ANTIMICROBIAL CONSUMPTION IN COMMUNITY HEALTH CARE CENTRES ACROSS GAUTENG, SOUTH AFRICA – A POINT PREVALENCE SURVEY

A mini-dissertation submitted by

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2018
DECLARATION

I 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.

Magongwa, NM (Mr)  
Date  

04/01/2018
DEDICATION

I dedicate this research to my mother, Mrs P Magongwa, for her understanding and encouragement. I would also like to dedicate this to my younger brother to encourage him to seek knowledge and strive for better achievements in life. My extended dedication is to my aunt (TR Tshitake) that assisted me financially throughout my undergraduate years and always believed in me.
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### ABBREVIATIONS AND ACRONYMS

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<th>Full Form</th>
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<tr>
<td>AMR</td>
<td>Antimicrobial Resistance</td>
</tr>
<tr>
<td>AMS</td>
<td>Antimicrobial Stewardship</td>
</tr>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
</tr>
<tr>
<td>AWS</td>
<td>Amazon Web Services</td>
</tr>
<tr>
<td>BRICS</td>
<td>Brazil, Russia, India, China, South Africa</td>
</tr>
<tr>
<td>CHC</td>
<td>Community Healthcare Centre</td>
</tr>
<tr>
<td>DDD</td>
<td>Defined Daily Dose</td>
</tr>
<tr>
<td>DID</td>
<td>DDD/100 people</td>
</tr>
<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
</tr>
<tr>
<td>ENAAABLERs</td>
<td>Enhancing Appropriate antimicrobial and vaccine use via health and other techniques in the Republic of South Africa</td>
</tr>
<tr>
<td>ESAC-Net</td>
<td>European Surveillance of Antimicrobial Consumption Network</td>
</tr>
<tr>
<td>HCP</td>
<td>Health Care Provider</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>IPC</td>
<td>Infection Prevention Control</td>
</tr>
<tr>
<td>LMIC</td>
<td>Lower Middle Income Country</td>
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<tr>
<td>M.HEALTH</td>
<td>Mobile Health</td>
</tr>
<tr>
<td>NHRD</td>
<td>National Health Research Database</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care</td>
</tr>
<tr>
<td>PPS</td>
<td>Point Prevalence Survey</td>
</tr>
<tr>
<td>SA</td>
<td>South Africa</td>
</tr>
<tr>
<td>SMUREC</td>
<td>Sefako Makgatho University Research &amp; Ethics Committee</td>
</tr>
<tr>
<td>WHA</td>
<td>World Health Assembly</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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ABSTRACT

Introduction: Antimicrobials have proven to be very effective when used appropriately to significantly reduce morbidity and mortality from microbial infections. Although they have shown great efficacy against micro-organisms, there is an increasing pattern of antimicrobial resistance. Studies on antimicrobial consumption have shown that the increase in resistance can be directly linked to the rate in which antimicrobials are consumed. Lower Middle Income Countries (LMICs) are mostly affected by declining efficacy of antibiotics because of their greater burden of infectious disease in both human and animal populations, the lack of access to affordable second- and third-line antibiotics, and because of suboptimal infection prevention measures in hospitals and communities. Also, the lack of appropriate antimicrobial consumption surveillance methods and population antimicrobial consumption data is a significant obstacle. In order to combat antimicrobial resistance, surveillance systems have to be implemented to track how antimicrobials are consumed at a patient level. Currently, there is a significant lack of vital information on patient-level antimicrobial consumption data in South Africa.

Objectives: To quantify antimicrobial usage in selected CHCs using a point prevalence survey; To list and describe antimicrobial consumption in CHCs using a point prevalence survey.

Method: The study was a quantitative descriptive study that used a point prevalence survey method. The studied included nine (9) CHCs across the five (5) municipalities in the Gauteng province. A total number of 786 patient files were surveyed of which the study group included all patients that visited the CHC the day prior to data collection, regardless of age, race or disease state. Data was collected using an m.Health mobile application by researchers that were trained prior to data collection. No interventions were made throughout the study.

Results: The study was conducted in order to fill in the paucity in antimicrobial consumption data. The nine (9) CHC that were surveyed had a sample size of 786 patients with only 30.79% (242) patients prescribed antimicrobials. Most of the antimicrobials that were prescribed were for the treatment of infections (209 units; 74.91%) whilst the others were used for medical prophylaxis (70 units; 25.01%). The most commonly prescribed antimicrobial was Amoxicillin (38.35%; 107/279) which was used for treatment of antimicrobial infections followed by isoniazid (14.70%; 41/279) which was used for medical prophylaxis, specifically in HIV positive, TB exposed patients. Most of the antimicrobial agents that were used could not be attributed to a specific infectious diagnosis to which it was indicated (60.1%; 472). The most
common infectious diagnosis that were documented were for laryngitis and otitis media (4.3%). followed by community acquired pneumonia then by sexually transmitted diseases in women. Monotherapy was most frequently prescribed as standard therapy used whilst only a few combination antimicrobial therapy was used. The most frequent combination therapy were Isoniazid plus Sulfamethoxazole/trimethoprim indicated for medical prophylaxis of TB and PJP, respectively and also a combination of Ceftriaxone plus Azithromycin plus Metronidazole (oral/rectal) which were commonly indicated to treat sexually transmitted diseases in women. There were varied differences in terms of the DDD/day consumption within the antimicrobials when compared with the recommended WHO DDD/day consumption. Some of the antimicrobial agents such as flucloxacillin showed a significantly elevated DDD/day consumption of surveyed patients as compared to the WHO DDD/day. On the contrary, antimicrobial agents such as ceftriaxone showed lower than recommended DDD/day consumption for the surveyed patients. The only antimicrobial agents that were equivalent to the WHO recommended DDD/day were isoniazid and Ciprofloxacin.

Although the data shows varieties in antimicrobial consumption throughout the different patient demographics, the sample size is not adequate to generalize the consumption rate to the South African CHC and PHC setting. The study served to motivate more studies to be conducted in the public healthcare setting in South Africa so that surveillance tools could be implemented and accurately report antimicrobial consumption which will possibly influence AMC and AMR guidelines that will be implemented through the SA national strategic framework and as a recommendation by the WHO.

Conclusion: Amoxicillin showed to be the most frequently prescribed antimicrobial, followed by Isoniazid. Most of the antimicrobial agents that were used could not be attributed to a specific diagnosis to which they were indicated. Infections of the ear, throat and nose were the most common infection to which antimicrobial agents were prescribed, this was followed by CAP then STDs in women. Antimicrobial consumption was observed to be relatively higher in CHCs with a larger HIV/AIDS population. The use of microbial cultures and antimicrobial sensitivity tests to guide antimicrobial selection was not observed in the CHCs. This reflects that there is still minimal information on antimicrobial resistance patterns in CHCs. This study is the first to be conducted in the community setting in South Africa. The results cannot be generalized to the South African antimicrobial consumption rate in the communities due to the relatively small sample size. The study served to motivate more studies to be conducted in the public healthcare setting in South Africa so that surveillance tools could be implemented and accurately report antimicrobial consumption which will possibly influence antimicrobial
consumption (AMC) and antimicrobial resistance (AMR) guidelines that will be implemented through the SA national strategic framework and as a recommendation by the WHO.

**Recommendations:** The filing system in the CHCs made it improbable to recover all the patient files of the patients that visited the clinics the day prior data collection. A prompt improvement of filing systems is essential for implementation in all the CHCs. The paper-based files make finding information difficult. Some documents are missing which means some vital information cannot be found and documented. The use of computer-based profiles might eliminate this predicament or at least reduce errors such as these.
INTRODUCTION

1.1 INTRODUCTION

This chapter entails a thorough description of the background and rationale for the study. The chapter also includes the aim, objectives and research questions. A brief discussion about the significance of the study and the outline of the whole dissertation then comes last.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

The effectiveness of antimicrobials has been proven continuously to significantly reduce morbidity and mortality from infections (Gelband & Laxminarayan, 2015). Although they have shown great efficacy against micro-organisms over the past 50 years, the high rate of use of these antimicrobials has shown to be associated with antimicrobial resistance (Bell, Schellevis, Stobberingh, Goossens & Pringle, 2014). Studies on antimicrobial consumption have shown that the increase in resistance can be directly linked to the rate in which antimicrobials are consumed regardless of the geographical region (Van Boeckel, Gandra, Ashok, Caudron, Grenfell, Levin & Laxminarayan, 2014).

Lower Middle Income Countries (LMICs) are significantly affected by antimicrobial resistance. This is because LMICs have a greater burden of infectious diseases in both human and animal populations, lack access to affordable second- and third-line antibiotics, and have suboptimal infection prevention measures in hospitals and communities (Laxminarayan & Gelband, 2015). This causes a decline in efficacy of antibiotics. The other challenge that has been observed in LMICs has been the lack of appropriate antimicrobial consumption surveillance methods and population consumption data which can be used to develop guidelines (Laxminarayan & Gelband, 2015).

The World Health Organization (WHO) has for many years promoted the global monitoring of antimicrobials across health sectors and raised awareness of the consequences of antimicrobial resistance (Versporten, Bolokhovets, Ghazaryan, Abilova, Pyshnik, Spasojevic, Korinteli, Raka, Kambaralieva, Cizmovic, Carp, Radonjic, Maqsudova, Celik, Payerl-Pal, Pedersen, Sautenkova & Goossens, 2014). Despite the call to introduce new policies to combat resistance, there is a disturbing increase in antimicrobial consumption and increasing antimicrobial resistance patterns (Versporten et al., 2014).
Chapter 1: Introduction

The absence in the development of new generations of antimicrobial drugs (Bell et al., 2014), as well as the diminishing effectiveness of antimicrobials, creates a major global predicament on how infections will be treated in the future (NDoH, 2015). Appropriate use of existing antimicrobials is crucial to ensure the long term availability of effective treatment for microbial infections. It is therefore crucial to gather information on antimicrobial consumption to help us understand what we are currently using and what the resistance patterns are on what we are currently consuming.

Currently, the lack of sufficient surveillance and reports on antimicrobial consumption in public health care service facilities in South Africa creates a predicament towards finding a valid and reliable method that will link antimicrobial consumption information between the pharmacy, prescribers and laboratory (Mendelson & Matsotso, 2015).

The purpose of this study was therefore to collect data on antimicrobial utilisation in selected Community Healthcare Centres across Gauteng province using a PPS in order to document and quantify current antimicrobial consumption.

1.3 RESEARCH QUESTION

The study posed the following research questions:

<table>
<thead>
<tr>
<th>Primary research question</th>
<th>Secondary research question</th>
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<tbody>
<tr>
<td>How were antimicrobials utilized across Community Healthcare Centres (CHC) in Gauteng, SA?</td>
<td>Which antimicrobials were being used in selected CHC’s in Gauteng, SA?</td>
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</tbody>
</table>

1.4 AIM OF THE STUDY

The aim for this study was to quantify the utilisation of antimicrobials in selected community healthcare centres (CHCs) across Gauteng, South Africa (SA).

1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To quantify antimicrobial usage in selected CHCs using a point prevalence survey.
• To list and describe antimicrobial consumption in CHCs using a point prevalence survey.

1.6 IMPORTANCE OF THE STUDY

There is a global concern that surrounds overuse of antimicrobials. Excessive and inappropriate use of antimicrobials overtime has led to a widespread increase in healthcare costs and emergence of microbial resistance (Bozkurta, Kayab, Tekina, Gulsunb, Devecia, Dayana & Hos, ogluua, 2013). Antibiotics are amongst the drugs associated with the highest costs worldwide and account for 20-30% of total drug expenditures (Pinar, 2012). Also, the observed antimicrobial efficacy decline against common pathogens has detrimental consequences towards different societies. In high-income countries, there has been an observed shift towards using more expensive drugs, which increases the total drug expenditure and creates a financial burden (Laxminarayan, Duse & Wattal, 2013). In low-income and middle-income countries, where affordability of second-line drugs restricts their use are observed, there is increased morbidity and mortality.

The indiscriminate and excess use of antimicrobial drugs appears the most significant factor in the emergence of resistant microorganisms in recent years (Sartelli, Weber, Ruppé, Bassett, Wright, Ansaloni, Catena, Coccolini, Abu-Zidan, Coimbra & Moore, 2016). Also, several research studies conducted in African countries show that communicable diseases are still the major result of death amongst African countries, especially in children below the age of 5 years (WHO, 2014). The extensive burden of communicable diseases especially HIV/AIDS has resulted in increased antimicrobial consumption which eventually leads to high resistance patterns (Leopold, van Leth & Tarekegn, 2014).

Global PPS of antimicrobial consumption and resistance are designed to provide current data on utilisation and resistance patterns using a standardised methodology in order to plan future interventions (Versporten et al, 2014). The use of antibiotic data is to drive policymakers to increase focus on the dangers of antimicrobial overuse and develop policies to combat antimicrobial resistance (Laxminarayan & Van Boeckel, 2014). When there is presence of antimicrobial consumption data, predictive mathematical modelling using patterns of antibiotic consumption could identify hotspots where resistance is most likely to originate, this will inform the selection of target sites for surveillance and policy changes (Laxminarayan & Van Boeckel, 2014).
To improve the quality of antimicrobial treatment and to reduce the related costs, several recent initiatives have been encouraged. Surveillance for antimicrobial consumption patterns is therefore essential (Bozkurta et al., 2013).

This study was designed to provide antimicrobial consumption data at a patient-level which is lacking currently in South Africa. The gathering of antimicrobial consumption data using a mobile application was also assessed as an antimicrobial consumption surveillance tool. This is done to fulfil the WHO AMR policy framework to improve surveillance systems in Africa in order to track and combat antimicrobial resistance. National policies can only be practical and effective if the consumption rate and resistance patterns specific to the South African health system are known and understood. This research is important as a first step approach to gathering antimicrobial consumption data and investigating effective surveillance systems to track antimicrobial consumption and resistance.

1.7 OUTLINE OF THE DISSERTATION

This dissertation consists of five chapters. Chapter 1 is the introduction which serves to introduce the reader to the background and rationale of the study, also, inform the reader about the aim and objectives of the study. Chapter 1 also includes an overview of the importance of the study. Chapter 2 gives an extensive literature review of the study, giving the reader information on what studies have been conducted on this topic and what the results were. The literature review mainly highlights how previously conducted studies have influenced the methodology of this study and also the importance of the study. Chapter 3 discusses the methodology applied in the study which entails the study design, study site, study population, data collection and analysis, data collection instrument, reliability and validity of the study, bias and all ethical principles considered in the study. Chapter 4 is a manuscript which contains the results of the study and the discussion of the results. Chapter 5 includes the summary, limitations of the study, recommendation and conclusion.

