenges with IT. Respondent (IDS1) also questioned whether the software developer would be able to integrate the DHIS with the proposed antimicrobial usage reporting tool.

"…You also talked about the hospital patient numbers. Obviously, there is quite a lot of IT issues there…" (IDS3: Post)

"…It's really by programme development number one, can they develop this tool and integrate it with the DHIS? To be able to say, can we draw DHIS data, which might have to be done. It depends how many steps there are, looking at the different systems. The DHIS is not complicated, it's just the politics behind that, and generation of reports…." (IDS1)

4.4.4 Theme 4: Practical solutions to be implemented

The last theme that was identified focused on practical solutions to be implemented in the process of collecting data for AMS monitoring purposes. The majority of the respondents had no suggestions for improving the framework for the proposed antimicrobial usage reporting tool.

As previously reported under Theme 2 (section 4.4.2), one of the respondents (P3) reflected on whether nurses would be able to make optimal use of the eMAR component. The respondent further stated that DOT requires accurate administration record of medication. The eMAR component was seen as essential to be included into the framework for the proposed antimicrobial usage reporting tool, as it would enable the compilation of DOT metric reports, track the antimicrobials being dispensed as ward stock and also obtain a standardised AMS metric for paediatrics. The respondent (P3) suggested that, while waiting for an eMAR system to be implemented in the public sector hospitals, a clerk with a clinical knowledge of antimicrobials could

possibly take all the patients' files and manually enter the specific antimicrobial data into a computer.

"…I assume, that at the end of the day the nurses would take all the files with antibiotics and then sitting at the computer and entering it manually, whether they would be administered or not. They just going to find them in the file and then put them and punch them into the computer…" (P3: Post)

"…The Days of Therapy is supposed to be accurate administration data. You can get someone else to enter the data, besides the nurse. That was the only sort of problem that I would see happening…" (P3: Post)

"A clerk could maybe do the work, but you would need someone with a clinical knowledge that knows what the antibiotics are." (P3: Post)

4.5 Summary

The quantitative component of the preliminary phase presented in this chapter focused on the views of antimicrobial stewardship (AMS) practitioners on the usage, usefulness and clinical relevance of the most commonly encountered AMS metrics in the South African healthcare setting. The quantitative data of the study only provided an overview regarding the application of the AMS metrics. Therefore, the qualitative component of the preliminary phase was conducted in order to provide a deeper insight into the current issues experienced by various healthcare professionals involved in AMS. The qualitative data obtained during the preliminary phase focused on the following themes: i) antimicrobial stewardship, ii) surveillance, iii) extraction of data, iv) challenges and v) implementation of an antimicrobial usage reporting tool. The qualitative data supported the need for an antimicrobial usage reporting tool for the South African public sector hospitals. Therefore, the findings obtained during the preliminary phase of the study allowed the researcher to develop a framework of AMS metrics to be included in an antimicrobial usage reporting tool, i.e. the developmental phase. The post-developmental phase presented qualitative data on the applicability and practicality of the framework for the proposed antimicrobial usage

reporting tool. The qualitative data obtained during the post-developmental phase focused on the following themes: i) overall impression of the framework for the proposed antimicrobial usage reporting tool, ii) factors related to the implementation of the framework for a proposed antimicrobial usage reporting tool, iii) challenges expected to be faced in the implementation of the framework for a proposed antimicrobial usage reporting tool and iv) practical solutions to be implemented. Chapter Five will present a discussion of the results obtained during the preliminary phase, developmental phase and post-developmental phase.

CHAPTER 5
DISCUSSION AND INTERPRETATION OF RESULTS

5.1 Introduction

The results obtained during the preliminary, development and post-development phases were presented in Chapter Four, while Chapter Five will link the results to the aims and objectives of the research. Chapter Five will also discuss the research findings in light of the current published literature in order to interpret the relevance of the research findings. A conclusion of whether the objective was achieved or not will be given at the end of each discussed objective. As described in Section 1.3, the primary aim of the research was to develop a framework for a proposed antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in a tertiary level, public sector hospital setting. In order to fulfill the aim of the research, the following objectives were achieved:

1. Identify the most commonly used Antimicrobial Stewardship (AMS) metrics, which focus on antimicrobial utilisation according to the published literature.
2. Describe practitioners' views on the usage, usefulness and clinical relevance of the AMS metrics, in the South African public healthcare setting.
3. Develop a framework of AMS metrics to be included in the antimicrobial usage reporting tool.
4. Explore the applicability and practicality of the proposed antimicrobial usage reporting tool prior to implementation, from the perspectives of the members of an AMS team.

5.2 Objective One

As described in Chapter One (section 1.4), the first research objective was "to identify the most commonly used AMS metrics which focus on antimicrobial utilisation, according to the published literature". In order to meet Objective One, an extensive literature review of various medical journal articles, websites and textbooks was

conducted and presented in section 2.6. Eight commonly encountered AMS metrics were identified (Table 2.1), namely Defined Daily Dose (DDD), Days of Therapy (DOT), Prescribed Daily Dose (PDD), Length of Therapy (LOT), exposure days, cost of antimicrobials, grams of antimicrobials and IV to oral switch.

Defined Daily Dose (DDD)

Both the WHO and the South African National Department of Health recommend using the DDD (Septimus, 2014; South African National Department of Health, 2016; WHO Collaborating Centre for Drug Statistics Methodology, 2016a). DDD, however, has limitations as an AMS metric. Beganovic and LaPlante (2018) were of the opinion that although the DDD is an AMS metric approved by the WHO, it is quite insignificant and presents many disadvantages in certain situations. The DDD relies on grams of antimicrobials and therefore, cannot be used in renally impaired patients, as an underestimate of antimicrobial usage is likely to be expected. Moreover, it cannot be applied to paediatric patients as lower doses not corresponding to the WHO-DDD values are often prescribed for this population (Brotherton, 2018). Despite being inaccurate in various circumstances, the ease of reporting and obtaining information to calculate the DDD makes it a convenient measure of antimicrobial usage (Brotherton, 2018).

Days of Therapy (DOT)

When contrasted with the DDD, the Centers for Disease Control and Prevention (CDC) encourages the use of DOT as a primary antimicrobial consumption metric as it produces more clinically relevant reports (Beganovic & LaPlante, 2018). Since variation in dosages does not affect the DOT values, DOT is often the most preferred AMS metric over DDD (B. R. Dalton et al., 2015). Yet, it is important to note that the DOT is not the ideal measure of antimicrobial usage when two antimicrobials are prescribed together, as this leads to a double DOT (Wong, 2018). In those circumstances, DOT would give no relevant information about appropriateness of antimicrobial treatment (Brotherton, 2018).

Length of Therapy (LOT) and Exposure days

According to the published literature, the LOT is another AMS metric which could be considered useful and it can be employed to complement the DOT when more than one antimicrobial is being administered to a patient (Polk et al., 2011). Even though LOT does not provide detailed information on antimicrobial usage, it can be employed to determine abnormal duration of antimicrobial treatment (Polk et al., 2011). Morris (2014) also introduced the concept of "exposure days" as a secondary complement to the DOT. LOT and exposure days are AMS metrics employed to bridge the gaps caused by the limitations of DOT (Morris, 2014; Polk et al., 2011). However, insufficient studies have been conducted about the application of exposure days in practice.

Prescribed Daily Dose (PDD)

In addition to the DDD and DOT, Grau et al. (2013) stated that the most common numerator used to express antimicrobial usage is the PDD. The AMS metric, PDD, can be compiled from prescription records (Gagliotti et al., 2014). Hence, an electronic prescribing system would facilitate the quantification of antimicrobials in terms of PDD. The avaibility of electronic prescribing in a healthcare setting would enable continuous data collection for monitoring antimicrobial usage (Curtis, 2010). However, a study conducted by Koopmans, Finlayson, Whitelaw, Decloedt, and Dramowski (2018) stated that electronic prescription tracking is not yet available in South Africa.

Cost

As outlined in Chapter Two, cost is one of the easiest AMS metrics to measure in an AMS programme (Morris, 2014). AMS interventions can considerably reduce costs associated with antimicrobial treatment by reducing the inappropriate usage of antimicrobials. However, it is important to highlight that cost should not be considered the primary focus of an AMS programme. The focus should be improved patient outcomes and antimicrobial usage (Brotherton, 2018).

Grams of antimicrobials

The volume or grams of antimicrobials dispensed is a more meaningful AMS metric than the DDD. It is usually extracted from pharmacy dispensing records and is used to calculate the DDD (Polk et al., 2007). As previously discussed, the volume or grams of antimicrobials can easily be obtained, therefore making the DDD a convenient measure of antimicrobial usage.

IV to oral switch

In addition, IV to oral switch was also identified as an AMS metric. IV to oral switch is not an AMS utilisation metric, however, the usage ratio of IV to oral antimicrobials can either be monitored in DDD, DOT, and/or PDD (Dik et al., 2016).

