The availability of recent antimicrobial policies in different wards/units at Dr. George Mukhari Academic Hospital, Gauteng Province

A mini-dissertation submitted by

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DEDICATION

I dedicate this research to my late mother Yvonne Modau, for her understanding, encouragement, motivation and wisdom, which influenced me to study further, she was a pillar when I started this research and unfortunately, she is not around to see the results. My Father Moses and Sister Refilwe Modau for their unending love and support; their believe in me pushes me further to achieve greater things.
DECLARATION

I, TM Modau, declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Science University for the degree of Master of Pharmacy, in the Faculty of Health Sciences, School of Health Care Sciences, 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.

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TM Modau (Mr) Date
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ABSTRACT

Background and Objectives: Antimicrobials are essential in the management of infections, but it is well known that inappropriate use of these agents leads to resistance. Effective implementation of antimicrobial policies through antimicrobial stewardship can curb resistance progression or development of new resistance. The aim of the study was to evaluate the availability of antimicrobial policies and to determine whether they are current and up-to-date. The objectives were to determine the availability of antimicrobial policies in the hospital, to examine the frequent sensitivity and resistance patterns, recommend review of the current antimicrobial policies that needs to be updated in accordance with the Essential Medicines List (EML) and susceptibility patterns seen at the hospital.

Method: This was a prospective, quantitative descriptive study. The researcher collected available antimicrobial policies from all the wards of Doctor George Mukhari Academic Hospital, and compared them against national guidelines and frequent susceptibility patterns obtained from the National Health Laboratory Services (NHLS).

Results: Between June 2015 and June 2016, data on antimicrobial policies as well as microbiological data were collected from 39 wards. Policies were found in six wards, resulting in 15.4% availability of antimicrobial polices, of which one was current and up-to-date. There were 36 different bacterial species identified from 371 organisms. The most common organisms identified from all the wards were Staphylococcus species, 23%, followed by Klebsiella spp 14%, Enterococcus spp 11%, E.coli 11% and Streptococcus spp 9%. Gram-positive organisms made up 43% (159) of the organisms and 57% (212) were gram-negative. Trimethoprim-sulphamethoxazole had the highest resistance, followed by beta-lactam antimicrobials (penicillin and cephalosporins respectively) while there was no resistance against vancomycin.

Conclusion: There were six antimicrobial policies available in the hospital and only one was current and up-to-date, other available policies were last updated in 2013. Although one is in accordance with the national guidelines and local prevalence and resistance despite being outdated. Trimethoprim-sulphamethoxazole had the highest resistance followed by penicillins and cephalosporins and this may be linked
to their frequent use. No resistance against vancomycin was reported during the study period.
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<td>CSF</td>
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<td>DGMAH</td>
<td>Doctor George Mukhari Academic Hospital</td>
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<td>SA</td>
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<td>SPP</td>
<td>Species</td>
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<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
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1.1 INTRODUCTION

This chapter describes the background and rationale for the research study in Section 1.2. The aim, objectives and, the significance of the study are discussed in Section 1.3 and the outline of the dissertation is included in Section 1.4.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Antimicrobials are essential in the prevention and cure of bacterial infections. However, the use of antimicrobials generates resistance to their therapeutic effects, thereby reducing their efficacy in the prevention and cure of disease (Action on antimicrobial Resistance, 2008). This is a global phenomenon and it has a negative impact on the global economy, society, healthcare system and individual patients (Barriere, 2015). When microorganisms become resistant to first-line antimicrobials, the prohibitive high cost of the second-line drugs may result in failure to treat diseases in many individuals (Laxminarayan, Matsotso, Pant, et al., 2016; Jyothsna, Nagaveni, Rama Rao, Vijaya Lakshmi, 2012). Globally, antibiotics account for approximately 30% of hospitals’ drugs expenditures (Bozkurt, Kaya, Tekin, Gulsun, Deveci, Dayan and Hosoglu, 2014). An antimicrobial stewardship programme (ASP) has become a key method of preventing the rise in antimicrobial resistance and reduce the use of broad-spectrum antimicrobials (Action on antimicrobial Resistance, 2008; Cooke, Stephens, Ashiru-Oredope, Johnson, Livermore, Sharland, 2014). There are several strategies used in antimicrobial stewardship programmes to prevent resistance and they include, streamlining/de-escalation, computer-assisted programmes, prospective auditing and feedback, pharmacodynamic dosing optimisation, parenteral-to-oral switch, formulary restrictions, education, prior approval and a controversial strategy, antimicrobial cycling and policies (protocols) and guidelines (Sulema and Meyer, 2012). Protocols and guidelines are important as they promote rational and evidence based prescribing (Wickens, Farrell, Ashiru-Oredope, Jacklin and Holmes, 2013). Since
there may be several agents from the same class available, protocols have become a beneficial guideline to assist prescribers in selecting the most appropriate agent (Araujo Da Silva, Zingg, Dramowski, Bielicki and Sharland, 2016; Avent, Hansen, Gilks, et al, 2016). These protocols have to take into account several aspects including the local microbiology and resistance patterns, possible contraindications, toxicity, drug costs, elimination of agents with similar activity and no added benefit, side effects profile and other significant factors (Avent, et al, 2016; Fishman, 2006; Paskovaty, 2005). The overall benefits of having an antimicrobial protocol have shown the ability to retard resistance, reduce healthcare costs and drug-related adverse events while improving clinical outcomes (Avent, et al, 2016; Drew, 2009). The aim of the study was to evaluate the availability of antimicrobial protocols in the different wards and to investigate if available protocols are current and up-to-date. One of the functions of an ASP is to update the antimicrobial policies annually. The chief executive officer of DGMAH through the Pharmaceutical and Therapeutic Committee (PTC) requested the evaluation of existing antimicrobial protocols in the hospital, following inconsistencies and inappropriate antibiotic therapies. A need for antibiotic protocols which are up-to-date based on a systemic review, inclusive of assessment of quality identified studies, taking into consideration the levels of evidence and applicability to the local and national microorganism prevalence’s and susceptibilities was identified (Araujo Da Silva, et al, 2016; Schellack and Gous, 2011).

1.3 RESEARCH QUESTION

Were existing antimicrobial policies available and updated in line with the resistance patterns in different wards/units of DGMAH?

1.4 AIM OF THE STUDY

The aim of the study was to investigate the availability of recent antimicrobial policies in the different units/wards of Dr George Mukhari Academic Hospital, Gauteng Province.
1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To investigate the availability of antimicrobial policies in the hospital and review existing policies.
- To examine the antibiotic susceptibilities and resistance patterns in different wards of DGMAH.
- To compare the antimicrobial policies to the Essential Medicines List (EML), and antibiotic susceptibilities and resistance patterns seen at the hospital.

1.6 IMPORTANCE OR SIGNIFICANCE OF THE STUDY

The significance of this study was to aid in the identification of the wards/units, which have an outdated or no antimicrobial protocol present, and to identify the local prevalent microorganisms and their susceptibility patterns.

This study may assist the antimicrobial stewardship programme team with one of their important functions which is to update the antimicrobial protocols annually, formulation and implementation of the protocols, with quality assured laboratory data to develop antimicrobial policies that are in accordance with standard national and local treatment guidelines, advocating evidence based immunotherapy or combination therapy. This must include consideration of spectrum of antimicrobials, pharmacokinetic/pharmacodynamic principles, adverse effects, cost and special needs of individual patient groups.

1.7 OUTLINE OF THE DISSERTATION

This dissertation consists of six chapters. Chapter 1 serves as an introduction to the dissertation, which includes the background and rationale, the aim and objectives of the study. It also includes an overview of the significance of the study. Chapter 2 provides an extensive literature review pertaining to the study. Chapter 3 covers the methodology used in this study which includes study design, study population, materials, apparatus and instruments, data collection and analysis, data collection instruments, reliability and validity of the study, bias as well as the ethical considerations. Chapter 4 presents the results of the study. Chapter 5 is the
discussion of the discussion and interpretation of the key findings of this research, while Chapter 6, the final chapter includes a summary, limitations, recommendations and conclusion of the study.

1.8 SUMMARY

Chapter 1 has deliberated on the background and rationale for this study. The research question if there are existing antimicrobial policies available and updated in line with the resistance patterns in different wards/units of DGMAH, the aim was provided followed by a list of objectives. The importance and significance of the study was discussed. Literature review will be the cornerstone of Chapter 2, This literature will be pertaining to the study at hand.
2.1 INTRODUCTION

In this chapter, an overview of published literature on the study topic and previous research done in this particular field is provided. Section 2.1 serves as an introduction; Section 2.2 discusses the inappropriate use of antimicrobials and the emergence of resistance followed by Section 2.3 which mentions some of the factors which led to resistance and Section 2.4 which describes the resistance seen in South Africa. Section 2.5 includes barriers to effective implementation of antimicrobial stewardship. Section 2.6 describes antimicrobial stewardship and its principles. Section 2.7 is the summary of the chapter.

2.2 INAPPROPRIATE USE OF ANTIMICROBIALS AND THE EMERGENCE OF RESISTANCE

Antimicrobials play a major role in treatment and prevention of infectious diseases. However, their inappropriate widespread use often reduces their efficacy and leads to antimicrobial resistance. Antimicrobial resistance is currently a common phenomenon in many hospitals globally. Increased hospital stay, toxicity, emergence of antimicrobial resistance, increased morbidity and mortality and increased health care costs are some of the potential consequences of inappropriate use of antimicrobials (Raap, Kaye, Cano, Hermsen, DePestel, unknown year; WHO, 2014).