1.8 SUMMARY

The development of resistance poses a significant threat on how we are going to treat microbial infections in future. The discussion in the background of the study has eluded to the fact that there is still a massive gap in antimicrobial consumption data in lower-to-middle income countries such as South Africa. This makes this study essential and necessary. The
importance of this study has been highlighted to be the quantification of antimicrobial use. The main aim of the study is to quantify antimicrobial consumption with the objective being listing and describing how antimicrobial agents are consumed in the CHCs. The next chapter comprises of an extensive literature review on antimicrobial consumption and resistance.
2.1 INTRODUCTION

Chapter 2 provides an overview of the literature review based on published studies that report on antimicrobial consumption and resistance patterns globally and locally. The chapter also includes how antimicrobials are quantified using the WHO drug classification system and the Be AWARE WHO antibiotic classification system which has recently been adopted. Surveillance methods using an application developed in South Africa are also explained and outlined. The chapter concludes with a summary that explains the discussions in Chapter 2.

2.2 ANTIMICROBIAL CONSUMPTION

2.2.1 Antimicrobial consumption

The data on antimicrobial consumption is essential as a provision benchmark for assessments of antibiotic stewardship programmes. Reductions in antibiotic consumption are a key part of comprehensive national strategies that have been shown to work in Canada, the EU, and the USA (Laxminarayan & Van Boeckel, 2014). Antimicrobial consumption can be defined as an aggregated rate of antimicrobial usage which is utilised for benchmarking purposes (Griffith, Postelnick & Scheetz, 2012). In order to accurately gather antimicrobial consumption data, prevalence surveys can be employed. Antimicrobial studies have been conducted globally to understand the pattern of antimicrobial consumption and resistance (Griffith, Postelnick & Scheetz, 2012).

2.2.2 Global antimicrobial consumption

There are several studies that have been conducted globally on antimicrobial consumption. One recent study was conducted by Van Boeckel, Gandra, Ashok, Caudron, Grenfell, Levin, & Laxminarayan (2014) titled “Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data”. The study used pharmaceutical sales data from retail and hospital pharmacies from the IMS Health MIDAS database. Trends for antimicrobial consumption of standard units of antibiotics were reviewed between 2000 and 2010 for 71 countries. This study included countries from Europe, Africa, North and South America making the data global. The following significant findings were made; consumption of
antimicrobials increased by 36% (from 54 083 964 813 standard units in 2000 to 73 620 748 816 standard units in 2010). Throughout the research period, the observed major antibiotics that increased in consumption were cephalosporins, broad spectrum penicillins and fluoroquinolones across all surveyed countries. The most concerning antibiotics that increased in consumption were carbapenems and polymixins by 45% and 13%, respectively which are usually used as a last resort to infections. Brazil, Russia, India, China, and South Africa (BRICS) were shown to have accounted for approximately three quarters (76%) of this global antimicrobial consumption increase. There was a significant increase in antimicrobial consumption in developing countries, which had a global population increase of 33% but contributed approximately three-quarters (3/4) of the increase in the global antimicrobial consumption rate. This indicates that the increase in antimicrobial consumption is not only a factor that can be attributed to demography but can also be influenced by factors such as increased access to antibiotics, increased expenditure in the medical sectors and several other factors (Van Boeckel et al, 2014).

The study confirms that even though there is a relatively high antimicrobial consumption rate per person in developed countries than developing countries, there is an alarming increase in antimicrobial consumption from developing countries (Van Boeckel et al, 2014). The increasing consumption rate has prompted more studies to be conducted in individual countries in order to develop antimicrobial consumption policies to improve antimicrobial consumption and to prevent antimicrobial resistance (Van Boeckel et al, 2014).

A large study was conducted across European Countries by the European Centre for Disease Prevention and Control (ECDC) between 2010 and 2014. The study collected antimicrobial consumption data both in the hospital and community sectors from 30 EU/EEA affiliated countries (ECDC, 2015). The antibiotic consumption data for this study was collected by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) at ECDC. The data was mainly on sales of antimicrobials in the country, or a combination of sales and reimbursement data (i.e. not including antibiotics obtained without a prescription and other non-reimbursed courses). The data was analysed using the Anatomical Therapeutic Chemical (ATC)/DDD index.

Antimicrobial consumption data was collected in the hospital setting from which it was observed that the relative proportion of antimicrobial consumption for different antibiotic groups in the hospital sector varied widely amongst countries. The EU/EEA population-weighted-mean consumption increased significantly during the period 2010-2014. In the hospital sector, the proportions of cephalosporin, other beta-lactams (including
carbapenem) and other groups of antibiotics were generally higher than in the community. There were several variations reported in the proportions of different antibiotic groups used in hospitals setting: consumption of cephalosporin and other beta-lactams, including carbapenem, ranged from 7% in the United Kingdom to 55% in Bulgaria; consumption of macrolides, lincosamides and streptogramin ranged from 3% in Sweden to 17% in Ireland; and consumption of quinolones ranged from 4% in the United Kingdom to 19% in Malta.

Antimicrobial consumption in the communities (outside hospitals) was also conducted and showed that there was an increased EU/EEA population-weighted mean consumption during the period 2010-2014. Penicillin drugs were the most frequently used antibiotics in all countries, ranging from 32% (Germany) to 67% (Slovenia) of the total consumption in the community, whereas the proportion of other antibiotic groups varied widely between countries- e.g. cephalosporin and other beta-lactams, from 0.2% (Denmark) to 21% (Slovakia); macrolides, lincosamides and streptogramin, from 5% (Sweden) to 27% (Slovakia); and quinolones, from 2% (United Kingdom) to 15% (Hungary).

The following figure summarizes the antimicrobial consumption pattern from the study conducted by the ECDC during 2010 to 2014;

**Figure 1: The antimicrobial consumption pattern from the study conducted by the ECDC during 2010 to 2014**

The above diagram compares the antibiotic consumption pattern between the hospital sector and the community sector across the European countries surveyed by the ECDC.

A study conducted by (Versporten, Bolokhovets, Ghazaryan, Abilova, Pyshnik, Spasojevic, Korinteli, Raka, Kambaralieva, Cizmovic, Carp, Radonjic, Maqsudova, Celik, Payerl-Pal, Pedersen, Sautenkova & Goossens, on behalf of the WHO/Europe-ESAC Project Group,
Chapter 2: Literature Review

2014) included 13 non-European Union (EU) countries and recently independent countries. These countries were selected based on the fact that there was no reliable antimicrobial utilization data for both the public and private sectors. The 13 countries included; (Armenia, Azerbaijan, Belarus, Georgia, Kyrgyzstan, Moldova, Tajikistan, Ukraine, and Uzbekistan) and six south and eastern European countries (Albania, Bosnia and Herzegovina, Macedonia, Montenegro, Serbia, Turkey), plus Kosovo.

The study reported that Co-amoxiclav (Amoxicillin+Clavulanic acid) was mainly used in Georgia (42.9% of total antibiotic use) and Turkey (30.7%). Newly independent states used substantial quantities of ampicillin and amoxicillin (up to 55.9% of total antibiotic use in Azerbaijan). Montenegro and Serbia were the highest consumers of macrolides (15.8% and 19.5% of total antibiotic use, respectively), azithromycin was the most consumed macrolide. Parenteral antibiotic treatment is a common practice: 46.4% of total antibiotic use in Azerbaijan (mainly ampicillin; 5·3 DID) and 31.1% of total antibiotic use in Tajikistan (mainly ceftriaxone; 4.7 DID).

The highlight of the study was that it showed a variety of antimicrobial consumption rate patterns amongst the surveyed countries. Some countries like Turkey showed a higher antimicrobial consumption rate than most ESAC-Net countries. This then prompted the Turkish government to implement antibiotic rational use policies to reduce antibiotic consumption between 2014 and 2017. The contrast was observed with countries such as Armenia which had a very low antimicrobial consumption rate that was similar to northern EU countries. This was however attributed to the fact that there was relatively limited access to antibiotics in Armenia compared to other European countries. Countries such as Belarus showed very low antimicrobial consumption rates even though there was very good access to antimicrobial agents. This was attributed to the relative efficiency of the country’s antimicrobial consumption policies. The significantly varied results from these countries could not prompt a consensus on whether there is an antimicrobial consumption pattern issue across non-EU countries. This has however, prompted more surveillance studies to be conducted in these countries to further establish whether antimicrobial consumption is a concern (Versporten et al, 2014).
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2.2.3 Antimicrobial consumption in African countries

An Egyptian study on antimicrobial consumption, which was the first of its kind, was conducted in 18 hospitals across the country (Talaat, Saied & Kandeel et.al, 2014). The point prevalence survey was conducted because there was no reliable data on antimicrobial consumption patterns. Talaat, Saied & Kandeel et.al (2014) eluded to the fact that appropriate and reliable antimicrobial consumption policies and programmes could not be implemented without the basic information on which antimicrobials were consumed, at what rate and used for which conditions. The study included 3408 patients of which 59% received at least one antibiotic during the duration of the study. The prevalence of antibiotic use in the participating hospitals ranged from 32.9%-91.7% with only 33% of hospitals having access to implemented antibiotic guidelines. Third generation cephalosporin’s were the most commonly prescribed antibiotics for all indications of antibiotic use, accounting for 28.7% of all antibiotic prescriptions. Penicillins with beta-lactamase inhibitors (e.g. Amoxicillin+Clavulenic acid) and metronidazole derivatives accounted for 19.7% and 15.2%; respectively (Talaat, Saied & Kandeel et.al, 2014). The results presented in this study has been long awaited and crucial to antimicrobial consumption policy making. The study was the first to quantify and characterize antimicrobial consumption in Egyptian hospitals. The researchers report that the study has assisted in identification of several specific opportunities to improve antibiotic use practices that may result in improved patient outcomes and lower healthcare costs within Egyptian hospitals (Talaat, Saied & Kandeel et.al, 2014).

2.2.4 Antimicrobial consumption in South Africa

South Africa is one of the countries that are actively involved in promoting antimicrobial consumption studies due to the paucity in antimicrobial consumption data (Schellack, Benjamin & Brink et.al, 2017). Between April and August 2015, a Point Prevalence Survey (PPS) was conducted in a large Tertiary Hospital in Cape Town as part of the 2015 Global Point Prevalence Survey (Finlayson, Versporten, Whitelaw, Goossens & Taljaard, 2016). The results showed that a third (31%) of patients were receiving antibiotics and the majority (83%) of antibiotic prescriptions were given as empirical treatment (Finlayson et al., 2016). In addition, only a limited number of doctors (11%) documented the stop/review date on the prescription which might lead to either lengthy or insufficient antimicrobial therapy (Finlayson et al., 2016).
In 2012, the South African Antibiotic Stewardship Programme (SAASP), a multidisciplinary group of experts across human and animal health, public and private health sectors, was formed to implement antibiotic stewardship programmes within hospitals and in primary care (South African Antibiotic Stewardship Programme, 2017). This group used wholesale antimicrobial sales data to determine antimicrobial consumption in the public sector. The results from the study showed that there is a significant level of antimicrobial consumption in the private and public sectors. The private sector in the South African hospitals showed an increase in 16% of last resort antimicrobial drugs which might indicate increased antimicrobial resistance rates (Schellack, Benjamin & Brink et.al, 2017). In the public sector, substantial increases were observed in four classes: ‘all other antibacterials’ (J1X9), injectable fluoroquinolones (J1G2), injectable cephalosporins (J1D2), and broad-spectrum penicillins oral (J1C1), which showed increases of 6876%, 287%, 169%, and 167%, respectively. Nearly 80% of the public market share was derived from trimethoprim combinations (J1E0) (37%), medium/narrow-spectrum penicillin (J1H1) (22%), and broad-spectrum penicillin oral (J1C1) (20%) (Schellack, Benjamin & Brink et.al, 2017).

This study shows that there is a possible increase in antimicrobial consumption in both the private and public sector. Because the antimicrobial consumption data was mostly wholesale data and not patient-level antimicrobial consumption data, the results from this study cannot be generalized antimicrobial consumption data to the South African population.

**Summary of antimicrobial consumption**

The analysis from the global antimicrobial consumption studies show that it is crucial to gather antimicrobial consumption data in order to characterize and quantify antimicrobial consumption in any country. European countries (EU/EEA) have actively conducted antimicrobial consumption data and have therefore been able to implement antimicrobial consumption guidelines and policies which have been seen to reduce antimicrobial consumption to a certain extent. The non-ESAAC European countries show varied antimicrobial consumption patterns due to mentioned reasons. Studies in these countries have however prompted further research into the reasons behind the variety in the antimicrobial consumption data within the different countries and how this could assist in developing antimicrobial consumption guidelines. In African countries, there is still a significant sparsity of information on antimicrobial consumption. Egypt has recently conducted an extensive antimicrobial consumption survey in their hospital setting. The results from the study showed that there is a relatively high antimicrobial consumption
pattern and this has prompted more investigational studies to be done on how guidelines
can be implemented in order to reduce the burden of antimicrobial consumption and the
negative implications that come with it. In South Africa, there is still lack of information on
antimicrobial consumption patterns. The SAASP group gathered antimicrobial consumption
data in the private and public hospital sectors, which showed that there is increased
antimicrobial consumption in both sectors. Due to the fact that the information on
antimicrobial consumption that was gathered was not patient-level data, this data cannot be
used to generalize the antimicrobial consumption characteristics and can therefore not be
accurately used to influence antimicrobial consumption guidelines to be used throughout
the country. The study also eluded to the fact that more antimicrobial studies that are
patient-level-based need to be conducted in the private and public health sectors in South
Africa. This will assist in implementing antimicrobial consumption guidelines as
recommended by the World Health Organization.

2.3 ANTIMICROBIAL RESISTANCE

2.3.1 Global data on utilization and resistance

The intensity of antimicrobial resistance can be a factor that can be controlled by the rate
of consumption of antimicrobials in a population regardless of whether these antimicrobials
are used correctly or not (Van Boeckel et al, 2014). An extensive meta-analysis study
conducted by Bell et al (2014) in Europe comprising of 243 studies concluded that there is
a definite link that exists between the rate of antimicrobial consumption and resistance. This
has also been highlighted by Sartelli et al, (2016), who states that there is a connection that
can be concluded between antimicrobial use and resistance. The indiscriminate and
excessive use of antimicrobials has played a major contributory role to the development of
resistance in recent years (Sartelli et. al, 2016).