Thus, research Objective One was met as the most commonly encountered AMS metrics, according to the published literature, were: i) Defined Daily Dose (DDD), ii) Days of Therapy (DOT), iii) Prescribed Daily Dose (PDD), iv) Length of Therapy (LOT), v) exposure days, vi) cost of antimicrobials vii) grams of antimicrobials and viii) IV to oral switch. It was identified that it has been a challenge to recognise the most convenient and reliable AMS metrics (Morris, 2014), although Grau et al. (2013) previously identified DDD, PDD and DOT as the most common measurements. Other AMS metrics were also considered in the clinical setting, however, it was concluded that the DDD was the only AMS metric currently recommended by the South African National Department of Health (South African National Department of Health, 2017a).

5.3 Objective Two

The second research objective was "to describe the practitioners' views on the usage, usefulness, and clinical relevance of the AMS metrics, in the South African public healthcare setting". In order to meet Objective Two, quantitative data was obtained through the use of a purpose-designed questionnaire as a data collection tool

(Appendix A) and the data obtained was further explored by collecting qualitative data from semi-structured interviews during the preliminary phase.

Usage

Despite being the most recommended AMS metric by the WHO, it was determined from the quantitative data collected during the preliminary phase of the study that the DDD was currently only being used in tertiary level public sector hospitals in the Eastern Cape province of South Africa, by 64.3% (f=9; n=14) of medical and 64.3% (f=9; n=14) of non-medical respondents (Figure 4.4) (WHO Collaborating Centre for Drug Statistics Methodology, 2016a). Although, no statistically significant differences were observed in the usage of the DDD between any of the groups (Medical (M) vs. Non-Medical (NM); Involved (I) vs. Not Involved (NI); AMS training (A) vs. No AMS training (NA)), it can be concluded that AMS training had created awareness about the DDD. A greater percentage of respondents with AMS training than respondents with no AMS training were using the DDD in practice (A vs. NA: 76.5% vs. 45.5%) (Figure 4.6).

From the quantitative data, it was also found that the respondents also used other AMS metrics in the workplace, for example, DOT (53.6%; f=15; n=28) and PDD (50.0%; f=14; n=28) in the workplace (Figure 4.3). However, conflicting results were found when the quantitative and qualitative data were compared, and it was concluded that the DDD was the only AMS metric currently being utilised, and only two of the five hospital research sites were using DDD.

"Yeah [yes], I use the DDD. I don't use the others [AMS metrics]." (P2: Prelim.)

"The DDD is the one [AMS metric] that we have been focusing on and I am aware that it does not give you the whole picture but we haven't looked at the others [AMS metrics]." (IDS3: Prelim.)

DOT was only used by 53.6% of the respondents (Figure 4.3). It was inferred from the qualitative data, that DOT might not be a feasible AMS metric to be currently used in the South African healthcare setting, due to the uncertainty of obtaining the

required information from Rx solution®, reinforcing why DOT was not employed as much in the clinical setting

"…I think something that could be considered is Days of Therapy [DOT] but I am not sure how they would get that information off the system [Rx Solution®]." (P3: Prelim.)

It was determined from the quantitative data that PDD was not commonly utilised by the respondents (50.0%; f=14; n=28) in their daily practice (Figure 4.3). Yet, the respondents identified this AMS metric as quite useful (i.e. extremely useful or useful) (75.0%; f=21; n=28) (Figure 4.7) and clinically relevant (i.e. extremely clinically relevant or clinically relevant) (82.1%; f=23; n=28) (Figure 4.11). As previously stated, the AMS metric, PDD, can be compiled from prescription records (Gagliotti et al., 2014). However, prescriptions are not often dispensed, resulting in an overestimate of antimicrobial usage (World Health Organization, 2003). It is evident that an electronic prescribing system would, therefore, assist and facilitate the compilation of accurate PDD metric reports (Curtis, 2010). It was confirmed from the qualitative data, that the facility of electronic prescribing was certainly not available in the public sector hospitals in the Eastern Cape and it can, thus, be concluded that although more respondents found the AMS metric, PDD, useful and clinically relevant, it was not frequently used due to the likelihood of limited access to PDD data.

"Only if the prescribing is done electronically…" (MP1: Prelim.)

From the quantitative data, LOT was being used by 71.4% (f=20; n=28) of the respondents (Figure 4.3). It was determined from the qualitative data that it was only possible to obtain the length of therapy of the antibiotics dispensed per patient from Rx Solution®. The respondent (P2) mentioned that it was not possible to follow up on those antibiotics dispensed as ward stock. Furthermore, the respondent mentioned that Rx Solution® does not have an option to credit medications and therefore, if a patient was discharged, the reports would show an overestimate of antimicrobial usage. Subsequently, the length of therapy had to be checked from the patient's file in order to obtain more accurate information.

"If you want to be sure that the information that you are gathering, you actually have to go to the file. A lot of the antibiotics that are frequently used are ward stocks in any case, they will have no information on the Rx Solution®, for example, which patient was on ceftriaxone and for how long. Only the one that you dispense per patient,…" (P2: Prelim.)

"…If it happens that they issued five days and after two days, the patient is discharged…there is no way on the Rx Solution® to actually do a credit or amended prescriptions or anything. So, it looks that the patient got five days and they only got two days…" (P2: Prelim.)

It was also observed that the AMS metric, exposure days, was used by the minority of the respondents (28.6%; f=8; n=28) (Figure 4.3). Very little literature supports the use of exposure days to monitor antimicrobial usage supporting why only a small percentage of the respondents were aware of this AMS metric.

From the quantitative data, it was noted that more non-medical respondents than medical respondents used cost to monitor antimicrobial usage. However, there was no statistically significant difference in the usage of cost between the medical and non-medical respondents (M vs. NM; 57.1% vs. 64.3%; Fisher's exact test p= .70). This finding is in line with the findings of Dalton K. and Byrne (2017), who emphasised on the fact that pharmacists, with their unique knowledge of medicines, are the healthcare professionals responsible for the cost-effective use of medicines. Though, it was confirmed from the qualitative data that cost was indeed not the primary focus of an AMS programme and it was only investigated when large amount of expensive antimicrobials were consumed. This finding is in agreement with the statement of Brotherton (2018), who cited that cost should not be considered the primary focus of an AMS programme.

"I don't actually put much focus on the cost at this point in time, we look at specifics, like we had an outbreak of candidiasis, invasive candidiasis in ICU, where we treated like 7 patients, but then obviously we looked at the cost because it is a major expense, but then in general the cost is not the biggest one that I look at, I look at consumption, quantities, at DDDs." (P2: Prelim.)

Furthermore, it can be observed that although no statistically significant differences in the usage of cost were observed between the following groups (M vs. NM – Figure 4.4 and I vs. NI – Figure 4.5), AMS training influenced the usage of cost between the two groups of the following respondents (A and NA – Figure 4.6). The odds that a respondent with AMS training uses cost is 10.06 times higher than the odds that a respondent with no AMS training uses cost (OR=10.06). It was noted that 57.1% (f=8; n=14) of the medical and 64.3% (f=9; n=14) of the non-medical respondents were using cost in the workplace (Figure 4.4). Eight medical respondents and nine non-medical respondents had completed AMS training, therefore, concluding that all the respondents who had completed AMS training were using cost to monitor antimicrobial.

From the qualitative data, it was also established that the data required to calculate the DDD, was extracted from Rx Solution®, the pharmacy dispensing programme used in the South African public healthcare setting in the Eastern Cape. It was confirmed by one of the respondents (P2) that the data extracted from Rx Solution® included the total number of grams of antimicrobials dispensed. The findings obtained from the qualitative data are consistent with the statement of Polk et al. (2007), who affirmed that 'the volume or grams of antimicrobials' dispensed is usually extracted from pharmacy dispensing records in order to calculate the DDD.

"I check the DDD from the WHO website, what gram equivalent the DDD is and then I check on the dispensing system basically, how many DDD or how many grams were dispensed and I convert it to that." (P2: Prelim.)

Beganovic and LaPlante (2018) stated that grams of antimicrobials could be considered as an AMS metric, however, it is not recommended as a suitable measure of antimicrobials as the grams of antimicrobials cannot be used to compare specific antimicrobial usage. In addition, from the quantitative data, grams of antimicrobials was reported to be used by 46.4% (f=13; n=28) of the respondents (Figure 4.3). It was formerly established from the qualitative data that grams of antimicrobials are available to use for the purpose of monitoring antimicrobial usage. However, one of the respondents (P3) described the DDD as being more clinically orientated than

grams of antimicrobials supporting why grams of antimicrobials was only used by a small percentage of the respondents (46.4%; f=12; n=28).

"I think it [DDD] is more sort of clinically orientated than grams of antibiotics or antibiotic expenditure…" (P3: Prelim.).

