POINT PREVALENCE SURVEY OF ANTIMICROBIAL UTILIZATION
AT DR GEORGE MUKHARI ACADEMIC HOSPITAL

A mini-dissertation submitted by

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in partial fulfilment of the requirements for the degree of

Master of Pharmacy

in the

School of Pharmacy

at the

Sefako Makgatho Health Sciences University

Supervisor: Prof N Schellack

Co-supervisors: Prof JC Meyer and Prof B Godman

2018
DECLARATION

I Nokuthula Dlamini declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University, for the degree of Master of Pharmacy, in the School of Pharmacy has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

Dlamini NN (Miss) Date: 20/02/2018
DEDICATION

To GOD Almighty for His love, grace and guidance. To my parents, Mr S.Z. Dlamini and Mrs E.U Dlamini for their continuous support, prayers and allowing me to choose my own path. My sister and rock star, Nompumelelo Dlamini for her endless support and being my pillar of strength all the time. I owe this accomplishment to you. Thank you all for believing in me and your never ending support.
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## ABBREVIATIONS AND ACRONYMS

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<tr>
<td>AMR</td>
<td>Antimicrobial Resistance</td>
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<tr>
<td>APP</td>
<td>Application</td>
</tr>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
</tr>
<tr>
<td>CARG</td>
<td>Compound Annual Growth Rate</td>
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<tr>
<td>DDD</td>
<td>Defined Daily Dose</td>
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<td>DUT</td>
<td>Drug Utilization</td>
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<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
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<td>EML</td>
<td>Essential Medicine List</td>
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<td>GARP-SA</td>
<td>Global Antibiotic Resistance Partnership- South Africa</td>
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<td>GAP</td>
<td>Global Action Plan</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>ICU</td>
<td>Intensive Care Unit</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>NDOH</td>
<td>National Department of Health</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>MURIA</td>
<td>Medicines Utilisation Research in Africa</td>
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<tr>
<td>SHCSRC</td>
<td>School of Health Care Sciences Research Committee</td>
</tr>
<tr>
<td>SMUREC</td>
<td>Sefako Makgatho University Research Ethics Committee</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>PDD</td>
<td>Prescribed Daily Dose</td>
</tr>
<tr>
<td>PPS</td>
<td>Point Prevalence Survey</td>
</tr>
<tr>
<td>PTCs</td>
<td>Pharmacy and Therapeutics Committees</td>
</tr>
<tr>
<td>URTI</td>
<td>Upper Respiratory Tract Infections</td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary Tract Infections</td>
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<td>WHO</td>
<td>World Health Organization</td>
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ABSTRACT

Introduction: Antimicrobial resistance (AMR) is a serious public health concern and a direct threat to patient safety as well as the economy of countries. Antimicrobials play a vital role in reducing morbidity and mortality through the management of infections. However, the misuse and overuse of these agents is taking us towards an era where there could be no antimicrobials available for use due to resistance. Extensive data on the reporting of antimicrobial utilization and consumption among hospitals in South Africa, especially public sector hospitals, is lacking. This study therefore aimed to determine antimicrobial consumption using a point prevalence survey (PPS) methodology in order to document current antimicrobial use in a leading public sector hospital in South Africa, as a first step in this process.

Objectives: The objectives of the study were to i) determine the appropriateness of the point prevalence survey (PPS) data collection instruments developed in Botswana for performing an antimicrobial utilisation study in selected public sector hospitals in Gauteng Province; ii) determine the point prevalence of antimicrobial utilisation in selected public sector hospitals in Gauteng Province; iii) evaluate the compliance of antimicrobials prescribed with the hospital formulary, the NDOH Essential Medicines List (EML) and the current Standard Treatment Guidelines (STGs) in South Africa; and iv) test the developed APP in practice to see if this could enhance data collection given concerns with the time and costs associated with a paper based method.

Method: A PPS was conducted in two phases at Dr George Mukhari Academic Hospital using data collection instruments developed and used in Botswana. Data was collected with the assistance of trained academic pharmacist interns. All patient files in one single in-patient ward were completely surveyed in a single day, which means, a ward was surveyed in one day but not all wards were surveyed on the same day. The number of patients who were on antimicrobials served as a numerator and the denominator comprised the total number of patients in the ward. Phase 1 was conducted over a period of two months in a summer season in 2017 and involved the surveillance of all in patient wards except for day admissions and psychiatry wards. The data was collected using paper-based forms. Parallel to the paper-based data collection, a web-based mobile application was developed, for simultaneous data collection and capture, using the PPS instruments.

Phase 2 was conducted in a period of a week with the aim to develop and test an electronic data collection instrument. A web based mobile application (APP), which was developed from the variables of the paper based data collection tool was tested, with data subsequently
entered on the mobile application and exported to MS Excel® for analysis. A questionnaire was administered to assess its usefulness. Ethical clearance was granted for the study (SMUREC/H210/2016:PG).

**Results**: A total of 39 wards and 512 patient files were surveyed in phase 1 using a paper-based tool. The overall prevalence of antimicrobial use was 38.5% with the highest use in the various ICUs. The use of beta lactamase inhibitors and TB drugs were the most prevalent antimicrobials used. More than two thirds (83%) of antimicrobial treatment was modified following culture sensitivity test (CST) results, and 98% of antimicrobials complied with the national Essential Medicine List. In phase 2, a total of 187 patient’s files was surveyed while documenting the challenges and areas of improvement for the APP. Users agreed that surveying the patient’s files took less time with the electronic tool compared to the paper based tool, and should be used in the future.

**Conclusion**: The Point Prevalence survey method offers a standardized tool that can be used to identify targets for quality improvement of antimicrobial use. In addition, the development of the APP appreciably reduces data collection time and analysis, and will be used in subsequent PPS studies among public hospitals in South Africa.
CHAPTER 1
INTRODUCTION

1.1 INTRODUCTION

This chapter provides an overview of antimicrobial use and resistance. It provides background information on the situation worldwide with regards to antimicrobial consumption and resistance and what the current situation is in South Africa (SA). It also explains the gaps in terms of antimicrobial stewardship and how this study is set to identify and close these gaps, which is the “rationale” of the study. The research questions, aims and objectives of the study are presented, followed by a description of the importance of the study. The chapter is concluded with an outline of the dissertation.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Antimicrobials play a vital role in reducing morbidity and mortality through the management of infections. They are estimated to increase life expectancy by 20 years (National Department of Health (NDoH), 2015). However, the excessive utilisation of these agents has brought about a global health concern, with increasing resistance against these lifesaving agents (Lior & Bjerrum, 2014; Van Boeckel, Gandra, Ashok, Caudron, Grenfell, Levin & Laxminarayan, 2014). For instance one of the leading pandemics in South Africa (SA), Tuberculosis, (Mendelson & Matsotsa 2015) has been reported to have increased resistant strains. Recent global data reported that 3.7% of new cases and 20% of previously treated TB cases have been caused by rifampicin and isoniazid resistant strains (Lior & Bjerrum, 2014). The increasing loss of efficacy of antimicrobials against common pathogens has not only led to high health cost, due to the compelled use of more expensive antimicrobials, but also increased morbidity and mortality (Van Boeckel et al, 2014).

With the diminishing effectiveness of antimicrobials, the world is facing a major predicament of how infections will be treated in the future (NDoH 2015). As a strategy to salvage and preserve the remaining antimicrobials, and prevent an era where infections are uncontrollable, member states of the World Health Organization (WHO) developed national action plans across countries, including improved governance, to reduce morbidity, mortality and costs associated with antimicrobial resistance (AMR), in response to the WHO’s antimicrobial resistance Global Action Plan (GAP) (Jinks et al, 2016). The GAP
Chapter 1: Introduction

intends to provide one health approach that will lead to the optimization of antimicrobial use in human and animal health through the knowledge and evidence obtained from surveillance and research (WHO, 2015)

Despite AMR being a matter of urgent concern, no single strategy can completely contain the emergence of resistance (Goosen, Ferech, Vander Stichel & Elseviers, 2005). Consequently, multiple strategies are typically needed across healthcare sectors including addressing issues of governance. For example every country can adopt the German policy in which an infection and protection act exists, which requires the collection of antimicrobial consumption data, assessing it and implementing appropriate strategies to combat AMR (With, Allerberger, Amann, Apfalter, Brod, Eckmanns, Fellhauer, Geiss, Janata, Krause, Lemmen, Meyer, Mittermayer, Porsche, Prester, Reuter, Sinha, Strau, Wechsler-Fördös, Wenisch & Kern, 2016). The development and implementation of effective strategies depends on the collection of accurate informative data including current utilisation and resistance patterns alongside current policies (Rezal, Hassai, Alrassheedy, Saleem, Yosof & Godman, 2015), which is starting to happen across countries to guide future interventions. However, obtaining accurate consumption data in South Africa has been a challenge due to economic and prescribing difficulties (Schellack, Benjamin, Brink, Duse, Faure, Goff, Mendelson, Meyer, Miot, Perovic, Pople, Suleman, van Vuuren & Essack, 2017). Another major challenge is that the South African health care system is divided into two levels of health care benefits and care (a two tiered health care system); the private and public sectors. This has resulted in a lack of standardized operation in certain areas such as availability of procurement data from Intercontinental Marketing Services (IMS), which was only available from the private sector and limited only to antibiotics (Schellack et al, 2017).

South Africa has a high burden of infectious diseases which contributes to the high use of antimicrobials (Mendelson & Matsotso, 2015). The antimicrobial consumption rate in South Africa has been reportedly to be very high (Mendelson & Matsotso, 2015). The use of broad spectrum penicillins in the country was recently recorded as 10 000 standard units per 1 000 population (Cddep.org, 2016). Antimicrobial consumption data has though recently been quantified at a population level using procurement data sources in SA (Schellack et al, 2017). In the public sector, the compound annual growth rate for antimicrobial use (CARG), which is a measure of market growth over this period, was reportedly to be 11%. A significant increase was evident in injectable cephalosporins (169%), injectable
fluoroquinolones (287%) and broad spectrum penicillins (167%). All other antimicrobials showed an increase of 6876% (Schellack et al, 2017).

With such high antimicrobial use, AMR will emerge. In South Africa, full penicillin-resistant *Streptococcus pneumonia* strains were already detected in 1977, and in 1978 the occurrence of multidrug-resistant and highly resistant strains was reported. Since then, the prevalence of *S.pneumonia* antibiotic resistance has increased around the world, not only to penicillin but also to non-β-lactam antibiotics, including the macrolides, tetracycline, chloramphenicol, the fluoroquinolones and co-trimoxazole (Crowther-Gibson, Govender, Lewis, Bamford, Brink, Gottberg, Klugman, Plessis, Fali, Harris, Keddy & Botha, 2011). Resistance to non-β-lactam drugs is often associated with decreased susceptibility to penicillin; consequently, the prevalence of multidrug-resistant strains is also increasing in South Africa (Crowther-Gibson et al, 2011).

Data from 2012 to 2014 showed a 27% resistance of *Escherichia coli* to fluoroquinolones, 27% methicillin resistant *Staphylococcus aureus* and an increasing rate (from 2.9% to 4.2%) of *Klebsiella pneumonia* resistance against carbapenems (Cddep.org, 2016). There are also concerns with current antibiotic prescribing practices in hospitals.

The WHO has for many years promoted the global monitoring of antimicrobial use across sectors and raised awareness of the consequences of resistance (Versporten, Bielicki, Drapier, Sharland, Goossens, Calle & Francis, 2016). Global Point Prevalence Surveys (PPSs) of antimicrobial consumption and resistance in hospitals are designed to provide current data on utilisation and resistance patterns using a standardised methodology to plan future interventions (Versporten et al., 2016). The European Centre for Disease Prevention and Control (ECDC) has also promoted similar activities (ECDC, 2013), with similar activities now being undertaken among African countries (Massele et al, 2017). The Medicine Utilization Research in Africa (MURIA) group annually brings African researchers together in a workshop to improve Drug Utilization (DU) research in Africa (Massele et al, 2017) and this study has been influenced by this group.

A PPS conducted between April and August 2015, as part of the 2015 Global Point Prevalence Survey, in a large tertiary hospital in Cape Town, South Africa, showed that 31% (359/1156) of patients were receiving antibiotics and the majority (83%) of antibiotic prescriptions were empirical (Finlayson, Versporten, Whitelaw, Goossens & Taljaard,
The implication of these results is that antibiotics were administered without the availability of cultures. In addition, only a few doctors (11%) documented the stop/review date on the prescription. This places patients at risk of being exposed to antimicrobials for a longer period than required (Finlayson et al, 2016).

However, extensive data on the reporting of antimicrobial utilisation and consumption among hospitals in South Africa, especially public sector hospitals, is currently lacking. A valid and reliable surveillance tool or method that will link information between the pharmacy, prescribers and laboratory is currently not in place yet (Mendelson & Matsotso, 2015). Data on antibiotic utilisation were collected in one of the hospitals in the Western Cape Province during World Antibiotic Awareness Week in 2015. However, the data are not sufficiently robust to make reliable and valid interpretations and recommendations. This highlights the need for assessing antimicrobial utilisation, using a valid and reliable surveillance tool, to provide a baseline for future surveys, ultimately aimed at promoting rational antimicrobial use. Recent evidence has also shown variable adherence to agreed antibiotic prescribing guidance across sectors and countries, which needs to be addressed as part of improving antimicrobial stewardship (Afriyie, Amponsah, Dogbey, Agyekum, Kesse, Truter, Meyer & Godman, 2017; Matsitse, Helberg, Meyer, Godman, Massele, Schellack, 2017).

In response to the lack of available antimicrobial consumption data as highlighted in the above sections, the aim of the study was to determine current antimicrobial consumption at Dr George Mukhari Academic Hospital (DGMAH) using a PPS methodology in order to document current antimicrobial use. Information was obtained with PPS data collection instruments developed and updated in Botswana with input from the WHO, building on the ECDC and Global studies (Massele, Tiroyakgosi, Matome, Desta, Muller, Paramadhas, Malone, Kurusa, Didimalang, Moyo & Godman, 2016). The study served as a pilot project for a follow-up national survey on antimicrobial utilisation among hospitals in South Africa. It was envisaged that the results of both these surveys would be used to identify targets for quality improvement programmes regarding antibiotic utilisation in individual public sector hospitals as well as for the country as a whole. This builds on current initiatives including defining the role for pharmacists as part of antimicrobial stewardship programmes in South Africa (Schellack, Bronkhorst, Coetzee, Godman, Gous, Kolman, Labuschagne, Malan, Messina, Naested, Schellack, Skosana & Van Jaarsveld, 2017).
1.3 RESEARCH QUESTION

The study posed the following research questions:

- The primary research question was what is the **prevalence of antimicrobial consumption** at Dr George Mukhari Hospital and how antimicrobials are currently being used in this facility.
- The secondary research question was if there are **antimicrobial stewardship programs** in place to improve antimicrobial prescribing and if national prescribing guidelines are being used to prescribe antimicrobials in the hospital.
- The last significant question was if the **PPS surveillance tool** can be used as a standardized tool to **measure antimicrobial consumption** in hospitals especially with the development of a web based application (APP) to reduce data collection times.

1.4 AIMS OF THE STUDY

The study posed the following aims:

- The principal aim was to **quantify and describe current antimicrobial utilisation** at DGMAH including adherence to current guidelines
- The secondary aim was to **develop and test an electronic data collection tool** in a form of a web based application (APP) to enhance data collection for PPS studies

1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- **To determine the appropriateness of the PPS data collection instruments** developed in Botswana for performing an antimicrobial utilisation study at DGMAH
- **To determine the point prevalence of antimicrobial utilisation** at DGMAH as a selected public sector hospital in Gauteng Province.
- To assess the potential of **using a web based APP** to reduce data collection time.
- **To determine the extent and utilisation of antimicrobial sensitivity testing to guide antibiotic prescribing.**
1.6 IMPORTANCE AND SIGNIFICANCE OF THE STUDY

The background presented in Section 1.2 alludes to the importance of this study, which is to enhance the appropriate use of antimicrobials in South Africa and consequently reduce AMR. This can be achieved by identifying areas of improvement and promoting the rationale use of antimicrobials, such as greater use of sensitivity analyses and faster descaling of IV medication to oral where necessary. Meyer and Suleman, (2012) in their summarised presentation of “Pharmacy beyond the imagination” stated that guidelines for antibiotic usage and infection control may be present, but evidence of implementation is scanty. This study was therefore aimed at providing a tool for documenting antimicrobial usage, which can serve as a stepping stone for implementation of antimicrobial usage guidelines to improve future use.