A study performed by the World Health Organisation in 129 countries globally reported that
there is a significantly elevated resistance to 3rd generation cephalosporin’s for
Escherichiae coli and Klebsiella pneumonia (Mendelson & Matsoto, 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 (Mendelson & Matsoso, 2015). The data clearly shows a
concerning prevalence of resistance, there is still lack of documentation and information
about antimicrobial consumption and resistance patterns in many countries globally (Mendelson & Matsotso, 2015).

A report called the ‘Antimicrobial Resistance Global Report on Surveillance’ by WHO exposed the global extent of antimicrobial resistance patterns in WHO regions (Essack, Desta, Abotsi & Agoba, 2016). The report eluded to the fact that there are high antibacterial resistance rates that are observed in the community and hospital settings. These high bacterial pathogen resistance patterns were observed across all six WHO regions at different rates and with different pathogens. Six WHO regions were surveyed and different bacterial pathogens were observed either in some regions or in all the regions at different rates that were quantified in percentages (Essack, Desta, Abotsi & Agoba, 2016). This is illustrated in the figure below;

![Figure 2: The different bacterial pathogens that are resistant in a number of WHO regions](image_url)

This study by WHO illustrates that there is a significant antimicrobial resistance predicament that is a global concern and needs immediate attention by implementing antimicrobial consumption policies and programmes that will reduce the rate of antimicrobial consumption and resistance (Essack, Desta, Abotsi & Agoba, 2016).

### 2.3.2 Utilization and resistance in developing countries (Africa)

A systematic review was conducted by Tadesse, Ashley, Ongarello, Havumaki, Wijegoonewardena, González & Dittrich (2017) on antimicrobial resistance in African and developing countries. The study highlighted that antimicrobial resistance data was not available for approximately 42.6% of the countries in the African continent. The final...
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The report observed the following findings: Penicillin resistance in Streptococcus pneumoniae was reported in 14/144 studies (median resistance (MR): 26.7%). Furthermore, 18/53 (34.0%) of Haemophilus influenza isolates were resistant to amoxicillin. Antimicrobial resistance of Escherichia coli to amoxicillin, trimethoprim and gentamicin was 88.1%, 80.7% and 29.8% respectively, while the microbial resistance to quinolones was 37.5%. Carbapenem resistance was common in Acinetobacter spp. and Pseudomonas aeruginosa but uncommon in Enterobacteriaceae (Tadesse et al., 2017). The study concluded that even though several antimicrobial resistance studies were found, there is still significant lack of antimicrobial studies in Africa and South East Asia. This was reported to be mainly due to the lack of surveillance systems that are necessary for the collection of quality antimicrobial resistance data that may be used to influence appropriate antimicrobial utilisation guidelines (WHO, AMR, 2014).

The general observation is that African countries have limited data on antimicrobial resistance, which creates a dilemma wherein the magnitude of antimicrobial resistance may be underestimated. The lack of data surveillance tools and studies plays a major role in insufficient data on antimicrobial resistance (WHO, 2011). Even though there is insufficient data, there have been several studies conducted that explicitly expose several cases of antimicrobial resistance. The Group for Enteric, Respiratory and Meningitis Disease Surveillance in South Africa (GERMS-SA) has reported on the emerging antimicrobial resistance in several micro-organisms (GERMS-SA, 2011). The growing resistance towards quinolones and cephalosporin’s towards the treatment of gonococcal diseases has raised valid concerns as stated by the report (WHO, HIV, 2011). One concerning report shows that even though there is an increase in the transmission of HIV/AIDS, data on antiretroviral therapy (ART) resistance patterns in Africa still remains very limited. Surveys conducted at sentinel clinics providing ART in several countries in the African Region estimated that HIV resistance to all drug classes is less than 5% (WHO, HIV, 2011).

HIV/AIDS is not the only condition of concern in low-income countries, TB has also been shown to present with detrimental drug resistance patterns which has shown to be a financial burden on the government of these African countries (Nugent, 2010). In the African continent, Since 2006, the African Region has observed a constant increase in the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) (Ndihokubwayo, Yahaya, Dester, Ki-Zerbo, Asamoah-Odei & Keita, 2013). Between the years 2004 and 2011, a total of 53 798 MDR-TB cases were reported by 42 countries in the Region, whilst, at the same time, 3 231 XDR-TB cases were reported from eight countries,
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with South Africa accounting for approximately 84% of MDR-TB and 96.8% of XDR-TB cases (Ndihokubwayo et al, 2013). Even though there are emerging cases of drug resistant TB, studies show that only 28 of the African countries reporting MDR-TB and XDR-TB have structured drug resistant treatment programmes in place (Ndihokubwayo et al, 2013). In the majority of African countries, the sparsity in laboratory capacity to confirm drug-resistant TB and other pathogens creates a knowledge gap on the true extent of drug resistance. Even where treatment programmes exist, not all confirmed cases are receiving attention, mostly due to the unavailability of adequate supplies of second-line anti-TB medicines and other second-and-third-line antimicrobial drugs (Ndihokubwayo et al, 2013).

2.3.3 Antimicrobial resistance in South Africa

South Africa is no exception to the emergence of resistance, in 1977 penicillin-resistant S. pneumoniae strains were detected, thereafter in 1978, multidrug-resistant and highly resistant strains was reported (Crowther-Gibson, Govender, Lewis, Bamford, Brink, Gottberg, Klugman, Plessis, Fali, Harris, Keddy & Botha, 2011). The prevalence of resistant strains to most antimicrobials was observed and recorded from then onwards (Crowther-Gibson et al., 2011).

In recent years, infections have been reported to constitute the majority of South Africa’s burden of disease, with HIV and TB attributed under some of the most commonly reported cases (WHO, TB, 2014); (Shisana, Rehle, Simbayi, Zuma, Jooste, Zungu, Labadarios & Onoya, 2014). In the second national burden of disease study (1997 – 2009), HIV was observed to be responsible for the highest number of deaths (31.2%), ahead of cerebrovascular disease (6.2%), tuberculosis (5.4%), lower respiratory tract infection (5.2%) and ischaemic heart disease (4.4%) (Pillay-van Wyk, Msemburi & Laubscher, 2014). Even though the report shows a high burden of infectious diseases, the true burden of bacterial infection (HIV- and non-HIV related) in South Africa remains incompletely documented due a high level of empiric management and an overall paucity of samples being sent for laboratory diagnosis (Von Gottberg, de Gouveia & Templa, 2014). The information available from public and private laboratory surveillance suggests very high levels of MDR-bacterial infections in hospitalized patients, MDR TB cases comprising 1.8% of new cases and 6.7% of retreatment cases respectively (WHO, TB, 2014). Studies that have been conducted on the South African population have shown the following AMR results;
Figure 3: The various AMR reports that have been observed in both the public and private health facilities in South Africa

Figure 3 shows the various AMR reports that have been observed in both the public and private health facilities in South Africa. In one of the reports, more than 50% of cases in the paediatric population included MRSA which is a resistant strain that cannot be treated with first line antibiotics used for S. aureus. The other cases include the prevalence and widespread of CPE in both the private and public hospitals.

South Africa faces an overwhelming burden of infectious diseases at the heart of the HIV and tuberculosis pandemics (Mendelson & Matsoso, 2015). Mendelson & Matsoso (2015) also advise that in order to reduce the high burden of infectious diseases, the main objectives of the Antimicrobial Resistance National strategy Framework need to be implemented. These strategies are mainly targeted towards legislative and policy reform, creation of surveillance systems, antimicrobial stewardship, and other strategies to reduce antimicrobial resistance (Mendelson & Matsoso, 2015).

The exceptional country in Africa has been reported to be South Africa which is moving towards nationalization of health. There are several strategies that were published under the AMR National Strategy Framework set out from 2014 to 2024. These structures have outcomes mainly aimed at managing AMR in order to reduce the prevalence of antimicrobial resistance (Essack, Desta, Abotsi & Agoba, 2016). The main objectives in this National Strategy Framework are depicted in the following illustration; (NDoH Pta, 2014).
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Figure 4: This illustration depicts the objectives of the South African AMR National Strategy Framework

The figure above shows the objectives that the South African government has set out as part of the AMR National Strategy Framework. These include enhancement of prevention and control of the spread of resistant microbes, optimization of surveillance, implementation of antimicrobial stewardship and establishment of national and health governance structures.

Currently South Africa has functioning programmes for 3 out of the 4 AMR policies that were set out for implementation in accordance with the WHO recommendation. There is still a large information paucity in antimicrobial surveillance and programmes that track antimicrobial resistance (NDoH Pta, 2014). Prior to 2007, a surveillance programme active in all nine of South Africa’s provinces was reporting data (Mendelson & Matsoso, 2015). However, the programme lost funding and was discontinued. This left a paucity in antimicrobial consumption and resistance data that is necessary to influence antimicrobial consumption guidelines in local, provincial and national settings. Organizations such as The National Institute for Communicable Diseases (NICD) conduct surveillance for human bacterial and fungal diseases of public health importance. Such surveillance platforms have
already demonstrated significant declines in invasive pneumococcal disease cases caused by bacteria resistant to one or more antibiotics, a very valuable added benefit of immunization (Mendelson & Matsoso, 2015). This NICD programme is a motivational programme that shows the major benefits of creating surveillance tools and how they can benefit reduction in antimicrobial resistance. The gathering of antimicrobial consumption data and the development of a surveillance tools forms the major part of this study. This study aims to fulfil the gap in the paucity of antimicrobial surveillance which is an essential component of combating AMR.

### 2.3.4 The cost implications of antimicrobial resistance

The financial implications of antimicrobial resistance can be calculated (Gandra, Barter & Laxminarayan, 2014). In Europe, the average cost of antibiotic resistance in the year 2007 was estimated to be at least €1.5 billion, with productivity loss accounting for 40% of this monetary cost (Gandra, Barter & Laxminarayan, 2014). In the United states of America (USA), the annual cost towards antimicrobial resistance was estimated to be approximately 21 to 34 billion US dollars (Gandra et al., 2014).

It is apparent that antimicrobial resistance and the development of resistant organisms is a major global concern according to the studies illustrated in the above topic. The increase in hospital stay and the several tests that have to be conducted add on to the costs that are incurred due to the debilitating effects of antimicrobial resistance (Gandra et al., 2014).

### 2.4 THE USE OF POINT PREVALENCE STUDIES IN ANTIMICROBIAL CONSUMPTION

Prevalence surveys are part of observational descriptive study methods that originated from the field of epidemiology (Bene, Paramadhas, Godman, Massele, Sinkala, Kgatwane, Tiroyakgosi, Zinyowera & Muller, 2016). The purpose of these studies are to observe, describe and document the frequencies of certain behaviour or occurrence of a condition or event observed in a sample or population as it naturally occurs without the use of any intervention (Bene et al., 2016). A point prevalence survey (PPS) can therefore be used for collecting antimicrobial consumption data.

There are different sources from which antimicrobial consumption data can be imported. These sources provide different quality levels of data and can therefore influence the generalization of the data reported (Robert, 2012). The following are the different sources in which antimicrobial consumption data can be collected;
The following data can be used as sources of antimicrobial consumption data (WHO, 2016):

- Import data: This is data from customs records.
- Wholesaler/ distributor data: This data refers to records of sales to pharmacies.
- Procurement records: This refers to data from the depots of the public health sector.
- Hospital purchasing data: The assumption is that the amount procured by the hospital from the supplier is equivalent to amount dispensed.
- Donations: This is especially relevant when it comes to certain public health programs where donations may be made e.g. HIV, Tuberculosis, and Cryptococcal Meningitis etc.
- Data from Health Insurance Providers.
- Prescribing or dispensing records.
- Information directly from the patient: This refers to information from the patient directly as to what medication was consumed (Also referred to as “patient-level-data”).

These different sources of data provide different levels of detail. Antimicrobial consumption can be evaluated from a population level or from a patient level (Robert, 2012). Population level data provides an overview of the quantities of antimicrobial agents used, however patient level data provides more specific information on the quality of use (Robert, 2012). Patient level data therefore provides more reliable estimates of antimicrobial consumption (WHO, 2015). The lack of patient level antimicrobial consumption data in South Africa creates a void in quality information on consumption. This study is projected towards collection of patient level data which provides quality and quantity information on antimicrobial consumption. This is proposed to mend the gap on the information that is critically sought on antimicrobial consumption (AMC) (WHO, 2015).

Global PPS of antimicrobial consumption and resistance are designed to provide current data on utilisation and resistance patterns using a standardised methodology to plan future interventions (Versporten et al., 2014). The choice for using a PPS study was then justified to measure antimicrobial consumption based on the observed research studies that have successfully conducted these studies with reliable reporting of results.
2.5 DRUG CLASSIFICATION SYSTEMS TO MEASURE ANTIMICROBIAL CONSUMPTION

2.5.1 The Anatomical Therapeutic Category (ATC) classification system

Medicines are classified by therapeutic categories, which is the system used by WHO and referred to as the Anatomical Therapeutic Chemical (ATC) classification system. This system was established by the Norwegian Medicinal Depot in the 1970s (Hutchinson, Patrick, Marra, Ng, Bowie, Heule, Muscat & Monnet, 2004) and is currently seen as the gold standard system for analysing drug utilisation patterns. Drugs are classified according to the organ or system on which they act and/or their therapeutic and chemical characteristics. An ATC code classified into groups at five different levels is assigned to each drug (Hutchinson et al., 2004; WHO, 2004).

The following table illustrates how the WHO ATC classification is conducted by using Ceftriaxone as an example; (Hutchinson et al., 2004; WHO, 2004).

<table>
<thead>
<tr>
<th>ATC Classification</th>
<th>ATC Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J</td>
<td>General anti-infectives for systemic use</td>
<td>1st level, anatomical main group</td>
</tr>
<tr>
<td>J101</td>
<td>Antibacterials for systemic use</td>
<td>2nd level, therapeutic main group</td>
</tr>
<tr>
<td>J101C</td>
<td>Cephalosporin antibacterials</td>
<td>3rd level, therapeutic/pharmacological subgroup</td>
</tr>
<tr>
<td>J101C A</td>
<td>3rd generation Cephalosporin antibacterials</td>
<td>4th level, chemical/therapeutic/pharmacological subgroup</td>
</tr>
<tr>
<td>J101C A04</td>
<td>Ceftriaxone</td>
<td>5th level, subgroup for chemical substance</td>
</tr>
</tbody>
</table>

2.5.2 The Defined Daily Dosage

The defined daily dose (DDD) is a technical unit that was created to use in conjunction with the ATC classification to enhance the ability to compare consumption data across time and geography (Hutchinson et al., 2004). It is defined as the average maintenance dose per day for a drug used for its main indication in adults. Different dosage forms of the same drug
may have different DDDs. A DDD is assigned to each drug in the fifth level (chemical substance classification).