Usefulness

When analysing the results from the quantitative component, the DDD was considered to be useful (i.e. extremely useful or useful) by 71.4% (f=20; n=28) of the respondents (Figure 4.7). It was observed that a greater percentage of non-medical respondents than medical respondents classified the DDD as useful (i.e. extremely useful or useful). It was explicated from the qualitative data that the medical respondents, with the exception of the infectious disease specialists, were not extensively involved in the monitoring of DDD consumption data, supporting this possible difference in the usefulness of the DDD between the medical and non-medical respondents (M: 64.3%; f=9; n=14 vs. NM: 78.6%; f=11; n=14) (Figure 4.8). Moreover, Rx Solution® is the dispensing programme utilised in the pharmacy, and it is the source, where the consumption data was extracted from, to calculate the DDD. The non-medical respondents, i.e. the pharmacists, were more acquainted with the dispensing programme and were, therefore, compiling the DDD metric reports. When the respondents with AMS training were considered, it was concluded that AMS training did not influence the perceptions of the respondents regarding the usefulness of the DDD (A: 64.7%; f=11; n=17 vs. NA: 81.8%; f=9; n=11) (Figure 4.10).

It was also noted from the quantitative data that being involved in an AMS team (p= .04) and undertaking AMS training (p= .018) certainly changed the views of the respondents on the usefulness of grams of antimicrobials. The odds that a respondent involved in an AMS team identifies grams of antimicrobials as useful (i.e. extremely useful or useful) is 10.92 times higher than the odds that a respondent who is not involved in an AMS team identifies grams of antimicrobials as useful (i.e. extremely useful or useful) (OR=10.92) while the odds that a respondent with AMS training identifies grams of antimicrobials as useful (i.e. extremely useful or useful) is 7.82 times higher than the odds that a respondent with no AMS training identifies grams of

antimicrobials as useful (i.e. extremely useful or useful) (OR=7.82). The odds ratios calculations highlighted that a multidisciplinary approach enlightened the views of the respondents on the usefulness of grams of antimicrobials. Furthermore, AMS training could have provided more information on the resources available for AMS monitoring purposes. One of the main barriers to the implementation of an AMS programme includes a lack of training, knowledge and education of AMS principles provided to healthcare professionals (Boeser, 2016). A. J. Brink et al. (2016) also emphasised on the fact that pharmacists require training for the purpose of monitoring antimicrobial usage. Thus, it can be concluded that AMS training is undeniably important for the healthcare professionals choosing to be actively involved in AMS activities.

It was observed from the quantitative data that the respondents who underwent AMS training and the respondents with no AMS training did not identify the same AMS metrics to be the most useful (i.e. extremely useful or useful) (Figure 4.10). This could related to the fact that the respondents who had AMS training had a more comprehensive knowledge of the AMS metrics and were, therefore, more aware of the usefulness of the various AMS metrics. This finding again emphasised on the fact that AMS training could have provided more information on the resources available for AMS monitoring purposes

From the quantitative data, IV to oral switch was considered to be useful (i.e. extremely useful or useful) by majority (96.4%; f=27; n=28) of the respondents (Figure 4.7). The qualitative data established that the DDD metric reports also comprised of the consumption of IV and oral antimicrobials.

"In the pharmacy, you have Rx Solution® and it both has the ordering as well as the dispensing component to that. On the dispensing component, the data is manually extracted, looking at all the different antibiotic classes, and in-patient versus outpatient, IV and oral, and then that is supplied on a monthly spreadsheet,… We look at the overall consumption which would be in Defined Daily Doses…" (IDS1: Prelim.)

Even though more medical respondents employed the practice of IV to oral switch, more of the non-medical respondents categorised IV to oral switch as useful (i.e.

extremely useful or useful) (100%; f=100; n=14) (Figure 4.8). The majority of the non-medical respondents comprised of pharmacists; they are the healthcare professionals, who recognise IV to oral switch as a cost saving situation (K. Dalton & Byrne, 2017). Moreover, pharmacists are well-informed on the available formulations and pharmacokinetic properties of antimicrobials when considering IV to oral switch. They are responsible for reinforcing the implementation of IV to oral switch guidelines, evaluating patients eligible for IV to oral switch and making interventions in recommending IV to oral therapy (Carver, Burgess, Cooper, Ty Elder, & Kramer, 2018; Chandrasekhar & PokkaVayalil, 2019; Waburton, Hodson, & James, 2014). On the other side, medical prescribers believe that IV antimicrobials have better bioavaibilities than oral antimicrobials, therefore, preferring IV over oral treatment (Chandrasekhar & PokkaVayalil, 2019). Furthermore, they only consider IV to oral switch as a cost-saving implementation (Waburton et al., 2014). Hence, it may be concluded that the pharmacists recognise IV to oral switch as an important AMS strategy but may not always be able to implement it due to their limited scope of practice, therefore explaining why the non-medical respondents, i.e. pharmacists, did not employ the practice of IV to oral switch as much as the medical respondents, but still perceived this AMS metric as useful.

When comparing with the respondents who used the eight AMS metrics, there were more respondents who found the AMS metrics useful (i.e. extremely useful or useful). This could be supported by the fact that the respondents identified the usefulness of the eight AMS metrics based on theoretical knowledge but were not commonly using all eight of the AMS metrics in the clinical setting.

Clinical relevance

Although, DOT was only used by 53.6% of the respondents (Figure 4.3), the highest number of respondents practicing at the research sites classified this AMS metric as clinically relevant (92.9%; f=26; n=14) (Figure 4.11). The respondents determined the clinical relevance based on theoretical knowledge but were not regularly employing DOT as an antimicrobial measure due to a lack of readily available and accessible of data required to determine DOT.

It was previously noted from the qualitative data that DDD was described as being more clinically orientated AMS metric than grams of antimicrobials. The quantitative data supports this statement, where more respondents perceived DDD as clinically relevant (Views on clinical relevance – DDD vs. grams of antimicrobials; 60.7% vs. 46.4%).

The odds that a respondent involved in an AMS team identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) is 26.87 times higher than the odds that a respondent who is not involved in an AMS team identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (OR=26.87) while the odds that a respondent with AMS training identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) is 11.40 times higher than the odds that a respondent with no AMS training identifies grams of antimicrobials as clinically relevant (i.e. extremely clinically relevant or clinically relevant) (OR=11.40). The odds ratios calculations again highlighted on the fact that a multidisciplinary approach towards AMS and AMS training changed the views of the respondents on the clinical relevance of grams of antimicrobials.

Overall views on DDD

Beganovic and LaPlante (2018) identified that the DDD has numerous disadvantages, including not being a useful AMS metric for the paediatric population. Many respondents were in agreement with the statement of Beganovic and LaPlante (2018). Despite being the only AMS metric currently being utilised at the two of the five research sites, the respondents described that the DDD is not the best AMS metric to evaluate antimicrobial usage. Some respondents also agreed on the fact that the DDD is not suitable for the paediatric population. Doron and Davidson (2011) emphasised on the fact that DDD reports are valuable for benchmarking purposes. This statement is line with the findings obtained from respondent (P2) who affirmed that, "*One of the advantages [of the DDD] is that you can benchmark between institutions"*. Brotherton (2018) concluded that the DDD is a convenient measure of antimicrobial usage, which is in agreement with one of the respondents (IDS1), who described the DDD as *"being a convenience more than anything".* The views of the respondents on

the application of DDD in general are illustrated in Figure 5.1. The quotations on the application of DDD in general were obtained from the qualitative component of the preliminary phase.

"One of the advantages [of the DDD] is that you can benchmark between institutions. It is a bit difficult for hospitals that don't have the computerised system, so you can't sort of benchmark against the smaller hospitals. The disadvantages, it depends on the drug. So for instance, the World Health Organization has a DDD of 1g for Ertapenem but the patient that we have in ICU have hypervolume anemia and they need a dose of 1 g BD. It [DDD] overestimates the usage whereas if you use Days of Therapy, the Days of Therapy would be 1 and the DDD would be 2 because we are using 2 vials. It depends on the dose used. It is not very accurate for specific populations. You can't use for paediatrics or neonates or even renally impaired patients. Then obviously when you compare between different hospitals, you have to take into account whether they are using the same formulary. For a specific indication if they use Kefzol® versus Ceftriaxone, or Kefzol® versus cloxacillin. Our institution uses cloxacillin, it is going to be very difficult to compare those." (P2: Prelim.)

"We are aware that there are some limitations and I have seen some studies that say that it may underestimate or overestimate in some context…it seems that there are no standard for paediatrics due variation of dosing in paeds according to the weight. In paeds, it's quite a non-representative value. It got some values just for some broad picture and trends…but for some antibiotics, it may underestimate or overestimate usage. Sometimes we are using higher doses than the Defined Daily Dose, so they skew the findings. It is useful over times in terms of trends but I am aware that it does not give you the full picture of your antibiotic usage." (IDS3: Prelim.)