Various studies demonstrated that there is a causal relationship between inappropriate antimicrobial use and resistance, and that changes in antimicrobial use lead to parallel changes in the prevalence of resistance, though these cannot be measured or quantified due to several uncontrolled variables and methodological differences (Avent, 2016; Timsit, Harbarth and Carlet, 2014). Up to 50% of prescribed antimicrobials are regarded unnecessary (Holmes, Moore, Sundsfford, et al, 2016). The reduction in unnecessary antibiotic prescriptions through AMS has shown moderate decrease in resistance over the past decade (Holmes, et al, 2016).
Even though there is a clear demonstration of the association between antimicrobial use and emergence of resistance, this link is complex as there must be confounding factors, which include:

- The interaction between the microorganism and the antimicrobial
- The microorganism and host interaction
- Microorganism mutation rate
- The development of effective antimicrobial resistant clones
- Rate of transmission of the microorganism between humans and animals

There has been an emergence of pathogens which are resistant to all currently available antimicrobials. Antimicrobial resistance is the result of a variety of mechanisms, which include but is not limited to:

- Producing enzymes that inactivate or destroy the antimicrobial;
- Altering the antimicrobial target site to prevent the drug from binding;
- Changing the permeability of the cell wall to prevent antimicrobial access to the target site;
- Actively pumping the antimicrobial from the cell (Raap, et al, unknown year).

Raap, et al, (year unknown) further explained that the most troublesome bacterial pathogens encountered in hospital are the ESKAPE pathogens – Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species. These pathogens are often resistant to available antimicrobial agents and regularly cause hospital acquired infections. The mechanism of resistance of ESKAPE pathogens often confers resistance to more than one agent (i.e. multidrug resistance) (Raap, et al, unknown year).
Following exposure to antimicrobials, whether rationally prescribed or not and years of evolution, pathogens have developed resistant mechanisms to protect their biochemical targets which antimicrobials are directed against (Courvalin, 2016; Spellberg, Bartlett and Gilbert, 2013). Most, if not all target binding sites have been exhausted which makes it a challenge to bringing novel antimicrobials to the market. There have been some clinically significant modifications made to antimicrobials, which are already in the market, and there were only two novel classes of antimicrobials, which emerged in the past thirty years, daptomycin - a cyclic lipopeptide and linezolid - an oxazolidinone, and a recently discovered teixobactin (Abdul, 2010; Homma, Nuxoll Gandt, et al, 2016; Penesyan, Gillings and Paulsen, 2015; So, Gupta, Brahmachari, et al, 2011). All of which are active against gram-positive organisms while there has not been a novel gram-negative antimicrobial, clinicians are forced to rediscover old agents such as polymixins and fosfomycin (Harbarth, Theuretzbacher and Hackett, 2015; So, et al, 2011).

2.3 FACTORS WHICH LED TO RESISTANCE

The epidemic of antimicrobial resistance was initially paved by lack of understanding of the unique features and risks of resistance (Laxminarayan, Dus, Wattal, et al, 2014). Research done in countries such as the Democratic Republic of Congo, showed that 73.9% of prescribers use pharmaceutical companies as their first source of information. They receive information from company representatives, conferences for prescribers and distribution of drug information pamphlets (Thriemer, Katuala, Batoko, et al, 2013). The use of such information sources to guide therapy might contribute to resistance, as pharmaceutical companies are profit orientated and rely on sales for survival of their companies. Selective information and material incentives are offered in order to influence prescribers who end up being biased when prescribing appropriate antibiotics and tend to use broader spectrum agents (Thriemer, et al, 2013). Antibiotic guidelines were found to be the second important source of information with 63.6%. Other sources of information include university courses, internet and WHO guidelines (Thriemer, et al, 2013).

Other factors include the irrational use of antibiotics against viral infections, inappropriate duration of treatment, self-medication (where doctors prescribe
antibiotics because the patient has requested it) and inadequate infection control measures to prevent the spread of resistant bacteria in both the hospital and community (Thriemer, *et al*, 2013). The availability of antibiotics without prescription was seen in 19 countries of which most are developing countries such as Nigeria, Vietnam, Syria and Sudan, although there might be laws against the non-prescription use of antibiotics (Gelband, Miller-Petrie, Pant, *et al*, 2015; Morgan, Okeke, Laxminarayan and Perencevich, 2011). Five countries provide antibiotics on the internet without a prescription while in 12 countries antibiotics are brought from other sources than a pharmacy such as the black market or veterinary clinics (WHO-Europe, 2014). Patients may also obtain antibiotics from friends, family members and at home from a previous incomplete course of antibiotic therapy (Gelband, *et al*, 2015; Morgan, *et al* 2011).

Human beings and animals use similar types of antimicrobials. It is estimated that agriculture, aquaculture and farming use up to four-times the quantity of antimicrobials that is used for medical purposes (Food and Drug Administration Department of Health and Human Services, 2010). In agriculture, antimicrobials are used to promote growth, as animals, which have received antimicrobials in their feed, gain approximately five percent more body mass than those which did not receive antimicrobials (Witte, 1998). Growth promoter antimicrobials, which are closely related to compounds used in humans have the same mechanism of action and exert selective pressure, which results in cross-resistance to humans. Some examples include the related resistance seen between vancomycin and avoparcin, which have resulted in resistance seen with enterococci (Gastmeier, Schroder, Behnke, Meyer and Geffers, 2014; Van den Bogaard and Stobberingh, 2000; Witte, 1998). Colistin was used in agriculture since the 1950’s. Its resistance in retail slaughtered animals such as pigs and chicken was found to be plasmid mediated. This mechanism was found in *Escherichia coli* and *Klebsiella pneumoniae* isolates from hospitalised patients and there is an increasing spectre of untreatable colistin resistant strains (Malhotra-Kumar, Xavier, Das, Lammens, Butaye, Goossens, 2016; Paterson and Harris, 2016).
2.4 RESISTANCE SEEN IN SOUTH AFRICA

A pathogen is classified as susceptible when the isolates are inhibited by usually achievable concentrations of an antimicrobial agent. There might be an imprecision due to host responses (Eldenstein, 2007; Niveditha and Sujatha, 2015), toxin production by the bacteria, site of infection, effect of biofilm if present, drug pharmacodynamics and other factors. Reciprocally, a resistant pathogen implies that the isolates are not inhibited by usually achievable concentrations (Harris, Tambyah and Paterson, 2015; Levy and Marshall, 2004). The intermediate category implies that there is clinical efficacy in body sites where the drug is physiologically concentrated or when higher than normal doses are used as in the case of beta-lactams (Detecting Antimicrobial Resistance, 2016; Eldenstein, 2007).

Multidrug resistance, which is defined as resistance to three or more classes of antimicrobials has become common globally. Recently, South Africa (SA) is moving closer to extensive drug resistance (XDR) which is susceptibility to two or less classes as seen with Mycobacterium tuberculosis. There have been increasing reports of gram-negative XDR cases evidenced with Klebsiella pneumoniae, E.coli, Enterobacter spp as well as Salmonella spp (Brink, Feldman, Ricards, Moolman and Senekal, 2008; Maharaj, Ross, Maharaj and Campbell, 2016).

One of the earliest resistant organisms seen in South Africa is the methicillin resistant Staphylococcus aureus (MRSA) which was reported as early as 1978, with an unquantified outbreak, which took place between 1986-1987 in Johannesburg (Falagas, Karageorgopoulos, Leptidis and Korbila, 2013). The spread of resistance in SA is a challenge, mostly due to inadequate financing, infrastructure, medical equipment, medications as well as a shortage of trained professionals. The spread is worsened by suboptimal sanitation (Falagas, et al, 2013). The Gauteng province has the highest number of invasive and non-invasive disease cases in the country. In 2013, the number of multidrug resistant cases detected by surveillance audit by province was 423 in the Gauteng province, while the entire country was at 1397, meaning that the Gauteng province alone contributed 30.3% of resistance (GERMS-SA, 2013).
2.5 ANTIMICROBIAL STEWARDSHIP

The goal of Antimicrobial Stewardship is to optimise clinical outcomes, reduce health care costs, without adversely affecting the quality of life, and minimise unintended consequences. It can be defined as the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy in conjunction with infection prevention and control measures, to prevent or slow down the emergence of antimicrobial resistance and transmission of antimicrobial-resistant pathogens (Raap, et al, unknown year; File, Srinivasan and Bertlett, 2014). Antimicrobial stewardship is an effective way of ensuring the prudent use of antimicrobials (WHO, 2014). Irrational use of antimicrobials is a serious problem that is wasteful and harmful (Holloway and Dijk, 2011; Laxminarayan, et al, 2016). In primary care in developing countries, less than 40% of patients in the public sector and 30% of patients in the private sector are treated in accordance with standard treatment guidelines (Holloway and Dijk, 2011). Namibia did a similar study where 26.2% (286; 1090) prescriptions complied with the strict criteria of the country’s standard treatment guidelines (Akpabio, et al, 2014).

The overall goal must be to preserve the ability to treat serious infections. In some contexts, preserving the effectiveness of antimicrobial medicines means to use them less (WHO, 2014). By reducing the use of antimicrobials, we would mitigate the selection pressure and diminish the prevalence of resistant bacterial organisms (Hollis and Ahmed, 2013; Laxminarayan, et al, 2016). There was a paucity of novel antimicrobial agents in the research and development pipeline. In 2010, the Infectious Diseases Society of America (IDSA) have illustrated that there are only a few potential novel agents in the pipeline with added benefits over licenced antimicrobials and a few agents moving forward that will be effective against the ESKAPE pathogens (Harbarth, Theuretzbacher and Hackett, 2015 Raap, et al, unknown year; Spellberg, Bartlett and Gilbert, 2013).