The following table illustrates the WHO DDD classification system by using cephalosporin’s as examples of this system; (Hutchinson et al., 2004; WHO, 2015).

Table 2: Examples of DDD classification system

<table>
<thead>
<tr>
<th>ATC Classification</th>
<th>ATC drug</th>
<th>Defined Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>J101C A04</td>
<td>Ceftriaxone</td>
<td>1 g (parenteral)</td>
</tr>
<tr>
<td>J101C A05</td>
<td>Cefixime</td>
<td>0.5 g (oral)</td>
</tr>
<tr>
<td>J101C A06</td>
<td>Cefotaxime</td>
<td>0.5 g (parenteral)</td>
</tr>
</tbody>
</table>

One of the most common ways to express antimicrobial consumption is to classify as a rate. It is important to note that in order to express a rate, a denominator and time unit need to be clearly defined first. The common units that are used for antibiotic consumption include DDD per 1000 inhabitant-days for out-patient data and DDD per 100 bed-days in hospitals (DID) (Brink, Messina, Feldman, Richards, Becker, Goff, Bauer & Nathwani, 2016). For expressions of antibiotic consumption at the level of a country, province or large region, census population estimates are appropriate (Brink et al., 2016).

2.5.3 The WHO beAWaRe classification of antibiotics

The WHO has recently designed a novel method for classifying antibiotics into three groups; Access, Watch, or Reserve (Gulland, 2017). The explicit recommendation by WHO is that this new categorization should be used to inform antibiotic stewardship at a national and global level (Hsia, Sharland, Jackson, Wong, Magrini & Bielicki, 2018). Access antibiotics are those that are to be used first-line or second-line treatments for key infections. First choices were generally narrow spectrum agents with a low toxicity risk. Second choices for specific syndromes were broader spectrum antibiotics than the first choices, which might have an increased risk of toxicity or resistance selection (Sharland, Pulcini, Harbarth, Zeng, Gandra, Mathur & Magrini, 2018). Also, access antibiotics are those that are high-quality formulations that are widely available at a low cost (Hsia, Sharland, Jackson, Wong, Magrini & Bielicki, 2018).

The Watch group includes antibiotic classes that were considered to have higher toxicity concerns or resistance potential compared with the Access group (WHO, AMR, 2017).
Watch antibiotics are considered to have a higher potential for selecting antibiotic resistance (WHO, EML, 2017). A small number of antibiotics from the Watch group were also recommended as first or second choice treatments for a few, specific indications (WHO, AMR, 2017). Active monitoring of the Watch antibiotics is encouraged through point prevalence surveys to ensure that use aligns with guidance (Sharland, Pulcini, Harbarth, Zeng, Gandra, Mathur & Magrini, 2018).

Reserve antibiotics should be considered antibiotics of last resort, to be used under specialist guidance and with specific monitoring (WHO, EML, 2017); (Sharland, Pulcini, Harbarth, Zeng, Gandra, Mathur & Magrini, 2018). These should be accessible when needed, but use should be tailored to very specific patients and clinical settings when other alternatives have failed or cannot be used (e.g. serious or life-threatening infections due to multidrug resistant bacteria). To preserve their effectiveness, these medicines should be protected and prioritised as key targets of high-intensity national and international stewardship programmes that involve central monitoring and reporting. The Reserve group also includes newer antibiotics (Sharland, Pulcini, Harbarth, Zeng, Gandra, Mathur & Magrini, 2018).

2.6 THE SOUTH AFRICAN HEALTH CARE SERVICES DISTRIBUTION

The 2011 General Household survey conducted a study where they asked respondents to indicate where most people in their households usually went first when they were ill and decided to seek medical help (Lehohla, 2013). They survey reported that 61.2% of the population visited the public sector clinics (PHC and CHC), 24.3% of patients visit the private doctors, 9.5% utilised public hospitals and 5% of the population utilised the private hospital, private clinic and other facilities (e.g. pharmacy, employer facilities, spiritual healers, homeopaths and traditional healers) (Lehohla, 2013).

The first point of entry for South Africans to health services at primary level through local clinics and community health centres (Cullinan, 2006). The Primary Health centers (PHC) cover a comprehensive range of “preventive, promotional, curative and rehabilitation services”. Both clinics and health centres offer services such as mother and child care, immunisation, family planning, treatment infections, minor trauma and care for those with chronic illnesses (e.g. diabetes, hypertension) (Cullinan, 2006).

Community Health Centers (CHC) are facilities cater mostly to the communities in a similar manner as a Primary healthcare facility but, have extra benefits of providing 24 hour
maternity, accident, emergency services, and up to 30 beds where patients can be observed for a maximum of 48 hours (Cullinan, 2006).

For a larger sample size and to have more detailed information, the CHCs were chosen as the primary data collection facilities based on the research conducted.

2.7 WEB-BASED APPLICATION USE IN ANTIMICROBIAL CONSUMPTION

2.7.1 m.Health Application

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. The web-based application allowed the global PPS to stretch over 53 countries and included 335 hospitals in 2015.

For the purpose of ongoing Point Prevalence Surveys, a web-based application was developed in South Africa as part of the ENAABLERS project. The web-application allows for anonymous patient data entry directly into the application via any mobile device connected to the web. The data encryption is done with both secure hash algorithm-256 (SHA-256) and Advance Encryption standard-265 (AES-256); these are the strongest encryption methods 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 back-up 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 like DOW Jones, Pfizer and the CDC. Every access to the data is logged and time-stamped and a log-file can be provided in the unlikely case (ref).

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.
2.8 SUMMARY

Entailed in this chapter is the background information on antimicrobial use. Research shows that there is increasing resistance that can be linked with the rate of antimicrobial consumption. This means it is very crucial to create surveillance systems that monitor the rate of antimicrobial consumption and resistance. Results would then be presented according to the world renowned WHO ATC/DDD system and the recently established be AWaRe system. An electronic data collection system was thoroughly explained which would be essential in modifying and easing data collection rather than using a paper-based system. The next chapter focuses more on the study methodology which comprises of the study site, population sample, data collection period, data analysis, and ethical considerations of the study.
3.1 INTRODUCTION

This chapter describes the methodology applied in this study. A brief discussion of the study design, followed by sections on the study sites, study population, data collection tool, data collection process, inclusion and exclusion criteria. Data analysis and methods applied to ensure reliability and validity of the data are also included. The final section discusses the importance of bias and ethical consideration applied in the study.

3.2 STUDY SITE

Data was collected from nine (9) CHCs in the five Gauteng municipalities which were chosen randomly. These facilities cater mostly to the communities in a similar manner as a Primary healthcare facility but, have extra benefits of providing 24 hour maternity, accident, emergency services, and up to 30 beds where patients can be observed for a maximum of 48 hours (Cullinan, 2006). The selection of healthcare centres over conventional primary healthcare clinics assisted with attaining a larger sample size and being able to collect data from both outpatient and impatient members of the community. The CHCs have both inpatient and outpatient departments from which data could be collected.

The selected CHCs in different municipalities in the Gauteng province as illustrated in Table 3.2.1.
Table 3: Nine (9) CHCs in five Gauteng municipalities

<table>
<thead>
<tr>
<th>Municipality/Metropolitan</th>
<th>Community Healthcare Centers (CHC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>City of Tshwane Metropolitan</td>
<td>Laudium CHC</td>
</tr>
<tr>
<td></td>
<td>Soshanguve CHC</td>
</tr>
<tr>
<td>City of Ekurhuleni Metropolitan</td>
<td>Phola-park CHC</td>
</tr>
<tr>
<td></td>
<td>Goba CHC</td>
</tr>
<tr>
<td>Sedibeng District</td>
<td>Boipatong CHC</td>
</tr>
<tr>
<td>City of Johannesburg</td>
<td>Zola CHC</td>
</tr>
<tr>
<td></td>
<td>Hillbrow CHC</td>
</tr>
<tr>
<td>West Rand District</td>
<td>Mohlakeng CHC</td>
</tr>
<tr>
<td></td>
<td>Thusanang CHC</td>
</tr>
</tbody>
</table>

3.3 STUDY DESIGN

This research was a quantitative descriptive study that used a point prevalence study method. Point prevalence methods form part of epidemiological study designs. A point prevalence study is a single assessment of a fixed point in time (Bhopal, 2016). Prevalence studies are usually measured as a rate or percentage and sampling calculation prior to commencing the study is not always necessary as it may be difficult to predict (Pearce, 2012). Point prevalence in this study can be defined as a measure of the prevalence of antimicrobial use during a patient visit to the CHC.

3.4 STUDY POPULATION AND SAMPLE

For a PPS study, no sampling was required. All the patient files of the patients seen the day before data collection were reviewed and surveyed. Two CHCs were chosen per district in Gauteng which totalled to 10 CHCs overall. Permission was attained for nine (9) CHCs, one (1) CHC could not provide permission and had to be omitted from the study which then resulted in data being collected in nine (9) CHCs. The CHCs were called two days prior to data collection to remind the CHC employees to put aside all the files of the patients that visited the
CHC on that specific day. This ensured that the patient files were not mixed in terms of dates and that all the patients that visited the CHC the day prior to data collection were reviewed and surveyed.

In a point prevalence study, the principle is to have a rate in which the prevalence of antimicrobial use can be calculated. The variables include having a denominator and a numerator. The denominator in this study comprised of the total number of patient files that were reviewed, which means all the files of patients that visited the CHC the day prior to data collection. The numerator is composed of patients that are on antimicrobials during the survey day. The numerator data has an inclusion and exclusion criteria. The criteria is listed below;

The study was conducted in patients that have been prescribed one or more of the following antimicrobials (numerator principle):

3.4.1 Inclusion criteria

- Systemic antibacterial drugs
- Antibiotics used for treatment of tuberculosis
- Antibiotics used as intestinal anti-infective agents
- Anti/protozoal used as antibacterial agents
- Anti-malarial agents

3.4.2 Exclusion criteria

- Patients who were admitted or visited the CHC after 8am on the day of data collection (denominator principle).
- Patients receiving topical antimicrobials (numerator principle).

3.4.3 Study sample calculation prior data collection

In a point prevalence study whereby all patients are going to be reviewed, it is not necessary to calculate the sample size needed for significance. All patients that visited the clinic prior to the day of data collection were reviewed and included in the study. Prior to data collection, the study was expected to include outpatients and inpatients that were served by the community. On the conclusion of the study, only outpatient data was collected from the CHCs.
The omission of inpatient data was due to a variety of factors that are elaborated on below:

- The inpatient and outpatient filing departments operate separately in most of the CHCs. The inpatient files were not easily accessible to the researchers hence data could not be collected.
- The inpatient departments were usually the emergency department whereby patients were only observed for less than 24 hours and transferred to a hospital with their file, so the files were not kept in the CHC which made data from these inpatients unattainable.
- Some of the CHCs were named CHCs but operated as PHCs which means they did not have inpatient departments from which data could be collected.

3.5 DATA COLLECTION

3.5.1 Data collection period

Due to the fact that the study is a point prevalence study, the data needed to be collected within one season. The data collectors had a day to finish collecting all the data at each CHC. The data was collected from May to July 2018 which was in one season (Winter) as requested for a PPS study.

The collection duration was applicable to a PPS study. The data from each CHC was collected in a day as recommended when using a PPS study design. Two CHCs were reviewed twice each. These CHCs were surveyed in March (autumn season) initially and had to be surveyed again since their data fell out of season. Their data from the March review period was omitted from the data analysis and therefore will not be presented in this research article.

The following figure shows how many CHCs were reviewed each month across the three-month data collection period;

![Figure 5: The CHCs that were reviewed each month across the three-month data collection period](image-url)
A total of nine (9) CHCs were surveyed from May to July, six (6) were reviewed in May, one (1) in June and two (2) in July.

This was all done in one seasonal period as expected in a PPS study.

3.5.2 Data collection training

Data collection commenced after the training workshop was conducted in February. Data collectors were thoroughly trained on the data collection tools and data collection techniques.

All participating CHCs were requested to select an antimicrobial stewardship champion. For the purpose of this study, an antimicrobial stewardship champion is defined as a pharmacist that is tasked with driving the initial antimicrobial stewardship activities in an institution. This follows a model that was used successfully in a study that demonstrated that the use on non-specialist pharmacists decreased antibiotic use by practicing antimicrobial stewardship in institutional settings (Brink, 2016). The AMS champions were trained on the methodology to collect the data and were also tasked to recruit and train other health care professionals to assist in the data collection procedure. A training session was done prior to the survey being conducted to ensure that all users are fully aware how to collect the data effectively. The lead researcher was available at all of the sites for the data collection. The CHCs were not able to provide the lead researcher with an AMS champion as requested. The lead researcher undertook the responsibility to request for volunteer academic intern pharmacists employed at the Sefako Makgathi Health Sciences University to assist with data collection in the different CHCs. For the purpose of this study the “lead researcher” is the student (Nicholus Magongwa), who is the chief researcher.

3.5.3 Data collection instruments

the PPS (Point Prevalence Study) data collection instruments were 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 the European Centre for Disease Control (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). This is the same tool that was used to conduct the study, except that instead of using a paper-based system, a web-based application was developed.
Chapter 3: Methodology

The data collection instruments have been adjusted to be applicable in a CHC setting so as to make the instrument as suitable to the CHC environment as possible. For the study to be specific and simplified, such acknowledgements have to be made because the data collection instruments were established to collect data primarily from hospitals so adjustments to the instruments had to be made.

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

3.5.3.1. The data collected from the CHCs were collected on the following levels;

Level 1: CHC data– to be completed only once (see Appendix 1)

Level 2: Patient data – to be 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 2)

Section 1 (level 2 data) is comprised of:

- CHC code, ward code, patient code, admission date, age, sex, employment and whether the patient was transferred there or not.
- Hospitalization in past 90 days, Antimicrobial use past 90 days, duration and names of antibiotics in past 90 days.
- Pre-existing medical conditions.

Section 2 (level 2 data is made up of the following:

- Prescriber classification (medical officer or nurse), Antimicrobial prescribed, indication, dose, frequency and route of administration.
- Culture sensitivity tests (CST) results and Bacterium name.
- Prescribed in International Non-proprietary Name (INN), according to SEDL (Standard Essential Drug List).
- Used for treatment or prophylaxis (surgical or medical).
Chapter 3: Methodology

The data collectors used the patient’s medical files as the only source of information and no patient or health professional was interviewed. If the information was not in the file then it was marked as “unknown”.