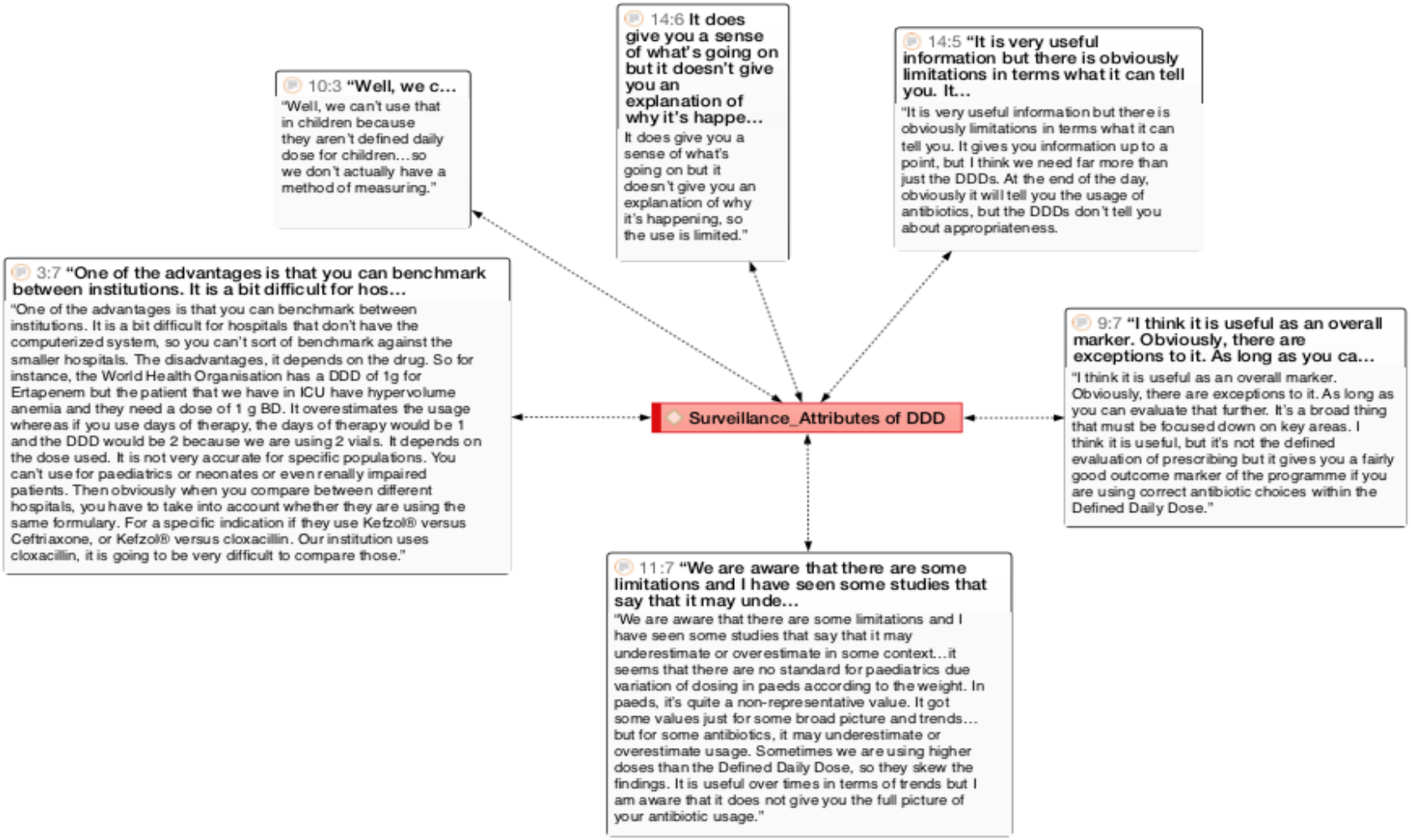

Figure 5.1. General views of the respondents on Defined Daily Dose (DDD)

Thus, Objective Two was met and the views of the practitioners on the usage, usefulness and clinical relevance of the eight commonly encountered AMS metrics were identified. The majority of the respondents used (75.0%; f=21; n=28) and classified IV to oral switch as useful (96.4%; f=27; n=28), while the most number of respondents classified DOT as clinically relevant (92.9%; f=26; n=28). Although the qualitative data concluded that DDD was the only AMS metric currently being utilised at two of the five research sites in the Eastern Cape province of South Africa, it was not the most used AMS metric (64.3%; f=18; n=28) and it was classified as clinically relevant (i.e. extremely clinically or clinically relevant) by just under two-thirds of the respondents.

5.4 Objective Three

The third research objective was "to develop a framework of AMS metrics to be included in the antimicrobial usage reporting tool". In order to meet Objective Three, the quantitative and qualitative data collected during the preliminary phase was integrated and interpreted during the developmental phase with the aim of formulating the proposed framework of AMS metrics for use in the South African public sector context (Figure 4.15).

The CDC emphasised on the use of electronic data in order to improve tracking and reporting of antimicrobial usage data (Minnesota Department of Health, 2018). It was recognised from the literature that the South African public sector hospitals mostly rely on pharmacy dispensing data for the tracking of antimicrobial consumption data (Koopmans et al., 2018). Indeed, the qualitative data confirmed that pharmacy dispensing data was being used to monitor the antimicrobial usage in terms of DDD, in the Eastern Cape province of South Africa. Furthermore, Koopmans et al. (2018) stated that pharmacy dispensing programmes were not originally designed to track antimicrobial consumption data and one of the respondents (IDS3) also confirmed on the uncertainty as to whether Rx Solution® was designed to be used for the generation of AMS metric reports. It was identified that AMS programmes tend to be less effective and successful without an electronic AMS monitoring programme (Pakyz et al., 2014). Furthermore, an effective antimicrobial surveillance system via an

electronic platform in resource-limited healthcare settings, particularly in Africa, is generally unavailable as it is perceived as a challenge (Koopmans et al., 2018; Rattanaumpawan, Boonyasiri, Vong, & Thamlikitkul, 2017).

Referring to Figure 4.15, the lack of accessibility of consumption data was identified as problematic as the relevant data had to be extracted from Rx Solution® into a Microsoft Excel® spreadsheet format. The data had to be re-entered in another Microsoft Excel® spreadsheet format, in order to manually calculate the DDD reports. This limitation was identified from the qualitative data obtained during the preliminary phase. Rx solution® was recognised as being *"not very user friendly in generating data"* as the programme lacks the ability of automatically extracting consumption data into an appropriate format. The dispensing programme, Rx solution® also lacks a built-in automatic AMS metric reports generating function. Hence, the need to implement an antimicrobial usage reporting tool was seen as imperative for the public sector hospitals in South Africa.

Ideally, the antimicrobial usage reporting tool should be interfaced with Rx Solution®, in such a way that the dispensing data extracted into the Microsoft Excel® spreadsheet format is automatically imported into the antimicrobial usage reporting tool from Rx Solution®. In addition to the dispensing component, an electronic medication administration records (eMAR) and electronic prescribing (E-prescribing) component are possible functions to be considered for addition into Rx Solution®.

It was clearly determined from the qualitative data that the option of eMAR was not available in the South African public healthcare setting as the DDD metric reports were only based on the number of issued antimicrobials and not the number of administered antimicrobials, producing inaccurate DDD metric reports. A direct quotation from one of the respondents is supportive of this statement.

"I look at the dispensing, but we have certain antibiotics that are ward stock, so we do them under demander transfer so that we have records of everything that goes either at ward stock or dispensed per patient on our dispensing system, so I look at that data… I don't look at what was actually administered. I look at what was issued." (P2: Prelim.)

Brotherton (2018) describes how DOT metrics reports can only be generated if eMAR data are available. However, this option is not always offered in all healthcare institutions (Brotherton, 2018). In a study conducted by Dalton B. R. et al. (2015), it was observed that, when compared to pharmacy dispensing data, a 23% lower DDD was obtained when DDD consumption data was calculated using eMAR data. Moreover, the literature identified that it was challenging to correlate certain antimicrobials being dispensed as ward stock with a patient in particular (Koopmans et al., 2018). This statement is in line with results obtained from the qualitative data obtained during the preliminary phase, where one of the respondents identified that antimicrobials dispensed as ward stock were difficult to monitor. Therefore, in the public healthcare sector in South Africa, the inclusion of an eMAR function linked to Rx Solution® would be beneficial for the purpose of accurate DDD reports and it would additionally allow better tracking of ward stock.

The literature also identified DOT as one of the most convenient antimicrobial measure for the paediatric population (Gravatt & Pakyz, 2013). A challenge highlighted by Koopmans et al. (2018) was the lack of an appropriate standardised metric for paediatrics. The qualitative data obtained during the preliminary phase also concluded that no AMS metrics were currently employed in the paediatric population at the research sites, as DDD values are not applicable in children. As a result, the eMAR function would also facilitate the generation of DOT reports, which could be utilised to monitor the antimicrobial usage in the paediatric population.

In August 2017, the South African National Department of Health (NDoH) had recently published new legislations regarding the status of E-prescribing in South Africa (Chowles, 2018). It was stated that, “every prescription for a medicine shall be prepared with an electronic agent as defined by and in compliance with the Electronic Communications and Transactions Act, 2002 (Act No. 25 of 2002)” (South African National Department of Health, 2017b). However, a study conducted by Koopmans et al. (2018) affirmed that electronic prescription tracking is still unavailable in South Africa. It was evident from the literature that the unavailability of an E-prescribing function would result in labour-intensive, time-consuming, manual collection of antimicrobial consumption data. The introduction of E-prescribing in a healthcare setting would be meaningful, as it would keep an electronic record of all prescriptions

instead of the current time-consuming option of a manual audit of prescriptions (Koopmans et al., 2018). It is important to note that E-prescribing is an option and many medical practitioners are not willing to accept technology in the clinical setting (Chowles, 2018). Moreover, E-prescribing systems would not only improve the quality of antimicrobial prescribing, but it would also be beneficial in supporting AMS. Other than keeping an electronic record of prescriptions, an E-prescribing system could also include other features such as a drug interaction prompt, dose checker and long IV treatment alerts (Hand et al., 2017). Hence, in addition to the assisting of PDD metric reports compilation, introduction of E-prescribing in a clinical setting would also promote the rational use of antimicrobials.