The process involves developing a proposal to obtain institutional support for the ASP, assembling and leading the ASP core team. Analysing current institutional practices, developing processes to meet ASP goals, analysing and reporting data demonstrating the impact of ASP processes, and developing and implementing
outreach plans directed to key hospital staff (Araujo Da Silva, *et al*, 2016; Raap, *et al*, unknown year).

The multidisciplinary antimicrobial stewardship team should ideally be composed of an infectious disease physician, clinical pharmacist, clinical microbiologist, infectious disease nurse, hospital epidemiologist and administrative support personnel (Barlam, Cosgrove, Abbo, *et al*, 2016; Goff, 2011). The infectious disease specialist will be responsible for overseeing the overall functioning of the ASP and ensure that all the decisions are in accordance with evidence based clinical and practical feasibility (Sulema and Meyer, 2012). The clinical pharmacist should preferably have infectious disease training and will be responsible for promoting evidence-based medicine and cost effective prescribing due to the scarcity of infectious disease specialists in South Africa. According to the Health Professions Council of South Africa (HPCSA), 2016, there are only 59 infectious disease specialist registered in 2016. The reason for this scarcity might be that most clinician graduates do not select primary care specialities like internal medicine and paediatrics where they can subspecialise in infectious diseases (Goff, 2011; Van der Plas and Mendelson, 2011).

Clinical pharmacists with infectious disease training should take a prominent role because of their knowledge and influence over antimicrobial use. They actively participate in ward activities on a daily basis, reviewing prescription charts, and individualise and optimise patient treatment to improve patient outcomes (Raap, *et al*, unknown year; Wickens, *et al*, 2013). During the ward activities, the clinical pharmacist can also do a prospective audit with intervention and feedback which involves a daily evaluation of targeted antimicrobials for appropriateness, conducting therapeutic drug monitoring and if required, contact the prescriber with recommendations (Drew, 2009; WHO, 2014). In a resource limited country like South Africa and scarcity of infectious disease specialists, a dedicated infectious disease pharmacist can effectively lead the antimicrobial stewardship team and have shown improved adherence to recommended antimicrobial practices (Gorman and Slavik, 2016; Van der Plas and Mendelson, 2011).
2.6 BARRIERS TO EFFECTIVE IMPLEMENTATION OF ANTIMICROBIAL STEWARDSHIP

Initially, two core ASP strategies were used which include prospective audit with intervention and feedback (also known as a back-end programme). Antimicrobial use is reviewed after antimicrobial therapy has been initiated and recommendations are made as to their appropriateness in terms of selection, dose, route, and duration. In prior authorization (or front-end) programmes, antimicrobials are made accessible only through an approval process (Owens Jr, 2008; Pogotzelska-Maziars, Herzig, Larson, Furuya, Parencevich and stone, 2015).

There are several barriers that hinder the implementation and sustainability of effective programmes. They include but are not limited to lack of funding, leadership and commitment, failure to regularly update standard treatment guidelines and implement them well (Broom, Broom, Plage, Adams and Post, 2016; Nabyonga, Bataringaya, Bakeera and Criel, 2012). In countries such as Uganda, the national guidelines are often outdated and not circulated amongst prescribers who resort to using either outdated guidelines, habits of their teachers or use international but locally irrelevant guidelines (Nabyonga, et al, 2012).

Compliance to guidelines can be driven by both supply and demand. Physicians, apart from their medical training, are influenced by their peers and patients, which makes it exhausting to comply with the treatment guidelines (Apisamthanarak and Mundy, 2009; Broom, et al, 2016). Whilst on the demanding side, patients self-medicate with antimicrobials, which they might obtain without a prescription. Patients have a positive attitude towards antimicrobials, as it is their perception that antimicrobials treat most illness, but paradoxically lack knowledge about these drugs and disease conditions (Morgan, et al, 2011). Suboptimum compliance, which includes taking left over antimicrobials from a previous treatment and sharing of antimicrobials is also common (Zarb and Goossens, 2012).

2.7 ANTIMICROBIAL POLICY PRINCIPLES

Antibiotic policies have shown to improve quality of patient care and safety where they have been used in optimising therapy and reduce adverse effects and
treatment failures with increased cure rates (Pollack and Srinivasan, 2014). In a resource-limited country like South Africa, antibiotic policies can also help with procurement where certain agents on the policy will be prioritised with the limited budget, with less treatment failures; there will be cost savings for the institutions. Antibiotic policies also complement existing guidelines, making it easier for the physician to make a decision when faced with multiple options and this can save time (Gould and Meer, 2008; Pollack and Srinivasan, 2014). The antimicrobial policy should be adapted for local needs with modifications based on various parameters which may include prevalent resistance and susceptibility patterns, cost analysis done, the outcome expected, the methods used for analysis and how recommendations were formulated (Acevedo, 2015; Leekha, Terrell and Edson, 2011). Depending on whether the policy is for prophylaxis (to prevent acquisition of infection), empirical (infective organism is unknown) or curative/definitive therapy, it should include recommendations for special population groups such as: paediatric patients, immunocompromised, hospital and community acquired infections (Leekha, Terrell and Edson, 2011). The policy should be based on the spectrum of activity (with the narrowest spectrum possible), pharmacokinetics and pharmacodynamics of these agents, adverse effects, potential for resistance, special needs of the individual patient groups and cost (Leekha, Terrell and Edson, 2011; Llewelyn, Hand, Hopkins and Walker, 2014; MacDougall and Polk, 2005).

The antimicrobial recommended should be effective against pathogens often seen locally. Information on optimal selection, dosage, route of administration, duration, and alternatives for allergy to first-line agents; adjusted dosage for patients with impaired liver or renal function should be provided (Acevedo, 2015; Duguid and Cruickshank, 2010; Leekha, Terrell and Edson, 2011). Surgical prophylaxis can be defined as specific procedures for which antimicrobials are needed. Optimal agents, dosage, timing, route and duration of administration should be considered. Recommendations should focus on specific clean as well as contaminated procedures (Sample Antimicrobial Stewardship Policy for a Local Health District or Network, 2014). Upon implementation, the policy should be reviewed by experienced peers, who are not members of the policy development team, but are experts in the relevant field
(Leekha, Terrell and Edson, 2011; Sample Antimicrobial Stewardship Policy for a Local Health District or Network, 2014).

A multidisciplinary team consisting of six to ten members must perform the following functions: develop a policy, monitor the implementation of the policy, receive feedback, assess the outcomes and discuss them with the clinicians. The policy needs to be updated annually (Pollack and Srinivasan, 2014; WHO, 2011). Other important functions of the multidisciplinary team include dose and regimen alteration, streamlining and sequential therapy, discontinuation of antimicrobials, advice as a result of therapeutic drug monitoring, automatic stop orders for antimicrobial prophylaxis, restricted antimicrobials, assistance in the interpretation of laboratory results, indication for use of specific antimicrobials (Leekha, Terrell and Edson, 2011; Pollack and Srinivasan, 2014).

Reliable data on antimicrobial resistance for important pathogens of public health importance is an essential pre-requisite for developing appropriate guidelines for use of antimicrobials, in order to reduce and de-escalate from broad-spectrum to narrower-spectrum targeted therapy (Llewelyn, et al, 2014; Srivastava, 2011).

Antimicrobial stewardship programmes (ASP) include antimicrobial policy structures, which consists of prescribing strategies to optimise the indication, selection, dosing, route of administration, duration and timing of antimicrobial therapy to maximise clinical cure or prevention of infection whilst limiting the unintended consequences of antimicrobial use, including toxicity. A secondary goal is to reduce healthcare costs without adversely affecting the quality of care (Gyssens, 2011; Llewelyn, et al, 2014). Najmi and Aiman (2013) explained that an antimicrobial policy should be revised each year, based on the national guidelines and susceptibility reports of the microbiology laboratory as this will help with the ASP in the following ways:

- It will improve patient care by promoting the best practice in antimicrobial prophylaxis and therapy.
- Make better use of resources by using cheaper drugs where possible.
- Retard the emergence and spread of multiple antimicrobial-resistant bacteria.
• Improve education of junior doctors by providing guidelines for appropriate therapy to eliminate the use of unnecessary or ineffective antimicrobials and restrict the use of high-cost and second-line antimicrobials.

2.8 SUMMARY

This chapter focused on the review of literature relating to this study. It gave an insight into the potential consequences of inappropriate antimicrobial use, mechanisms of resistance to antimicrobials and the emergence of multiple drug resistance. Events that led to initial resistance to antimicrobials were discussed briefly followed by resistance seen in South Africa. It went on to define antimicrobial stewardship, its overall goal and secondary goals. Core antimicrobial stewardship strategies were discussed including the team members and barriers that hinder the implementation and sustainability of effective programmes. The next chapter will focus on the methods used to conduct this research.
CHAPTER 3:  
METHOD

3.1 INTRODUCTION

This chapter describes the methodology used to conduct this study. In Section 3.2, the study design is discussed. The study site, the study population and data collection instruments as well as the data collection process is discussed in the following sections. Data entry and analysis are described as well as methods put in place to ensure the reliability and validity of the data. The chapter ends with a discussion of bias and the ethical considerations for this study.