The diagnosis and indication for prophylaxis or treatment used the same diagnosis group, which is anatomically related to an organ (e.g. skin or lungs) based on the European Centre for Disease Control (ECDC, 2013) study (see Appendix 3). Actual prescribed doses were recorded for both adults and children for single and combination antibacterial (e.g. 625mg of amoxicillin plus clavulanic acid). Antibacterial were presented by their individual chemical substance names (e.g. amikacin). The route in which the antimicrobials were administered was also taken into consideration. Whether the antimicrobial was used for prophylaxis or treatment of a microbial infection was noted and recorded, including what type of microorganism was responsible for the infection and whether this was a community-or-nosocomial acquired infection.

3.6 PILOT STUDY

A PPS study on antimicrobial consumption was conducted in Botswana in 2016. The study was conducted to test the feasibility of a PPS study using the selected data collection instruments (Massele et al., 2016; ECDC, 2013). The results of this study were presented at the MURIA symposium and concluded that a PPS study can reliably be conducted using these data collection instruments (Paramadhas, Tiroyakgosi & Godman, 2016). A m. Health (named knack) application was piloted in one academic hospital in a study conducted by N Dlamini, (2017) (SMUREC/H/210/2016: PG). This study by N Dlamini served as a pilot for this research to be conducted. Although this study was not conducted in CHCs, the reliability of it in the hospital setting made it suitable for use in other healthcare facility settings with minor adjustment to be made for specific settings. The app was developed so that it can reduce errors and make data collection convenient.

3.7 DATA ENTRY AND ANALYSIS

All the data collectors had the application either on their Smart phones or the personal computers. After data was collected from each patient file, the data collected is then fed into an excel spreadsheet.

The data was imported on Microsoft Excel™ spread sheets. Entered data was checked for accuracy and correctness prior to analysis. This was a descriptive, explanatory analysis since
Chapter 3: Methodology

the study is quantitative. Categorical variables were summarized as frequency counts and percentage calculations. Continuous variables were summarized by mean, standard deviation, median, interquartile range, minimum and maximum values.

The prevalence (percentage) of utilization of all the antimicrobials was calculated together with 95% confidence intervals.

All results were presented in the form of tables and graphs.

Antimicrobials prescribed were analyzed according to the WHO’s ATC of medicines (ATC level 5), the dose, frequency and route of administration.

All statistical analyses were performed on IBM SPSS version 25 SPSS (Statistical Package for Social Sciences).

3.8 RELIABILITY AND VALIDITY

Reliability is commonly observed as a reflection of research consistency and replicability over time. Also, reliability is observed as the degree to which a test is free from measurement errors, since the more measurement errors occur the less reliable the test (Fraenkel & Wallen, 2003). Reliability can also be defined as a measure of precision (Cherry, 2014) and refers to the consistency of a measure (Gravetter & Forzano, 2011).

The study used a reliable data collection instrument which was used for a study on antimicrobial consumption. The data collection instruments were developed by a group of researchers based on the ECDC (2013) PPS with input from WHO, which have already been piloted and subsequently refined in Botswana. This provides some level of reliability of the data collection instruments and thus made the study feasible.

The data collection was conducted strictly by individuals who were trained by the lead researcher on utilizing the Mhealth app (Knack® app), as a data collection instrument and also on how to submit data to the Microsoft Excel™ spread sheet. Assistance from a statistician was sought to accurately define the statistical significance of the collected data.

The following tables explain the principles of internal and external validity. They assist in recognizing what threats there might be that might influence unreliability or rather invalidate the study. Included is also how these validity threats were observed to potentially affect the study and the measures that were taken to avoid this.
The two tables that follow below put into perspective internal and external validity principles and how they were applied to the study;

### Table 4: Threats to internal validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to current study</th>
<th>What was done to minimize the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attrition</td>
<td>Occurs when participants who have been selected to take part in the study, do not take part at all or fail to take part during every stage of the research process.</td>
<td>Can occur when potential research participants forget to collect data from the patient files in their respective clinics.</td>
<td>All the data collectors were called on the day of data collection to ensure they did not forget. The lead researcher also checked the spreadsheet to ensure that data was collected on the day set for data collection.</td>
</tr>
<tr>
<td>Performance bias</td>
<td>Systemic differences in standard procedure and deviation from protocol design.</td>
<td>Occurs in this study when a uniform procedure according to the protocol is not followed e.g. data collection not started at 8h00 in the morning.</td>
<td>The Mhealth app (Knack®) was able to clock in the time when information was logged in and therefore showed if time constraints were not followed. There could not be additional information added as the app only allows for information that has already been installed on the data base to be analysed.</td>
</tr>
<tr>
<td>Researcher bias</td>
<td>Occurs when the researcher has a personal bias/preference towards a technique.</td>
<td>The researcher may create a predetermined hypothesis regarding the results that were obtained with the various testing procedures.</td>
<td>An electronic data collection instrument, Knack®, was used to collect data. Thorough training was conducted to make sure the researcher(s) comprehend the purpose of this study and how to properly utilize app data collection tools.</td>
</tr>
</tbody>
</table>
Table 5: Threats to external validity

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What will be done to minimize the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population validity</td>
<td>Refers to the extent to which the findings can be generalized from the sample group towards a larger population.</td>
<td>Due to external factors, the sample may not be representative of the population. Random sampling was used.</td>
<td>Data was collected in 2 randomly selected CHCs in all 5 major municipalities in Gauteng province. This gave a large sample size and also a rough estimate of antimicrobial consumption in Gauteng primary health care setting.</td>
</tr>
<tr>
<td>Ecological validity</td>
<td>The extent to which the findings from a given study can be generalized across settings, conditions, variables and contexts.</td>
<td>The data and final results in this study were dependent on the setting and the location in which it is obtained in.</td>
<td>The findings of this study were only used to assess antimicrobial consumption in primary health care settings. No data will be used to make conclusions about consumption in hospital settings or other health facilities.</td>
</tr>
</tbody>
</table>

3.9 BIAS

To avoid the study being bias, the CHCs were chosen randomly throughout the five Gauteng municipalities. The CHCs. The random selection and number of the CHCs can then be used to analyze whether the study could have unbiasedly be generalized to represent antimicrobial consumption in Gauteng province. Selection bias was eliminated since medical files of all patients in the wards and outpatients that visited the clinic the day before data collection were reviewed. These files were assessed not excluding any age groups, race, gender and/or medical condition.

The data had to be captured by the researcher and different voluntary data collectors in different facilities. This might result in altering of true data and misrepresentation of results. To avoid this, the data collectors had to be trained on avoiding misrepresentation of data and how that will impact on the study.
The following table illustrates the different types of Bias that can influence a study and how they were avoided in this particular research study.

**Table 6: Threats to bias**

<table>
<thead>
<tr>
<th>Threat</th>
<th>Definition</th>
<th>Applicability to the current study</th>
<th>What will be done to minimise the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation Bias</td>
<td>Occurs when the protocol designed for the intervention is not followed in the intended manner (also known as protocol bias)</td>
<td>Can occur if the protocol used for all patients are not the same, i.e. time of measurement, method of measurement.</td>
<td>The researcher followed the same protocol throughout the research</td>
</tr>
<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></td>
<td>Usually occurs when the researcher evaluates open-ended responses and allows his/her prior knowledge of the research participants to influence the scores given.</td>
<td>No influence, as data analysis was done by an objective statistician with no prior knowledge relating to the participants, with the use of objective data given to him.</td>
<td>-</td>
</tr>
</tbody>
</table>

### 3.10 ETHICAL CONSIDERATIONS

- Permission

For the study to be performed, ethical clearance was sought from the Sefako Makgatho University Research & Ethics Committee (SMUREC), (SMUREC/P/33/2018:PG). Approval from the National Health Research Database (NHRD) was needed in order to conduct this study in the selected CHCs and the managers of the CHCS were contacted before collecting data. (Appendix 4-10)
• **Informed consent**

There was no need to obtain consent from the patients or the health care providers (HCP) as the only information needed was obtained from the patient files. No confidential information like the name of the patient and/or HCP, ID number of the patient or practice number of the HCP were recorded. The patients and HCPs were not asked any questions or communicated with both directly or indirectly. If required information was not found in the patient files, it was just marked as “Not Available”. Approval to conduct the research in all facilities was obtained from the individual districts that govern the CHCs and permission to extract data from the patient files was obtained from the facility manager in each of the CHCs that were surveyed.

• **Anonymity**

No identifiable names were taken from the patient files. Codes were used to identify the patients. The Prescriber’s names were also not recorded when collecting the data. This was to ensure that maximal anonymity is exercised. The codes used for the patients were only known to the researcher, who had the information stored in a locked password protected data base for study purposes alone.

• **Confidentiality**

Each data collector that used the Knack® mobile application had an individual password in order to login to the mobile app. Once data was submitted to the spreadsheet, only the lead researcher had access to the collected data. The researcher made sure that the data collectors understood that no patient names, HCP names or CHC names were recorded and that only identifiable codes to the researcher were used.

### 3.11 SUMMARY

This chapter has provided the detailed methodology of the study, which was a quantitative descriptive study that used a point prevalence study method.

quantitative, observational descriptive study conducted prospectively. The study was conducted at nine (9) CHCs in Gauteng province that were chosen using random convenient sampling. Data was collected exclusively from patient medical files by trained data collectors and no interviews or interventions were made. Data collection was conducted using a web-based application that was developed from paper-based data collection instruments that were developed by MURIA and tested in Botswana. A pilot study was not conducted as the web-based application was tested and found to be reliable in a South African hospital. Data analysis
was conducted by a trained statistician. The reliability of the study including factors that may affect validity of the study were discussed. Bias in this study was avoided through various means which are extensively discussed in the above chapter. The chapter concludes with ethical considerations which were made through application for ethical approval and permission to conduct the study from institutions such as SMUREC and NHRD, respectively. The next chapter, Chapter 4 will include a manuscript which would contain the results obtained in this study and the discussion of these results.
4.1 INTRODUCTION

The results and discussion of this study are presented in the form of a manuscript.

The manuscript is titled: Antimicrobial consumption in Community healthcare centres in Gauteng, South Africa

4.2 MANUSCRIPT FOR PUBLICATION

Antimicrobial consumption in Community Healthcare Centres in Gauteng, South Africa.

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²Private Hospital, Pretoria, South Africa

Corresponding author: NM Magongwa, email: magonnm@gmail.com
ABSTRACT

Objectives:

To quantify antimicrobial usage in selected CHCs using a point prevalence survey; To list and describe antimicrobial consumption in CHCs using a point prevalence survey.

Methods:

The study was a quantitative descriptive study that used a point prevalence survey method. The study included nine CHCs across the five municipalities in the Gauteng province. The study reviewed medical files of all patients that visited the CHC the day prior to data collection.

Results:

The Nine (9) CHC that were surveyed had a sample size of 786 patients. There were only 30.79% (242) patients that were prescribed antimicrobials. The most commonly prescribed antimicrobial was Amoxicillin (38.35%; 107/279) followed by isoniazid (14.70%; 41/279). Some of the antimicrobial agents such as flucloxacillin showed a significantly elevated DDD/day consumption of surveyed patients as compared to the recommended WHO DDD/day. On the contrary, antimicrobial agents such as ceftriaxone showed lower than recommended DDD/day consumption for the surveyed patients. The only antimicrobial agents that were equal to the WHO recommended DDD/day were isoniazid and Ciprofloxacin.

Conclusion:

This study is the first to be conducted in the community setting in South Africa. The results cannot be generalized to the South African antimicrobial consumption rate in the communities due to the relatively small sample size. More and larger studies are required to give sample data that can be used to give a more accurate generalization of antimicrobial consumption in the communities.

Keywords: Antimicrobial consumption, community healthcare centers m.Health, antimicrobial resistance, surveillance, WHO, ATC, DDD/DID
INTRODUCTION

Antimicrobials have proven to be very effective when used appropriately to significantly reduce morbidity and mortality from microbial infections over the past 50 years.\textsuperscript{1,2} Research have shown that increased antimicrobial consumption can be directly linked with an increase in antimicrobial resistance.\textsuperscript{3} Antimicrobial resistance (AMR) has currently been attributed to accounting for more than 700,000 deaths per year globally with an expected ten million deaths by 2050.\textsuperscript{4} The current global expenditure of antibiotics contribute approximately 20-30\% of total drug expenditure and AMR is expected to cost an estimated US$100 trillion per year by 2050, if no appropriate measures are employed to combat it’s progress.\textsuperscript{4,5}

The absence in the development of new generations of antimicrobial drugs\textsuperscript{2}, as well as the diminishing effectiveness of antimicrobials, creates a major global dilemma on how infections will be treated in the future.\textsuperscript{6} The provision of reliable antimicrobial consumption data is a prerequisite to understanding antimicrobial resistance (AMR), since selection pressure from antimicrobial use is one of the main drivers of resistance.\textsuperscript{6} The World Health Organization (WHO) has promoted the global monitoring of antimicrobial consumption and resistance, despite this call to introduce new policies to combat resistance, there is a disturbing increase in antimicrobial consumption and increasing resistance patterns.\textsuperscript{7}

The WHO together with the World Health Assembly (WHA) have since the 1990’s conducted several global strategic meetings that have resulted in publication of AMR policies to be implemented throughout the globe.\textsuperscript{8} One of the policies that were implemented was the WHO launching of a six-point AMR policy package to combat AMR\textsuperscript{8}, this six-point policy package consists of the following; Should have overarching national infection prevention policies, have national medicine lists, implement national AMR plans, implement national medicines policies and treatment guidelines intimating rational use, create surveillance systems on antimicrobial use and resistance and participate in the innovation, research and development of novel antimicrobial agents.\textsuperscript{9} Very little of the surveillance tracking policies have been implemented in the African setting to track antimicrobial use and resistance patterns.\textsuperscript{9}

In South Africa there are several strategies that were published under the AMR National Strategy Framework set out from 2014 to 2024. These structures have outcomes mainly aimed at managing AMR in order to reduce the prevalence of antimicrobial resistance.\textsuperscript{9} One of the main objectives in this National Strategy Framework was to optimize surveillance and early detection of AMR and enable reporting of resistance trends at local, regional and national levels to optimize empiric and targeted antibiotic choice.\textsuperscript{6}
The lack of sufficient surveillance reports on antimicrobial consumption in community public health care service facilities in South Africa is a novel area for improvement.

METHODS

STUDY DESIGN

The research was a quantitative descriptive study that used a point prevalence study method. Point prevalence methods form part of epidemiological study designs. There were no interventions that were made during the study. Only information from the files were collected. If the information was not found, it was marked “N/A” (Not available).