Thus, Objective Three was met and a framework of AMS metrics was developed to be included in the antimicrobial usage reporting tool. The following AMS metrics, DDD, DOT and PDD were considered for inclusion in the framework for the proposed antimicrobial usage reporting tool. Even though DDD metric reports were already being compiled at two of the five research sites in the Eastern Cape, the reports were not at all times accurate and were not suitable to monitor the antimicrobial usage in paediatrics. Therefore, the eMAR could be considered for inclusion in order to obtain better DDD reports. Furthermore, using the DDD as the only AMS metric is not ideal as it does not always provide a realistic picture of antimicrobial usage (Stanic Benic et al., 2018). Hence, DOT reports could also be generated and a suitable measure for use in paediatrics would be obtained. The legislations regarding the status of E-prescribing in South Africa have been approved (Chowles, 2018) ,therefore, incorporation of an E-prescribing function could also be considered for Rx Solution®, with the purpose of facilitating the generation of PDD reports.

5.5 Objective Four

The fourth research objective was to “explore the applicability and practicality of the proposed antimicrobial usage reporting tool prior to implementation, from the perspectives of the members of an AMS team.” In order to meet Objective Four, the framework for the proposed antimicrobial usage reporting tool was electronically

distributed to the respondents who participated in the semi-structured interviews of the preliminary phase. The respondents were then interviewed in order to investigate the applicability and practicality of the framework for the proposed antimicrobial usage reporting tool.

It was noted that the majority of the respondents favored the idea of the framework for the proposed antimicrobial usage reporting tool. In addition, Rattanaumpawan et al. (2017) stated that an electronic antimicrobial surveillance system could provide better data in terms of quality and accuracy. A policy on the development of eHealth Strategy in South Africa was developed in 2012, which stated that South African hospitals must "implement patient-based information systems at all facilities where healthcare is delivered" (South African National Department of Health, 2012). For the South African public sector hospitals to generate accurate AMS metric reports, it is, therefore, important for those hospitals to deviate from paper-based collection of data. It was noted from the preliminary phase of the study, that Hospital A was not always using Rx Solution® for dispensing and the pharmacists were manually dispensing medications. Hence, it can be concluded that, even though, patient-based information systems are currently recommended throughout the South African hospitals, some institutions are not currently using an electronic system even for dispensing.

"…Rx solution® is not used properly. They use it [Rx Solution®] today and after three days, they [the pharmacists] don't use it because nobody is watching them or the computers are off. They [the pharmacists] decide to give it [the prescription] out manually." (P7: Prelim.)

It was previously established from the preliminary phase that electronic prescribing was unavailable at the research sites. Though, it must be noted that the data collection process for the preliminary phase took place following the publication of the new legislatives regarding the status of E-prescribing in South Africa. It was revealed from the post-developmental phase that one ward of Hospital C had started prescribing medication via an electronic platform. This is seen as a good initiative from the medical prescribers' side, who are not only taking into consideration the eHealth Strategy but are also slowly planning of moving away from paper-based prescriptions in the public sector. However, it may be interesting to note that an E-prescribing

system can be costly in terms of purchasing, implementing and maintaining of the system, as well as training the staff on the use of the system, explaining a possible reason why not all research sites had started using E-prescribing (du Toit, Naicker, & Bodenstein, 2015).

Wright, O'Mahony & Cilliers (2017) identified that data for the purpose of monitoring is currently being hand written by nurses. It was recognised from the post-developmental phase that a lack of human resources at the ward level, at the research sites was regarded as problematic. Respondent (IDS3) stated that nurses struggle to perform their daily routine work while respondent (P3) related that the nurses are negligent towards signing off in the patient's file after the administration of medications, therefore, doubting the accuracy of the information captured by the nursing staff. Those findings are in line with the statement of Wright et al. (2017), who concluded that nurses are generally overworked and data collected by the nurses were perceived as being of poor quality (Wright, O'Mahony, & Cilliers, 2017). Even though one respondent (P7) had seen that the future inclusion of an eMAR system would enable to track the antimicrobials being dispensed as ward stock, another respondent (P3) questioned the inclusion of the eMAR component in the framework for the proposed antimicrobial usage reporting tool, as a result of negligence from the nursing staff.

Other than a lack of human resources, training was also recognised as a challenge towards the successful implementation of the proposed antimicrobial usage reporting tool. Though, training was not recognised as a major challenge towards using the proposed antimicrobial usage reporting tool, as one respondent (P3) emphasised that it would require only one pharmacist to compile the AMS metric reports. Other respondents discussed that the only training required would be related to the nursing staff and medical prescribers, if the eMAR and E-prescribing components were further carried out in the public sector hospitals.

One of the other major challenges discussed by Wright et al. (2017) on the failure of implementing an electronic system, was associated with cost of implementing an electronic system. Lack of appropriate IT infrastructure, such as lack of computers and reliable Internet connection at a facility was also seen as a barrier. The findings of

the post-developmental phase affirmed that funding, a lack of computers and poor Internet connections at the research sites would be considered as the problems contributing to the successful implementation of the proposed antimicrobial usage reporting tool.

The literature acknowledged that a lack of leadership and dedication to support AMS are barriers to the implementation of AMS in general (Cho, Dunn, Loredo, & Brazill, 2018). It was established from the preliminary phase that AMS is slowly gaining momentum in the South African public sector hospitals and a lack of leadership by pharmacy management at one of the research sites was influencing the lack of AMS activities. One of the respondents (P2) further discussed that a lack of support from the National Department of Health (NDoH) would be seen as a barrier to the implementation of the proposed antimicrobial usage reporting tool. Hence, it was concluded from two respondents (P3 and P4), that if sufficient importance is first given to AMS from the hospital's management, then the AMS metrics would be seen as feasible reports.

"...It definitely has to get the standard approval from the Department of health and their support and permission." (P2: Post)

"...As it becomes part of daily routine, if it's [AMS] made mandatory to hospital's management, I can see that being done with the other reports as well." (P3: Post)

"...I will also try and work through opinion leaders, for example, the management. If it is enforced from management's side...If you are told you have to fill in these stats...If one is able to make it as important as reporting bed occupancy, then there is no argument. If it has to be done and it becomes one of those things that has to be done, I would probably go down that avenue and make it part of daily stats." (P4: Post)

It can be concluded that, the implementation of the proposed antimicrobial usage reporting tool for the public sector hospitals is a good initiative towards fulfilling the requirements of South African National Department of Health (NDoH), i.e. reporting of DDD consumption data (South African National Department of Health, 2017a).

However, it was noted from the preliminary phase, that one of the research sites was not using the dispensing component of Rx Solution®. In consequence, it would be impossible for such public sector hospitals to generate DDD metric reports as part of their daily routine. It is, therefore, important for all public sector hospitals to adopt an electronic platform, beginning at the dispensing level, so as to begin with generating DDD metric reports. On the other side, the practice of E-prescribing had recently started, therefore, implying that, in the near future, this option could be considered as feasible for all the public sector hospitals. Furthermore, the eMAR component was not seen as practical and feasible, due to a lack of negligence by the nursing staff. While waiting for an eMAR system to be implemented for the public sector hospitals, a more practical solution to this challenge would be for a clerk with a clinical knowledge to be appointed in the ward, and manually entering the information related to administration of antimicrobials from the patients' files on a computer. However, it was emphasised by respondent (P3) that the nurses would need to be trained so that they could understand the importance of taking down accurate data. Irrespective of the person appointed to record the administration of antimicrobials on a computer, it is, hence, essential that nurses record the correct information in the patients' files, in order to produce accurate DDD and DOT metric reports.

"...I think the nursing staffs are overwhelmed with work. So, this would be an additional job for them. You know, if they are trained properly and they understand the importance of it, that would obviously make a difference." (P3: Post)

Thus, Objective Four was met and the applicability and practicality of the proposed antimicrobial usage reporting tool prior to implementation, from the perspectives of the members of an AMS team was explored. Most of the respondents were in agreement of using all three AMS metrics: DDD, DOT and PDD. Though, the South African National of Health had only emphasised on the reporting of DDD consumption data (South African National Department of Health, 2017a). Hence, the South African public sector hospitals should be focusing on obtaining accurate primary data so as to obtain accurate DDD metric reports. DOT would be considered as the next most feasible AMS metric and it could be considered only for the paediatric wards. PDD would be considered useful in order to complement for the DDD, in instances, where high doses of antimicrobials are prescribed, however, until

E-prescribing is integrated into one platform, it would be labour-intensive to compile PDD metric reports. It could be concluded that a tool with the ability to produce automated AMS metric reports would be essential for the South African public sector hospitals. Yet, many challenges such as the lack of appropriate IT support and funding were seen as barriers to the implementation of the proposed antimicrobial usage reporting tool. With appropriate support from the National Department of Health, the implementation of the proposed antimicrobial usage reporting tool could be regarded as a feasible endeavor.