3.2 STUDY DESIGN

This study was a prospective, quantitative, observational study, with data collected over 13 months from June 2015 until June 2016. Two consecutive months were spent per department. The data was analysed descriptively.

3.3 STUDY SETTING

Doctor George Mukhari Academic Hospital (DGMAH) is a 1652-bed tertiary health institution. It has 39 wards, which comprises of nine clinical departments, including adult ICU, neonatal ICU, paediatrics, obstetrics and gynaecology, renal unit, spinal clinic, psychiatry, surgical and internal medicine wards (Shelembe, 2015). It is the second largest hospital in Africa, located in the north of Pretoria, near the township of Ga-Rankuwa 30km’s from the city of Tshwane (Mabuza, Omole, Govender, and Ndimand, 2014).

3.4 DATA COLLECTION INSTRUMENTS

Data collection tool

Previous and current antimicrobial policies, which are

AIM: The researcher obtained existing antimicrobial protocols by going to each ward in the hospital and asking
available in the wards/units.

the sister in charge or the physician for a copy of the protocol which they keep in the ward.

Rationale: To evaluate protocols by comparing them to current available guidelines, namely the latest national standard treatment guidelines and any other guideline used in the ward.

Current Essential Medicines List (EML) and any other prescribing tools used in the hospital wards.

AIM: These are the tools, which were used to compare to the antimicrobial policies/protocols in order to evaluate if these policies or protocols are in line with the national guidelines.

Rationale: To parallel the local policies/protocols with the national guidelines such as the EML, which was developed by the South African National Department of Health (NDoH). This list has been aligned with current developments in medicine and scientific advances and clinical evidence was used in the selection of these medicines. The relation between the EML and local policies/protocols were an indication of how well the hospital is keeping up with the pace of changes in health care and incorporating the two to achieve positive health outcomes for patients and minimising the progression of resistance.

Antibiogram results from the National Health Laboratory Service (NHLS) database situated in the hospital.

AIM: Antibiogram reports was used to show the results of antimicrobial susceptibilities i.e. susceptible, intermediate or resistant by means of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) interpretative criteria. This laboratory tests were done for the susceptibility of isolated bacterial strains to different antimicrobials. Antimicrobials, which the isolates had inherent resistance against, were automatically excluded.
By definition, an antibiogram test is an in vitro study, but the correlation of in vitro to in vivo susceptibility is often high enough for the test to be clinically useful.

Rationale: Was to obtain antibiogram data from the (NHLS) on frequent susceptibilities and resistance patterns seen in the hospital. This was done on a daily basis, with the researcher spending two months per department (surgical, ICU, Paediatric ward etc.), identifying patients on antimicrobials to see if any microbiology tests were requested. If so, the information would be recorded on the data collection sheet (Appendix 2). This was done in order to allow the researcher to evaluate existing antimicrobial protocols, which were compared to current available guidelines and then relate them to the local prevalence and susceptibilities seen in the hospital.

**Data collection forms:**

**Appendix 1: Data collection questionnaire**

This tool was used to record the ward/unit number, if an antimicrobial policy was available, the last date of review and if they are in accordance with the latest guidelines or not, it was designed based on the objectives of the study and validated via the pilot study.

**Appendix 2: Prevalence and susceptibility in different wards**

This tool was used to capture antibiogram test results data from the NHLS and illustrates the bacterial strains that are frequent in the specific ward, susceptibilities and the source of specimen. This data collection tool was designed based on both the NHLS microbiology laboratory report (excluding patient demographics information) and it was lined up with the objectives of this study.
Chapter 3: Method

Pilot Study

Reliability and validity of the collection instruments was tested during the pilot study: A pilot study was conducted in the Neonatal ICU using appendix 1 (data collection questionnaire), where the antibiotic policy was obtained from the ward and all the required information was recorded on the questionnaire. Appendix 2 (prevalence and susceptibilities in different wards), five antibiogram results were recorded on this appendix so that we can determine what changes are needed to make sure that the data collected meets the objectives of this study. The pilot study measured the stability, internal consistency and equivalence of the instruments. No amendments were made to the data collection instruments subsequent to the pilot study.

Sampling

A census sampling method was used when collecting policies, meaning that every ward of the hospital was visited. Purposive sampling was utilised when obtaining antibiogram results. Only patients with positive antibiogram results were included in this study.

Inclusion criteria

- Patients who were admitted from June 2015 until June 2016
- Presented with or suspected of having an infection
- Was on antibiotics and antibiogram data was requested
- Antibiogram results, which have an isolated organism.

Exclusion criteria

- Patients who were admitted outside the study period (between June 2015 and June 2016)
Chapter 3: Method

- Antibiogram results, which did not isolate any microorganism
- Antibiogram results which isolated viruses or fungal organisms
- Antibiogram which only isolated mycobacteria
- Duplicate cultures from the same episode, with the same organisms.
3.5 DATA COLLECTION PROCESS

**Collection of protocols**

- The researcher visited all the wards in the hospital where data on availability of antimicrobial policies and protocols was obtained.
- The wards which did not have any policies were asked for the guidelines which are used in place of a policy.
- This information was recorded on the data collection tool (appendix 1).

**Collection of antibiogram data**

- The researcher spent two months collecting data per department, as shown on the data collection timeline illustrated below. Data from the renal unit and spinal clinic was collected simultaneously, in one month. The psychiatric wards data was also collected in one month due to the low level of requests for antibiogram data.
- An additional month was spent at the surgical wards due to its extensive number of wards.
- Microbiology tests for individual patients were identified by reviewing the patient files.
- The specimen reference were obtained from the patient files to attain the microbiology test results on the National Health Laboratory Service (NHLS) system of the hospital.
- Appendix 2: prevalence and susceptibility in different wards was used to capture these results.

**Figure 3.1: Data collection process**
### 3.6 ANALYSIS

**Statistical Package for the Social Sciences - SPSS® statistical software**  
This statistical tool was utilised for descriptive statistics to summarise the antibiogram data. Numerous category codes were generated to easily group the data and identify the distribution of frequent bacterial isolates and drug susceptibilities. This data was captured on an

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<td>Surgical Wards</td>
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<td>Spinal and Renal unit</td>
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**Figure 3.2: Data collection time line**
Excel™ spreadsheet to be analysed descriptively using percentages.

**Microsoft Excel™ 2010** This tool was used to capture the data collected from the wards, by transferring the information from Appendix 1 (data collection questionnaire) and Appendix 2 (prevalence and susceptibility in different wards) onto the Excel spreadsheet. Data was utilised again for descriptive statistics using percentages and to construct the graphs after running the data through the SPSS statistical software. The susceptibility percentage of each antimicrobial was calculated and reported per isolates, after grouping isolates from the same genus family together.

The researcher will make the necessary recommendations to update the antimicrobial policies in accordance to the Essential Medicines List (EML), frequent susceptibilities and resistance patterns seen at the hospital. The policy should be simple, clear, clinically relevant, flexible and applicable to day-to-day practice and available in user-friendly format.

### 3.7 RELIABILITY AND VALIDITY

Reliability is the consistency of a measurement, or the degree to which an instrument measures the same way each time it is used under the same condition with the same subjects. In short, it is the repeatability of a measurement (Fogelholm, Leppinen, Auvinen, Raitanen, Nuutinen and Vaananen, 2012). The researcher recorded the data from the patients’ antibiogram report and no alterations were made. Whenever necessary, it is possible to access these records and assess the reliability of the data. The researcher did not alter the susceptibility report of microorganisms that was obtained from the NHLS in anyway and such reports are available, therefore another researcher can obtain the same results should these records be made available to him/her.
Validity refers to the extent to which a research design is scientifically sound or appropriate (Struwig and Stead, 2009). A pilot study was conducted in the Neonatal ICU of DGMAH using appendix 1 (data collection questionnaire), where the antibiotic policy was obtained from the ward and all the required information was recorded on the questionnaire. Appendix 2 (prevalence and susceptibilities in different wards) was used to record data on prevalent organisms and their susceptibilities. This allowed the researcher an opportunity to become familiar with the data collection procedure, materials and apparatus, as well as an option to make the necessary amendments if needed.

For the purpose of ensuring that the claims made about the availability of antimicrobial policies in the wards were valid, the researcher has visited each ward in the hospital to obtain these policies and also obtained a distribution list of these policies from the Pharmaceutics and Therapeutics Committee (PTC). This research claimed to demonstrate the most frequent susceptibility and resistance patterns seen in the hospital. These were validated by the actual laboratory test records, collected from different wards.

Validity can be either internal or external. Internal validity refers to the extent to which the study design and data obtained allowed the researcher to draw accurate conclusions about the associations within the data (Leedy and Ormrod, 2001). External validity refers to the extent to which the results obtained during the study could be generalized to other contexts (Leedy and Ormrod, 2001).

3.8 BIAS

Bias is defined as any tendency that prevents unprejudiced consideration of a question. In research, bias occurs when one outcome or answer over another is selected by introducing systematic error into sampling or testing. Bias can occur at any phase of research, including study design or data collection, as well as in the process of data analysis and publication (Pannucci and Wilkins, 2011). In this study, duplicate isolates were excluded to minimise bias due to over-representation as some patients required microbiology cultures to be performed more than once, unless different organisms were identified. Length bias might have occurred in this study as data depends on the prevalence during the period at which the researcher...
was collecting data at that particular ward or department. The protocol methodology was strictly followed and there were no deviations.