STUDY SITES AND STUDY PERIOD

This research study was conducted in nine (9) Community Health Centers (CHCs) in the five (5) Gauteng municipalities. These were chosen using random convenient sampling. The data for the study was collected from May to July (winter season) in 2018. CHCs are facilities that cater mostly to the communities in a similar manner as a Primary healthcare (PHC) facility but, have extra benefits of providing 24 hour maternity, accident, emergency services, and up to 30 beds where patients can be observed for a maximum of 48 hours. The CHCs were estimated to have a larger sample size than PHCs and were therefore the best facilities to conduct the study.

DATA COLLECTION AND ANALYSIS

Data was collected using a web-based application (Knack® application) that was developed in South Africa (SA) as part of the appropriate antimicrobial and vaccine use via mobile health and other techniques in the Republic of South Africa (ENAABLERS) project. The web-application allows for anonymous patient data entry directly into the application via any mobile device connected to the web. The data encryption is done with both secure hash algorithm-256 (SHA-256) and Advance Encryption standard-256 (AES-256); these are the strongest encryption available and the same level of encryption used by international banks.

Each clinic was assigned a date where data was collected. Data was only collected on working week days, not on weekends or public holidays. Data was collected from 08:00 AM until all necessary data were gathered.
All results are presented in text, tables and graphs. Statistical analysis were performed on SAS (SAS Institute Inc., Carey, NC, USA) Release 9.4 or higher. All statistical tests are two-sided and p-values $\leq 0.05$ (5%) are considered significant.

**ETHICAL CONSIDERATIONS**

Ethical clearance was obtained from the Sefako Makgatho University Research and Ethics Committee (SMUREC) *(SMUREC/P/33/2018: PG)*. Permission and approval was also granted by the Chief Executive Officers (CEOs) of the contributing clinics. Permission was again obtained from The National Health Research Data Base (NHRD). Approval to conduct research in the individual CHCs was obtained from the district authorities that regulate the CHCs and permission to use the patient files was obtained from the facility managers at each CHC.

**RESULTS**

**Demographic data**

There were a total number of 786 patient files that were surveyed in total across the nine (9) CHCs that were included in the study. In the final analysis of the data, there were one-third (35.88%) of the surveyed population that were prescribed antimicrobials. The majority of patients were between 35 and 55 years of age (n=282; 35.9%; SD 20.267). More than half of all the patients (58.9 %) (n=463/786) of the total number of patients were female. Patients that were reported to be HIV positive were 24.3% (n=191), HIV negative patients were 22.9% (180) and the HIV status of 52.8% (n=415) of patients could not be confirmed. All the patients that were HIV positive were on highly active antiviral therapy (HAART) and eight (8) patients were TB positive but only two (2) patients received TB treatment. Table 1 provides an overview of the study demographic characteristics.

<table>
<thead>
<tr>
<th>Table 1: Demographics of the study population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surveyed patients (n)</strong></td>
</tr>
<tr>
<td><strong>Total number of patients</strong></td>
</tr>
<tr>
<td><strong>Age group</strong></td>
</tr>
<tr>
<td>Adolescent (12 years - 18 years old)</td>
</tr>
<tr>
<td>Adult (18 years - 35 years old)</td>
</tr>
<tr>
<td>Adult (older than 55 years)</td>
</tr>
<tr>
<td>Adult (36-55)</td>
</tr>
<tr>
<td>Child</td>
</tr>
<tr>
<td>Infant (1 month - 11 months old)</td>
</tr>
</tbody>
</table>
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### Neonate (1 - 28 days old)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>463</td>
<td>58.9</td>
</tr>
<tr>
<td>Male</td>
<td>323</td>
<td>41.1</td>
</tr>
</tbody>
</table>

#### Hospitalization in the past 90 days

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>354</td>
<td>45.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>427</td>
<td>54.3</td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

#### Antimicrobial use in the past 90 days

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>308</td>
<td>39.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>411</td>
<td>52.3</td>
</tr>
<tr>
<td>Yes</td>
<td>67</td>
<td>8.5</td>
</tr>
</tbody>
</table>

#### TB Status

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>232</td>
<td>29.5</td>
</tr>
<tr>
<td>Positive</td>
<td>8</td>
<td>1.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>546</td>
<td>69.5</td>
</tr>
</tbody>
</table>

#### HIV Status

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>180</td>
<td>22.9</td>
</tr>
<tr>
<td>Positive</td>
<td>191</td>
<td>24.3</td>
</tr>
<tr>
<td>Unknown</td>
<td>415</td>
<td>52.8</td>
</tr>
</tbody>
</table>

### Diagnosis

The data shows that the majority of antimicrobials did not have a specified indication for why they given, this was observed to account for 60.1% (n=472) of total diagnosis. The second most prevalent condition for which antimicrobials were indicated included infections of ear/nose/throat/larynx and mouth (Upper respiratory tract excluding bronchi) (4.3%). The most common diagnosis in the latter were laryngitis, otitis media. The other prevalent diagnosis included community acquired pneumonia (2.2%) and sexually transmitted infections in females (1.3%).

### Table 2: The diagnosis distribution for patients on antimicrobials

<table>
<thead>
<tr>
<th>Disease</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRON; Acute bronchitis or exacerbations of chronic bronchitis</td>
<td>5</td>
<td>0.6</td>
<td>0.6</td>
<td>28.6</td>
</tr>
<tr>
<td>CYS; Symptomatic lower urinary tract infection/ (Urethra and Bladder) e.g. cystitis</td>
<td>6</td>
<td>0.8</td>
<td>0.8</td>
<td>29.4</td>
</tr>
<tr>
<td>ENT; refers Infections of ear/nose/throat/ larynx and mouth (Upper respiratory tract excluding bronchus)</td>
<td>34</td>
<td>4.3</td>
<td>4.3</td>
<td>33.7</td>
</tr>
</tbody>
</table>
### ANTIMICROBIAL CONSUMPTION DATA

There were 279 units of antimicrobials dispensed in total for both treatment and medical prophylaxis. Of the total antimicrobial units, 209 units (74.91%) of antimicrobials were used for treatment compared to 70 units (25.01%) of antimicrobials that were used for medical prophylaxis. On average, 0.3 antimicrobials were prescribed per patient.

**The WHO beAWaRe antibiotics**

The beAWaRe classification only includes antibiotics and other antimicrobials are not included within this classification. In total 279 units of antimicrobial agents were prescribed, the beAWaRe antibiotics constitute 83.87% (234 units) of total antimicrobial prescriptions whilst the non-

<table>
<thead>
<tr>
<th>Category</th>
<th>Code</th>
<th>Code</th>
<th>Code</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>EYE; refers to eye infections/ e.g. endophthalmitis</td>
<td>1</td>
<td>0.1</td>
<td>0.1</td>
<td>33.8</td>
</tr>
<tr>
<td>GI; Gastrointestinal infections (e.g. salmonellosis/ antibiotic-associated diarrhoea)</td>
<td>2</td>
<td>0.3</td>
<td>0.3</td>
<td>34.1</td>
</tr>
<tr>
<td>GUM; Prostatitis/ epididymo-orchitis/ and STD in men</td>
<td>5</td>
<td>0.6</td>
<td>0.6</td>
<td>34.7</td>
</tr>
<tr>
<td>ML; Malnutrition</td>
<td>2</td>
<td>0.3</td>
<td>0.3</td>
<td>35.0</td>
</tr>
<tr>
<td>NA; &quot;Not applicable; for antimicrobial use other than treatment&quot;</td>
<td>472</td>
<td>60.1</td>
<td>60.1</td>
<td>95.0</td>
</tr>
<tr>
<td>OBGY; Obstetric or gynaecological infections (e.g. STDs in women/ abortion related sepsis/ post-partum sepsis etc.)</td>
<td>10</td>
<td>1.3</td>
<td>1.3</td>
<td>96.3</td>
</tr>
<tr>
<td>PNEU; &quot;Pneumonia (other than TB; if TB see below for different code)&quot;</td>
<td>17</td>
<td>2.2</td>
<td>2.2</td>
<td>98.5</td>
</tr>
<tr>
<td>PYE; Symptomatic upper urinary tract infection/ (Ureter and Kidney) e.g. pyelonephritis</td>
<td>1</td>
<td>0.1</td>
<td>0.1</td>
<td>98.6</td>
</tr>
<tr>
<td>SST; Soft tissue infections (e.g. cellulitis/ wound/ and deep soft tissue) not involving bone</td>
<td>8</td>
<td>1.0</td>
<td>1.0</td>
<td>99.6</td>
</tr>
<tr>
<td>TB; Pulmonary Tuberculosis</td>
<td>3</td>
<td>0.4</td>
<td>0.4</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>786</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
AWaRe classified antimicrobials were 16.13% (45 units). Access antibiotics accounted to 79.60% (185 units) of antibiotics in the AWaRe classification compared to watch antibiotics which amounted to 20.94% (49 units). The data revealed that there were no patients that were prescribed antibiotics in the reserve group. Amoxicillin accounted for more than half (57.84%) of the access group antibiotics, while Azithromycin (46.94%) was the most commonly prescribed antimicrobial in the watch group.

The total antimicrobial consumption

Amoxicillin was the most frequently consumed antimicrobial which accounted for 38.35% (107/279) of total antimicrobial consumption. Isoniazid was the second most frequently consumed antimicrobial (14.70%; 41/279), followed by azithromycin (8.24%; 23/279). The least consumed antimicrobials was Fluconazole, contributing 0.36% (1/279) of the total antimicrobial consumption. The DDD for Acyclovir and Sulfamethoxazole/trimethoprim could both not be compared with the WHO recommended DDD because the DDD recommendation is currently not available for both drugs.

Antimicrobial for prophylaxis of infections

There were 279 units of antimicrobials prescribed in total, of these units, medical prophylaxis accounted for 25.01% (70 units) of the total antimicrobials prescribed.
Table 3: The utilization of antimicrobials for prophylaxis

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>DDD patient total</th>
<th>Number of patients on antimicrobial</th>
<th>Average patient DDD</th>
<th>WHO DDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin ; J01CA04</td>
<td>4</td>
<td>5</td>
<td>0.8g</td>
<td>1g</td>
</tr>
<tr>
<td>Amoxicillin and enzyme inhibitor ; J01CR02</td>
<td>5.25</td>
<td>3</td>
<td>1.75g</td>
<td>1g</td>
</tr>
<tr>
<td>Azithromycin ; J01FA10</td>
<td>2</td>
<td>2</td>
<td>1g</td>
<td>0.3g</td>
</tr>
<tr>
<td>Flucloxacillin; J01CF05</td>
<td>6.5</td>
<td>2</td>
<td>1.3g</td>
<td>2g</td>
</tr>
<tr>
<td>Isoniazid ; J04AC01</td>
<td>11.95</td>
<td>41</td>
<td>0.3g</td>
<td>0.3g</td>
</tr>
<tr>
<td>Sulfamethoxazole and trimethoprim ; J01EE01</td>
<td>13.44</td>
<td>14</td>
<td>0.96g</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Isoniazid 58.57% (41/70) was the most prescribed antimicrobial, followed by Sulfamethoxazole/trimethoprim 20% (14/70). The least consumed antimicrobial was Azithromycin 2.86% (2/70).

Figure one below depicts the use of antimicrobials that were used as prophylaxis.

![Antimicrobial used for prophylaxis](image)

**Figure 1:** Shows the average DDD antimicrobial consumption per day of surveyed patients compared with the WHO recommended DDD consumption per day for medical prophylaxis.
The antimicrobials depicted above are antimicrobials that were used for medical prophylaxis to prevent infections. The data shows varied values amongst the different antimicrobial consumption rates. The only antimicrobial that was compliant with the WHO DDD consumption per day (in grams) was Isoniazid that was used for medical prophylaxis for patients that were TB exposed or were HIV/AIDS positive and were therefore high risk patients for TB co-infection. Amoxicillin and flucloxacillin were on average below the WHO recommended consumption rate per day whilst amoxicillin and enzyme inhibitor combination was on average above the WHO recommendation.

Antimicrobials for treatment of infections

Depicted below is the average consumption of antimicrobials used for treatment of infections also including how many units where dispensed on average, the average DDD consumption per day, the recommended WHO DDD and the calculated consumption rate.

**Table 4: The utilization of antimicrobials for treatment**

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>DDD total</th>
<th>Number of antimicrobials dispensed (units)</th>
<th>Average patient DDD</th>
<th>WHO DDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>1.2</td>
<td>1</td>
<td>1g</td>
<td>N/A</td>
</tr>
<tr>
<td>Amoxicillin ; J01CA04</td>
<td>146.375</td>
<td>102</td>
<td>1.435g</td>
<td>1g</td>
</tr>
<tr>
<td>Amoxicillin and enzyme inhibitor ; J01CR02</td>
<td>20.1</td>
<td>12</td>
<td>1.675g</td>
<td>1g</td>
</tr>
<tr>
<td>Azithromycin ; J01FA10</td>
<td>18.25</td>
<td>21</td>
<td>0.869g</td>
<td>0.3g</td>
</tr>
<tr>
<td>Ceftriaxone ; J01DD04</td>
<td>4.25</td>
<td>15</td>
<td>0.283g</td>
<td>2g</td>
</tr>
<tr>
<td>Ciprofloxacin ; J01MA02</td>
<td>11</td>
<td>11</td>
<td>1g</td>
<td>1g</td>
</tr>
<tr>
<td>Cloxacillin; J01CF02</td>
<td>1</td>
<td>1</td>
<td>1g</td>
<td>2g</td>
</tr>
<tr>
<td>Doxycycline ; J01AA02</td>
<td>1.1</td>
<td>6</td>
<td>0.183g</td>
<td>1g</td>
</tr>
<tr>
<td>Flucloxacillin; J01CF05</td>
<td>17.5</td>
<td>8</td>
<td>2.1875g</td>
<td>2g</td>
</tr>
<tr>
<td>Fluconazole ; J02AC01</td>
<td>0.4</td>
<td>1</td>
<td>0.4g</td>
<td>0.2g</td>
</tr>
<tr>
<td>Metronidazole (oral/rectal) ; P01AB01</td>
<td>25.8</td>
<td>20</td>
<td>1.29g</td>
<td>2g</td>
</tr>
<tr>
<td>Phenoxymethylpenicillin; J01CE02</td>
<td>4.5</td>
<td>3</td>
<td>1.5g</td>
<td>2g</td>
</tr>
<tr>
<td>Rifafour 400/275/150/75</td>
<td>400/275/150/75</td>
<td>2</td>
<td>400/275/150/75</td>
<td>N/A</td>
</tr>
<tr>
<td>Sulfamethoxazole and trimethoprim ; J01EE01</td>
<td>6.12</td>
<td>6</td>
<td>1.02g</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Amoxicillin was the most frequently prescribed antimicrobial (48.80%; 102/209), followed by Azithromycin (10.05%; 21/209), then metronidazole (9.57%; 20/209).