To combat AMR, the WHO developed a policy package that addressed the critical actions to be taken by all governments and stakeholders in fighting resistance. One of the components of this policy was the importance of antimicrobial use surveillance. The surveillance of antimicrobial utilization provides the basis for monitoring antimicrobial consumption and prescribing behaviours. This is very important as it provides understanding in making sound and rational decisions on antimicrobial therapy and helps in assessing the health consequences of antimicrobial overuse (WHO, 2015).

This study, in alignment with possible policies to strengthen antimicrobial surveillance capacity and combat AMR, aimed at providing a tool for documenting current antimicrobial usage in hospitals. The findings can serve as a stepping stone for the future implementation of pertinent antimicrobial usage guidelines in especially public hospitals in South Africa. This study also served as a basic study for the instigation of further surveys on antimicrobial utilization in South Africa. Through this study, an electronic data collection tool was developed and tested to serve as a more convenient data collection tool for antimicrobial prevalence studies for consideration in South Africa as well as other countries in Africa. Further, the study also contributed to knowledge of consumption and prescribing patterns in this hospital, and this information forms a baseline for implementation of strategies and policies to reduce future AMR rates.

In 2014, the South African Department of Health released an implementation plan for the antimicrobial resistance strategy framework for 2014-2024 (NDoH, 2015). One of the aims
was the development of surveillance tools for antimicrobial use. The results of the study will form the basis for promoting appropriate use of antimicrobials in hospitals.

Information was obtained through the use of PPS data collection instruments developed and updated in Botswana with input from the WHO, building on the ECDC and Global studies (Massele, Tiroyakgosi, Matome, Desta, Muller, Paramadhas, Malone, Kurusa, Didimalang, Moyo & Godman, 2016). The study served as a pilot project for a follow-up national survey on antimicrobial utilisation among hospitals in South Africa. It was envisaged that the results of both these surveys would be used to identify targets for quality improvement programmes regarding antibiotic utilisation in individual public sector hospitals as well as for the country as a whole. This builds on current initiatives including defining the role for pharmacists as part of antimicrobial stewardship programmes in South Africa (Schellack, Bronkhorst, Coetzee, Godman, Gous, Kolman, Labuschagne, Malan, Messina, Naested, Schellack, Skosana & Van Jaarsveld, 2017).

1.7 OUTLINE OF THE DISSERTATION

The details of the study are outlined and described in five chapters. Chapter 1 is an introduction to the study. It is structured into the background and rationale of the study, research questions, objectives, aims and significance of the study. Chapter 2 is a literature review and reflects studies that previously have been undertaken on the topic as well as literature and current information on key aspects of the study. It is organized into topics that form concepts and the framework of the study. Chapter 3 explains the methodology used to collect the data needed to meet the objectives of the study. Chapter 4 consists of the results and findings of the study as well as the discussion and analysis of the results. Chapter 5 gives a summary and overview of the study and this is incorporated into conclusion, limitations and recommendations of the research.

1.8 SUMMARY

Increased antibiotic resistance at both population and individual level has shown to be the consequence of overuse of antimicrobials. South Africa in accordance with the World Health Assembly (WHA,2014), resolution to fight antimicrobial resistance has developed an AMR strategy framework which includes the optimization of antimicrobial use surveillance. The
surveillance data will be of benefit in developing and implementing effective policies of AMS at both the national and institutional level.

This study addresses one of the pillars of the strategic framework of the South African plan to reduce AMR and aims to enhance antimicrobial utilization surveillance by quantifying and describing current antimicrobial utilization in public hospitals and the development of an appropriate tool for antimicrobial surveillance nationwide. Furthermore, it gives knowledge and a snapshot on the prescribing patterns and appropriate use of antimicrobials in a leading public sector hospital in South Africa. It also serves as a stepping stone for future surveillance studies to be conducted in a larger setting, and possibly nationwide, to determine national surveillance and reporting systems that will be effective and accurate to plan future pertinent policies.
CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

This chapter reviews available literature and already published research on antimicrobial consumption. It explains the definition of antimicrobials, antimicrobial consumption and how antimicrobial consumption can be measured. It also reviews the quality indicators used in antimicrobial consumption studies. The chapter further provides literature on AMR and the current situation globally as well as in South Africa.

2.2 DEFINING ANTIMICROBIAL CONSUMPTION AND PREVALENCE SURVEYS

Antimicrobials are pharmaceutical agents that encompass antibacterial, antiviral, antifungal, antiparasitic drugs (Leekha, Terrell & Edson, 2011). Appropriate use of these agents is essential in combating AMR, and involves giving the correct antimicrobial for the correct indication, after being certain that an antimicrobial is indicated for the obtained diagnoses, understanding the dosing effect on antimicrobial activity and administering the right dose, as well as switching intravenous (IV) to oral antimicrobials as soon as possible (Leekha et al, 2011). Unfortunately these concepts are not practiced in most parts of the world, hence antimicrobial PPSs have been used in health care institutions to provide baseline knowledge. Furthermore PPSs are a useful means of measuring antimicrobial utilization in hospitals and have shown to be advantageous in cases where time and resources do not permit continuous surveillance (Zarb & Goossens, 2011). PPSs of antimicrobial utilization form the bases in creating policies for antimicrobial stewardship strategies, and can be repeated in institutions to monitor the trends and success of antimicrobial stewardship initiatives. (Zarb & Goossens, 2011).

A PPS is a count of the number of patients with a particular condition/treatment (in this case an antimicrobial agent) at a particular time (in this case a day), as a proportion of the total number of patients who are hospitalized at that particular time. A PPS only counts the condition/treatment if present at the time (on the day) of the survey, but does not count if it is present at other times during the patient stay in the hospital (WHO, 2015).
These type of surveys provide consumption data based on information on dose used, indication and duration of therapy. PPSs provide both quantitative and qualitative information on utilization of antimicrobials. On the day of survey, the required information as shown on Table 2.1 is obtained by assessing prescriptions or patient files.

<table>
<thead>
<tr>
<th>Antimicrobial therapy adheres to standard guidelines with respect to:</th>
<th>Antimicrobial prophylaxis adheres to standard guidelines with respect to:</th>
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<tr>
<td>Choice of agent</td>
<td>Choice of agent</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Route of administration</td>
</tr>
<tr>
<td>Dose</td>
<td>Dosing</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>Timing of preoperative prophylaxis</td>
</tr>
<tr>
<td>Duration of infusion</td>
<td>Dosing interval</td>
</tr>
<tr>
<td></td>
<td>Duration of administration</td>
</tr>
</tbody>
</table>

Source: Zarb & Goossens (2011)

2.2.1 Antimicrobial surveillance

According to the WHO, surveillance is a systematic method of continuous collection of health related information to be used for the assessment, analysis, implementation and evaluation of health practices. Surveillance of antimicrobial consumption is vital in providing information that can be used to control AMR and implement policies and strategies that can be used to control resistance (WHO, 2014). Obtaining this data requires continuous and repeated surveillance in hospitals and at national level. The main goal is to explore antimicrobial use trends and misuse which is the cause of resistance.

2.2.2 Antimicrobial consumption

According to the WHO’s methodology for a global programme on surveillance of antimicrobial consumption, the following antimicrobial consumption and utilization data is explained as follows (WHO 2017):
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**Antimicrobial consumption** is defined as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g. days, months, and year).

**Consumption data** refers to estimates derived from aggregated data sources such as import or wholesaler data, or aggregated health insurance data where there is no information available on the patients who are receiving the medicines or why the antimicrobials are being used. These data sources provide a representation estimate of the use of antimicrobials. Consumption data may be presented as total consumption for a country or may be disaggregated by setting (community or hospital; public or private sectors).

**Antimicrobial use data** refer to estimates derived from patient-level data. These data may allow disaggregation of data based on patient characteristics (gender, age), or indication for which the medicine is being used. Depending on the source of information, it may be possible to determine the patients’ symptoms, physician diagnoses and medication ordered. This will facilitate assessment of clinical practice against agreed protocols and treatment guidelines.

### 2.2.2 Quality indicators for antimicrobial use

The WHO, in its quest to combat AMR, developed a policy package to address this. One of the objectives is the implementation of antimicrobial use surveillance studies, because appropriate use of antimicrobials is necessary in fighting antimicrobial resistance (van den Bosch, Geerlings, Natsch, Prins, & Hulscher, 2014).

Further to this, the WHO states that to understand how antimicrobials are used, indicator studies and focused surveys of patients, prescribers, and dispensers are used to explore the factors that drive antimicrobial use decisions. Examples of indicators used to assess the quality of antibiotic prescribing include the following:

A) Ambulatory care/total utilisation (Adriaenssens, Coenen, Versporten, Muller & Vankerckhoven, 2011):

- Percentage of physician encounters where an antibiotic is prescribed (averaging 46.8% across Africa (Ofori-Asenso, Brhlikova & Pollock, 2016)
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- Total utilization of antibiotics expressed as Daily Drug Dose (DIDs) (DDDs/ 1000 inhabitants/ day)

- Utilization of penicillins (J01C) in DIDs and as a % of total antibiotic use

- % utilization of combination penicillins such as co-amoxiclav as a percentage of amoxicillin use

- Total utilization of cephalosporins (J01D) in DIDs and as a % vs. total antibiotics

- % utilization of third- and fourth-generation cephalosporins vs first and second generation cephalosporins

- Total utilization of macrolides (J01F) in DIDs and as a % vs. total antibiotics

- Utilization of quinolones (J01M) expressed in DIDs as well as % vs. total antibiotic use

- Ratio between users of broad to narrow-spectrum penicillins, cephalosporins and macrolides (B/N ratio) (de Bie, Kaguelidou, Verhamme, De Ridder, Picelli, Straus, Giaquinto, Stricker, Bielicki, Sharland & Sturkenboom, 2016).

B) Hospitals

Potential indicators include the following (van den Bosch et al, 2016):

- Prescribe empirical antibiotic therapy according to national guidelines

- An antibiotic plan should be documented in the case notes at the start of systemic antibiotic therapy

- Empirical antibiotic therapy should be changed to pathogen directed therapy when culture results become available

- Antibiotic therapy should be switched from intravenous to oral therapy within 48 to 72 hours

- A current local antibiotic guideline should be present in the hospital and an evaluation of whether an update should be considered should be performed every 3 years

- Local antibiotic guidelines should correspond to the national antibiotic guidelines, but should deviate based on local resistance patterns

Table 2.2 explains how quality indicators are used in a prevalence survey
### Table 2.2: The use of quality indicators in a prevalence survey

<table>
<thead>
<tr>
<th>Quality indicator</th>
<th>Numerator description</th>
<th>Denominator description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The national treatment guideline must be followed when empirical antibiotic treatment is prescribed</td>
<td>Number of patients who were prescribed empiric antibiotic treatment according to the national guidelines</td>
<td>Total number of patients who started with empiric antibiotic therapy</td>
</tr>
<tr>
<td>Prior to antimicrobials administration blood cultures or specimen for culture from suspected site of infection must be taken.</td>
<td>Number of patients who were started on antimicrobial treatment after taking blood cultures</td>
<td>Number of patients on antimicrobial therapy</td>
</tr>
<tr>
<td>Systemic antimicrobial therapy must be switched from iv to oral as soon as oral treatment is rendered adequate preferable within 48 to 72 hrs on the based on the clinical condition</td>
<td>Number of patients that were switched from iv to oral antimicrobial therapy</td>
<td>Number of patients that were not switched from iv to oral in whom switching from iv to oral therapy on the basis of the condition was indicated.</td>
</tr>
<tr>
<td>Empirical antimicrobial therapy must be deescalated to pathogen specific therapy as soon as culture results become available</td>
<td>Number of patients in which empirical antimicrobial therapy was deescalated after positive culture results</td>
<td>Total number of patients on empiric therapy whose cultures were positive</td>
</tr>
<tr>
<td>Empirical antibiotic therapy for presumed bacterial infection should be discontinued based on the lack of clinical and/or microbiological evidence of infection. The maximum duration of empirical systemic antibiotic treatment should be 7 days</td>
<td>Number of patients whose empirical antibiotic therapy was discontinued within 7 days</td>
<td>Total number of patients who started empirical systemic antibiotic therapy, but lacked clinical and/or microbiological evidence of infection</td>
</tr>
<tr>
<td>A current local antibiotic guideline should be present in the hospital and an evaluation of whether an update should be considered and should be performed every 3 year</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Source: Van den Bosch et al (2016)
2.3 OBTAINING AND QUANTIFYING ANTIMICROBIAL CONSUMPTION /UTILIZATION DATA

In obtaining and quantifying data for antimicrobial use, a number of aspects must be put into consideration. There must be a common system of antimicrobial classification and a standard measurement metric. The most recommended classification system is the Anatomical Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) is a widely used measurement metrics,(WHO 2015). There must be a potential data source of information on antimicrobial use. Various data sources are used that help to quantify antimicrobial consumption at patient and population levels (WHO, 2015).

2.3.1 Data sources to estimate consumption rate

Different data sources can be used and they all provide information on antimicrobial consumption and use with varying levels of detail. The nature and degree of difficulty in obtaining information from these sources must be well understood before commencing with data collection as there may be a risk of over or under estimating antimicrobial consumption and use.