3.9 ETHICAL CONSIDERATIONS

Permission to perform the study was obtained from the Chief Executive Officer (CEO) of Dr George Mukhari Academic Hospital (DGMAH) (Appendix 3). Ethical clearance was obtained from the Sefako Makgatho Health Sciences University Research and Ethics committee (SMUREC). (Protocol reference number - SMUREC/H/127/2015: PG) (Appendix 4). Patient consent was not required as patient data was not utilised during the study, Confidentiality was ensured as patients’ personal information was not used, only the NHLS track number was obtained from the patients file to retrieve antibiogram results and this was recorded on a data collection sheet (Appendix 2) without information which lead to the patient. Patient data cannot be linked back to the patient.

3.10 SUMMARY

This chapter has described in detail the methodology used to conduct this research, which was a prospective, quantitative, observational descriptive study. It took place in all 39 wards of DGMAH, including psychiatry, ICU and the renal unit where antimicrobial policy availability was evaluated and compared to the current national guidelines. Materials used, which included data collection questionnaires, antimicrobial policies, antibiogram data, current essential medicines list and other prescribing tools were discussed. Data collection and analysis methods were explained together with reliability and validity of the study. Bias and ethical considerations concluded the chapter. Chapter 4 will present the results obtained in this study and the discussion of these results.
CHAPTER 4:
RESULTS

4.1 INTRODUCTION

Results based on the data collected during this study are presented and described in this chapter. Section 4.2 reports on the data obtained from the policies. Section 4.3 and 4.4 reports on the organism prevalence and antibiotic susceptibility respectively and includes graphs and tables, with a brief description of the reported figures. Section 4.5 is the last section, which is the summary of the chapter.

4.2 POLICIES

Between June 2015 and June 2016, data was collected from a total number of 39 wards, which consisted of 16 surgical wards, six paediatric wards, the neonatal ICU, the adult ICU, seven internal medicine wards, four obstetrics and gynaecology wards, the renal unit, the spinal clinic, and the psychiatric wards. From these wards, there were six (15.4%) antimicrobial policies/protocols present. From the six, which were obtained, only one (2.6%) was current and up to date. The remainder of the wards (33 wards) were using the standard treatment guidelines from the National Department of Health, some the 2012 version, while others were using the mobile application which contains the primary health care standard treatment guidelines and essentials medicines list for 2015 (NDoH, 2016).

4.3 ORGANISM PREVALENCE

Non-duplicate specimen results data from 39 wards was obtained, and a total number of 346 results were recorded. The source of the samples were as follows: swab (including wound, abscess, superficial) 34.7% (120), urine 24.9% (86), blood culture 23.7% (82), aspirate (tracheal, wound) 8.1% (28), sputum 5.5% (19), tissue 2.0% (7), 0.3% for CSF (1), intravenous catheter tip (1) and ventriculo-peritoneal shunt (1) respectively.

During the 13 months of data collection, two months was spent in each department, with the exception of three departments, namely psychiatry, renal unit and spinal
clinic where data was collected over one month and the surgical department, where data was collected over three months. There were 371 organisms identified, which were isolated from all nine departments. The distribution of these organisms is illustrated on Figure 4.1 reporting separately on the ICU organisms in order to show the differences and similarities between the adult and neonatal ICU. This decision was influenced by several publications indicating that more organisms in the ICU settings are multi-drug resistant to antibiotics compared to general wards (Adrie, Garrouste-Orgeas, Essaied, 2016).

**Figure 4.1: The distribution of organisms**
Figure 4.2: Prevalence of organisms in the general wards

Figure 4.2 demonstrates the organisms, which were prevalent during a two-month period in each of the general wards, identifying 293 organisms. Within the paediatric wards, 20 *Staphylococcus* spp were isolated (6.8%), seven isolates of *Streptococcus* spp (2.4%), *K. pneumoniae* and *Enterococcus* spp had six isolates (2%) each, followed by five *E.coli* isolate (1.7%).

In the internal medicine wards, the reported *Staphylococcus* spp during the two-month period were 20 (6.8%). *K. pneumoniae* and *P. aeruginosa* were both isolated seven times (2.4%) followed by *Enterococcus* spp and *E.coli* which were isolated six times (2%). In the surgical wards, the data collection period was three months, as the surgical department has more wards. There were 33 isolates of *Staphylococcus* spp (11.3%), 21 isolates of *E. coli* (7.2%), *P. aeruginosa* isolates were 18 (6.1%), while *Klebsiella* spp (includes *K. pneumoniae* and *K. oxytoca*) were 16 isolates (5.5%) and *Enterococcus* spp (Includes *E. faecium, E. faecalis and E. gallinarum*) were 11 isolates (3.7%).

In the obstetrics and gynaecology wards, nine isolates of *K. pneumoniae* (3%) were found, followed by five *Enterococcus* spp (1.7%), three isolates of *E. coli* (1%),
*Streptococcus* and *Citrobacter spp* were also prevalent both with five isolates (1.7%).

The prevalent organisms isolated in the renal unit, spinal clinic and psychiatric wards rendered only 15 positive results, which was collected over one month per unit, since there were few requests for cultures. In the renal unit nine organisms were isolated, the most prevalent being *M. morganii* and *Staphylococcus spp* with two isolates each. In the spinal unit the most prevalent organisms were *K. pneumoniae* and *P. mirabilis* both with two isolates (13.3%). The only isolate found in the psychiatric wards during the data collection period was *S. aureus*.

![Graph showing prevalence of organisms in ICU](image)

**Figure 4.3: Prevalence of organisms in ICU**

Figure 4.3 compares the prevalent isolates in both the Adult ICU and the Neonatal ICU, where data was collected for two months respectively. In the adult ICU, *Enterococcus spp* (*E. faecium* and *E. faecalis*) was the most prevalent with six isolates (9.5%), *K. pneumoniae* and *A. baumannii* both had five isolates (7.9%), and *Staphylococcus spp* three (4.8%). In the neonatal NICU, the most prevalent organisms were *K. pneumoniae* and *S. marcescens* both with eight isolates (12.7%), followed by three isolates of *Staphylococcus spp* (4.8%).
A total of 371 isolates (N=371) were found during the study period. The distribution of these organisms based on their gram staining classification was calculated and 57% (212) were gram-negative.

### 4.4 ANTIBIOTIC SUSCEPTIBILITY

![Figure 4.4: Antibiotic susceptibility](image)

Figure 4.4 illustrates the susceptibility percentages of antibiotics in the hospital as reported by the NHLS. A total of 2258 antibiotics were tested against the 371 organisms.

Folic acid synthesis inhibitors, e.g. trimethoprim-sulfamethoxazole, had the lowest susceptibility, followed by cell wall inhibitors (beta-lactam-penicillins). Vancomycin reported 100% susceptibility.
Chapter 4: Results

Figure 4.5: Antimicrobial susceptibility of gram-positive organism

Antimicrobial susceptibility against gram-positive organism (Staphylococcus, Enterococcus and Streptococcus spp) are depicted in Figure 4.5. with their respective susceptibilities to ampicillin/amoxicillin, vancomycin, cloxacillin, erythromycin/azithromycin, clindamycin and trimethoprim-sulfamethoxazole.
Figure 4.6: Antimicrobial susceptibility of gram-negative organism

Figure 4.6 shows the antimicrobial susceptibility against gram-negative organisms Klebsiella spp, Enterobacter spp and Pseudomonas spp, A. baumannii, E. coli and S. marcescens together with their respective susceptibilities to ciprofloxacin, amoxicillin-clavulanic acid, piperacillin/tazobactam, amikacin, imipenem and trimethoprim-sulfamethoxazole.

4.5 SUMMARY

In this chapter, the results of the data collected over 13 months between June 2015 and June 2016 were reported for the 39 wards of DGMAH. The data was reported for nine departments starting with the availability of antibiotic policies, followed by
use of graphs, showing the prevalent organism in the wards or units and their respective antibiotic susceptibility.
CHAPTER 5:

DISCUSSION

5.1 INTRODUCTION

The results from chapter 4 are discussed in this chapter. Section 5.2 is the discussion of the policies which were either present and current or not, Section 5.3 and 5.4 discusses prevalent organisms and antibiotic susceptibility respectively. Section 5.5 is the last section which is the summary of the chapter.

5.2 POLICIES

Antimicrobial policies aid, rationalise and reduce antimicrobial use, which results in retardation of antimicrobial resistance progression and cost savings (Gant, 2001; Visschers, Backhans, Collineau, et al, 2015). Policies should be relevant to a particular setting for eradication of common infections without driving selection pressure for resistance through dependence on a few key antibiotics, which are regarded as first-line (Shallcross, Howard, Fowler and Davies, 2015). Every department or ward should have its own antimicrobial policy in addition to a formulary, which acts as a passive tool to ensure rational prescribing. Investigating this principle in a South African teaching hospital, DGMAH, only six out of 39 wards had an antimicrobial policy, meaning that the availability of relevant antimicrobial policies is 15.4%. Out of the six policies available, only one from the adult ICU was current and up-to-date, denoting that the hospital has a 2.6% availability of up-to-date antimicrobial policies.