Figure two shows the comparison of the antimicrobials used for treatment against the DDDs giving by the WHO.

**Figure 2:** Antimicrobial consumption per day for treatment of infections have relatively significant disparities as compared to the recommended WHO DDD per day.

The average DDD antimicrobial consumption per day of surveyed patients compared with the WHO recommended DDD consumption per day for the treatment of infections showed a varied spectrum. The most commonly prescribed antimicrobial agents for the treatment of infections that had significant differences between recommended and prescribed included amoxicillin, flucloxacillin, azithromycin and Amoxicillin/enzyme inhibitor. All of these antimicrobials had a DDD/day consumption rate that was above the recommended WHO DDD. Flucloxacillin, azithromycin and Amoxicillin/enzyme inhibitor had the most significantly observed elevated antimicrobial consumption DDD/day as compared to the WHO DDD. Ceftriaxone and metronidazole were some of the antimicrobial agents that had a lower consumption rate as
compared to the WHO DDD that was recommended. The only antimicrobial that matched the WHO DDD/day consumption was Ciprofloxacin and Isoniazid.

Combination of antimicrobial agents

There were 242 (30.79%) patients that were prescribed antimicrobials. Out of these patients, 24 (9.9%) patients received more than one antimicrobial. The most commonly prescribed combinations were Isoniazid plus Sulfamethoxazole/trimethoprim that were indicated for the medical prophylaxis of TB and *pneumocystis jirovecii* pneumonia in immunocompromised patients (HIV/AIDS). The second most frequent combination was triple therapy consisting of Ceftriaxone; J01DD04 + Azithromycin; J01FA10 + Metronidazole (oral/rectal); P01AB01 which were indicated for treating sexually transmitted diseases in females. The other combinations that were used could not be attributed to any specific indication. Although combination therapy was used, monotherapy was more frequently prescribed more than combination antimicrobial therapy.

**Table 5:** Top antimicrobial combinations and respective indications for which they were used

<table>
<thead>
<tr>
<th>Combination</th>
<th>Number</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimicrobial for treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin ; J01CA04 + Ceftriaxone ; J01DD04</td>
<td>2</td>
<td>Acute and chronic bronchitis; Pneumonia</td>
</tr>
<tr>
<td>Ceftriaxone ; J01DD04 + Azithromycin ; J01FA10 + Metronidazole (oral/rectal) ; P01AB01</td>
<td>8</td>
<td>STD³ in women;ENT¹</td>
</tr>
<tr>
<td>Azithromycin ; J01FA10 + Metronidazole (oral/rectal) ; P01AB01</td>
<td>4</td>
<td>ENT¹</td>
</tr>
<tr>
<td>Ciprofloxacin ; J01MA02 + Metronidazole (oral/rectal) ; P01AB01</td>
<td>2</td>
<td>Asymptomatic bateriuria</td>
</tr>
<tr>
<td>Amoxicillin ; J01CA04 + Metronidazole (oral/rectal) ; P01AB01</td>
<td>2</td>
<td>Gastrointestinal infections; ENT¹ infections</td>
</tr>
<tr>
<td><strong>Antimicrobial for prophylaxis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid ; J04AC01 + Sulfamethoxazole and trimethoprim ; J01EE01</td>
<td>8</td>
<td>TB³ and PJP⁴ prophylaxis</td>
</tr>
</tbody>
</table>

1 ENT Infections of the Ear/nose/throat; 2 STD Sexually transmitted disease; 3 TB Tuberculosis; 4 PJP *Pneumocystis jirovecii* pneumonia
Discussion

The study was conducted in order to fill in the paucity in antimicrobial consumption data. The nine (9) CHC that were surveyed had a sample size of 786 patients with only 30.79% (242) patients prescribed antimicrobials. Most of the antimicrobials that were prescribed were for the treatment of infections (209 units; 74.91%) whilst the others were used for medical prophylaxis (70 units; 25.01%). The most commonly prescribed antimicrobial was Amoxicillin (38.35%; 107/279) which was used for treatment of antimicrobial infections followed by isoniazid (14.70%; 41/279) which was used for medical prophylaxis, specifically in HIV positive, TB exposed patients. Most of the antimicrobial agents that were used could not be attributed to a specific infectious diagnosis to which it was indicated (60.1%; 472). The most common infectious diagnosis that were documented were for laryngitis and otitis media (4.3%). followed by community acquired pneumonia then by sexually transmitted diseases in women. Monotherapy was most frequently prescribed as standard therapy used whilst only a few combination antimicrobial therapy was used. The most frequent combination therapy were Isoniazid plus Sulfamethoxazole/trimethoprim indicated for medical prophylaxis of TB and PJP, respectively and also a combination of Ceftriaxone plus Azithromycin plus Metronidazole (oral/rectal) which were commonly indicated to treat sexually transmitted diseases in women. There were varied differences in terms of the DDD/day consumption within the antimicrobials when compared with the recommended WHO DDD/day consumption. Some of the antimicrobial agents such as flucloxacillin showed a significantly elevated DDD/day consumption of surveyed patients as compared to the WHO DDD/day. On the contrary, antimicrobial agents such as ceftriaxone showed lower than recommended DDD/day consumption for the surveyed patients. The only antimicrobial agents that were equivalent to the WHO recommended DDD/day were isoniazid and Ciprofloxacin.

Although the data shows varieties in antimicrobial consumption throughout the different patient demographics, the sample size is not adequate to generalize the consumption rate to the South African CHC and PHC setting. The study served to motivate more studies to be conducted in the public healthcare setting in South Africa so that surveillance tools could be implemented and accurately report antimicrobial consumption which will possibly influence AMC and AMR guidelines that will be implemented through the SA national strategic framework and as a recommendation by the WHO.

Disclaimer

The information reported cannot be generalized to the entire picture of antimicrobial consumption in primary healthcare in South Africa.
References


CHAPTER 5
LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS

5.1 INTRODUCTION

This chapter discusses the limitations of this study and recommendations which include possible practice changes that are based on findings in this study.

5.2 LIMITATIONS OF THE STUDY

The following are the limitations that were encountered from the commencing of the study to the study conclusion. It includes predicaments with collection of data, patient filing, study site categorization etc.

- During the study period, some data could not be collected due to the following factors;
  - The inpatient and outpatient filing departments operate separately in most of the CHCs. The inpatient files were not easily accessible to the researchers hence data could not be collected.
  - The inpatient departments were usually the emergency departments whereby patients were only observed for less than 24 hours and transferred to a hospital with their file, so the files were not kept in the CHC which made data from these inpatients unattainable.
  - Some of the CHCs were named CHCs but operated as PHCs which means they did not have inpatient departments from which data could be collected.
  - The filing system in the CHCs made it improbable to recover all the patient files of the patients that visited the clinics the day prior to data collection so some files could have been missed.
  - The paper-based files make finding information daunting. Some documents are missing which means some vital information cannot be found and documented.
  - During data collection, there were no microbial cultures or sensitivity tests that were found in any of the patient files. This opens the possibility that patients are prescribed and dispensed antimicrobials (sometimes frequently on different occasions). This means that patients are potentially exposed to developing antimicrobial resistance.
5.3 RECOMMENDATIONS

The following is list of recommendations that could help to improve the data collection procedure and decrease the consumption of antimicrobials.

- Improvement of the filing-system is very crucial in the CHCs. Files go missing in the filing rooms and there is no integration of information. It is very important that the filing system and filing rooms be reviewed and improved to prevent these predicaments.

- The medical profiles of patients should be computerized due to the fact that when the paper-based files get lost, all the patient’s information is also lost. Loss of critical information may lead to catastrophic implications for the patients as patients may be prescribed contraindicated medication by health professionals that are not aware of the patient’s health history and other unwanted consequences that may arise. Computerized medical profiles might reduce this problem.

- Some clinics were named CHCs but performed as PHCs. Improvement of the department of health categorization of healthcare facilities is pivotal as the information is misleading.

- Training of nurses in infectious diseases and prescribing is essential in the CHCs as these facilities were observed to have limited trained staff.

- CHCs and PHCs should be aligned to laboratories. Healthcare professionals should be given more liberty to request microbial culture tests with a good turnover time for accessing results. The observation was that there was very limited sensitivity results obtained from the surveyed patient files. Some patients were on the same antibiotics on separate CHC visits without any cultures which might increase the risk for developing AMR if the antimicrobial agent is dispensed irrationally.

5.4 CONCLUSIONS

The study was conducted in order to fill in the paucity in antimicrobial consumption data. The nine (9) CHC that were surveyed had a sample size of 786 patients with only 30.79% (242) patients prescribed antimicrobials. Most of the antimicrobials that were prescribed were for the treatment of infections (209 units; 74.91%) whilst the others were used for medical prophylaxis (70 units; 25.01%). The most commonly prescribed antimicrobial was Amoxicillin (38.35%; 107/279) which was used for treatment of antimicrobial infections followed by isoniazid (14.70%; 41/279) which was used for medical prophylaxis, specifically
in HIV positive, TB exposed patients. Most of the antimicrobial agents that were used could not be attributed to a specific infectious diagnosis to which it was indicated (60.1%; 472). The most common infectious diagnosis that were documented were for laryngitis and otitis media (4.3%). followed by community acquired pneumonia then by sexually transmitted diseases in women. Monotherapy was most frequently prescribed as standard therapy used whilst only a few combination antimicrobial therapy was used. The most frequent combination therapy were Isoniazid plus Sulfamethoxazole/trimethoprim indicated for medical prophylaxis of TB and PJP, respectively and also a combination of Ceftriaxone plus Azithromycin plus Metronidazole (oral/rectal) which were commonly indicated to treat sexually transmitted diseases in women. There were varied differences in terms of the DDD/day consumption within the antimicrobials when compared with the recommended WHO DDD/day consumption. Some of the antimicrobial agents such as flucloxacillin showed a significantly elevated DDD/day consumption of surveyed patients as compared to the WHO DDD/day. On the contrary, antimicrobial agents such as ceftriaxone showed lower than recommended DDD/day consumption for the surveyed patients. The only antimicrobial agents that were equivalent to the WHO recommended DDD/day were isoniazid and Ciprofloxacin.

Although the data shows varieties in antimicrobial consumption throughout the different patient demographics, the sample size is not adequate to generalize the consumption rate to the South African CHC and PHC setting. The study served to motivate more studies to be conducted in the public healthcare setting in South Africa so that surveillance tools could be implemented and accurately report antimicrobial consumption which will possibly influence AMC and AMR guidelines that will be implemented through the SA national strategic framework and as a recommendation by the WHO.


References


Hsia Y, Sharland M, Jackson C, Wong IC, Magrini N, Bielicki JA. Consumption of oral antibiotic formulations for young children according to the WHO Access, Watch, Reserve (AWaRe) antibiotic groups: an analysis of sales data from 70 middle-income and high-income countries. The Lancet Infectious Diseases. 2018 Dec 3.


APPENDICES

Appendix 1: CHC Data

PART 1 – CHC DATA

Point Prevalence Survey

*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 CHC:</td>
<td></td>
</tr>
<tr>
<td>CHC Code <em>(Refer to the CHC 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/CHC</td>
</tr>
<tr>
<td>Full Names of the Data Collector: <em>(Print in capital letters)</em></td>
<td></td>
</tr>
</tbody>
</table>

| CHC Codes |
|-----------------|-----------------|
| **CHC Name** | **CHC Code** |
| Soshanguve CHC | C1 |
| Laudium CHC | C2 |
| Zola CHC | C3 |
| Goba CHC | C4 |
| Phola-park CHC | C5 |
| Boipatong CHC | C6 |
| Hillbrow CHC | C7 |
| Mohlakeng CHC | C8 |
| Thusanang CHC | C9 |
## Appendix 2: Patient Data

### PART 3 - PATIENT DATA

#### Point Prevalence Survey

**Section 1 - To be completed for all patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Code:</td>
<td></td>
</tr>
<tr>
<td>Ward Code:</td>
<td></td>
</tr>
<tr>
<td>Patient Code:</td>
<td></td>
</tr>
<tr>
<td>Consented:</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Admission Date:</td>
<td>DD/MM/YY</td>
</tr>
<tr>
<td>Age:</td>
<td>Yrs/M</td>
</tr>
<tr>
<td>Sex:</td>
<td>M/P/T</td>
</tr>
<tr>
<td>Employed:</td>
<td>Yes/No/UN</td>
</tr>
<tr>
<td>Transfer in:</td>
<td>Yes/No/UN</td>
</tr>
<tr>
<td>Prior Hospitalization:</td>
<td>Yes/No/UN</td>
</tr>
<tr>
<td>Antibiotic use last 90 days?:</td>
<td>Yes/No/UN</td>
</tr>
<tr>
<td>Duration of Use:</td>
<td>days</td>
</tr>
<tr>
<td>Catheterization:</td>
<td>U/P/C/O/N</td>
</tr>
<tr>
<td>Intubation:</td>
<td>Yes/No</td>
</tr>
<tr>
<td>HIV:</td>
<td>P/N/UN</td>
</tr>
<tr>
<td>Name of last Antibiotics:</td>
<td>Abbreviate</td>
</tr>
<tr>
<td>CD4 Count:</td>
<td>cells/mm³</td>
</tr>
<tr>
<td>On HAART:</td>
<td>Yes/No</td>
</tr>
<tr>
<td>On Antibiotics now?:</td>
<td>Yes/No</td>
</tr>
</tbody>
</table>