5.6 Summary

In summary, the study identified that the DDD was the only AMS metric currently recommended by the South African National Department of Health (South African National Department of Health, 2017a) and it was used at only two of the five research sites in the Eastern Cape. It was concluded from the qualitative data obtained during the preliminary phase, that the dispensing programme, Rx Solution® does not have the capacity for automatically generating AMS metric reports for the purposes of AMS monitoring. Hence, a framework for a proposed antimicrobial usage reporting tool was developed. The following AMS metrics, DDD, DOT and PDD, were considered for inclusion in the framework for the proposed antimicrobial usage reporting tool. Feedback on the applicability and practicality of the proposed antimicrobial usage reporting tool prior to implementation, from the perspectives of the members of an AMS team was also explored. Even though the utilisation of all three AMS metrics: DDD, DOT and PDD, was not regarded as feasible, most of the respondents were in agreement that using all three AMS metrics would be ideal for the public sector hospitals in South Africa. However, it may be interesting to note the implementation of the eMAR and E-prescribing system for the public sector hospitals can be costly in terms of infrastructure upgrades. If appropriate support is given from the National Department of Health (NDoH), the implementation of the proposed antimicrobial usage reporting tool would be seen as a success for the public sector hospitals.

CHAPTER SIX
CONCLUSION

6.1 Conclusion

The primary aim of the research was to develop a framework for a proposed antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in a tertiary level, public sector hospital setting. From the results obtained during the three phases of the study, it can be concluded that the aim of the study was achieved and a framework for a proposed antimicrobial usage reporting tool was developed (Figure 4.15).

With the aim of fulfilling the requirements of the National Department of Health (NDoH), i.e. reporting of Defined Daily Doses (DDD), it is important for all public sector hospitals to utilise the dispensing component of Rx Solution®. It was identified that the dispensing programme, Rx Solution® had all the information required to produce DDD metric reports. However, the programme did not have the ability of automatically producing the reports, hence, resulting in labour-intensive manual calculation of the DDDs. The findings obtained during qualitative component of the preliminary phase, therefore, established the need for an electronic platform for the purpose of monitoring antimicrobial usage for the South African public sector hospitals. Yet, many challenges obstructing the implementation of the proposed antimicrobial usage reporting tool were identified. It was, therefore, concluded that AMS in general, should be considered as an important focus from the management's point of view so as to ensure success of the antimicrobial usage reporting tool.

6.2 Limitations of the Study

One of the limitations of study was that the data obtained during the study was only limited to the public sector hospitals in the Eastern Cape province of South Africa. Therefore, the results obtained could not be generalised to all the provinces of South Africa. Furthermore, the sample size for the quantitative component of the

preliminary phase was relatively small (n=28). Hence, it was difficult to identify significant relationships from the data obtained.

6.3 List of Recommendations

From the findings obtained throughout the study, certain recommendations could be made. It was noted from the qualitative findings obtained during the preliminary phase that the respondents were not familiar with all the AMS metrics. It is, therefore, important for the AMS practitioners to be formally trained on the application of AMS metrics, so as to understand the importance of quantifying antimicrobial usage via a standardised metric.

The qualitative results obtained during the preliminary phase of the study identified that AMS was not the biggest concern from the management's point of view at the public sector hospitals. It is, therefore, recommended for the management to be more involved and consider AMS in general as a key focus for the South African public sector hospitals. Hence, the success for the antimicrobial usage reporting tool would also be seen as achievable and realistic for the South African public sector hospitals.

Furthermore, it was found during the post-developmental phase that nurses generally struggle to sign correctly in the patients' files after administration of medications. It is recommended that nurses should be made more involved in AMS. They should be educated on the importance of correctly administering and recording the administration of antimicrobials, with the purpose of obtaining accurate data for AMS monitoring.

It was also recognised from the qualitative data obtained during the preliminary phase and post-developmental phase that one of the hospital research sites in the Eastern Cape was not always using the dispensing component of Rx Solution® and was, therefore, unable to compile DDD metric reports. Thus, it is recommended for all South African public sector hospitals to start utilising the dispensing component of Rx Solution®, so as to start generating the DDD metric reports.

It was seen from the data obtained from the post-developmental phase that only ward at one of the research sites had started electronically prescribing medications. Recommendations should be made that all public sector hospitals should invest in an E-prescribing system so as to facilitate the generation of PDD metric reports.

It was also identified that the respondents were unable to track the antimicrobials being dispensed as ward stock. The findings obtained during the developmental phase concluded that an eMAR system would be ideal for this purpose. It is recommended that, while waiting for an eMAR system to be implemented for the South African public sector hospitals, paper-based audits could be done in order to investigate if a high DDD is obtained for the antimicrobials being dispensed as ward stock.

6.4 Future Areas of Research

Future research could come up with a strategy to implement the framework for the proposed antimicrobial usage reporting tool. Another area of research, which could possibly be considered, is the integration of lab results together with the AMS metric reports into one consolidated database.

It was concluded from the qualitative component obtained during the preliminary phase that other provinces in South Africa also use other dispensing programmes and are not limited to Rx Solution®. Further studies could be done in order to investigate what are other programmes being utilised and if the programmes can be used for the purpose of obtaining better reports for AMS monitoring.

It was reported that one of the hospital research sites in the Eastern Cape was not always using the dispensing component of Rx Solution®. This finding could possibly be investigated further at a national level. Another possible study could arise with a strategy to implement an electronic medication administration record (eMAR) system for the public sector hospitals and investigate the adherence of nurses to that system. This would, therefore, determine if eMAR would a feasible system to implement for the purpose of AMS monitoring.

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Appendix A: Questionnaire: Use of Metrics in Antimicrobial Stewardship (AMS) – Preamble email to questionnaire

Dear participant,

My name is Yumna Ramjan (Student no. 213398826), currently registered for a M.Pharm degree at the Nelson Mandela University.

You are being asked to participate in the preliminary phase of a Master's study. You will be required to complete a questionnaire, which will involve questions related to the use of antimicrobial stewardship utilisation metrics in the workplace. The research to be conducted for the Master's dissertation involves the **"**Development of a framework for an antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in the South African public sector hospital setting". This project will be conducted under the supervision of Dr. Jane McCartney.

Approval for the study has been received from the Faculty Post Graduate Studies Committee (FPGRSC) and the Research Ethics Committee (REC-H) at the Nelson Mandela University, the Eastern Cape Department of Health (ECDOH) and the Senior Manager Medical Services of Hospital X. I am hereby seeking your consent to complete the questionnaire.

To participate, you will be required to agree or not agree in the first section of the electronic questionnaire to verify that you understand and agree to the conditions. Participation in the research is completely voluntary. Although your identity will at all times remain confidential, the results of the research study may be presented at scientific conferences or published in a peer-reviewed journal. It is expected that the questionnaire will take you about 10 minutes to complete. Please complete the questionnaire by the 2nd June 2018.

Thank you very much for your time and participation in the study. If you have any questions pertaining to the study, please feel free to contact me on my email address: s213398826@mandela.ac.za or contact number: +27714325943.

Yours sincerely,
Yumna Ramjan (RESEARCHER)

Questionnaire: Use of Metrics in Antimicrobial Stewardship (AMS)

I agree to participate in the research and therefore will complete the questionnaire.

Yes ☐

No ☐

Use of Metrics in Antimicrobial Stewardship (AMS)												No.
	Section A – Demographical Information											
1.	Gender	Female		Male								
2.	Home language	Afrikaans		English		Xhosa		Other: (specify)				
3.	Occupation											
	Infectious disease specialist		Pharmacist		Medical prescriber		Clinical Pathologist					
4.	Are you involved in an AMS team?	Yes		No								
5.	Do you or did you undergo AMS training?	Yes		No								
	If yes, choose one of the following option:											
	Short/online course		Workshop		University course		Other: (specify)					

	Section B – Perceptions regarding the application of the AMS metrics				
1.	**Have you ever utilised the metrics listed below to monitor antimicrobial utilisation? Please circle the appropriate response.**				
1.1	Defined Daily Dose (DDD)	**Yes**		**No**	
1.2	Days of Therapy (DOT)	**Yes**		**No**	
1.3	Prescribed Daily Dose (PDD)	**Yes**		**No**	
1.4	Length of Therapy	**Yes**		**No**	
1.5	Exposure days	**Yes**		**No**	
1.6	Costs of antimicrobials	**Yes**		**No**	
1.7	Grams of antimicrobials	**Yes**		**No**	
1.8	Intravenous (IV) to oral switch	**Yes**		**No**	
2.	**Please indicate the degree of usefulness of the following AMS utilisation metrics by circling the appropriate number:**	**Not useful**	**Slightly useful**	**Useful**	**Extremely useful**
2.1	The usefulness of Defined Daily Dose (DDD) to monitor antimicrobial usage is:	1	2	3	4
2.2	The usefulness of Days of Therapy (DOT) to monitor antimicrobial usage is:	1	2	3	4
2.3	The usefulness of Prescribed Daily Dose (PDD) to monitor antimicrobial usage is:	1	2	3	4
2.4	The usefulness of Length of Therapy (LOT) to monitor antimicrobial usage is:	1	2	3	4
2.5	The usefulness of exposure days to monitor antimicrobial usage is:	1	2	3	4
2.6	The usefulness of costs of antimicrobials to monitor antimicrobial usage is:	1	2	3	4
2.7	The usefulness of grams of antimicrobials to monitor antimicrobial usage is:	1	2	3	4
2.8	The usefulness of intravenous (IV) to oral switch to monitor antimicrobial usage is:	1	2	3	4