The wards that did not have policies were using the standard treatment guidelines and essential medicines list from the South African National Department of Health. The 2012 version was the only version available in the adult wards while the paediatric wards were using the hospital level paediatrics 2013 version of the guidelines. A selected few prescribers in the different wards were using the mobile application which contains the primary health care standard treatment guidelines and essentials medicines list for 2015. This application includes a searchable list of the latest guidelines, decision-support tools and a directory service (NDoH, 2016).
The absence of antimicrobial policies was attributed to nationally available formularies in the form of standard treatment guidelines (2013 for the paediatric guidelines and 2012 for adults, which were found in the wards). These guidelines offer the prescriber a number of choices available for a variety of clinical conditions, enabling the prescriber to make a selection on antimicrobials based on clinical grounds, and other factors (Akpabio, *et al.*, 2014; Emmerson, 2000). Policy makers also lack evidence about the generalisability, effectiveness and cost-effectiveness of these initiatives as they fail to properly implement the policies, target prescribing behaviour, conducting surveillance and antimicrobial use data to ensure accountability, regularly updating the policy using evidence based data (Dar, Hasan, Schulundt, *et al.*, 2016).

However, no single formulary will suit all hospitals and all departments or wards, which is why it is crucial for antimicrobial policies to be adopted for a certain department (Gelband and Laxminarayan, 2015). Antimicrobial resistance patterns and frequent organisms vary from time to time and based on the settings of a specific area. An example will be pathogens prevalent in a tropical rural area might have different susceptibilities to antimicrobials when compared to pathogens prevalent in an urban area of another province. What is observed nationally does not always reflect locally (Essak, Connolly and Sturm, 2005; Gelband and Laxminarayan, 2015). An effective policy must be updated annually and relevant to the type of patients admitted. It should guide, educate and essentially lead to improvements in patient care while achieving acceptability to both the population and stakeholders from the regulatory, political, technical and financial environments (Akpabio, *et al.*, 2014; Dar, *et al.*, 2016; Emmerson, 2000).

Patients admitted to the intensive care units are at greater risk of hospital-acquired infections than patients in the general wards, hence it is important for these wards to have a policy (Gant, 2001; Sharma, Mamoria and Jain, 2016). As mentioned, the adult ICU had a current antimicrobial policy, which was relevant to the national guidelines, as well as to the local frequent organisms and resistance patterns. The Neonatal ICU had an outdated policy which was last reviewed in 2013. This policy is nonetheless in accordance with the national guidelines and local prevalent organisms and resistance patterns (NDoH, 2012; NDoH, 2013).
Chapter 5: Discussion

The obstetrics and gynaecology department had several protocols and seven of these protocols involved antimicrobials. They were updated in August 2013 and they are not in accordance with local resistance patterns obtained from our study. As seen with the high resistance to beta-lactam penicillins, especially amoxicillin and ampicillin, which are still included in treatment regimes, although they were showing high resistance. Without knowledge of the prevalence and resistance patterns, it is impractical to develop appropriate, evidence-based guidelines and policies (Bamford, Brink, Govender, et al, 2011; Friedlander, Haznoun and Aghazadehsanai, 2015).

5.3 ORGANISM PREVALENCE

The prevalent organisms in the hospital are described separately under the general wards (paediatrics, internal medicine, surgical and obstetrics and gynaecology wards, psychiatric, renal unit and spinal clinic) and ICU’s – intensive care unit (adult and neonatal ICU’s). The data was collected over a period of 13 months. It is noteworthy to take into consideration that two months was spent in each department, with the exception of the surgical wards (three months) the renal unit, spinal clinic and psychiatry wards (one month) since few requests for microbial cultures were seen in these departments.

A total of 371 (N=371) organisms were isolated in the different departments collectively over the study period. The distribution of these organisms based on their gram staining classification showed a higher prevalence of gram-negative organisms at 57% (212). The general wards isolated 308 organisms where 54.4% were gram-negative, while there were 63 organisms isolated in the ICU of which 69.8% were gram-negative organisms. A study done in China reported that the general wards had 93.6% of gram-negative organisms while the ICU had 89.0% gram-negative organisms (He, Luo, Hu, Li and Niu, 2014). In South Africa, a similar study done in a Cape Town tertiary hospital has reported that gram-negative organisms were 59.8% in the general wards and 56.8% in the ICU. Both of these studies concur with the findings of our study where gram-negative organisms were more prevalent (McKay and Bramford, 2015).

General wards
Chapter 5: Discussion

The most frequent organism cultured in the hospital’s general wards is *Staphylococcus* spp, which include *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*. This prevalence correlates with that seen in Cape Town, South Africa (McKay and Bramford, 2015). Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified by means of resistance to cloxacillin, and constituted 5% of frequent *Staphylococcus* spp in the hospital. Ramsay, Muckart and Han (2013), explained that this low prevalence was due to lack of exposure to antibiotics in the general population, deduced from their cohort study done in Durban, South Africa.

The paediatric wards organism prevalence are illustrated in Figure 4.2, and has reported that *Staphylococcus* spp was the most prevalent organism in these wards followed by *Streptococcus* spp. Both *K. pneumoniae* and *Enterococcus* spp were equally present as the third most prevalent organisms in the paediatric wards. A similar study conducted in a western African teaching hospital in Ghana, also excluding neonates, showed a high prevalence for *Staphylococcus* spp, in accordance with our study as the most prevalent organism. The second most isolated organism in their study was *Salmonella* spp, which was different from this study, where *Salmonella* spp were not isolated at all in the paediatric wards during the study period (Obeng-Nkrumah, *et al*, 2016). This shows that guidelines used in other countries do not necessarily apply to our country, even though we are on the same continent as seen with *Salmonella* spp.

Locally, in South Africa, a study conducted at Tygerberg children’s hospital in Cape Town, excluding the neonatal wards has reported that *Klebsiella* spp was the most prevalent organism, followed by *Staphylococcus* spp. *Enterococcus* spp was not part of the top five most prevalent organisms (Dramowski, Cotton, Rabie and Whitelaw, 2015). This further elaborates the statement made by Gelband and Laxminarayan (2015) that prevalence and resistance patterns will differ from region to region, even though those regions are in the same country or province.

The internal medicine wards revealed that *Staphylococcus* spp was the most prevalent organism, followed by *K. pneumoniae* and *P. aeruginosa*, which both had seven isolates, while *Enterococcus* spp and *E. coli* had six isolates. Several similar studies on the African continent have been done. One study done in the internal
medicine wards of a tertiary hospital in Rwanda found *E. coli* as the most prevalent organism followed by *Klebsiella* spp and *Staphylococcus* spp (Ntirenganya, Manzi, Muvunyi and Ogbuagu, 2015). A study done in Cape Town showed *Staphylococcus* spp and *E. coli* as the most common isolated organisms, soon followed by *K. pneumoniae*, *Enterococcus* spp and *A. baumannii* (McKay and Bramford, 2015). From these results, it can be deduced that gram-negative organisms are more prevalent than gram-positive organisms in the African continent while it is the opposite in the United States where there is challenge with high prevalence of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium* and drug-resistant *Streptococcus pneumoniae* (Munita, Bayer and Arias, 2015).

In the surgical wards, *Staphylococcus* spp was the most prevalent organism, followed by *E. coli*, *P. aeruginosa* and *Klebsiella* spp (*K. pneumoniae* and *K. oxytoca*). A study conducted in a secondary non-teaching hospital in Northern India reported that the most prevalent organisms in descending order were *A. baumannii*, *Enterococcus* spp and *E. coli*. In contrast to what were found in DGMAH, *Staphylococcus* spp was not the most prevalent organism in the surgery department in Northern India (Ginawi, Saleem, Sigh, et al, 2014). A study done in Cape Town, concurred with these results as it showed *E. coli* and *Klebsiella* spp as the predominant organisms in general surgical wards (McKay and Bramford, 2015). It is known that 30% of healthy humans carry *S. aureus* on their skin and nasopharynx. If the incorrect sampling technique is used to collect the sample, it might show a positive result for *Staphylococcus* spp, which may not be pathogenic, so sample collection technique, should be reviewed in this ward (Cashin-Garbutt, 2016).

The prevalent organisms in the obstetrics and gynaecology wards included nine isolates of *K. pneumoniae*, followed by five isolates of *Enterococcus*, *Streptococcus* and *Citrobacter* spp (including *C. youngae*, *C. freundii* and *C. koseri*). A retrospective study collecting data from a Greece teaching hospital over a calendar year including 761 women was done and *E.coli* was the most prevalent organism, followed by *Streptococcus* spp, *Enterococcus* spp and *K. pneumoniae* (Tansarli, Skalidis, Legakis and falagas, 2016). A study done at an academic hospital in Cape
Town reported *A. baumannii* as the most prevalent organism, while other isolates included *Klebsiella spp* and *Pseudomonas spp* (McKay and Bramford, 2015). These results show that *K. pneumoniae* is an important organism in these wards.

The prevalent organisms seen in the renal unit, spinal clinic and psychiatric wards are part of the general wards and they are not illustrated on the graph as they have been categorised as minor wards by the researcher as depicted on Figure 4.1, based on their size (number of beds) and the frequency of antibiogram requests.

The renal unit has reported two isolates for both *M. morganii* and *Staphylococcus spp* followed by a single isolate of *Enterobacter spp*, *Enterococcus spp*, *E. coli*, *P. mirabilis* and *S. agalactiae*. *M. morganii* is part of the gram-negative organisms believed with increased incidence of peritonitis as a consequence of recent decrease in gram-positive peritonitis (Kitterer Latus, Alscher and Kimmel, 2016). An academic hospital in Bloemfontein conducted a study on catheter-related bloodstream infections in the nephrology unit where *Staphylococcus spp* was the most prevalent, followed by *Enterococcus spp* and *Enterobacter spp* (Bisiwe, Van Rensburg, Barrett, Van Rooyen, and Van Vuuren, 2015). These results are similar to our study as they are both in agreement that *Staphylococcus spp* is the most prevalent organism although there was no indication of *M. morganii* in the study conducted at Bloemfontein.