*If you answered “Yes” then fill Section 2 below*

**Section 2 - To be completed only for patients currently on Antimicrobial therapy**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribed by:</td>
<td>S/M/N</td>
</tr>
<tr>
<td>Prophylaxis/Treatment?:</td>
<td>P/T</td>
</tr>
<tr>
<td>Medical or Surgical prophylaxis?:</td>
<td>M/S</td>
</tr>
<tr>
<td>Duration of Prophylaxis:</td>
<td>days</td>
</tr>
<tr>
<td>Indication:</td>
<td></td>
</tr>
<tr>
<td>Type of Infection:</td>
<td>CA/HA +LI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the Antibiotic: 1</th>
<th>INN (Generic Name)</th>
<th>Dose:</th>
<th>Frequency:</th>
<th>Route:</th>
<th>Prescription on Drug sheet?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>mg</td>
<td>OD/BID/TID/QID</td>
<td>PO/IM/IV</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Start Date:</td>
<td>DD/MM/YY</td>
<td>No. of Doses Missed:</td>
<td>Antibiotic O/S?:</td>
<td>Yes/No</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes/No</td>
<td>Prescription on Drug sheet?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of the Antibiotic: 2</th>
<th>INN (Generic Name)</th>
<th>Dose:</th>
<th>Frequency:</th>
<th>Route:</th>
<th>Prescription on Drug sheet?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>mg</td>
<td>OD/BID/TID/QID</td>
<td>PO/IM/IV</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Start Date:</td>
<td>DD/MM/YY</td>
<td>No. of Doses Missed:</td>
<td>Antibiotic O/S?:</td>
<td>Yes/No</td>
<td>Prescription on Drug sheet?</td>
</tr>
<tr>
<td>Name of the Antibiotic:</td>
<td>INN (Generic Name)</td>
<td>Dose:</td>
<td>Frequency:</td>
<td>Route:</td>
<td>Start Date:</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------</td>
<td>-------</td>
<td>------------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>Name of the Antibiotic: 3</td>
<td>[Blank]</td>
<td>mg</td>
<td>OD/BID/TID/QID</td>
<td>PO/IM/IV</td>
<td>DD/MM/YY</td>
</tr>
<tr>
<td>Name of the Antibiotic: 4</td>
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<td>OD/BID/TID/QID</td>
<td>PO/IM/IV</td>
<td>DD/MM/YY</td>
</tr>
<tr>
<td>Name of the Antibiotic: 5</td>
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<td>mg</td>
<td>OD/BID/TID/QID</td>
<td>PO/IM/IV</td>
<td>DD/MM/YY</td>
</tr>
</tbody>
</table>

Rx in INN (generic name)? | Yes/No | CST prior to Empiric Treatment? | Yes/No | CST Results? | Yes/No | Name of Bacteria: | K. pneumonia |
Was Rx changed to sensitive Abx? | Yes/No | Diarrhoea/Vomiting? | Yes/No | Oral Switch? | Yes/No | All Antibiotics from SEDL? | Yes/No |

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### Appendix 3: Indication list

<table>
<thead>
<tr>
<th>Indication/Diagnosis Code as per site for antimicrobial use (based on ECDC list)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS – refers to infections of the central nervous system</td>
</tr>
<tr>
<td>EYE – refers to eye infections, e.g. endophthalmitis</td>
</tr>
<tr>
<td>ENT – refers infections of ear, nose, throat, larynx and mouth</td>
</tr>
<tr>
<td>BRON - Acute bronchitis or exacerbations of chronic bronchitis</td>
</tr>
<tr>
<td>PNEU – Pneumonia</td>
</tr>
<tr>
<td>CVS - Cardiovascular infections: endocarditis, vascular graft</td>
</tr>
<tr>
<td>GI - Gastrointestinal infections (e.g. salmonellosis, antibiotic-associated diarrhoea)</td>
</tr>
<tr>
<td>IA - Intra-abdominal sepsis, including hepatobiliary</td>
</tr>
<tr>
<td>SST - Cellulitis, wound, and deep soft tissue not involving bone</td>
</tr>
<tr>
<td>BJ - Septic arthritis (including prosthetic joint), osteomyelitis</td>
</tr>
<tr>
<td>CYS - Symptomatic lower urinary tract infection, e.g. cystitis</td>
</tr>
<tr>
<td>PYE - Symptomatic upper urinary tract infection, e.g. pyelonephritis</td>
</tr>
<tr>
<td>ASB - Asymptomatic bacteriuria</td>
</tr>
<tr>
<td>OBGY - Obstetric or gynaecological infections, e.g. STDs in women</td>
</tr>
<tr>
<td>GUM - Prostatitis, epididymo-orchitis, and STD in men</td>
</tr>
<tr>
<td>BAC - Laboratory-confirmed bacteraemia</td>
</tr>
<tr>
<td>CSEP - Clinical sepsis (suspected bloodstream infection without lab confirmation/results are not available, no blood cultures collected or negative blood culture), excluding febrile neutropenia</td>
</tr>
<tr>
<td>FN - Febrile neutropenia or other form of manifestation of infection in immunocompromised host, e.g. HIV, chemotherapy, etc., with no clear anatomical site</td>
</tr>
<tr>
<td>SIRS - Systemic inflammatory response with no clear anatomical site</td>
</tr>
<tr>
<td>UND - Completely undefined; site with no systemic inflammation</td>
</tr>
<tr>
<td>NA - Not applicable; for antimicrobial use other than treatment</td>
</tr>
</tbody>
</table>
Appendix 4: SMUREC Clearance certificate

APPENDICES

APPROVAL NOTICE - NEW APPLICATION

01 February 2018

Mr NM Magongwane
Department of Pharmacy
P.O.Box 286
Meiduna, 0004

MEETING:

01/2018

SMUREC Ethics Reference Number:

SMUREC/PI33/2018: PG

The New Application received on 17 January 2018, was reviewed by members of Sefako Makgatho University Research Ethics Committee 01 February 2018 and was provisionally approved on 01 February 2018.

Title:

Antimicrobial consumption in community health care centres

Researcher:

Mr NM Magongwane

Supervisor:

Mrs P Skosana

Co-supervisor:

Prof N Schellast

Prof JC Meyer

Department:

Pharmacy

School:

Pharmacy

Degree:

M Pharm

Please note the following information about your approved research protocol:

Approval Period:

01 February 2018 – 01 February 2019

Please remember to use your protocol number (SMUREC/PI33/2018: 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.
Appendix 5: SMUREC Ammendment letter

Mr NM Magongwa
Department of Pharmacy
P.O Box 218
Medunsa, 0204

Dear Mr Magongwa

RE: SMUREC/P/33/2018: PG – AMENDMENT TO PROTOCOL

Researcher: Mr NM Magongwa
Supervisor: Mrs P Skosana
Co-supervisor: Prof N Schellack

SMUREC approved title: An antimicrobial consumption in community health care centres

SMUREC NOTED your letter dated 20 September 2018 requesting permission to amend the following:

a) To change some of study sites, Changa Kwa-Theme CHC to Goba CHC.

Motivation: The Ekurhuleni municipality recommended that I remove Kwa-Theme from the study sites and replace it with Goba CHC. This is due to the small capacity of Kwa-Theme and the continuous protests that were on-going. Permission was granted to rather go to Goba CHC.

b) Permission to omit a study site (Leval-Mbatha CHC)

Motivation: The protocol was supposed to survey 10 CHCs. The researcher managed to obtain approval for nine (9) with the exception of Leval-Mbatha CHC which has been delayed for more than three (3) months. Since the researcher is doing a point-prevalence study, he cannot collect data over two different seasons. The researcher already collected data for the other CHCs (winter) and can therefore no longer collect data now since it is autumn. He therefore requests to remove Leval-Mbatha as one of her CHCs and only have nine (9) CHCs to analyze for the results.

SMUREC NOTED and APPROVED your request to change the study sites, Kwa-Theme CHC to Goba CHC and omit a study site, Leval-Mbatha CHC as mentioned above.

Yours Sincerely,

PROF GA OGUNBAJO
CHAIRPERSON SMUREC
04 October 2018
Cc.: Mrs P Skosana
Appendices

Appendix 6: Approval letters: JHB District

JOHANNESBURG HEALTH DISTRICT

Faculty Of Health Sciences
Research Ethics Committee,
Sefako Makgatho University
Pretoria North, South Africa
natalie.schellack@smu.ac.za

DRC Ref: 2018-02-006
NHRI Ref no: GP_201802_005

Dear: Prof Natalie Schellack

Re: APPROPRIATE ANTIMICROBIAL AND VACCINE USE VIA mobile HEALTH AND OTHER TECHNIQUES IN THE REPUBLIC OF SOUTH AFRICA

Your application for Research Approval refers

The District Research Committee has reviewed your application. This letter serves as an in-principle approval to access the Districts Health facilities (mentioned below) for the above project subject to following conditions:

• The facility to be visited: HILLBROW CHC, ZOLA CHC
• This facility will be visited from 16/04/2018 to 16/14/2019
• The research can only commence after you submit an ethics clearance certificate from a recognized institution.
• You will report to the Facility Manager before initiating the study.

<table>
<thead>
<tr>
<th>Region</th>
<th>Regional Health Manager</th>
<th>Contact No.</th>
<th>Cell phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABEF</td>
<td>Ms Matlala</td>
<td>011 440 1259</td>
<td>082 307 0267</td>
</tr>
<tr>
<td>D</td>
<td>Ms. Maria Mazibuko</td>
<td>011 674 1200</td>
<td>082 781 9919</td>
</tr>
</tbody>
</table>

The following conditions must be observed:

• Participants’ rights and confidentiality will be maintained all the time.
• No resources (Financial, material and human resources) from the above facilities will be used for the study. Neither the District nor the facility will incur any additional cost for this study.
• The study will comply with Publicly Financed Research and Development Act, 2008 (Act 51 of 2008) and its related Regulations.
Appendices

- Your supervisor and University of the Witwatersrand will ensure that these reports are being submitted timeously to the District Research Committee.
- The District must be acknowledged in all the reports/publications generated from the research and a copy of these reports/publications must be submitted to the District Research Committee.

We reserve our right to withdraw our approval, if you breach any of the conditions mentioned above.

Please feel free to contact us if you have any further queries. On behalf of the District Research Committee, we would like to thank you for your interest.

Regards,

Dr EM Osaifa
Chairperson: District Research Committee
Johannesburg Health District
Date: 24/04/2018

Mrs M. Morewane
Chief Director
Johannesburg Health District
Date: 24/04/2018
Appendices

Appendix 7: Approval letters: Sedibeng District

TO : PROF. N. SCHELLACK
     SEFAKO MAKGATHO UNIVERSITY

FROM : MS. S. HLAHANE
       DIRECTOR SEDIBENG DHS

DATE : 25 APRIL 2018

SUBJECT : PERMISSION TO CONDUCT RESEARCH – APPROPRIATE
           ANTIMICROHAL AND VACCINE USE VIA MOBILE HEALTH
           AND OTHER TECHNIQUES IN THE REPUBLIC OF SOUTH
           AFRICA.

Please be informed that permission has been granted for you to carry out the abovementioned
research at Boipatong CHC. It is noted that you have already obtained Provincial Ethics
Committee as well as the Sefako Makgatho University Research Ethics Clearance.

Kindly note that a copy of the report on the findings (especially) that concerns Sedibeng District
must be submitted to the Director’s office at the completion of the study.

This permission is also subject to the conditions stated in the protocol and any change in design
and methodology must be communicated to the District Director.

We wish you success in your research endeavours.

MS. S. HLAHANE
DIRECTOR SEDIBENG DHS
DATE: 3/04/2018

RESEARCH PROPOSAL DETAILS: GP_201802_005
Appendices

Appendix 8: Approval letters: Tshwane District

Gauteng Province

TSHWANE RESEARCH COMMITTEE: CLEARANCE CERTIFICATE

MEETING: 07/2017
PROJECT NUMBER: 39/2018
NHID REFERENCE NUMBER: GP_201802_005

TOPIC: Appropriate Antimicrobial and Vaccine Use Via mobile Health and Other Techniques in the Republic of South Africa

Principal Investigator: Professor Natalie Schellack
Professor Marion Bennie

Co-investigator:
Professor Johannes Meyer
Dr Andrew Shax
Professor Marc Mendelson
Professor Brian Goodman
Mr Derie Kruger

Dr Marilyn London
Dr Zanele Baker
Dr Samantha Alvarez-Modraco
Professor Detria Goff

Facility:
Senzisa Bepape CHC
Laudium CHC
Jubilee District Hospital

Name of the Department:
Sefako Makgatho Health Sciences University

NB: THIS OFFICE REQUEST A FULL REPORT ON THE OUTCOME OF THE RESEARCH DONE AND

NOTE THAT RESUBMISSION OF THE PROTOCOL BY RESEARCHER(S) IS REQUIRED IF THERE IS DEPARTURE FROM THE PROTOCOL PROCEDURES AS APPROVED BY THE COMMITTEE.

DECISION OF THE COMMITTEE: APPROVED

Dr Robert Gyedirpe
Acting Chairperson: Tshwane Research Committee
Date: 5/08/2018

Mr. Pitsi Mshomone
Chief Director: Tshwane District Health
Date: 9/08/2018
Appendix 9: Approval letters: Ekhuruleni District

EKURHULENI RESEARCH CLEARANCE CERTIFICATE

Research Project Title: Appropriate Antimicrobial and Vaccine Use via Mobile Health and other Techniques in the Republic of South Africa.

NHRD No: GP_201802_005

Research Project Number: 08/03/2018-06

Name of Researcher(s): Prof Natalie Schellack

Division/Institution/Company: Sefako Makgatho Health Science University

DECISION TAKEN BY THE EKURHULENI HEALTH DISTRICT RESEARCH COMMITTEE (EHDC)

- THIS DOCUMENT CERTIFIES THAT THE ABOVE RESEARCH PROJECT HAS BEEN FULLY APPROVED BY THE EHDC. THE RESEARCHER(S) MAY THEREFORE COMMENCE WITH THE INTENDED RESEARCH PROJECT.

- NOTE THAT THE RESEARCHER WILL BE EXPECTED TO PRESENT THE RESEARCH FINDINGS OF THE PROPOSED RESEARCH PROJECT AT THE ANNUAL EKURHULENI RESEARCH CONFERENCE.

- THE RESEARCH COMMITTEE WISHES THE RESEARCHER(S) THE BEST OF SUCCESS.

Deputy Chairperson: Ekurhuleni Metropolitan Municipality
Dated: 08/03/2018

Chairperson: Gauteng Department of Health (Ekurhuleni Region)
Dated: 08/03/2018
Appendices

Appendix 10: Approval letters: West Rand District

GP_201802_005
Prof Natalie Schellack

RE: PERMISSION TO CONDUCT RESEARCH IN WEST RAND DISTRICT.

Your correspondence on the above matter refers. Thank you for your request to conduct research in West Rand District in determining appropriate use of antimicrobials and vaccines.

Permission is hereby granted to you to conduct research in PHC clinics in West Rand. I am anticipating that you will conduct your research with the knowledge of all relevant Managers in respective clinic and Sub-district.

You are expected to share the findings and recommendations with the district in order to improve service delivery to people of west rand.

I hope you find the above in order.

Yours faithfully,

Signature

MS Puleng Muso
Director
WDOCA
Date: 07-02-2018