Data sources believed to give a more accurate estimate of antimicrobial consumption are the ones that provide data on the patient’s gender and age, as well as provide detailed information on the antimicrobial prescription and indication thereof (WHO, 2015). Table 2.3 shows the different data sources that can be used as well as their advantages and disadvantages (WHO, 2015).
<table>
<thead>
<tr>
<th>Data source</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Import data</td>
<td>Customs declaration requires product name (both generic and branded), volume, batch number, expiry date and country of origin.</td>
<td>These records are administrative and not structured for research and analyses.</td>
</tr>
<tr>
<td></td>
<td>These records are centralized as they are permitted by Government and include OTC medicines</td>
<td>Products that are illegally imported or smuggled are not accounted for and there may be incomplete documentation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Data corresponds to import cycles and not necessarily consumption data.</td>
</tr>
<tr>
<td>Wholesalers</td>
<td>Purchase and supply data is provided at all levels supplied e.g. the facility type and region.</td>
<td>Large number of wholesales may make it difficult to obtain data.</td>
</tr>
<tr>
<td></td>
<td>Where there is limited number of wholesalers, data collection can be easier.</td>
<td>Does not only supply end users but other small wholesales and where consumption data is focused at the human level, supply data can be problematic as they supply agriculture and veterinary sectors as well</td>
</tr>
<tr>
<td></td>
<td>Supply data is a more reliable source for consumption data than purchase data</td>
<td></td>
</tr>
<tr>
<td>Public sector procurement</td>
<td>Can possibly have reliable documentation of purchases and decentralized distribution data to facility types and location</td>
<td>Provide data for public sector only and may include procured stock that was never supplied</td>
</tr>
<tr>
<td>Community and hospital</td>
<td>Provides “close to” patient data.</td>
<td>Data collection may be intensive especially in settings where manual records are used.</td>
</tr>
<tr>
<td>pharmacies, drug stores</td>
<td>Can separate community and hospital sectors and private and public sectors.</td>
<td>Compliance with therapy is not taken into consideration</td>
</tr>
<tr>
<td>dispensaries data</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Chapter 2: Literature Review

### Data source | Advantage | Disadvantage
--- | --- | ---
Prescribing records of (health professionals or databases) | May have patient details, indication, dose, duration, co-prescribed medicines | Prescribed medicines may not be dispensed
| | | Samples of prescribers may not be representative and therefore not reflect national data
Commercial data sources (e.g. IMS Health) | Standardized data collection
Capacity to combine data from multiple sources including manufacturer records, hospital and pharmacy data | There may be limited data collection in some countries as data must be purchased
| | Does not disaggregate data information to facility or prescriber level.
| | May not collect data in DDDs but other units making comparisons across countries difficult
Health insurance data | Provides consumption data at a patient level as well as geographic data. Easily accessible data | May not represent the whole population and may be difficult to get information from the private sector
| | May often not include diagnosis or outcome data – just recording utilization data


### 2.3.2 Units of measurement for antimicrobial utilization

There has been variation in the units used in measurement of antimicrobial utilization data in published surveillance studies over the years. The WHO has proposed the ATC classification and DDD’s as the standardised units for the quantification of antimicrobial use.
2.3.2.1. Defined Daily Dose

The DDD is defined by the WHO as “the average maintenance dose per day for a drug used for its indication in adults” (WHO 2011). It is used in conjunction with the ATC classification to measure antimicrobial use in hospitals. WHO express antimicrobial use in hospitals as the number of DDDs per 100 or 1000 patient-days or per 100 admissions. The DDDs however have limitations (Haug, 2014):

- They often set a lower dose, hence typically do not reflect the actual dose given to the patients. This leads to non-accurate data and it could reflect higher antimicrobial usage
- DDDs are not applicable in paediatric patients as a measure of antimicrobial utilization
- DDDs do not put into consideration dose adjustments due to patient factors such as weight and renal impairment
- The use of DDDs in combination agents is a challenge as this typically under-reports actual utilization

2.3.2.2. Prescribed daily doses (PDD)

PDDs are defined by WHO as average dose prescribed according to standard guidelines or representative sample of prescriptions. PDDs vary according to the condition or illness treated and its severity. PDDs reflect the average daily amount of the drug prescribed (Mittel, 2014). According to WHO they do not reflect actual antimicrobial utilization as the patient does not always take all the prescribed medication. Other units used for measurement of antimicrobial consumption include prescribed packages, and minimum marketed dose, which is the minimum dose required for a therapeutic effect. However none of these methods are superior over DDDs (Haug, 2014).

2.3.2.3. Anatomical Therapeutic Chemical (ATC) classification

The ATC methodology is used by WHO as a standardized coding and classification system in which active substances are categorized according to their system or organ site of action, therapeutic, chemical and pharmacological properties. The medicines are classified into five groups and five different levels (see Table 2.4). In the first level, the drugs are divided into fourteen main groups. The group that relates to antimicrobials is the systemic anti-effectives group, J. However some antimicrobials are classified into other groups. The second level
is the pharmacological/therapeutic subgroup, the third level is the chemical/pharmacological subgroup, fourth level is the pharmacological subgroup and fifth level is the chemical substance (WHO, 2011).

Table 2.4: ATC classification

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Anatomical main group e.g J is the group that relates to most antimicrobials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 2</td>
<td>Therapeutic subgroup, e.g. J01 is antibiotics for systemic use</td>
</tr>
<tr>
<td>Level 3</td>
<td>Pharmacological /chemical subgroup e.g J01C beta lactam penicillins</td>
</tr>
<tr>
<td>Level 4</td>
<td>Pharmacological group e.g J01CA extended spectrum penicillins</td>
</tr>
<tr>
<td>Level 5</td>
<td>Chemical substance e.g J01CA04 Amoxicillin</td>
</tr>
</tbody>
</table>

Source: WHO (2011)

2.4 ANTIMICROBIAL UTILIZATION IN SOUTH AFRICA

Between 2000 and 2010, the overall consumption of antibiotics increased significantly across countries with India, China, Brazil, Russia, and South Africa, accounting for the greatest increase (Van Boeckel et al, 2014). Regardless of this appreciable increase, access to and miss-use of antibiotics is still a matter of concern globally (Laxminarayan, Matsotso, Pant, Rottinga, Klugma & Davier, 2016). Excess consumption is attributed to the inappropriate prescribing, use, and dispensing of antibiotics (Laxminarayan et al, 2016). The lack of antimicrobial usage policies also plays a role with enhancing antimicrobial resistance (Hoffman & Outterson, 2015). A situational analysis on the current antimicrobial use in SA, using antimicrobial procurement as data source (one of the approaches in obtaining antimicrobial utilization data), showed a substantial increase in the use of antibiotics in the public sector(11%) (Table 2.5) (Schellack et al, 2017).
Table 2.5: Antibiotic use in South Africa

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>J1A0 TETRACYCLINES + COMBS</td>
<td>114 988 400</td>
<td>168 296 842</td>
<td>21%</td>
</tr>
<tr>
<td>J1B0 CHLORAMPHENICOLS + COMBS</td>
<td>109</td>
<td>93</td>
<td>-8%</td>
</tr>
<tr>
<td>J1C1 BROAD SPEC PENICILL ORAL</td>
<td>54 045 080</td>
<td>385 061 012</td>
<td>167%</td>
</tr>
<tr>
<td>J1C2 BROAD SPEC PENICILL INJ</td>
<td>34 687 670</td>
<td>54 987 307</td>
<td>26%</td>
</tr>
<tr>
<td>J1D1 CEPHALOSPORINS ORAL</td>
<td>1 455 300</td>
<td>7 300 010</td>
<td>124%</td>
</tr>
<tr>
<td>J1D2 CEPHALOSPORINS INJ</td>
<td>10 565 000</td>
<td>76 629 057</td>
<td>169%</td>
</tr>
<tr>
<td>J1E0 TRIMETHOPRIM COMBS</td>
<td>783 509 493</td>
<td>700 365 086</td>
<td>-5%</td>
</tr>
<tr>
<td>J1F0 MACROLIDES + SIMILAR TYPE</td>
<td>8 019 700</td>
<td>16 427 840</td>
<td>43%</td>
</tr>
<tr>
<td>J1G1 ORAL FLUOROQUINOLONES</td>
<td>23 465 600</td>
<td>33 679 945</td>
<td>20%</td>
</tr>
<tr>
<td>J1G2 INJ FLUOROQUINOLONES</td>
<td>144 100 2</td>
<td>158 000</td>
<td>287%</td>
</tr>
<tr>
<td>J1H1 MED/NARRW SPEC PEN PLAI</td>
<td>515 183 440</td>
<td>424 833 433</td>
<td>-9%</td>
</tr>
<tr>
<td>J1K0 AMINOGLYCOSIDES</td>
<td>6 975 300</td>
<td>6 295 783</td>
<td>-5%</td>
</tr>
<tr>
<td>J1P2 PENEMS AND CARBAPENEMS</td>
<td>460 000</td>
<td>809 878</td>
<td>33%</td>
</tr>
<tr>
<td>J1X1 GLYCOPEPTIDE ANTIBACT</td>
<td>285 700</td>
<td>651 093</td>
<td>51%</td>
</tr>
<tr>
<td>J1X9 ALL OTHER ANTIBACTERIALS</td>
<td>5 899 28</td>
<td>704 650</td>
<td>6876%</td>
</tr>
<tr>
<td><strong>Grand total</strong></td>
<td><strong>1 553 790 791</strong></td>
<td><strong>1 906 200 029</strong></td>
<td><strong>11%</strong></td>
</tr>
</tbody>
</table>

Total QTY units: Total number of antimicrobial units. The pack size was taken into consideration (units per pack). CARG: Compound annual growth rate
Source: Schellack et al (2017)

Many studies have reported on rational antibiotic prescribing patterns and practices but less has been reported on antibiotic consumption (Hutchinson et al., 2004). This information is vital in obtaining the desirable levels of antibiotic consumption, but must include local disease prevalence, prescribing patterns and the philosophy of use (Hutchinson, Patrick, Marra, Bowie, Heule, Muscat & Monnet, 2004).

2.5 **ANTIMICROBIAL UTILIZATION SURVEILLANCE IN SA**

In South Africa, antimicrobial consumption data in hospitals are mostly obtained at the patient level through surveillance of prescription charts. The distribution of medicines in
South African hospitals is illustrated in Figure 2.1 (Meyer, Schellack, Stokes, Lancaster, Zeeman, Defty, Godman & Steel, 2017).

Figure 2.1: Distribution of medicines in SA

Figure 2.1 shows that surveillance of antimicrobial utilization can be undertaken at all three levels namely, wholesale, pharmacy and patient level. Wholesale and pharmacy data provide utilization data at a population level and patient level surveillance is undertaken by assessing hospital prescription charts. As previously mentioned, to obtain accurate antimicrobial utilization data, a standardised surveillance tool that allows continuous surveillance is essential (WHO, 2014).

Accurate hospital antimicrobial utilization data can be obtained using patient level surveillance. Computerised prescription databases are of great use in the accurate quantification of antimicrobial use. However, currently in South Africa most hospitals use a paper-based system, and obtaining antimicrobial utilization data is done through surveillance of prescription charts, which is laborious and time consuming (Meyer et al, 2017). Time limited surveys such as PPSs are mostly used to obtain utilization data in the hospitals and although they give an overview of consumption data they do not represent overall antimicrobial utilization within a hospital. These surveys involve collection of information on the dose, dosage interval and duration of therapy (Zarb & Goossens, 2011).

Population-level surveillance data can be obtained from pharmacy dispensing data. For aggregate data to be obtained, the pharmacy must effectively manage their stock and keep record of expired stock and returned stock from the wards. Population level surveillance is the most feasible method for continuous monitoring of antimicrobial use (With et al, 2016),
whilst continuous surveillance is useful in monitoring utilization trends and identifying areas of improvement for appropriate use of antimicrobials (With et al, 2016).

2.6 RELATIONSHIP BETWEEN ANTIMICROBIAL USE AND RESISTANCE

The relationship between antimicrobial use and resistance is complex and affected by multiple factors (Cantón, Horcajada, Oliver, Garbajosa, & Vila, 2013). One of the factors leading to dissemination of antimicrobial resistant strains is selection pressure brought forth by exposure to antimicrobials. Mathematical models and population analysis methods have proved that the overuse of antimicrobials triggers the emergence of resistance (Canton et al, 2013). Multiple studies have shown the increased risk of antimicrobial resistance in patients previously exposed to these agents than patients unexposed patients. A meta-analysis undertaken among 76 clinical studies at Scotland presented a risk of 1.8 for MRSA for patients previously exposed to antimicrobials compared to patients not exposed (Cosgrove & Li, 2017).

The main focus over the years has been on consumption of antimicrobials by humans but recent studies have shown that the overconsumption of antimicrobials by livestock plays an appreciable role in antimicrobial resistance and it cannot be overlooked. A recent discovery in the US that about 80% of antimicrobials are consumed by livestock has led to the call for surveillance of antimicrobial use in agriculture and veterinary as well (Huttner, Harbarth, Carlet, Cosgrove, Goossens, Holmes, Jarlier, Voss & Pittet, 2013). In South Africa, this is reflected in measures to limit the use of colistin (Mendelson, Brink, van Vuuren, Naidoo, Gouws, Schellack & Rees, 2017).

2.7 ANTIMICROBIAL RESISTANCE

Alexander Fleming upon discovering penicillin gave a warning on the emergence of resistance. He specified that the overuse of these agents will eventually lead to an era of antibiotic resistance and that to avert this evil antibiotics must be used rationally. Unfortunately we have reached the era which Alexander warned us of (Spelberg, 2014)

According to the WHO, 2011 antimicrobial resistance is defined as the “ability of microorganisms to prevent or stop antimicrobial such as antibiotics, antivirals and antimalarials from working against it. This results in ineffective treatment of infections, hence they persist and spread to others”. Antimicrobial resistance is caused by a number
of factors e.g. the use of low doses below the minimum inhibitory concentration or a dose not strong enough to kill or inhibit the growth of the pathogen cause some organisms to develop mechanisms of survival such that it becomes resistant to that antimicrobial. The organisms use the following mechanisms to resist antimicrobials (Blair et al, 2015):

- Change the permeability of their cell wall or pumping the drugs out of the cells
- Changing the target cells structure or producing enzymes that destroy antimicrobials
- Obtaining genes that are resistant from other bacteria. They do this by DNA transfer and this can be passed down to the next descendants of the organism. The rapid multiplication of microorganisms expands resistance (see Figure 2.2)

When two bacteria come in contact, they can easily pass along DNA segments containing antimicrobial resistant genes (red segments). (Source: National Institute of Allergy and Infectious Diseases)

**Figure 2.2:** Antimicrobial resistance mechanism

As mentioned previously, the increase in antibiotic resistance is a global concern to the health care system including South Africa. South Africa has recently been outlined as a major contributor to the global increase in antibiotic utilization (Van Boeckel et al, 2014), which needs to be addressed. A survey on situational analysis of antibiotic resistance performed by the Global Antibiotic Resistance Partnership-South Africa (GARP-SA) in 2011 identified a clear need of action against antibiotic resistance (Mendelson & Matsotso, 2015). One of the key findings of a recent WHO among 129 states across the world is that there are very high rates of resistance to bacteria that cause common health-care associated and community acquired infections such as urinary tract infections and pneumonia (Mendelson & Matsotso, 2015). This includes high resistance to 3rd generation cephalosporins for
Escherichia coli and Klebsiella pneumonia (Mendelson & Matsotso, 2015). This implies that the last resort to treating severe infections of this cause is the use of carbapenems. Klebsiella pneumonia resistant to carbapenems with average proportions of up to 50% was detected in a number of countries. Furthermore, the lack of documented information about resistance in many states around the world is of great concern (Mendelson & Matsotso, 2015).

2.8 SUMMARY

Excessive use of antimicrobials has been proven to parallel the emergence of resistance and has led to the global call for all nations to implement effective strategies in combating AMR. AMR increases mortality and morbidity rates caused by infections. It also contributes to the high health costs. The WHO is at the forefront in promoting global monitoring of antimicrobials and one of the strategies implemented in preventing the loss of efficacy of these agents is antimicrobial utilization surveillance. Antimicrobial use surveillance forms the basis of developing national antimicrobial policies as well as governance. The effectiveness of such strategies depends on the collection of accurate and informative data on antimicrobial use and consumption. Point prevalence surveys have been proven to be effective in obtaining such information and are advantageous in cases where time and resources are limited. A ward is surveyed in a single day and the numerator and denominator data serve as variables for calculating prevalence. Antimicrobial use surveillance is currently carried out in numerous countries and South Africa is one of them.

In line with the international call to combat antimicrobial resistance and promote rational use of medicine, this study served as an initiative for surveillance in the Gauteng province public sector hospitals. In the next chapter the methodology use in this study is described in detail.
3.1 INTRODUCTION

This chapter gives a detailed discussion of the study’s methodology in a systemic description of the study design, site and population. The population covered is explained in detail, followed by the data collection procedures and the training of data collectors. An informative description of the data collection tool used for the study is described as well as how it was tested for feasibility. It further explains reliability, validity and bias of the study. The chapter end with a brief explanation of the necessary ethical consideration and how ethical clearance was obtained.

3.2 STUDY DESIGN

This was an observational, descriptive study using a point prevalence survey (PPS) design. Data was collected in two phases. Phase 1 data was collected using a paper-based system and in Phase 2, the data was collected electronically. Phase 2 also included a survey of data collectors regarding the web based APP that was developed with the aim of making data collection and entry less complicated and less time consuming.

3.2.1 Point Prevalence Survey

As described in the previous chapter, prevalence studies are used for drug utilization research to describe the nature, extent and cause of drug consumption. They can be conducted retrospectively to review prescribing patterns and the rationale use of medicine (Lee & Bergman, 2012).