Only five organisms were isolated from the spinal unit and they are as follows; *K. pneumoniae* and *P. mirabilis* both with two isolates, while *E. coli* had one isolate. Extensive research has not been done with respect to prevalent organisms in spinal units, and the researcher could not find a similar recent study. A study conducted in San Diego, California on children with cerebral palsy after spinal fusion surgery, reported *E. coli* as the most prevalent organism, followed by *Pseudomonas spp*, *Staphylococcus spp* and *Proteus spp* (Sponseller, Jain, and Shah, *et al*., 2013). As seen from the two studies, it can be deduced that gram-negative organisms are the most frequent causative pathogens in these wards.

Only one organism, namely *S. aureus* was isolated from the psychiatric wards during the data collection period. According to Moftah, Kamel and Attia, *et al*., (2013), most patients in the psychiatric wards have skin infections with the most common
cause of bacterial infection Acne vulgaris and pyogenic infections (which are most frequently caused by \textit{S. aureus}). A study done at DGMAH reported that 80-90\% of intravenous drug users have positive \textit{S. aureus} cultures and this concurs with our isolated organism (Henema, 2015).

\textit{Intensive care units (ICU)}

The ICU setting is usually associated with high rates of multi-drug resistant organisms (Pappa, Sarris, Pavlou and Eforakopoulou, 2015). Figure 4.3 has compared the prevalent organisms in both the adult and neonatal ICU collected over a period of two months per ICU.

In the Adult ICU, the most prevalent organism during the two-month study period was \textit{Enterococcus spp} with six isolates, \textit{K. pneumoniae} and \textit{A. baumannii} both with five isolates, \textit{Staphylococcus spp} were three. No \textit{S. marcescens} was isolated in this ward. These results did not vary much with a similar study done at a tertiary hospital in Cape Town, which revealed \textit{A. baumannii} as the most prevalent organism, followed by \textit{Klebsiella spp} (McKay and Bramford, 2015). Another study done at an academic hospital in Johannesburg, reported \textit{P. aeruginosa} as the most common isolated organism in their ICU, which is in contrast with the results of this study as \textit{P. aeruginosa} was not part of the top five prevalent organisms. Other organisms, which are in accordance with this study included \textit{Klebsiella spp}, \textit{A. baumannii} and \textit{Staphylococcus spp} (Pillai Yazicioglu and Moeng, et al, 2015). Patel, Panchal, Mahendra and Vegad, (2016). In India reported the most common gram-negative organisms to be \textit{P. aeruginosa}, \textit{A. baumannii} and \textit{Klebsiella spp} while the most common gram-positive organisms were \textit{Staphylococcus spp} and \textit{Enterococcus spp}.

This study has reported that the most prevalent organisms in the neonatal ICU (NICU) were \textit{Klebsiella spp} and \textit{S. marcescens} each with eight isolates. \textit{Staphylococcus spp} had three isolates, followed by \textit{A. baumannii} and \textit{Enterococcus spp} both with only one isolate. \textit{Enterococcus spp} and \textit{Streptococcus spp} also each had one isolate. \textit{K. pneumoniae} had the highest prevalence, in accordance with a study done in Nepal where \textit{Klebsiella spp} were the most prevalent organism. There were no \textit{S. marcescens} isolates and \textit{Staphylococcus spp} was the second most prevalent organism (Shrestha, Shrestha and Gurung, 2012). Another study done in
Nepal showed *Staphylococcus spp* as the most prevalent organism in their NICU, followed by *Klebsiella spp* and *Enterobacter spp* (Shrestha, Shrestha, and Dongol-Singh, *et al*, 2013).

### 5.3 ANTIBIOTIC SUSCEPTIBILITY

Antimicrobial resistance has been linked to antimicrobial use. Figure 4.4 shows that folic acid synthesis inhibitors (e.g. trimethoprim-sulfamethoxazole) have the lowest susceptibility of all the recorded antibiotics (41%), followed by beta-lactam-antibiotics (penicillins (43%) and cephalosporins (54%)). Susceptibility to fluoroquinolones (ciprofloxacin) and aminoglycosides (amikacin and gentamicin being the most reported on) showed a susceptibility of 75% and 76% respectively. Vancomycin was 100% susceptible in all the reported isolates. This susceptibility is in accordance with a consumption of antimicrobials study done globally over a period of 10 years, which reported that antibiotic consumption has increased by 36%, of which beta-lactam cell wall inhibitors contributed 55%, followed by fluoroquinolones (Van Boeckel, 2014). This shows that antibiotic consumption is directly proportional to resistance.

Trimethoprim-sulfamethoxazole had the lowest susceptibility in accordance with several studies done in South Africa and globally. Trimethoprim-sulfamethoxazole has been linked to treatment failure and it is no longer considered as a first-line agent due to its high resistance (Bosse, Li and Walker, *et al*, 2015). In developing countries like South Africa, the use of this inexpensive drug for treatment of urinary tract infections, respiratory tract infections and also for the prophylaxis of *Pneumocystis jiroveci* infection in HIV-positive patients, has contributed greatly to this resistance (Bosse, *et al*, 2015; Lewis, Gumede and van der Hoven, *et al*, 2013). A study done in South African health facilities showed that trimethoprim-sulfamethoxazole was the least efficacious antimicrobial agent against urinary tract infections and had a susceptibility of 44.3% (Lewis, *et al*, 2013).

**Gram-positive organism susceptibility**

Gram-positive organism susceptibility is shown in Figure 4.5 where the susceptibility of gram-positive organisms (*Staphylococcus, Enterococcus* and *Streptococcus*)
spp) is reported against several antibiotic agents. In DGMAH, gram-positive organisms are still susceptible to ampicillin/amoxicillin. *Staphylococcus spp* was 100% susceptible to vancomycin, clindamycin and trimethoprim-sulfamethoxazole, while there was 93.7% and 66.7% susceptibility to cloxacillin and erythromycin/azithromycin respectively. A tertiary hospital in the Democratic Republic of Congo, conducted a similar study from February 2013 until January 2014 and has reported *S. aureus* to be 100% resistant to ampicillin and trimethoprim-sulfamethoxazole. No resistance to other agents such as clindamycin, vancomycin and aminoglycosides was indicated, and similar to our study, erythromycin was 66.7% susceptible (Irenge, Kabego, Kinunu, *et al*, 2016). The antimicrobial resistance surveillance report done at Charlotte Maxeke hospital in Johannesburg has shown that *S. aureus* is 54% susceptible to clindamycin, 100% susceptible to vancomycin and 51% susceptible to cloxacillin while erythromycin/azithromycin is 46% susceptible (Perovic and Chetty, 2015). Erythromycin/azithromycin seem to have a low susceptibility as reported by these South African studies whilst there were other susceptibilities of this report do not correspond with those found from our study and this might be attributed to the differences in geographical locations.

*Enterococcus spp* was 100% susceptible to vancomycin and 51.1% susceptible to ampicillin/amoxicillin. The surveillance report of DGMAH has reported *E. faecalis* to be 58% susceptible to penicillin/ampicillin and 100% susceptible to vancomycin while *E. faecium* was 2% susceptible to ampicillin/amoxicillin and 100% susceptible to vancomycin (Perovic and Chetty, 2015). It is recommended that penicillins not be used for *E. faecium* infections. This shows that penicillin resistance is prevalent at our hospital and that protocols should be revised and implemented effectively with proper guidelines denoting that penicillins should only be used when susceptibility is known.

*Streptococcus spp* was 100% susceptible to ampicillin/amoxicillin and erythromycin/azithromycin, with only 50% susceptibility to trimethoprim-sulfamethoxazole. The results concur that South Africa has very high trimethoprim-sulfamethoxazole resistance, making this agent the least efficacious (Lewis, *et al*, 2013). In a study done in the Democratic Republic of Congo (DRC), there was only
one isolate of *S. pneumoniae* and it was resistant to amikacin, with 100% susceptibility to gentamicin and erythromycin (Irenge, *et al*, 2016). A study done in the Gauteng province has revealed 33% resistance to penicillin, this is in contrast with our study where no resistance to ampicillin/amoxicillin against *Streptococcus spp* was reported during the study period (Crowther-Gibson, Govender and Lewis, *et al*, 2011). Resistance patterns may differ depending on the site of specimen collection, age of patient, and geographical location. In South Africa, penicillin resistance remains intermediate (Crowther-Gibson, 2011).

*Gram-negative organism susceptibility*

On Figure 4.6, prevalent gram-negative organism susceptibilities are presented. *Klebsiella spp* showed 100% susceptibility to ciprofloxacin and imipenem, there was 94.4% and 85.7% susceptibility to amoxicillin-clavulanic acid and amikacin respectively, piperacillin/tazobactam and trimethoprim-sulfamethoxazole both had less than 50% susceptibility each being 33.3% and 44% susceptibility respectively. In a study conducted in the DRC, *Klebsiella spp* was 100% susceptible to imipenem, 94.4% susceptible to amikacin, 92.6% susceptible to amoxicillin-clavulanic acid and 68.5% susceptible to ciprofloxacin. Trimethoprim-sulfamethoxazole was 100% resistant (Irenge, *et al*, 2016). The susceptibility reports obtained in DGMAH surveillance report showed susceptibility for ciprofloxacin (79%), imipenem (100%), amikacin (92%) and piperacillin/tazobactam (69%) against *Klebsiella spp*. (Perovic and Chetty, 2015).