3.	**Please indicate the degree of clinical relevance of the following AMS utilisation metrics clinically by circling the appropriate number:**	**Not clinically relevant**	**Slightly clinically relevant**	**Clinically relevant**	**Extremely clinical relevant**
3.1	The clinical relevance of Defined Daily Dose (DDD) is:	1	2	3	4
3.2	The clinical relevance of Days of Therapy (DOT) is:	1	2	3	4
3.3	The clinical relevance of Prescribed Daily Dose (PDD) is:	1	2	3	4
3.4	The clinical relevance of Length of therapy (LOT) is:	1	2	3	4
3.5	The clinical relevance of exposure days is:	1	2	3	4
3.6	The clinical relevance of costs of antimicrobials is:	1	2	3	4
3.7	The clinical relevance of grams of antimicrobials is:	1	2	3	4
3.8	The clinical relevance of IV to oral switch is:	1	2	3	4

Thank you for completing this questionnaire.

Appendix B: Informed consent form for qualitative component: semi-structured interviews – preliminary phase and post-developmental phase

NELSON MANDELA UNIVERSITY

INFORMED CONSENT FORM

RESEARCHER'S DETAILS	
Title of the research project	**Development of a framework for an antimicrobial usage reporting tool for public sector hospitals**
Reference number	**H17-HEA-PHA-020**
Principal investigator	**Yumna Ramjan**
Address	**Faculty of Health Sciences** **Department of Pharmacy** **Building 12, South Campus** **P.O. Box 77000** **Nelson Mandela University** **Port Elizabeth**
Postal Code	**6031**
Contact telephone number (private numbers not advisable)	**+27 415042128**

A. DECLARATION BY OR ON BEHALF OF PARTICIPANT		**Initial**
I, the participant and the undersigned	(Full names)	
ID number		
Address (of participant)		

A.1 HEREBY CONFIRM AS FOLLOWS:		**Initial**
I, the participant, was invited to participate in the above-mentioned research project		
that is being undertaken by	Yumna Ramjan	
from	The Department of Pharmacy in the Faculty of Health Sciences	
of the Nelson Mandela University.		

2. THE FOLLOWING ASPECTS HAVE BEEN EXPLAINED TO ME, THE PARTICIPANT:					**Initial**
2.1	**Aim:**	The researcher is investigating the development of a framework for an antimicrobial usage reporting tool, which would integrate with various data sources in order to be used by AMS practitioners in order to optimise antimicrobial usage in the South African public sector hospital setting. The information will be used to/for the purpose of a Masters Degree.			
2.2	**Procedures:**	I understand that I will need to participate in a semi-structured interview.			
2.3	**Risks:**	None. All information related to the participants will remain anonymous			
2.4	**Possible benefits:**	As a result of my participation in this study – None			
2.5	**Confidentiality:**	My identity will not be revealed in any discussion, description or scientific publications by the investigators.			
2.6	**Access to findings:**	Any new information or benefit that develops during the course of the study will be shared as follows:			
2.7	**Voluntary participation / refusal / discontinuation:**	My participation is voluntary	**YES**	**NO**	
		My decision whether or not to participate will in no way affect my present or future care / employment / lifestyle	**TRUE**	**FALSE**	

3. THE INFORMATION ABOVE WAS EXPLAINED TO ME/THE PARTICIPANT BY:	**Initial**
Yumna Ramjan	
In **English**	
I was given the opportunity to ask questions and all these questions were answered satisfactorily.	

4.	No pressure was exerted on me to consent to participation and I understand that I may withdraw at any stage without penalization.	

5.	Participation in this study will not result in any additional cost to myself.	

A.2 I HEREBY VOLUNTARILY CONSENT TO PARTICIPATE IN THE ABOVE-MENTIONED PROJECT:	
Signed/confirmed at	on 20
Signature or right thumb print of participant	Signature of witness: Full name of witness:

B. STATEMENT BY OR ON BEHALF OF INVESTIGATOR		
I, Yumna Ramjan, declare that:		
1.	I have explained the information given in this document to	(Name of patient/participant)
2.	He / she was encouraged and given ample time to ask me any questions;	
3.	This conversation was conducted in English and no translator was used	
Signed/confirmed at	On	20
Signature of interviewer	Signature of witness: Full name of witness:	

C. IMPORTANT MESSAGE TO PATIENT/REPRESENTATIVE OF PARTICIPANT	
Dear participant/representative of the participant Thank you for your/the participant's participation in this study. Should, at any time during the study: - You require any further information with regard to the study	
Kindly contact	Yumna Ramjan
At telephone number	+27 415042128/ +27 714325943

Appendix C: Written information given to the respondents prior to participation in the semi-structured interviews – preliminary and post-developmental phase

Faculty of Health Sciences
Department of Pharmacy
Building 12, South Campus
Nelson Mandela University

Tel: +27 (0) 41 504-2128
Fax: +27 (0) 41-504-2744
E-mail Faculty Chairperson: ilse.truter@mandela.ac.za

Date XXXX
Ref: H17-HEA-PHA-020

Contact person: Miss Yumna Ramjan

Dear participant,

You are being asked to participate in the preliminary phase of a Master's study. You will be required to participate in a semi-structured interview, which will involve questions related to the use of antimicrobial stewardship utilisation metrics in the workplace. The research to be conducted for the Master's dissertation involves the **"**Development of a framework for an antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in the South African public sector hospital setting". This project is being conducted under the supervision of Dr. Jane McCartney.

We will provide you with the necessary information to assist you to understand the study and explain what would be expected of you. These guidelines would include the risks, benefits, and your rights as a study subject. Please feel free to ask the researcher to clarify anything that is not clear to you. To participate, it will be

required of you to provide a written consent that will include your signature, date and initials to verify that you understand and agree to the conditions.

You have the right to query concerns regarding the study at any time. Immediately report any new problems during the study, to the researcher. Telephone numbers of the researcher are provided. Please feel free to call these numbers.

Furthermore, it is important that you are aware of the fact that approval for the study has received from the Faculty Post Graduate Studies Committee (FPGRSC) and the Research Ethics Committee (REC-H) at the Nelson Mandela University, the Eastern Cape Department of Health (ECDOH) and the Senior Manager: Medical Services of Hospital X. I am hereby seeking your consent to conduct a semi-structured interview. Queries with regard to your rights as a research subject can be directed to the Research Ethics Committee (Human), Department of Research Capacity Development, PO Box 77000, Nelson Mandela University, Port Elizabeth, 6031.

Participation in research is completely voluntary. If you do partake, you have the right to withdraw at any given time, during the study without penalty or loss of benefits. Although your identity will at all times remain confidential, the results of the research study may be presented at scientific conferences or published in a peer-reviewed journal.

A second round of semi-structured interview may take place in the post-developmental phase of the framework for the proposed antimicrobial usage reporting tool. You will be invited to participate in the semi-structured interview for feedback on applicability and practicality of the framework for the proposed tool. More information will be communicated at a later stage.

This informed consent statement has been prepared in compliance with current statutory guidelines.

Yours sincerely,

Yumna Ramjan (RESEARCHER)

Appendix D: Oral information given to the respondents prior to participation in the semi-structured interviews – preliminary phase and post-developmental phase

No oral information was given to the respondents prior to participation in the semi-structured interviews.

Appendix E: Institutional Permission: Letter to request for permission from the Chief Executive Officer to conduct research at hospital X

NELSON MANDELA
UNIVERSITY

Miss Yumna Ramjan
Faculty of Health Sciences
Department of Pharmacy
Building 12, South Campus
Nelson Mandela University
Tel: +27 415042128

Attention: The Chief Executive Officer of Hospital X

RE: REQUEST FOR PERMISSION TO CONDUCT RESEARCH AT HOSPITAL X

Dear Sir or Madam,

My name is Yumna Ramjan, and I am a pharmacy student at the Nelson Mandela University in Port Elizabeth. The research I wish to conduct for my Master's dissertation involves the "Development of a framework for an antimicrobial usage reporting tool which would integrate with various data sources in order to be used by AMS practitioners to optimise antimicrobial usage in the South African public sector hospital setting". This project will be conducted under the supervision of Dr. Jane McCartney.

I have received approval for the study from the Faculty Post Graduate Studies Committee (FPGRSC) at the Nelson Mandela University and the Eastern Cape Department of Health (ECDOH). I have included copies of the approval letter. I am hereby seeking your consent to carry out a questionnaire and interview members of the antimicrobial stewardship team at Hospital X.