The prevalence survey design was selected because it has been proven to be effective in describing and providing a snap shot of antimicrobial consumption and the problems that cause irrational drug use. Furthermore, it forms the basis for development of policies regarding antimicrobial use and future interventions.
3.2.2 Descriptive study design

This study aimed to describe the prevalence of antimicrobial consumption and the appropriate use of antimicrobials. Descriptive designs’ value is based on the principle of improving practices through observation and analysis (Koh & Owen, 2000), and as such they help in the growth of new knowledge, generating questions and hypotheses that could form the basis of further research (Walker, 2005). Survey research like this study are the most common type of descriptive research and involve questionnaires to provide an account of the characteristics of individuals, groups or situations (Koh & Owen 2000). The overall aim is to discover new meanings, describe what currently exists and as well correlate the relationship between variables (Walker, 2005). The advantage of these studies is that numerous variables can be measured with a single instrument (Koh & Owen 2000).

3.3 STUDY SITE

The study took place in Dr George Mukhari Academic Hospital (DGMAH), which is a provincial and academic hospital situated in the Tshwane/Metsweding district (north-west part of Gauteng). It offers a teaching platform to Sefako Makgatho Health Sciences University and Garankuwa Nursing college. DGMAH has 1652 beds with a catchment area population of 1 200 000. It also serves as a referral hospital, receiving referrals from North West, Limpopo and Mpumalanga as well as neighbouring countries. (DGMAH, 2016). It has four clusters namely, surgical, medical, critical care, mother and child and diagnostic cluster. The hospital provides all three levels of health care service and has 28 clinical departments.

3.4 STUDY POPULATION AND SAMPLE

3.4.1 Phase 1

The study population included all in-patients; patients who were admitted and stayed overnight in the hospital. No sampling was done since the study included all in-patients. Data was collected only ONCE, from ALL the in-patient wards in the hospital who stayed overnight and remained admitted at 8 am on the day of survey. Each ward within the hospital was surveyed only one time. Day case wards, including those for dialysis and chemotherapy were excluded. Accidents and Emergencies’ and ‘Out-Patients Department (OPD)’ were excluded.

The following hospital wards were surveyed:
Chapter 3: Methodology

- Paediatric medical wards
- Haematology-Oncology
- Paediatric surgical wards
- Paediatric intensive care unit
- Neonatal medical ward
- Neonatal intensive care unit
- Adult medical ward
- Haematology-oncology ward
- Adult surgical wards
- Adult intensive care units
- Obstetrics and gynaecology ward

3.4.2 Phase 2

For Phase 2, representative wards from each of the adult and paediatric wards of the hospital were included but NOT ALL the wards or departments were included. A purposive sampling technique was used because the objective of this phase was to compare a paper-based data collection tool (used in Phase 1) to an electronic data collection tool (used in Phase 2), with the aim of improving the paper-based data collection tool rather than completing the full PPS again. The wards in the hospital were not necessarily all surveyed on the same day, but all beds in one single ward were completely surveyed in one single day. This ensured that the denominator (number of admitted patients) is calculated correctly. The following wards were surveyed:

- Adult ICU
- 3 Adult medical wards
- 3 Adult surgical wards
- Haematology-Oncology paediatric medical ward
- 2 Obstetrics and gynaecology wards
3.4.3 Inclusion criteria

All in-patients admitted in a ward (excluding day admissions such as endoscopy or renal units) at 08H00 on the day of the survey served as the denominator. All in-patients "on antimicrobial agents" at 08H00 on the day of the survey were used as the numerator (total number of patients on antimicrobials in the ward on the day of survey).

3.4.4 Exclusion criteria

Day hospitalizations and outpatients were excluded. This included data from “day” surgery and “day” hospital units. Consequently, they were also NOT counted in the denominator data (total number of inpatients at 08H00 of the ward surveyed). Data from patients discharged before 8H00 and/or patients admitted after that time was not collected. Emergency admissions admitted on the day of the survey were excluded and also NOT counted in the denominator data.

3.5 DATA COLLECTION

3.5.1 Data collection period

Data collection commenced after the necessary ethical clearance and permissions were granted. Table 3.1 shows how the objectives were addressed in the data collection process. For Phase 1, data was collected over a period of two months, from February to March 2017. With a PPS design, ALL beds in one single ward, were completely surveyed in ONE single day, to be able to correctly calculate the denominator and the numerator. Data was collected on weekdays only, and not on weekends. Phase 2 data collection was undertaken from the 11th to the 12th of July 2017.
Table 3.1: Objectives addressed in data collection process

<table>
<thead>
<tr>
<th>Objective</th>
<th>Objective addressed by data collection</th>
</tr>
</thead>
</table>
| To determine appropriateness of the data collection tool                   | Face validity and content validity: Used experts and people who are knowledgeable about the topic to review the data collection instrument for relevance and appropriateness of content  
Pilot tested the DCI in a few wards to determine its suitability and feasibility. |
| Determine the point prevalence of antimicrobial utilisation               | Total number of patients in the ward were used as the denominator and patients on antimicrobials as the numerator to determine the percentage of antimicrobial use. Total number of antimicrobials used by each patient were calculated and compared to the number of all medication received by the patient |
| To evaluate if prescribed antimicrobial was from the SA treatment guidelines(EML and STG) | Prescribed antimicrobials were checked if they complied with the EML and STG |
| To determine the extent and utilisation of antimicrobial sensitivity testing | Evaluating if empiric antimicrobial treatment was initiated after taking a culture and sensitivity test or if there was any culture taken even thereafter |

3.5.2 Data collection training

The researcher collected the data with a team of trained academic intern pharmacists who had a B. Pharm degree. The training included a mini pilot involving all data collectors to determine if they understood the data collection instrument. A proper training that took about 8 hours was given in a form of a power point presentation where all data collectors were given the exact procedure of collecting the data.

3.5.3 Data collection instruments

3.5.3.1 Phase 1

The PPS data collection instruments, which was used to collect the data in this study, was developed in February 2016, by a group of key stakeholders, principally from Botswana. Variables included in the data collection instruments were aligned mainly to those included in
Chapter 3: Methodology

the ECDC PPS study with input from WHO (Massele et al., 2016; ECDC, 2013). The data collection instruments were tested in a pilot study in Botswana in June 2016 and the results presented at the Medicines Utilisation Research in Africa (MURIA) Symposium in Botswana in July 2016 (Paramadhas, Tiroyakgosi & Godman, 2016; Massele et al, 2017).

The instruments were subsequently refined during the MURIA Symposium at a meeting attended by a group of researchers from across Africa, again with input from WHO. The aim of this collaborative effort was to have a set of data collection instruments for PPS, which could result in comparable data across multiple countries in Africa.

Three sets of data was collected and recorded on pre-printed data collection sheets, as shown in Appendices 1 to 3:

- Hospital data – collected only once for the hospital (see Appendix 1)
- Ward data – collected on entrance to each ward (see Appendix 2)
- Patient data – collected from the medical folder of each patient: Section 1 completed for all patients; Section 2 completed for patients on antimicrobial therapy only (see Appendix 3)

Patients’ medical folders served as the main data collection source. No patient was interviewed directly and any lack of information was recorded as such. Data was collected by reviewing patient medical records and information was captured on the data collection sheets.

3.5.3.2. Phase 2

The data collection tool used in this phase was an online web based application which allowed centralization of the captured data and also exported the data to an Ms excel™ spreadsheet. This web based application was developed on a web based builder and used the same variables as the data collection tool used in Phase 1. The web based APP allowed users to view, edit and delete the data they had entered. It was designed with the aim of making data collection and entry less complicated and less time consuming, which was subsequently assessed for feasibility and ease of use.

The researcher was the main administrator of the data collection tool and could see all the data entered by the data collectors as well as monitor what each single user entered. Patients’
files still served as the main data collection source and three sets of data was collected as explained above under Phase 1.

**3.5.3.3. Variables collected**

Both data collection tools covered the same variables. The patient data included the patients' demographics (age, gender, employment status), factors contributing to previous use of antimicrobials (previous hospitalization, HIV, TB and malaria status), previous use of antimicrobials and duration and if the patient was currently on antimicrobials or not. If the answer was “yes”, Section 2 of the patient data was completed and this was used for the assessment of appropriateness, quantification of antimicrobials used and reason for use of the antimicrobials. Appropriateness was based on whether the antimicrobials used were in accordance with current Essential Medicine Lists (EML) and South African Standard Treatment Guidelines (STGs).

The data collected included diagnosis, prescribed antimicrobials, indication, dose, duration and route of administration. Diagnosis and indication for prophylaxis or treatment used the same diagnosis group, which is anatomically related to an organ (e.g. skin or lungs) and based on the ECDC (2013) study. It was also noted whether there were any missed doses and whether the prescriptions were noted on the drug sheets. In addition, whether any sensitivity analyses were requested and whether the results were acted upon. Actual prescribed doses were recorded for both adults and children for single and combination antibacterials (e.g. 960mg of cotrimoxazole). Antibacterials were either presented by a group (e.g. cephalosporins) or by individual chemical substance (e.g. cefazolin). The route of administration was also be specified.

**3.6 PILOT STUDY**

A pilot study is a small scale study that can be conducted for two main reasons. It can signify a small scale feasibility study or trial runs conducted in preparation for the main study or testing the validity and reliability of a research instrument (Polit, Beck and Hungler, 2001). The pilot study was undertaken after receiving ethical clearance from the University.
3.6.1 Pilot study to Phase 1

An initial pilot study was conducted in three wards in the hospital before the main data collection commenced. The aim of the pilot study was to determine the suitability and feasibility of the PPS data collection instruments developed in Botswana for use in the South African setting. Similar to the main study, medical folders of ALL beds in one single ward, were completely surveyed in ONE single day. Based on the results of the pilot study, amendments were made to the data collection instruments before roll-out across the hospital.

3.6.2 Pilot to Phase 2

Since this was the first time using the web based application in practice, a pilot test was undertaken to establish its feasibility. This objective was to assess whether this data collection tool could be used in this setting and was sufficient in obtaining all the information to meet the objectives of the study. The pilot study also helped in identifying areas of improvement on the web based APP for its optimal use and efficient collection of data. Through this process, the data collection tool was adjusted accordingly for efficient use.

3.7 DATA ENTRY AND ANALYSIS

The data was captured on the web-based APP and exported it to Microsoft Excel™ spreadsheets. Data was checked for accuracy and correctness prior to analysis using SPSS Version 8.0 for Windows, in consultation with a statistician. This was a descriptive, explanatory analysis since the study was quantitative. Categorical variables were calculated as frequencies and percentages. Measures of central tendency for continuous variables included the mean with standard deviation, and median with inter quartile range.

Antimicrobials prescribed were analysed according to the WHO ATC classification (ATC level 5), the dose, frequency and route of administration. Appropriateness of the prescribed antimicrobials with guidelines were evaluated based on the hospital formulary, the NDOH Essential Medicines List (EML) and Standard Treatment Guidelines (STGs). Further analysis included whether antibiotic sensitivity analysis was requested and subsequently acted upon, and whether treatment was empiric or not.
3.8 RELIABILITY, VALIDITY AND BIAS OF DATA

3.8.1 Reliability

Reliability is defined as the consistency of results over time when taken with the same instrument under a similar methodology and also an accurate representation of the total population being studied (Bashir, Afzal & Azeem, 2008). Inter-rater reliability is used to assess the degree to which different observers give consistent estimates of the same phenomenon (Bashir et al, 2008). To ensure precision, only data obtained through the data collection tool was used. All errors identified were discussed with the supervisor and subsequently corrected. Reliability was achieved by means of a pilot study whereby the instrument was tested for feasibility and suitability. The instrument was tested in three different wards to check for consistency and any errors on the instrument.

All data collectors, who were academic pharmacists interns, were trained on the use of the data collection instruments. Collected data was first captured on pre-printed data collection sheets and then entered on Microsoft Excel™ spread sheets, to allow verification of data if necessary. All captured data was be double checked for accuracy.

3.8.2 Validity

Validity is a measure of accuracy (Cherry, 2014) and refers to whether the study was able to scientifically answer the questions that it was intended to answer (Gravetter & Forzano, 2011). When looking at validity during a research study, two aspects, internal and external validity need to be taken into account. Internal validity refers to the extent to which the research design and data obtained will allow the researcher to draw accurate conclusions about relationships within the data. External validity refers to the extent to which the results obtained during the study can be generalised to other contexts (Leedy & Ormrod, 2001).

The validity of this study was ensured by using data collection instruments developed by a group of researchers based on the ECDC (2013) PPS with input from WHO (Massele et al 2016), which had already been pilot-tested and subsequently refined in Botswana. A pilot study was also conducted in a few wards prior to commencement of data collection to further test the suitability and feasibility of the tool. In this study we used face and content validity.
Chapter 3: Methodology

Content validity was checked by people who are experts or who knew and understand the topic read through the questionnaire. They evaluated whether the question captured the topic under investigation and if the questions were appropriate. The construction of the questionnaire was checked for common errors such as double barrelled questions. Furthermore, the instrument had already been assessed by a group of researchers based on the ECDC PPS with input from WHO.

Face validity pertains to whether the test looks valid to the administrative person using it or other untrained personnel, it does not require experts in the field to assess it. This was achieved by going through the questionnaire myself together with my supervisors.

Table 3.2: Threats to external validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to current study</th>
<th>What was done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illusory Correlation</td>
<td>The propensity to overestimate the relationship between variables. This normally relates to confirmation bias.</td>
<td>Researcher can over or under estimate the relationship between variables.</td>
<td>External statistician was consulted, so to limit predetermined views of the researcher influence on the analyses of the data obtained.</td>
</tr>
</tbody>
</table>
### Table 3.3: Threats to internal validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What was done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Design / Data Collection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity</td>
<td>Refers to the extent to which the findings can be generalised form the sample group towards a larger target population.</td>
<td>The researcher could assume that the accessible population is representative of the target population.</td>
<td>Data collected was specific to one public hospital. There was no comparison between this study population and the rest of the public hospitals population.</td>
</tr>
<tr>
<td>Ecological Validity</td>
<td>The magnitude to which the results from a certain study can be used as a broad view or generalization across conditions, settings, variables and contexts.</td>
<td>Will influence the study, as the data and final results are dependent on the setting and location in which they are obtained.</td>
<td>Researcher did not use the results to generalize on what is happening in similar public sector hospitals.</td>
</tr>
<tr>
<td><strong>Data Analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity</td>
<td>Occurs when a researcher analyses a subset of data, compared to when the total sample would have been used.</td>
<td>Limited influence, as the total sample selected during the data collection phase, will be utilised during the data analysis phase of the study.</td>
<td>This is a point prevalence survey and included analysis of all in-patients files mentioned in inclusion criteria.</td>
</tr>
<tr>
<td>Specificity of variables</td>
<td>Relates to aspects such as location, time and type of participants used during the study.</td>
<td>Can influence external validity when variables are categorised using local norms.</td>
<td>Where possible, standardised norms were used so that variables can be transferable to a different context.</td>
</tr>
<tr>
<td><strong>Data Interpretation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Validity, ecological validity and temporal validity</td>
<td>The magnitude to which the results from a study can be used as abroad view or generalization</td>
<td>Can occur when the researcher over-generalise the data obtained.</td>
<td>Results obtained were comprehensively as possible compared to available literature so that the results can be placed in a realistic context.</td>
</tr>
</tbody>
</table>
3.8.3 Bias

Bias can be defined as any systematic error with a tendency for selectivity or influence, meaning that the research findings deviate from the ‘true findings’. Bias can occur at any stage of the research (Pannucci & Wilkins, 2010). As noted during the discussion on internal and external validity, various biases could have an influence on the current research study. These have been accounted for and, as far possible, various techniques will be employed to decrease or minimise the effect of bias on the data obtained. Definitions of bias and how this was addressed are contained in Table 3.2.

Table 3.4: Threats to bias

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What was done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researcher Bias</td>
<td>Occurs when the researcher has a personal bias/preference towards a particular result</td>
<td>The researcher may create predetermined hypothesis regarding the results that will be obtained</td>
<td>The researcher did not discuss any pre-conceived notions regarding the possible results.</td>
</tr>
<tr>
<td>Matching Bias</td>
<td>Occurs when the researcher only group patients after the data on the total sample group has been collected.</td>
<td>No influence, as research participants were already grouped into the sample group during the data collection phase of the research study.</td>
<td></td>
</tr>
<tr>
<td>Confirmation Bias</td>
<td>Occurs when confirmation and conclusions made from the current data are overly consistent with the preliminary hypothesis.</td>
<td>Limited influence, as this study was not be approached with a predetermined hypothesis (due to a lack of previous studies), but rather a research question.</td>
<td>There was no research hypothesis.</td>
</tr>
</tbody>
</table>


3.9 ETHICAL CONSIDERATIONS

Ethical considerations and principles were applied in the study so to maintain honesty, confidentiality and prevent bias and harm to participants. The following aspects of ethical principles were considered.

3.9.1 Non-maleficence

The Helsinki principle states that research involving humans as participants must obtain ethical approval from a recognised ethics and research committee (General Assembly of the World Medical Association, 2014). For this study ethical clearance was sought from the Sefako Makgatho University Research Ethics Committee (SMUREC) (SMUREC/H/210/2016: PG) (see Appendix 4). The committee was also informed of any amendments to the protocol. The protocol was submitted for review and approval to the hospital and Chief Executive Officers (CEOs) of Dr George Mukhari Hospital, permission was thereafter attained from the CEO to conduct the study in the hospital.

3.9.2 Beneficence

The declaration of Helsinki states that any research conducted using humans as subjects must not confer any risk to the participant and if any risk at all, the benefit must outweigh the risk (General Assembly of the World Medical Association, 2014). In this study there was no intended risk to the patients as only the patients’ files were used. There was no interaction with the patient.

3.9.3 Confidentiality and anonymity

Patient confidentiality was maintained throughout the study by assigning a unique study number to each patient. All documented and captured data were locked away in the School of Pharmacy. Patients were kept anonymous by assigning a unique subject number to each participant instead of using their real identities.

3.10 SUMMARY

The study was conducted in two phases with Phase 1 being the fundamental of the study and Phase 2 aimed at improving the data collection tool for further studies. The data was collected in all the wards in Phase 1 and representative wards for Phase 2. In both cases, the patient
files were used as source of data. The methodology used for collecting the data was considered to be relevant in meeting the objectives of the study and a conclusion can be made that reliable and valuable results were.

3.11 CONCLUSION

The next chapter, discuss the results and the discussion thereof are presented as two manuscripts for publication in a peer reviewed journal.
Chapter 4: Results and Discussion

CHAPTER 4
RESULTS AND DISCUSSION

4.1 INTRODUCTION

The results and discussion of this study are presented in a form of two manuscripts

**Manuscript one** is titled “Feasibility of using point prevalence surveys to assess antimicrobial utilization in public hospitals in SA; pilot study and implications” will be submitted to the Hospital Practice journal. A cover letter to the Editor-in-Chief of the selected journal is provided (see Appendix 6) followed by the guidelines for authors (see Appendix 7)

**Manuscript two** is titled “Development of an APP to improve data collection for point prevalence surveys in the public system in SA; findings and implications’ This paper will be submitted after Manuscript one has been submitted. A cover letter to the Editor-in-Chief of the selected journal is provided (see Appendix 7) followed by the guidelines for authors (see Appendix 8)
Feasibility of using point prevalence surveys to assess antimicrobial utilisation in public hospitals in South Africa; a pilot study and implications

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(Target Journal – Hospital Practice)
ABSTRACT

Introduction: Antimicrobial resistance (AMR) is a serious health concern and direct threat to patient safety. Although antimicrobials play a vital role in reducing morbidity and mortality through the management of infections, their misuse and overuse is moving the world towards an era where antimicrobials will be unavailable for treatment due to AMR. Extensive data on the reporting of antimicrobial utilization and consumption among hospitals in South Africa (SA), especially public sector hospitals, is currently lacking. This study aimed to address this by determining antimicrobial consumption using a point prevalence survey (PPS).

Methods: A PPS was conducted in Dr George Mukhari Academic Hospital using previously tested data collection instruments. Data was collected with the assistance of trained academic pharmacist interns. All patient files in one single in-patient ward were completely surveyed in a single day. The number of patients who were on antimicrobials served as the numerator and the denominator comprised the total number of patients in the ward.

Results: A total of 39 wards were surveyed and 512 patient files were surveyed. The overall prevalence of antimicrobial use was 38.5%. Beta lactamase inhibitors and antimicrobials for TB drugs were the most prevalent antimicrobials. More than two thirds (83%) of antimicrobial treatment was modified following culture sensitivity test (CST) results, and 98% of antimicrobials complied with the national Essential Medicine List. However, there is concern with the lack of IV to oral switching where appropriate.

Conclusion: The PPS method offers a standardized tool that can be used to identify targets for quality improvement.

INTRODUCTION
Antimicrobials play a vital role in reducing morbidity and mortality through the management of infection\textsuperscript{1-3}. They reduce mortality by 10\% to 75\% depending on the disease area, with estimations of increasing life expectancy by 20 years\textsuperscript{4}. However, their excessive utilisation has appreciably increased resistance rates, which is now a global concern\textsuperscript{5-7}. With the diminishing effectiveness of antimicrobials, the world is facing a major predicament of how infections will be treated in the future, leading to calls to develop global and national action plans to reduce morbidity, mortality and costs associated with antimicrobial resistance including increased governance\textsuperscript{3-4,8-12}.

The World Health Organization (WHO) and others have for many years promoted the monitoring of antimicrobial use across sectors and raised awareness of the consequences of Antimicrobial Resistance (AMR), which includes the WHO Africa region\textsuperscript{8,13-19}. These activities include the instigation of Point Prevalence Study in hospitals to provide data on current utilisation and resistance patterns using a standardised methodology to plan future interventions\textsuperscript{20-22}. This is particularly important with growing resistance rates to penicillins as well as non-\(\beta\)-lactam antibiotics, including the macrolides, tetracycline, chloramphenicol, the fluoroquinolones and co-trimoxazole in South Africa\textsuperscript{23}. It has been estimated that over 50\% of isolates in hospitals in SA are Methicillin Resistant \textit{Staphylococcus Aureus} (MRSA), with up to 75\% of \textit{Klebsiella pneumoniae} isolates extended spectrum beta-lactamase (ESBL) and also outbreaks of Vancomycin-Resistant Enterococci (VRE), as well as other studies showing \textit{K. pneumoniae} resistance against carbapenems\textsuperscript{3,17}, resulting in the development of plans to improve antibiotic utilisation and reduce resistance rates across all sectors in South Africa in the coming years\textsuperscript{4,24}.

In addition, a PPS conducted between April and August 2015 in a large tertiary hospital in Cape Town, South Africa, indicated that 31\% (359/1156) of patients were receiving antibiotics and the majority (83\%) of antibiotic prescriptions were empirical\textsuperscript{25}. The implication of these results is that antibiotics were administered in public hospitals without the availability of cultures. In addition, only a few doctors (11\%) documented the stop/review date on the prescription. This is not helped by concerns with the availability of valid and reliable surveillance tools or methods linking information between the pharmacy, prescribers and laboratory in South Africa\textsuperscript{26}. Data on antibiotic utilisation were collected in a number of hospitals in the Gauteng Province during World Antibiotic Awareness Week in 2015. However, these data were not sufficiently robust to make reliable and valid interpretations and
recommendations, highlighting the need for assessing antimicrobial utilisation using valid and reliable surveillance tools to provide a baseline for future surveys, ultimately aiming at promoting rational antimicrobial use. More recently, a situational analysis on the current antimicrobial use in SA, using antimicrobial procurement as data source (one of the approaches in obtaining antimicrobial utilization data), showed a substantial increase in the use of antibiotics in the public sector in recent years, which needs to be addressed to reduce AMR rates.11.

Overall though, there is a paucity of data on the use of antimicrobials among public hospitals in South Africa, which prompted the study to determine antimicrobial consumption at Dr George Mukhari Academic Hospital (DGMAH) using a PPS method. Information was obtained with a PPS data collection instruments developed and updated in Botswana with input from the WHO, building on the ECDC and Global studies.27-29 The findings will assist with the instigation of pertinent programs in this hospital to improve future antimicrobial use, furthermore the study results will help with the development of a follow-up national survey on antimicrobial utilisation among public hospitals in South Africa to further identify targets for quality improvement programs regarding antimicrobial utilisation in individual public sector hospitals as well as for the country as a whole.

METHODS
Study design, setting and study period
The study design was a point prevalence survey. With a PPS design, all beds in one single ward, were completely surveyed in one single day, to be able to correctly calculate the denominator and the numerator. Data was collected on weekdays only. The principal researcher collected the data together with a team of trained data collectors. Data collectors reviewed medical records on the survey date to determine whether patients may have been receiving an antimicrobial on the day of survey. If so, the information was collected on antimicrobial use.

Data was collected over a period of two months, from February to March 2017. For each antimicrobial, data collectors recorded the rationale for use; i.e. treatment of infection surgical prophylaxis, medical prophylaxis, a non-infection-related reason, or an unknown rationale. Empirical use of antimicrobial drugs for suspected infection was considered treatment. For
antimicrobial drugs given to treat infections, data collectors identified the anatomical site of infection.

Data was collected at DGMAH. This teaching hospital is one of four in the province and situated in Ga-Rankuwa, Pretoria, Gauteng Province. This is a 1,650-bed hospital with 28 clinical departments, 20 approved ICU beds, 60 high care beds and 17 surgical theatres, providing services to an estimated 1.7 million people from the surrounding area.

**Study population and sample**
As this was a PPS, no sampling was undertaken. Data was collected only once, from all the in-patient wards in the hospital except for day admissions such as renal and emergency and accidents wards. Each ward within the hospital was surveyed only one time. The wards in the hospital were not all necessarily surveyed on the same day, but all beds in one single ward were completely surveyed in one single day. This ensured that the denominator (number of admitted patients) was calculated correctly.

**Data entry and analysis**
The data was taken from patients' bed charts, which are paper-based and organized in a file, as they have all the patients' records. The data was subsequently captured onto Microsoft Excel™ spread sheets and analysed using SPSS Version 8.0 for Windows, in consultation with a statistician. Entered data was checked for accuracy and cleaned prior to analysis. This was a descriptive, explanatory analysis of information such as epidemiologic parameters, the prevalence and degree of consumption of antimicrobials, which is, number of prescriptions and drug prescription profiles considering different ages and genders. Descriptive statistics were performed on retrieved data. Categorical variables were calculated as percentages and measures of central tendency for continuous variables and included the mean with standard deviation, the median with inter quartile range and 95% confidence interval (CI).

Antimicrobials prescribed were analysed according to the WHO’s Anatomical Therapeutic Chemical (ATC) classification of medicines (ATC level 5), the dose, frequency and route of administration. The appropriateness of the prescribed antimicrobials were evaluated based on the hospital formulary, the NDOH Essential Medicines List (EML) and Standard Treatment Guidelines (STGs) in line with other publications. Further analysis included whether
antimicrobial sensitivity analyses were requested and subsequently acted upon, and whether treatment was empiric or not.

**Ethical considerations**
Data collection commenced after receiving ethical approval from the Sefako Makgatho University Research Ethics Committee (SMUREC/H/210/2016:PG). Permission was thereafter obtained from the Chief Executive Officers of DGMAH. Patient confidentiality was maintained at all times and unique identification numbers were used for all patients so to keep them anonymous.

**RESULTS**
A total of 512 patient files were surveyed which included 400 adults of which 175 (44%) were males and 225 (56%) females. The mean age (SD) for males was 42.25 (17.29) and median age (IQR) was 43 (28.5). For females the mean age (SD) was 46.10 (18.8), and median age 43 (28) (Table 1). Most (85%) of the admitted adults were less than 65 years, with the occupation of nearly two thirds (61%) of patients unknown (Table 1). In the paediatric wards, there were more infants and children than neonates, with a mean (SD) age of 3 years (± 3.65) and median (IQR) age of 1 (4.17).

**Table 1: Demographics of adult patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of adults; n(%)</td>
<td>175 (44)</td>
<td>225 (56)</td>
<td>400 (100)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65; n (%)</td>
<td>153 (38)</td>
<td>185 (46)</td>
<td>338 (84.5)</td>
</tr>
<tr>
<td>≥ 65; n (%)</td>
<td>22 (6)</td>
<td>40 (10)</td>
<td>62 (15.5)</td>
</tr>
<tr>
<td>Mean (± SD)</td>
<td>42.25 (17.29)</td>
<td>46.10 (18.8)</td>
<td>45.05 (17.9)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>43 (28.5)</td>
<td>44 (28)</td>
<td>43 (28.25)</td>
</tr>
<tr>
<td>Occupation; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>13 (3)</td>
<td>9 (2)</td>
<td>22 (5.5)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>45 (11)</td>
<td>89 (22)</td>
<td>134 (33.5)</td>
</tr>
<tr>
<td>unknown</td>
<td>117 (29)</td>
<td>127 (32)</td>
<td>244 (61)</td>
</tr>
<tr>
<td>Transferred in; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45 (11)</td>
<td>25 (6)</td>
<td>70 (17.5)</td>
</tr>
<tr>
<td>No</td>
<td>118 (30)</td>
<td>190 (48)</td>
<td>308 (77)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (3)</td>
<td>10 (3)</td>
<td>22 (5.5)</td>
</tr>
</tbody>
</table>
Antimicrobial use prevalence

Of the total number of 512 patients surveyed, 193 patients received at least one antimicrobial. The total prevalence of antimicrobial use was 38.5%. The prevalence of antimicrobial use was the highest in the various ICUs (Table 2).