I have provided you with a copy of my research proposal, for further information, and consent and assent forms to be used in the research process.

Upon completion of the study, I undertake to provide the Department of Health with a bound copy of the full research report. If you require any further information, please do not hesitate to contact me s213398826@mandela.ac.za. Thank you for your time and consideration in this matter.

Yours sincerely,

Yumna Ramjan (213398826)
Nelson Mandela University

Appendix F: Approval letter from the Faculty Postgraduate Research Committee at the Nelson Mandela University

NELSON MANDELA
UNIVERSITY

Copies to:

Supervisor: PROF SI BOSCHMANS
Co-supervisor: MS JA MC CARTNEY
Summerstrand South
Faculty of Health Sciences
Tel. +27 (0)41 5042956 Fax. +27 (0)41 5049324
Marilyn.Afrikaner@mandela.ac.za

Student number: 213398826
Contact person: Ms M Afrikaner
07-NOV-2017
MS RAMJAN
27 SIESTA SANDS
GARDNER CIRCLE
SOUTH END
PORT ELIZABETH
6070

OUTCOME OF FINAL RESEARCH/PROJECT PROPOSAL:

65500 MPharm (Research)
DEVELOPMENT OF A FRAMEWORK FOR A PROPOSED ANTIMICROBIAL USAGE REPORTING TOOL FOR PUBLIC SECTOR HOSPITALS

Please be advised that your final research project was approved by the Faculty

Postgraduate Studies Committee (FPGSC).

FPGSC grants ethics approval. The ethics clearance reference number is H17-HEA-PHA-020 and is valid for three years.

We wish you well with the project.

Kind regards,

Ms M Afrikaner

Faculty Postgraduate Studies Committee (FPGSC) Secretariat

Faculty of Health Sciences

Appendix G: Approval letter from the Eastern Cape Department of Health

Eastern Cape Department of Health

Enquiries:	Madoda Xokwe	Tel No:	040 608 0710
Date:	27 November 2017	Fax No:	043 642 1409
e-mail address:	madoda.xokwe@echealth.gov.za		

Dear Ms. Y. Ramjan

Re: Development of a Framework for a Proposed Antimicrobial Usage Reporting Tool for Public Sector Hospitals (EC_201711_019)

The Department of Health would like to inform you that your application for conducting a research on the abovementioned topic has been approved based on the following conditions:

1. During your study, you will follow the submitted protocol with ethical approval and can only deviate from it after having a written approval from the Department of Health in writing.
2. You are advised to ensure, observe and respect the rights and culture of your research participants and maintain confidentiality of their identities and shall remove or not collect any information which can be used to link the participants.
3. The Department of Health expects you to provide a progress on your study every 3 months (from date you received this letter) in writing.
4. At the end of your study, you will be expected to send a full written report with your findings and implementable recommendations to the Epidemiological Research & Surveillance Management. You may be invited to the department to come and present your research findings with your implementable recommendations.
5. Your results on the Eastern Cape will not be presented anywhere unless you have shared them with the Department of Health as indicated above.

Your compliance in this regard will be highly appreciated.

SECRETARIAT: EASTERN CAPE HEALTH RESEARCH COMMITTEE

Appendix H: Approval letter to conduct research at Dora Nginza Hospital

Province of the
EASTERN CAPE
HEALTH

Office of the Senior Manager: Medical Services • Room DG 25 • Dora Nginza Regional Hospital • Spondo Street • Zwide • Port Elizabeth • Eastern Cape
Private Bag X11951 • Algoa Park • Port Elizabeth • 6005 • REPUBLIC OF SOUTH AFRICA
Tel: +27 (0)41 406 4201 • Cell: +27 (0)82 956 6709 • Fax: +27 (0)866 413 211
Email: Jaline.Kotze@ECHEALTH.GOV.ZA or jaline.kotze@gmail.com • Website: www.echealth.gov.za

7 December 2017

Ms Y Ramjan

RE: REQUEST TO DO RESEARCH

Dear Ms Ramjan

Your request to do research at Dora Nginza Regional Hospital is hereby approved.

The approval is granted with the following conditions attached:

1. Adherence to the conditions as set out in the ethical approval by NMU.
2. Adherence to the conditions as set out in the approval from the ECDOH.

I wish you all the success with your research.

Regards,

Dr Jaline Kotze
Senior Manager: Medical Services
Dora Nginza Hospital

Appendix I: Approval letter to conduct research at Livingstone Hospital and Port Elizabeth Provincial Hospital

It must be noted that Port Elizabeth Hospital Complex consists of Livingstone Hospital and Port Elizabeth Provincial Hospital. The Senior Manager Medical Services of Livingstone Hospital is the same for Port Elizabeth Provincial Hospital, therefore, the letter in Appendix I also applies to Port Elizabeth Provincial Hospital.

Province of the
EASTERN CAPE
HEALTH

Office of the Senior Manager: Medical Services • 1st Floor • Nurses' Home • Livingstone Hospital • Stanford Road • Korsten • Port Elizabeth
PO Korsten • Port Elizabeth • 6014 • REPUBLIC OF SOUTH AFRICA
Tel.: +27 (0)41 405 2100/2101/2102 • Fax: +27 (0)41 405 2103

16 February 2018

Ms Y Ramjan
Nelson Mandela University

Via email: s213398826@mandela.ac.za

Dear Ms Ramjan

Re: REQUEST TO BE GRANTED PERMISSION TO DO RESEARCH – *"Development of a framework for a proposed Antimicrobial usage reporting tool for Public sector hospitals"*

Your request to do research at Livingstone hospital refers.

Authorisation is herewith granted to do your research at Livingstone Hospitals.

Kindly contact Mrs. B Koopman, Pharmacy Department, Livingstone Hospital - on 041 405 2167 to make the necessary logistic arrangements.

You are to ensure that your study does not disrupt services and you must maintain strict confidentiality at all times.

On conclusion of your study, a research report detailing your findings and recommendations is to be made available to the hospital.

May I take this opportunity to wish you success with your studies.

.....
DR MJ MASELOA
SENIOR MANAGER MEDICAL SERVICES
MJM/jhm

Together, moving the health system forward

Fraud prevention line: 0800 701 701
24 hour Call Centre: 0800 032 364
Website: www.echealth.gov.za

2030 NDP

Appendix J: Approval letter to conduct research at Frere Hospital

Province of the
EASTERN CAPE
HEALTH

Non Interventional Hospital Review Board

Postal Address:
Frere Hospital
Private bag x 9047
Amalinda
East London
5200
Enquiries: B. Willie

Tel: 043 709 2389

Email:babalwa.willie@echealth.gov.za

Physical Address:
Frere Hospital
4th Floor Room 4.18
Amalinda
East London
5200

09th April 2018

Ms Y. Ramjan
Nelson Mandela Metropolitan University
Faculty of Health Sciences
Summerstrand South
Port Elizabeth
6000

RE: REQUEST FOR PERMISSION TO CONDUCT RESEARCH

" Development of a framework for a proposed antimicrobial usage reporting tool for public sector Hospitals."

We acknowledge receipt of the above mentioned proposal.

Having gone through your proposal, the committee has no ethical problems noted.

Please be advised that the committee has granted you the consent to do the research and confidentiality be maintained.

Yours sincerely

.....

Dr J. Thomas
Clinical Governance Frere Hospital

Appendix K: Approval letter to conduct research at Cecilia Makiwane Hospital

Province of the
EASTERN CAPE
HEALTH

Office of the Chief Executive Officer : Cecilia Makiwane Hospital
Billie Road, Mdantsane, 5219. Private Bag X9047: East London, 5200
Tel: 043 708 2300. E-mail: yoliswa.ngcanga@echealth.gov.za: Website: www.ecdoh.gov.za

12 March 2018

Ms Y. Ramjan
Faculty of Health Sciences
Department of Pharmacy
Nelson Mandela University
Port Elizabeth
Eastern Cape Province

Dear Ms Ramjan

RE: REQUEST FOR PERMISSION TO CONDUCT RESEARCH STUDY AT CECILIA MAKIWANE HOSPITAL –DEVELOPMENT OF A FRAMEWORK FOR A PROPOSED ANTIMICROBIAL USAGE REPORTING FOR PUBLIC SECTOR HOSPITALS (ec 2017 11 019).

Permission is hereby granted for you to conduct the abovementioned research study at Cecilia Makiwane Hospital subject to the following provisions:

1. Complying with the provisions of the permission letter from the Eastern Cape Health Research Committee dated 27 November 2017.
2. Complying with your Research Methodology Plan as approved by the relevant Ethics Committee.
3. Introducing yourself to the relevant management division of the hospital and providing necessary documentation showing permission and approval of your research study to be conducted at the hospital.
4. Ensuring minimal disturbance to the day to day operations of the relevant department of the hospital.
5. Observe the confidentiality of participants and their rights not to participate in the research study.

Your compliance in this regard will be highly appreciated and wishing you all the best in your research study.

Dr M. V. Nkohla
Acting Chief Executive Officer