Table 2: Antimicrobial use prevalence in the wards

<table>
<thead>
<tr>
<th>Ward speciality</th>
<th>Total number of patients</th>
<th>Number of patients receiving antimicrobials</th>
<th>Prevalence (%)</th>
<th>95% CI for prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal ICU</td>
<td>24</td>
<td>17</td>
<td>70.8</td>
<td>52.6, 89.0</td>
</tr>
<tr>
<td>Paediatric ICU</td>
<td>9</td>
<td>6</td>
<td>66.7</td>
<td>35.9, 97.5</td>
</tr>
<tr>
<td>Adult ICU</td>
<td>28</td>
<td>15</td>
<td>53.6</td>
<td>35.1, 72.1</td>
</tr>
<tr>
<td>Adult medical ward</td>
<td>128</td>
<td>60</td>
<td>46.9</td>
<td>38.3, 55.5</td>
</tr>
<tr>
<td>Haematology - Oncology Paediatric Medical Ward</td>
<td>12</td>
<td>5</td>
<td>41.7</td>
<td>13.8, 69.6</td>
</tr>
<tr>
<td>Adult surgical ward</td>
<td>194</td>
<td>56</td>
<td>28.9</td>
<td>17.0, 40.8</td>
</tr>
<tr>
<td>Paediatric Medical Ward</td>
<td>58</td>
<td>19</td>
<td>32.8</td>
<td>20.7, 44.9</td>
</tr>
<tr>
<td>Obstetric and Gynaecology</td>
<td>50</td>
<td>15</td>
<td>3.3</td>
<td>-1.7, 8.3</td>
</tr>
<tr>
<td>Paediatric Surgical Ward</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0.0, 0.0</td>
</tr>
<tr>
<td>Total</td>
<td>512</td>
<td>193</td>
<td>38.5</td>
<td></td>
</tr>
</tbody>
</table>

Antimicrobial drugs administered to treat infections

Of all the antimicrobials used to treat infections in the 193 patients, 46 (15%; 95% CI: 10.92-18.88) antimicrobials were used to treat clinical sepsis in 28 patients, 37 (12.0, 95% CI,8.37 -15.63) for pulmonary tuberculosis (TB) in 19 patients, 32 (10.4%, 95% CI,6.99 -13.81) for pneumonia, and 21 (6.8%,3.99 -9.61) for bone and joint infection as well as obstetrics and gynaecological infections in 17 and 14 patients respectively (Table 3). Lower urinary tract infections accounted for the lowest number of prescribed antimicrobials. Antimicrobials were also used for prophylaxis, with 17 antimicrobials having no clear indication or defined infection site for their use documented in the patient records (Table 3).
Table 3: Infection sites for which patients received antimicrobials

<table>
<thead>
<tr>
<th>Infection site</th>
<th>Number of antimicrobials (%) [95% CI (n = 308)]</th>
<th>Number of patients (%) [95% CI (n = 193)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical sepsis (bloodstream)</td>
<td>46 (14.9%) [10.92-18.88]</td>
<td>28 (14.5%) [9.53 -19.47]</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>37 (12.0%) [8.37 -15.63]</td>
<td>19 (9.8%) [5.61 -13.99]</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>32 (10.4%) [6.99 -13.81]</td>
<td>24 (12.4%) [7.75 -17.05]</td>
</tr>
<tr>
<td>Bone and joint infections</td>
<td>21 (6.8%) [3.99 -9.61]</td>
<td>17 (8.8%) [4.80 -12.79]</td>
</tr>
<tr>
<td>Obstetrics and gynaecology</td>
<td>21 (6.8%) [3.99 -9.61]</td>
<td>14 (2.1%) [15.25 -26.75]</td>
</tr>
<tr>
<td>Soft tissue infections</td>
<td>19 (6.2%) [3.51 -8.89]</td>
<td>14 (2.1%) [0.08 - 4.12]</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>17 (5.5%) [2.95 -8.05]</td>
<td>15 (7.8%) [4.02 -11.58]</td>
</tr>
<tr>
<td>Undefined site with no systemic inflammation</td>
<td>17 (5.6 %) [3.03 -8.17]</td>
<td>15 (7.8) [4.02 - 11.58]</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>17 (5.5%) [2.95 -8.05]</td>
<td>13 (6.7%) [3.17-10.23]</td>
</tr>
<tr>
<td>Ear, nose, and throat</td>
<td>12 (3.9%) [1.74- 6.06]</td>
<td>10 (5.2) [2.07 -8.33]</td>
</tr>
<tr>
<td>Upper urinary tract</td>
<td>11 (3.6%) [1.52 -5.68]</td>
<td>10 (5.2%) [2.07 -8.33]</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>11 (3.6%) [1.52 -5.68]</td>
<td>9 (4.7%) [1.71 -7.69]</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>7 (2.3%) [0.63 -3.97]</td>
<td>6 (3.1%) [0.65 -5.55]</td>
</tr>
<tr>
<td>Intraabdominal</td>
<td>7 (2.3%) [0.63 -3.97]</td>
<td>4 (2.1%) [0.07-4.13]</td>
</tr>
<tr>
<td>Extra pulmonary TB</td>
<td>4 (1.3%) [0.034 -2.57]</td>
<td>3 (1.6%) [-0.17 - 3.37]</td>
</tr>
<tr>
<td>Eye infections</td>
<td>3 (0.9%) [-0.15- 1.95]</td>
<td>3 (1.6%) [-0.17-3.37]</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3 (0.97%) [-0.12 -2.06]</td>
<td>3 (1.6%) [-0.17 -3.37]</td>
</tr>
<tr>
<td>Asymptomatic bactearia</td>
<td>2 (0.65%) [-0.25 - 1.55]</td>
<td>2 (1.0%) [-0.40 -2.40]</td>
</tr>
<tr>
<td>Genitourinary for males</td>
<td>2 (0.6%) [0.26 – 1.46]</td>
<td>2 (1.0%) [-0.40 -2.40]</td>
</tr>
<tr>
<td>Laboratory confirmed bacteremia</td>
<td>1 (0.32 %) [-0.31 - 0.95]</td>
<td>1 (0.5%) [-0.50 -1.50]</td>
</tr>
<tr>
<td>Antimicrobial use other than treatment</td>
<td>16 (5.2%) [2.72 -7.68]</td>
<td>16 (8.3%) [4.41 -12.19]</td>
</tr>
</tbody>
</table>

*Antimicrobials could be used for more than one anatomical site of infection.

Antimicrobial Use by ATC

Broad spectrum penicillins were the most commonly prescribed antimicrobials (34.1. followed by the cephalosporins (17.9%) and anti-tuberculosis agents (12.0%). The least used antimicrobials were the tetracyclines (0.3%) (Figure1).
Figure 1: Antimicrobial use by ATC

Antimicrobial use in the past 90 days
Figure 2 shows that less than half (44.5%) of the patients (137) who were on antimicrobials in the last 90 days used antimicrobials for up to five days, while 8.8% were on antimicrobials for more than 14 days.
Chapter 4: Results and Discussion

Figure 2: Antimicrobial use in the past 90 days (n=137)

Culture and sensitivity testing (CST) (n=193)
The majority (83%) of antimicrobial treatment was modified following CST results when requested and 12 (8.8%) was not modified as per CST results. The rest of the patients' files (21%) had no culture and sensitivity tests results recorded.

Compliance to national guidelines (EML/STGs)
Most of the antimicrobial agents prescribed (98%) were from the national EML/STG. However, the treatment was not evaluated for compliance with the STGs.

Discussion
Antimicrobial utilization in a leading public hospital in South Africa (DGMAH) was prevalent as approximately 38.5% of patients were on antimicrobials (Table 2). This high rate was envisaged in view of the prevalence of infectious diseases in South Africa, and in line with previous publications.\textsuperscript{6,25,33}

It was encouraging to see a high level of modification of antimicrobial treatment following CST results when requested. However, there were concerns that the antimicrobial treatment was not modified in a minority (17%) following the results, and there may well have been situations when CST could have been ordered but not recorded or available in the files at the time of data collection. These are considerations for the future.
Most antimicrobials were used to treat infection rather than prophylaxis, similar to other studies. The high burden of Tuberculosis (TB) in South Africa is a possible reason for the relatively high use of anti-TB agents in DGMAH (Figure 1). In line with other studies performed in SA, the penicillins had a high utilization rate. This may be due to restrictions on second line antibiotics such as cephalosporins and fluoroquinolones. Antibiotic policies to optimize the use of penicillins also help preserve newer antimicrobials. However care is needed as their high use poses a risk in the development of resistance such as methicillin resistant Staphylococcus aureus (MRSA). This will be monitored closely in the hospital.

The majority of antimicrobials prescribed were medicines that were available as part of the EML. Standard treatment guidelines and the EML, alongside support measures to promote the prescribing of medicines according to these guidelines, has been in place in South Africa since 1996. Procurement of medicines in public hospitals is highly influenced by national standard guidelines such as the EML, hence the high compliance.

The switch from oral to intravenous (IV) medication is the most economical approach and associated with fewer complications but most physicians are still reluctant to perform this. The WHO encourages the switching to oral antibiotics as soon as possible without failure of therapy or loss of efficacy to reduce costs and hasten hospital discharge where appropriate. In this study there is no antimicrobial that was switched from IV to oral even if the patient had a stable GIT. This lack of switching will be explored in future studies in view of the cost implications.

Prior antimicrobial exposure promotes colonization and subsequent infection with antimicrobial-resistant pathogens leading to prolonged exposure to antimicrobials and the emergence of resistance. The results showed that just under a third (27%) of patients had used antimicrobials in the past 90 days, and this places them at risk of having infections, consequently contributing to high use of antimicrobials. This will also be explored further in future studies.

**Limitations**

The accuracy of the results depends on the accuracy of the documentation in the patient’s files as this was not an interventional survey. The use of data collectors had a positive impact in accelerating the process of data collection, however, they had to be continuously monitored.
and data collected was greatly influenced by their accuracy and level of commitment. Further to this, the data collection tool was adequate but time consuming and the need to search for information in the files lead to other data collectors not completing all variables. Variables such as hospital or community acquired infections were not a clear cut.

In addition, we are aware that the results presented on this study were obtained from one public hospital in the country and any generalization to all public sector hospitals in SA based on these results would not be possible. However, this is a leading public sector hospital in South Africa and the findings can be used to suggest improvement programmes in this and other hospitals in South Africa.

Conclusion
The results showed a high use of broad spectrum penicillins and low use of restricted or newer antimicrobials (e.g. carbapenems) which is encouraging. In addition, there was high adherence to the EML. However, there is a concern with the lack of IV to oral switching in suitable patients and that not all suitable patients have CST and not all results are acted upon. These are suggested quality improvement programmes for the future.

This study formed the basis of future studies to be undertaken in the Province and Country to further record current antimicrobial utilisation rates in hospital, as well as instigating quality improvement programmes in this and other hospitals. Further work is needed to develop a standard data collection tool for such surveys which are less time consuming such as a web-based application. This is now underway for use in South Africa and possibly other African countries.

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The authors declare they have no other conflicts of interest.

References
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publication of the *European Society of Clinical Microbiology and Infectious Diseases*, 20(10):973-80.


30. WHO. WHO Collaborating Centre for Drug Statistics Methodology. ATC/ DDD Index. Available at URL: https://www.whocc.no/


MANUSCRIPT 2

Development of a web-based application to improve data collection for antimicrobial point prevalence surveys in the public health care system in South Africa; findings and implications

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Journal – to be determined
ABSTRACT

Introduction: Surveillance of medicine use is one of the global action plans in combating antimicrobial resistance. It is a key strategy for the development of pertinent antimicrobial policies, increasing governance and future interventions. Determining antimicrobial utilisation at patient-level in South Africa can be a challenge, with one of the reasons being that there is currently no standardized data collection tool for obtaining this information. Most countries in Africa currently undertake antimicrobial utilisation surveillance using paper-based data collection tools. Unfortunately, paper-based systems have some disadvantages as they are time consuming, increasing costs and challenges with personnel. Consequently, an electronic data collection tool, a web-based application (APP) was developed and tested to try and address this.

Methods: A web based application (APP) was developed based on previous studies conducted in Botswana and South Africa using a paper-based data collection tool. The developed APP was evaluated for data quality by measuring the number of errors, work flow, time taken for the survey. User acceptance was also measured via a questionnaire to the data collectors.

Results: A total of 187 patients’ files was surveyed while documenting the challenges and areas of improvement for the App. Users agreed that surveying the patients’ files took less time with the electronic tool compared to the paper based tool, and should be used in the future. Conclusion: The APP development process has proven to be of great use and is a potential tool to be used in future antimicrobial consumption surveys in South Africa and wider. This is currently happening.

INTRODUCTION

Antimicrobials have played a vital role in improving care and reducing mortality in patients with infections. However, there are now concerns that their increasing and often inappropriate use is appreciably increasing resistance rates. This has resulted in the development of global and national action plans to reduce morbidity, mortality and costs associated with antimicrobial resistance (AMR) including South Africa, which are ongoing.

Strategies include the instigation of point prevalence surveys (PPSs) in hospitals to provide data on current utilisation and resistance patterns using a standardised methodology to plan future interventions. There are concerns with antibiotic prescribing in South Africa with high
rates of AMR², and a PPS conducted in 2015 in a large tertiary hospital in South Africa showed that 31% of patients were receiving antibiotics with the majority (83%) of antibiotic prescriptions empirical.¹⁶ High empiric use is not helped by concerns with reliable surveillance tools or methods linking information between pharmacies, prescribers and laboratories in South Africa.⁶ In addition, data on antibiotic utilisation collected in the Gauteng Province during World Antibiotic Awareness Week in 2015 were not sufficiently robust to make reliable and valid interpretations and recommendations, highlighting the need for valid and reliable surveillance tools to provide a baseline for pertinent quality improvement programmes to enhance future antimicrobial use within the public hospitals in South Africa.²,⁶ This is particularly important since as part of the AMR National Strategy Framework in South Africa, one of the domains is the strengthening of antimicrobial consumption surveillance, with a situational analysis on AMR performed by Global Antibiotic Resistance Partnership (GARP) South Africa in 2011 identifying the urgent need for South Africa to take action against AMR.²

However, there have been concerns with the length of time taken to undertake PPSs using a paper based approach, which has implications for both manpower and costs since the data from a single ward has to be collected in one day and there can be large hospitals in countries such as South Africa.¹⁷ We are also aware of possible data errors through data collection and entry. Hopefully, the use of a web–based application (APP) can try and address these concerns.¹⁸ We are aware that in the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global PPS), a web-based application was used for data-entry, validation and reporting, which allowed the global PPS to stretch over 53 countries and include 335 hospitals. Following the challenges experienced with a paper based data collection tool for PPSs, an APP was developed in April 2017 in South Africa by one of the researchers (DK) based on the PPS forms developed and refined from the ongoing PPS study in Botswana.¹⁸,¹⁹

Consequently, the aim of the study was to test the developed APP in practice in South Africa to see if this could enhance data collection, given concerns with the time and costs associated with a paper method. Subsequently, use the findings to further refine the APP if needed before expanding the PPS study to cover more public hospitals in South Africa as well as potentially across Africa.

**METHODS**

**Study design, period and study setting**
The design of the original study was a point prevalence survey. With a PPS design, all beds in one single ward, were completely surveyed in one single day.

Following the completion of an initial paper based study, this study involved data being collected during two week days, from 11th to 12th of July 2017, by 15 trained data collectors using a newly developed APP. The training included a mini pilot involving all data collectors to see if they understood the APP data collection instrument. Training was given via a power point presentation where all trainers were instructed on the exact procedure for collecting the data and given the opportunity to ask questions.

Data was collected at Dr George Mukhari Academic Hospital (DGMAH). This teaching hospital is one of four in the province and situated in Ga-Rankuwa, Pretoria, Gauteng Province. This is a 1,650-bed hospital with 28 clinical departments, 20 approved ICU beds, 60 high care beds and 17 surgical theatres, providing services to an estimated 1.7 million people from the surrounding area.

**Development of the APP**

An APP was developed in South Africa to enable anonymous patient data to be entered directly into the application via any mobile device connected to the web. Data encryption is undertaken with both secure hash algorithm-256 (SHA-256) and Advance Encryption standard-265 (AES-256), which are the strongest encryption technology currently available and the same level of encryption used by international banks.

The data backups consist of both active and manual backups, and both the active backup and archives use the same encryption as the database. To minimize the risk of data mitigation failure, the data is stored in different geographic locations. The infrastructure is powered by Amazon Web Services (AWS) the industry leader in cloud services and is trusted by organizations such as DOW Jones, Pfizer and the CDC in Atlanta. Every access to the data is logged and time-stamped, and a log-file can be provided if needed. Only authenticated users can access the database, various passwords protect the application, and passwords are protected by double encrypted password technology.
The raw data can be exported in comma separated values (.csv) text (.txt) a JavaScript object notation (json) formats to Microsoft Excel for data analysis and statistical purposes. Data collection within the application consists of the following fields:

- Hospital code, ward code, patient code, admission date, age, sex, employed, transferred.
- Hospitalization in past 90 days, antimicrobial use past 90 days, duration and names of antibiotics in past 90 days
- Catheterization, intubation
- Pre-existing medical conditions
- Prescriber classification, antimicrobial prescribed, indication, dose, frequency, route
- Date, missed doses, out of stock
- CST results, bacterium name, sensitivity, IV to oral switch
- Prescribed in INN, according to EDL
- Unrelated surgery, prophylaxis

Furthermore, no patient sensitive data is stored directly within the APP and patient confidentiality is maintained through the use of anonymous coding system build directly into the application.

As mentioned, the APP was developed using variables from a paper based PPS data collection tool developed by a group of researchers principally from Botswana. Variables included in the data collection tool were aligned mainly to those included in the ECDC and Global PPS studies with input from WHO. This included data on the treatment of the infection if an antimicrobial was prescribed, the rationale including whether surgical or medical prophylaxis, whether empirical or not, the route of administration, as well as other criteria to help assess appropriateness. The presence of HIV, TB and malnutrition were also included as variables as they will influence potential antimicrobial use in sub-Sahara Africa.

**Study variables**

A number of variables were measured, which included entries related to work flow, data quality and usability of the APP. Work flow was measured by estimating the time it took to prepare the data collection instrument, data collection from the source of the data and actual data entry, validation and cleaning. The data quality was measured by evaluating the number of errors and if they could be amended. The usability of the APP was evaluated through a questionnaire completed by data collectors to give feedback on the usability of the APP
Time taken for collecting the data was also measured by requesting the data collectors to document the starting and ending time for data collection for each patient.

**Data collection and analysis**

Following the training of the data collectors on the APP, a pilot test was undertaken to ensure that data collectors were competent in data collection using the APP. The APP was subsequently used across 13 wards at DGMAH (adult ICU, three adult medical wards, three adult surgical wards, haematology-oncology paediatric medical ward, two obstetrics and gynaecology wards, paediatric ICU and two paediatric medical wards). Data collectors reviewed medical records on the survey date to determine whether patients may have been receiving an antimicrobial on the day of the survey, with details subsequently entered onto the APP. The APP allowed users to view, edit and delete the data they had entered, and was designed with the aim of making data entry less complicated and less time consuming. Additional features included on the APP were the list of medications and organisms to choose from. It also had automated show/hide functionality to ensure that only relevant fields are displayed, hence reducing data collection time and reducing the risk of data errors.

Antimicrobials prescribed were analysed according to the WHO’s anatomical therapeutic chemical (ATC) classification of medicines (ATC level 5), their dose, frequency and route of administration.

All data during this study was collected through the data collectors’ cell phones. The APP automatically exported the data to Microsoft Excel™ spread sheets and analysed using SPSS Version 8.0 for Windows, in consultation with a statistician. Entered data was checked for correctness and cleaned prior to analysis. Descriptive statistics were performed on retrieved data, in a form of table, graphs and bar charts. It was further on analysed for error rates as one of the qualitative variables.

The second part involved administering a questionnaire to the 15 data collectors, completed anonymously. The questionnaire was developed using a set of questions developed by an IT specialist from Scotland (ML) and included questions on the usefulness of the APP, its ease of use and the time it took to survey a patient’s file.
ETHICAL CONSIDERATIONS
Data collection commenced after receiving ethical approval from the Sefako Makgatho University Research Ethics Committee (SMUREC/H/210/2016:PG). Subsequently permission was obtained from the Chief Executive Officers of DGMAH. Patient confidentiality was maintained at all times with a unique identity number allocated to each patient’s record so to keep them anonymous.

RESULTS
In total 181 files were reviewed from 13 wards collected over two days in July 2017 of whom 151 were adults with 55% females. The mean age (SD) and median age (IQR) for males was 45.25 (17.29) and 45.5 (25.5) respectively. The mean and median age for females was 44.57 (±18.28) and 42 (27) respectively. The overall prevalence of antimicrobial use was 44%. Whilst a considerable number of patients in the adult surgical ward received antimicrobial (31 patients, prevalence 38%, 95% CI 27.49-48.51), the prevalence was highest in the paediatric medical wards (78%, 50.94 – 105.06). Less than half (42%) of the patients had not been hospitalized in the past 90 days and less than a third of those had used antimicrobials, with 30% patients’ files having no history of hospitalization. Amoxicillin and clavulanic acid was the most used antimicrobial followed by co-trimoxazole. 54% of the antibiotics were initiated before taking a culture and 19% after taking a sample for a culture and sensitivity test (CST).

DATA QUALITY
The data quality was measured by evaluating the number of errors encountered with the data recorded in the APP. Errors were further assessed to determine whether the APP could be refined to eliminate these errors or whether the errors were due to data collectors’ non-compliance with instructions. In total, 31 variables were included in the APP and six variables had errors. All errors were due to data collectors’ mistakes by choosing the wrong option provided on the APP and four of these errors were eliminated by refining the APP.

Although no consent was needed to survey patient files at DGMAH, some data collectors selected the option in the APP to indicate “patient did not give consent”. This requires the data collectors to be attentive when entering the data. This could not be refined on the current APP because the APP is intended for use in other countries and hospitals where consent to survey patients’ files might be required.
The variable to determine if HIV patients are on HAART had one error where a data collector indicated an HIV negative patient to be on HAART. This error was eliminated by modifying the APP to only show the variable “on HAART” if the patient is HIV positive.

For the variable, route of administration, ceftriaxone was captured as being given orally yet there is no oral formulation for this medication. The APP could not be refined to eliminate this error but the data collectors can avoid this error by making sure they enter the correct information.

Regarding culture sensitivity test (CST) requests and analysis, there was no option to capture a record of unknown or unavailable culture tests on the APP so these results were captured as no culture taken before initiation of the antimicrobials. However, two of the antimicrobials were captured as initiated without taking any cultures and no culture taken even after initiation of the antibiotics. Despite this, the data collectors selected the option for results available. This error was eliminated by automating the APP to skip the question on results available or not when an option for CST not ordered is chosen.

On entering the names of the antimicrobials used for prophylaxis, the field containing the name of the antimicrobial was empty for a few patients. The APP was programmed to ensure the field is compulsory to reduce the risk of missing data.

Concerns occurred when the type of infection was not documented on the files and data collectors had to use information on the physicians’ and nurses’ notes to check the onset of infection and establish what type of infection it is. This will be the subject of future quality improvement programmes in the hospital. A few of the patients were captured as having home-based care/facility acquired infection and this information was perceived as inaccurate as it would be almost impossible to know if it is a home-based care/facility infection if not documented on the file. This can be avoided by having the hospital and community acquired infection only option on the APP as home-based care/facility closely relates to community acquired infection.
WORK FLOW FOR DATA COLLECTION
The work flow of the survey process was evaluated by looking at the time taken for the preparation of the data collection tool, actual data collection from the data source as well as data entry and analysis.

Preparation of data collection tool
The preparation of the paper-based data collection tool was time consuming as it involved printing of the forms, stapling, organizing them into files and distribution to data collectors. The estimated time for this process was 9 hours. In case of any changes on the original forms, it would result in the recall of all previously distributed forms and re-issue of the updated forms. The APP involved loading the data collectors on the system and from there they could access it from their electronic devices. Any changes on the APP are made centrally and reflect immediately on the system.

Data collection time
The data collection time was measured by requesting data collectors to document the time it took them to collect data from each patient file. The same data collectors who had used the paper-based tool were the ones undertaking data collection using the APP. Out of the 15 data collectors who used the APP, 2 of them recorded that it took them 5 to 10 minutes to survey each patient file, ten of them said it took 15 to 20 minutes to survey one patient file and for three data collectors it took longer than 2 minutes (Table 1). The time taken for the paper based tool was considerably longer.

Data entry and analysis
With the paper based tool the data needed to be captured manually into an Ms Excel® spreadsheet. The estimated time it took to capture 512 patient files was 48 hours. Analysing the data took approximately 24 hours. The APP automatically exported the entered data into an Ms Excel® spreadsheet which provided automatically generated tables and graphs to summarise the data.

USABILITY OF THE APP
According to the data collectors’ responses to the questionnaire they were all confident in using the APP and found not complex at all. A majority of the data collectors (14) found the functions of the APP to be well integrated and consistent. Only one person disagreed with this.
A total of 11 users strongly agreed that the APP could be useful in PPS surveys while the other 4 users just agreed. All the users agreed that they needed training with the APP before they could use it. (Table 1).

Table 1: Usability of APP according to data collectors (n=15)

<table>
<thead>
<tr>
<th></th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The APP was easy to use</td>
<td>4</td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I think that I would need the support of a technical person to be able to use the APP</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>I found the APP unnecessarily complex</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>I found the various functions in this system were well integrated</td>
<td>2</td>
<td>12</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I thought there was too much inconsistency in this system</td>
<td>0</td>
<td>1</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>I would imagine that most people would learn to use this APP very quickly</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I found the APP very difficult to use</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>I felt very confident using the APP</td>
<td>10</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I needed to learn a lot of things before I could get going with this APP</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>It enables me to accomplish task more quickly compared to the forms</td>
<td>12</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Overall, I find this product useful in PPS surveys</td>
<td>11</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>How much time did you take to survey one patient file with the APP</td>
<td>2</td>
<td>10</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>How much time did you take to survey one patient file with the form</td>
<td>0</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

DISCUSSION

The aim of developing an APP is to provide an electronic data collection tool that is less time consuming and less costly than a paper-based system and to facilitate data entry analysis. Several other studies that have compared electronic and paper based data collection instruments have already shown that electronic data collection saves time, costs and is more reliable.22 This study sought to build on this.
The APP allowed an appreciable amount of data to be collected for each patient. A measure of data accuracy using errors showed that all the errors can be avoided by having trained data collectors who are compliant to instructions and attentive in capturing the data using the APP. A total of 31 variables used for surveying antimicrobial consumption and rationale of use were assessed with the APP. Errors occurred in six of the variables and the APP was refined in four of these variables to prevent and eliminate occurrence of similar errors. The errors with the other two variables can also be avoided by having data collectors that are compliant to instructions and consistent when collecting the data.

The electronic data collection tool (DCI) proved to be less time consuming in terms of all the processes. Once data collectors are loaded on the APP all the fields are available in electronic format and data collection can be initiated. The paper based DCI needed printing, collating of the forms and distributing them. This whole process took about nine hours.

Increased efficiency with data entering and validation was seen with the APP as it automatically exported the data to an excel spread sheet. The paper DCI required manual entering of the data into an Excel spreadsheet, which was time consuming and increased the risk of errors.

Users indicated that the APP was easy to use, well integrated and they preferred it over the paper-based DCI (Table 1). There were comments received from the users on how to improve the APP and such as “an auto fill” once the first two alphabets of an organism or medication is typed. The majority of the users also found the use of electronic devices more convenient than numerous paper-based forms that needed to be printed and filed. Other users felt that the forms were more labour intensive compared to the electronic DCI. These findings were in line with other studies\(^2\) where participants’ acceptance of an electronic DCI was significantly more satisfactory compared to that of a paper based DCI.

The APP is currently being further refined to suit the South African hospital setting and other African countries. PPSs in the Gauteng Province aiming to use this APP are underway, and during this research programme the APP will further be refined and reports given on its usability.
Chapter 4: Results and Discussion

LIMITATIONS
The accuracy of the data captured is dependent on the accuracy of documentation in the files and the level of commitment of the data collectors. Web-based applications is dependent on good internet connection. This might impose a limitation on this application as data collection in rural areas of South Africa where internet access is a challenge might be impaired.

In a case where the internet connection or signal is lost before submitting the captured information, the user has to recapture that information as it does not get saved. Alternatively the APP can be downloaded and be a non-internet dependant APP whereby once downloaded it does not require internet to be used. Another concern is that certain countries in Africa impose that patient level data may not be exported, imposing a limitation to the use of the web-based application on a larger scale in Africa.

The errors were based on logical inconsistencies amongst the data collectors by entering the incorrect data and this can be avoided by having committed and data collectors fully compliant to the instructions.

RECOMMENDATIONS
It would be recommendable that a mobile application that does not require internet connection be developed for data collection. A mobile application of this kind will have the advantage of being able to collect data without an active internet connection and update the information once a connection is available/ established. As mobile applications run directly on mobile devices the limitation imposed by certain countries to export patient level data might also be overcome.

A detailed comparison on all the processes and statistical comparison of error rates and mean durations between the two tools can be performed in future studies. Furthermore the costs for both DCI’s can be evaluated to make accurate calculations on the total costs for each type of DCI to better plan for the future. Errors on the paper-based tools can then be evaluated so to make a reliable conclusion on data quality for both tools.

Data collectors could also potentially be given incentives to motivate them to collect data efficiently.

CONCLUSION
Chapter 4: Results and Discussion

The APP is a potential tool to be used in antimicrobial surveillance studies as it proved to be user friendly and time saving. The APP has been tested in a public hospital and will continue being used in studies across South Africa. This tool can also be used in antimicrobial consumption surveillance studies across Africa. Further research is also ongoing to refine the APP if needed as part of more extensive studies in South Africa. We will be reporting on this in the future.

REFERENCES


Chapter 4: Results and Discussion


21. WHO. WHO Collaborating Centre for Drug Statistics Methodology. ATC/ DDD Index. Available at URL: https://www.whocc.no/

Chapter 5: Limitations, Recommendations and Conclusions

CHAPTER 5
LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS

5.1 INTRODUCTION

The limitations and recommendations of this study are discussed followed by a conclusion. A summary for the study ends this chapter.

5.2 LIMITATIONS OF THE STUDY

Due to the study being conducted in one hospital, due care should be given to the generalisation of study results for antimicrobial utilization in South African health care. This study did not investigate the cause and relationship of the results. Hospital charts were used for data collection, thus the accuracy depended on the accuracy of the hospital files. Further studies, which will take these limitations into consideration, are needed.

Data collectors were not motivated and this required the researcher to constantly monitor them to limit errors and inappropriate data. Financial support or incentives can be provided to improve results and efficiency. Patient history e.g. previous medication, hospitalization etc, were not always documented and if documented it was not easy to find and one had to go through all the notes and files to get information so the accuracy of the data largely depended on the information on the files.

5.3 RECOMMENDATIONS

Reliable data collection systems for antimicrobial utilisation are urgently needed to collect accurate data, and a follow-up on the findings of this study through education of health care professionals e.g. order and record CST, recording all information in patient records can help to achieve optimal antimicrobial use and improve prescribing practices. Lastly a culture within health care of regularly recording antibiotic utilisation, using the PPS data collection instruments, now available on a mobile application must be created.

5.4 CONCLUSIONS

The use of broad spectrum penicillins was high, followed by cephalosporins. Even though 60% of patients were not on antibiotics, more than 50% of them had used antibiotics in the
past 90 days. The use of antibiotics without taking cultures was high, which is an appreciable concern if antimicrobials are being used inappropriately. Information recorded in patient records was often incomplete. The PPS method offers a standardised tool that can be used to identify targets for quality improvement.


References


WHA | Resolutions on antimicrobial use and resistance.(2014) [online] Available at: http://www.who.int/drugresistance/AMR_DC_Resolutions/en/


APPENDICES

Appendix 1: Hospital Data

<table>
<thead>
<tr>
<th>PART 1 - HOSPITAL DATA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point Prevalence Survey</td>
</tr>
</tbody>
</table>

*Do not leave any field in this form unfilled; all details are required.*

<table>
<thead>
<tr>
<th>Date:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of the Hospital:</td>
<td></td>
</tr>
<tr>
<td>Hospital Code <em>(Refer to the Hospital Codes provided in the table below)</em></td>
<td></td>
</tr>
<tr>
<td>Level of Healthcare Facility <em>(Choose and circle the correct one)</em></td>
<td>Regional / District / Provincial</td>
</tr>
<tr>
<td>Full Names of the Data Collector: <em>(Print in capital letters)</em></td>
<td></td>
</tr>
<tr>
<td>Telephone no:</td>
<td></td>
</tr>
<tr>
<td>Mobile No:</td>
<td></td>
</tr>
<tr>
<td>Email:</td>
<td></td>
</tr>
</tbody>
</table>

### Hospital Codes

<table>
<thead>
<tr>
<th>Hospital Name</th>
<th>Hospital Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr George Mukhari Academic Hospital</td>
<td>P1</td>
</tr>
</tbody>
</table>
# PART 2 - WARD DATA

<table>
<thead>
<tr>
<th>Name of the Ward</th>
<th>Ward Code</th>
<th>Ward Specialty</th>
<th>No. of patients in the ward at 7 a.m.</th>
</tr>
</thead>
</table>

Write the name of the ward as you state in your hospital. Use the Ward Codes provided on the right side of the sheet. State if the ward has a particular specialty name as "Burn’s Unit, Coronary Care Unit, Stroke Unit, Spine Unit etc..."

## NAME OF THE WARD

<table>
<thead>
<tr>
<th>WARD CODE</th>
<th>NAME OF THE WARD</th>
</tr>
</thead>
</table>

### I. Paediatric Departments

- Paediatric Medical Ward: PMW
- Haematology-Oncology Paediatric Medical Ward: HO-PMW
- Transplant BMT/Solid Paediatric Medical Ward: T-PMW
- Paediatric Surgical Ward: PSW
- Paediatric Intensive Care Unit: PICU

### II. Neonatal Departments

- Neonatal Medical Ward / Special Care Baby Unit: NMW
- Neonatal Intensive Care Unit: NICU

### III. Adult Departments

- Adult Medical Ward (Male, Female & General, Private, TB, Isolation): AMW
- Haematology-Oncology - Adult Medical Ward: HO-AMW
- Transplant BMT/solid Adult Medical Ward: T-AMW
- Pneumology Adult Medical Ward: P-AMW
- Adult Surgical Ward (Male, Female): ASW
- Adult Intensive Care Unit: AICU
Appendices

Appendix 3: Patient Data

**PART 3 - PATIENT DATA**

### Section 1 - To be completed for all admitted patients

<table>
<thead>
<tr>
<th>Hospital Code:</th>
<th>Ward Code:</th>
<th>Patient Code:</th>
<th>Consented:</th>
<th>Admission Date:</th>
<th>Age:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed:</td>
<td>Transfer in:</td>
<td>Prior Hospitalization:</td>
<td>Antibiotic use last 90 days?</td>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>Catheterization:</td>
<td>Intubation:</td>
<td>HIV:</td>
<td>Name of last Antibiotics:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 Count:</td>
<td>On HAART</td>
<td>On Antibiotics now?:</td>
<td>(If you answered “Yes” then fill Section 2 below)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Section 2 - To be completed only for patients currently on Antibiotic therapy

<table>
<thead>
<tr>
<th>Prescribed by:</th>
<th>Prophylaxis/Treatment?</th>
<th>Medical or Surgical prophylaxis?</th>
<th>Duration of Prop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication:</td>
<td>Type of Infection:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the Antibiotic: 1</th>
<th>Dose:</th>
<th>Frequency:</th>
<th>Route:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start Date:</td>
<td></td>
<td>No. of Doses Missed:</td>
<td>Antibiotic O/S?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the Antibiotic: 2</th>
<th>Dose:</th>
<th>Frequency:</th>
<th>Route:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start Date:</td>
<td></td>
<td>No. of Doses Missed:</td>
<td>Antibiotic O/S?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the Antibiotic: 3</th>
<th>Dose:</th>
<th>Frequency:</th>
<th>Route:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start Date:</td>
<td></td>
<td>No. of Doses Missed:</td>
<td>Antibiotic O/S?</td>
</tr>
</tbody>
</table>

*Rx in INN (generic name)?* | CST prior to Empiric Treatment? | CST Results? | Name of Bacteria |

*Was Rx changed to sensitive Abx?* | Diarrhoea/Vomiting? | Oral Switch? | All Antibiotics from *
Appendices

Appendix 4: SMUREC clearance certificate

Sefako Makgatho Health Sciences University
Research & Postgraduate Studies Directorate
Sefako Makgatho University Research Ethics Committee
(SMUREC)

Molotlegi Street, Ga-Rankuwa 0208
Tel: (012) 521 5617/3698 | fax: (012) 521 3749
Email: lorato.phiri@smu.ac.za
P.O. Box 163 Medunsa 0204

APPROVAL NOTICE - NEW APPLICATION

01 September 2016
Ms N Dlamini
Department of Pharmacy
P.O. Box 218
Medunsa, 0204

MEETING: 07/2016
SMUREC Ethics Reference Number: SMUREC/210/2016: PG

The New Application received on 18 August 2016, was reviewed by members of Sefako Makgatho University Research Ethics Committee 01 September 2016 and was approved on 01 September 2016.

Title: Point prevalence survey of antimicrobial utilization in selected public sector hospitals in the Gauteng Province of South Africa

Researcher: Ms N Dlamini
Supervisor: Prof N Scholtz
Co-supervisor: Prof JC Meyer
Department: Pharmacy
School: Health Care Sciences
Degree: Master of Pharmacy

Please note the following information about your approved research protocol:

Protocol Approval Period: 01 September 2016 - 01 September 2017

Please remember to use your protocol number (SMUREC/210/2016: PG) on any documents or correspondence with the REC concerning your research protocol.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modification, or monitor the conduct of your research and the consent process.

After Ethical Review: Please note a template of the progress report is obtainable in the Research Office and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit. Translation of the consent document in the language applicable to the study participants should be submitted.

International Organisation [ORG0003691], Institutional Review Board [IRB000070386] Expiry date: 09 December 2018,
Federal Wide Assurance [FWA000023943] Expiry date: 31 August 2017 and NHREC No: REC 210408-003

Sincerely,
DR C BAKER
DEPUTY CHAIRPERSON SMUREC

Date: 01/09/2016

Chairperson
SMU Research Ethics Committee
Appendices

Appendix 5: Amendments Approval SMUREC clearance certificate
Dear Prof Ogunbanjo,

Protocol amendment: Point Prevalence Survey of Antimicrobial Utilisation in Selected Public Sector Hospitals in the Gauteng Province of South Africa

The above mentioned protocol received ethical clearance from the Sefako Makgatho University Research Ethics Committee (SMUREC) on 01 September 2016 (SMUREC/H/210/2016: PG).

I hereby request the following amendments to the above protocol:

a) To change the study site from the three hospitals which were Sebokeng hospital, South Rand hospital and Dr. George Mukhari Academic Hospital (DGMAH) to one study site which is only Dr George Mukhari Academic Hospital (DGMAH).

b) To change the title to: Point Prevalence Survey of Antimicrobial Utilisation at Dr George Mukhari Academic Hospital.

Motivation: Since this is a point prevalence survey it is ideal that all the data be collected at a certain point and in one season in all the sites, for it to be comparable. The use of antimicrobials is greatly influenced by seasons e.g. upper respiratory infections are more
prevalent in winter than in summer and this can have a great influence on the results of the study as it can create a case-mix. I already have the data and results from George Mukhari which I obtained in February –March 2017 but due to lack of enough data collectors to assist with the data collection I could not collect the data in the other sites on the same season.

c) To include enablers application on the methodology as an additional data collection instrument.

d) To include testing and piloting of the enablers app on methodology

**Motivation:** The enablers application is an electronic data collecting instrument. As I was conducting the study we realized that the forms we were using as DCI’s were taking too much time to fill in and this app may be a solution with further consumption studies as it is less time consuming and the data automatically get exported into an excel spreadsheet making it easier to be captured rather than manually entering the data into a spread sheet.

All changes to the text in the protocol, as a result of the above amendments, have been highlighted. Attached please kindly find a copy of the original protocol dated July 2016, the revised protocol dated July 2017 and the SMUREC clearance certificate.

Thank you for your valuable time and input into reviewing this study, if there are any more questions please do not hesitate to contact me.

Kind regards

Nokuthula Dlamini

Prof N Schellack (supervisor)

Master’s Degree Candidate

CC: Prof JC. Meyer (Co-supervisor)
Managing Editor - Hospital Practice

Dear Dr Dearman

I am pleased to submit this original research article entitled “Feasibility of using point prevalence surveys to assess antimicrobial utilisation in public hospitals in South Africa; a pilot study and implications” by Dlamini, Schellack, Meyer, Kruger, Kurdi, and Godman for consideration for publication in the Hospital Practice Journal. The co-authors have had good experience with this Journal - hence this submission.

This manuscript underlines the importance of collecting antibiotic utilisation among public hospitals in South Africa as a critical step with improving future antibiotic prescribing in South Africa and reduce future antimicrobial resistance rates. We believe the findings have important policy implications for antibiotic stewardship programmes in this and other public hospitals in South Africa in terms of maintaining high adherence rates to essential medicine lists/guidelines, requesting and using sensitivity analysis as well as addressing currently limited IV to oral switching.

Consequently, we believe that this manuscript will be suitable for publication in Hospital Practice Journal, and builds on other publications regarding antibiotic utilisation among African countries in your and other journals. We are happy to confirm this manuscript has not been submitted to any other journal for consideration and that all Tables and Figures are originals. We also have no conflicts of interest to disclose.

Thank you for your consideration!

Sincerely,

Ms Nokuthula Dlamini
Appendix 8: Guidelines for the authors for the journal of hospital practice

Hospital Practice is an international, peer reviewed journal, publishing high-quality, original research. Please see the journal’s Aims & Scope for information about its focus and peer-review policy.

Please note that this journal only publishes manuscripts in English.

This journal accepts the following article types: 1) Original Research, 2) evidence-based Review articles, 3) Health Outcomes, 4) Editorials 4) Supplements, and 5) Letters to the Editor.

We allow a maximum of five authors on submitted papers. The maximum quantity of authors on any submitted manuscript is at the discretion of the publisher. In addition, once a manuscript is submitted, we do not allow the inclusion of additional authors on the manuscript; additional authors may be added to the acknowledgements section. The addition of more authors is at the discretion of the Editorial Office.

Please also be sure that your submission is written clearly and avoid jargon and/or colloquialisms. We do not accept manuscripts that have plagiarized content within them—this includes self-plagiarism. Please be sure to cite all sources (even your own previously published work) and ensure that your words are your own.

We accept unsolicited manuscripts and encourage authors to contact the Editorial Office to discuss any unsolicited article topics in order to avoid replication of previously published or already submitted articles.

Article types

• Original Research Articles: formal investigative studies that focus on timely clinical issues. These reports include clinical trials, randomized trials, intervention studies, cohort studies, case-control studies, epidemiologic assessments, other observational studies, surveys with high response rates, cost-effectiveness analyses and decision analyses, and studies of screening and diagnostic tests. As a condition of consideration for publication, all clinical trials must be registered at an appropriate online public registry before submission of a manuscript based on the trial.

• Review Articles: evidence-based, comprehensive analyses and meta-analyses of current developments in the field of clinical medicine relevant to our readers. Reviews present content that is accessible to readers who are not intimately familiar with the subject being reviewed,
increase readers' interest in the subject, and describe important developments in the relevant medical area.

- **Health Outcomes:** Articles featured in the Health Outcomes section of Hospital Practice address specific economic issues in clinical medicine, health care policy, or medical research.

- **Editorials:** Editorials are short articles on issues of topical importance to our readers. We encourage our editorial writers to express their opinions, giving the author the opportunity to present criticism or address controversy. The intention is very much that the article should offer a personal perspective on a topic of recent interest.

- **Supplements:** Publishing a sponsored supplement to Hospital Practice offers an efficient way to distribute a large volume of research in one of the oldest and most widely-read medical journals in the world. Supplements are peer-reviewed, indexed, and covered by the major databases and content services (Medline, PubMed, EMBASE) in the same manner as articles published in the journal.

- **Letters to the Editor-in-Chief:** discuss a specific article published in Hospital Practice. All letters to the Editor are subject to editing and abridgement; we try to ensure that letters are not censored or suppressed, but a letter may be returned to the author if the information in the letter is inaccurate or misleading. The Editor-in-Chief will make the final decision on author revisions of the letter and may solicit comments from authors of the original article published in Hospital Practice. The letter and response will be published together, either online or in print.

  - **Peer review**

Taylor & Francis is committed to peer-review integrity and upholding the highest standards of review. Once your paper has been assessed for suitability by the editor, it will then be double blind peer-reviewed by independent, anonymous expert referees. Find out more about what to expect during peer review and read our guidance on publishing ethics.

  - **Preparing your paper**

All authors submitting to medicine, biomedicine, health sciences, allied and public health journals should conform to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, prepared by the International Committee of Medical Journal Editors (ICMJE).

  - **Structure**
All manuscripts should follow the basic format below. Not all sections are required for all manuscripts, but we do encourage authors to be as thorough as possible during submission.

1. Title Page (including manuscript title, author names and degrees, professional affiliations (institute, etc), and corresponding author, with the latter's postal address, phone, fax, and email address)
2. Abstract (in Original Research articles, the abstract should be structured using the following headings: Objectives, Methods, Results, Conclusion.)
3. Keywords (approximately 5-10, for indexing)
4. Introduction
5. Materials and Methods
6. Results (original research articles)
7. Discussion
8. Conclusion/Summary
9. Acknowledgements (if any)
10. Conflict of Interest Statements (if any)
11. References
12. Figure Legends
13. Tables
14. Figures
15. Treatment algorithm(s) (optional)

On a separate page, provide the article title (120-character maximum), running title (50-character maximum), full name of each author, his/her highest degree(s) attained, institutional affiliations (for all authors), and title of current position. One author must be designated as the corresponding author with full contact information (mailing address, office phone number, mobile phone number, fax number, and e-mail address).

- **Word limits**

Please include a word count for your paper.

A typical Original research article, review article, or health outcome for this journal should be more than 3000 and no more than 6000 words; this limit does not include keywords, references, legends, and a maximum of 6 figures and 8 tables.

A typical Letter to the Editor for this journal should be more than 300 and no more than 1200 words.

A typical Editorial for this journal should be no more than 1500 words.
Appendices

- **Style guidelines**

Please refer to these style guidelines when preparing your paper, rather than any published articles or a sample copy.

Please use American spelling style consistently throughout your manuscript.

Please use single quotation marks, except where 'a quotation is "within" a quotation'. Please note that long quotations should be indented without quotation marks.

Each manuscript should clearly state an objective or hypothesis; the design and methods; a comment section placing the results in context with the published literature and addressing study limitations; and the conclusion. Data included in research reports should be as current as possible. Full sentences and paragraphs should be used in writing the content of the paper—bullet points are not an acceptable format for the presentation of information.

Please be sure that your submission is written clearly and avoid jargon and colloquialisms.

We do not accept manuscripts that have plagiarized content within them – this includes self-plagiarism. Please be sure to cite all sources (even your own previously published work) and ensure that your words are your own.

**English-Language Editing Services**

Prior to submission, please ensure that your manuscript is written in good English grammar and language. If you are concerned about the English language in your manuscript, it will be helpful to you to use an English language editing service prior to peer review, to ensure that the peer review process will be meaningful for you and so that the editorial processing of your manuscript can be efficient. We provide an in-house language editing service, at a charge. Please see our website for more information about this, as well as other editing services we offer.

- **Formatting and templates**

Papers may be submitted in any standard format, including Word and LaTeX. Figures should be saved separately from the text. To assist you in preparing your paper, we provide formatting templates.

A LaTeX template is available for this journal.
Word templates are available for this journal. Please save the template to your hard drive, ready for use.

If you are not able to use the templates via the links (or if you have any other template queries) please contact authortemplate@tandf.co.uk

Before submission, please blind your manuscript to expedite the processing of your work. This means that no author-identifying information should be included in the main text or in the file name of the main document. The only author-identifying information should be on the title page, which should be submitted online as a separate document.

The manuscript text should be separated into relevant sections and paragraphs with appropriate headings. Please be sure that all main and subheadings are clearly delineated.

Authors of original research manuscripts should contact the Editorial Office (jonathan.patience@informa.com) if they are interested in submitting more than the maximum amount of figures or tables. Authors must obtain permission via the original publisher for any adapted/reproduced table or figure material and must use the exact credit wording as specified by the original publisher. Please also ensure that informed consent is obtained for all figures and images containing any identifying features or information.

• References

Please use this reference style guide when preparing your paper. An EndNote output style is also available to assist you.

Please ensure that your manuscript follows our style to expedite your manuscript's processing. The accuracy of all references is the author's responsibility. Please include only published references and cite full sources. References should be current and numbered consecutively in the order in which they are cited in the text. A minimum of 30 references should be included in your manuscript; lists with fewer than 30 references will be reviewed at the discretion of the editorial office.

References should be denoted numerically and in sequence in the text, using Arabic numerals placed in square brackets, i.e., [12].

Please note: A maximum of 20 references are permitted in Editorials.
• **Checklist: what to include**

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