*Acinetobacter baumannii* was 100% susceptible to ciprofloxacin, amikacin and imipenem. In a study done in the DRC, *A. baumannii* was 100% susceptible to ciprofloxacin, amikacin and imipenem, which is in accordance with the results from our study (Irenge, *et al*, 2016). Antimicrobial resistance surveillance done in South African public hospitals has reported on the *A. baumannii* isolates seen at Dr George Mukhari Academic hospital had 68% susceptibility to amikacin, a low 28% for ciprofloxacin and an even lower 18% susceptibility to imipenem, even though these results contradict with the results from our study. This resistance is said to be due to the ability of *A. baumannii* to encode and upregulate various mechanisms of resistance such as the loss of external membrane porins and permeability, efflux pumps and other mechanisms (Perovic and Chetty, 2015).
Enterobacter spp were 100% susceptible to ciprofloxacin and imipenem. There was 75% susceptibility to amikacin while trimethoprim-sulfamethoxazole only had 33.3% susceptibility. Enterobacter spp reported from DRC showed 100% susceptibility to amikacin and imipenem, ciprofloxacin had 42.9% susceptibility while trimethoprim-sulfamethoxazole had 100% resistance (Irenge, et al, 2016). In South Africa at Dr George Mukhari Academic hospital, a surveillance report has described that Enterobacter spp was 79% susceptible to ciprofloxacin, 98% susceptible to imipenem and 81% susceptible to amikacin which somewhat coincides with our study (Perovic and Chetty, 2015).

Escherichia coli showed 100% susceptibility to ciprofloxacin, 60.7% susceptibility to amoxicillin-clavulanic acid, 50% susceptibility to amikacin, and only 15.8% susceptibility to trimethoprim-sulfamethoxazole. The study done in the DRC showed that this organism was 68.5% susceptible to ciprofloxacin, 92.6% susceptible to amoxicillin-clavulanic acid, amikacin had a susceptibility of 94.4% while trimethoprim-sulfamethoxazole was not susceptible (Irenge, et al, 2016). According to the surveillance report for microbial resistance, Dr George Mukhari academic hospital has reported 78% susceptibility of ciprofloxacin against E. coli, while amikacin was 89% susceptible, trimethoprim-sulfamethoxazole was not reported (Perovic and Chetty, 2015).

Pseudomonas spp was not susceptible to piperacillin/tazobactam and trimethoprim-sulfamethoxazole, while ciprofloxacin had 89.3% susceptibility. The study done in the DRC, showed that Pseudomonas spp was 66.7% resistant to ciprofloxacin and 100% resistant to trimethoprim-sulfamethoxazole, which shows that there are similarities in the trimethoprim-sulfamethoxazole resistance pattern, but this was not true for ciprofloxacin. In the DRC, there is high consumption of ciprofloxacin due to its broad spectrum of activity, ease of administration, attractive pharmacokinetic profile (excellent oral bioavailability, drug serum concentrations equivalent to intravenous administration), relatively cheap and few adverse effects (Irenge, et al, 2016). The surveillance report for microbial resistance has also reported antimicrobial susceptibility in other South African public hospitals such as Charlotte Maxeke hospital where Pseudomonas spp was 83% susceptible to piperacillin/tazobactam, which is in contrast to our study since Pseudomonas spp
was not susceptible to this antibiotic, while ciprofloxacin was 84% which correlates with our study (Perovic and Chetty, 2015).

*Serratia marcescens* was 100% susceptible to ciprofloxacin, amikacin and carbapenems (imipenem, meropenem and ertapenem). A study done in in the Western Cape Province in South Africa has reported that *S. marcescens* was 100% susceptible to amikacin and carbapenems, which is in accordance with our study (Morkel, Bekker, Marais, Kirsten, van Wyk and Dramowski, 2014).

Penicillin resistance was the second highest in our study following trimethoprim-sulfamethoxazole. The resistance to ampicillin and other beta-lactams was almost exclusively due to beta-lactamase production. Organisms that confer resistance through this mechanism are still susceptible to beta-lactamase-inhibitor combinations such as amoxicillin-clavulanic acid. Another mechanism is through mutation of the penicillin-binding protein-3, which results in decreased affinity by beta-lactams (Crowther-Gibson, *et al*, 2011; Blair, Webber, Baylay, Ogbolu and Piddock, 2015).

Recent studies have reported an increase in the prevalence of antibiotic resistance amongst infectious organisms and numerous classes of antibiotics have become less susceptible as a result of emergence of resistance, initiated by selective pressure of antibiotic usage (Holmes, *et al*, 2016; Moyo, *et al*, 2010). It is clear that there is high resistance against aminopenicillins as a result of extensive and inappropriate use of these agents in the treatment and prophylaxis of common infections (Mantadakis, *et al*, 2015; Woolhouse, *et al*, 2016). Current guidelines suggest that aminopenicillins alone may not be used as monotherapy to treat several serious infections and additional agents need to be added for this purpose (Mantadakis, *et al*, 2015; Woolhouse, *et al*, 2016). Vancomycin resistant gram-positive organisms were not identified in this study and this is in accordance with similar studies done in Spain, Sweden and Mozambique (Fransen, *et al*, 2016; Marco and Dowzicky, 2016; Preziosi, Zimba, Lee, *et al*, 2015).
5.4 SUMMARY

In this chapter, the results collected over 13 months between June 2015 and June 2016 were discussed. The discussion included the interpretation of the study results and comparisons with similar studies done both locally and internationally.
CHAPTER 6:
LIMITATIONS, RECOMMENDATIONS AND CONCLUSION

6.1 INTRODUCTION

This chapter presents Section 6.2, which discusses the study limitations, which are due to the study design and methodology and restrictions on the generalisability and applications of the research findings. Recommendations of this study are discussed in Section 6.3, and include suggestions for changes based on the research findings. The chapter concludes the study with Section 6.4.

6.2 LIMITATIONS

- The study does not represent other teaching hospitals in South Africa, only data from DGMAH has been collected and therefore the results may not be used to generalise prevalence and antibiotic susceptibilities in other facilities as these differ based on the geographical locations.

- The distinction between community and hospital acquired infections could not be made since data was collected from patients who were currently in the wards irrespective of what condition they initially presented with or how long they have been in the ward.

- The data does not illustrate susceptibility patterns over time and only demonstrates the susceptibilities at the point in time when the data was collected either over one, two or three months.

- The study does not correlate patient outcomes with antimicrobial susceptibility testing data, as the antibiotics, which were used for the reported pathogens and the patient outcome is not described by this study.

- The antibiogram data was collected manually, collecting data from patients files to obtain the specimen number to extract the results from the NHLS system. Some of the data may have been missed due to several reasons, the most important one being that the prescribers do not always put the specimen number on the patients file.
Doctors do not routinely request microbiological specimens, so some patients may have many other microorganisms which were not recorded, while some doctors would request them when the patient is already on antimicrobials or they are switching antimicrobials (mostly in cases of sepsis). There are no policies or guidelines in place for requesting microbiological specimens, so this practice varies from one prescriber to the next.

The correlation between resistance and usage is not illustrated.

6.3 RECOMMENDATIONS

The antimicrobial policies in the neonatal ICU and adult ICU do not require any changes. The review date on the neonatal ICU policy needs to be updated to keep it current.

The protocols in the obstetrics and gynaecology department need to be updated, as they are not in accordance with the local prevalence; penicillin resistance needs to be closely monitored in these wards.

The surgical wards require an antimicrobial policy, especially for surgical prophylaxis. Since they use cefazolin or amoxicillin-clavulanic acid which is correct, but they do not have these guidelines written anywhere and we do not know of the duration of prophylactic use of these agents is correct. The use of amoxicillin-clavulanic acid is correct but it is not first line. Prophylaxis depends on the type of procedure and duration, in most cases, cefazolin is the first line prophylactic agent, combined with metronidazole. Clindamycin may be used in cases of beta-lactam allergy.

Sample collection techniques should be reviewed, especially in the surgical wards. Emphasis on correct site of sample collection is also important and it shows that the disease process is well understood.

It would be beneficial to have a clinical pharmacist, who will spend time in the wards, monitoring the overall therapy and paying extra attention to patients on antimicrobials and their response to treatment. This clinical pharmacist may also do surveillance and ensure that clinical advice is available for the prescribers.
Chapter 6: Limitations, Recommendations and Conclusion

- Microbiologists may also be available for clinical advice and assist with unmediated management of infected patients by guiding specimen collection, handling and transportation and interpretation of results.
- Most of the prescribers were not aware of the existing policies. Distribution and education on these policies is important.
- The Pharmacy and Therapeutics Committee (PTC) to initiate and establish an antimicrobial stewardship team, which will lead the antimicrobial stewardship programme, and update the antimicrobial policies regularly according to local trends.

6.4 CONCLUSION OF THE STUDY

The overall aim of this study was to investigate the availability of current and up-to-date antimicrobial policies in the different wards of DGMAH. The availability of antimicrobial policies was determined and found to be 15.4%. Policies were obtained from the adult ICU, neonatal ICU, and obstetrics and gynaecology (in four wards). Only one policy is current and up-to-date, the other available policies were last updated in 2013 and only one of them was in accordance with the national guidelines and local prevalence and susceptibility reports. The most frequent organisms isolated included Staphylococcus species, Klebsiella spp, Enterococcus spp, E. coli and Streptococcus spp while Salmonella typhi, Providencia stuartii and Stenotrophomonas maltophilia were amongst the least frequent organisms. Trimethoprim-sulphamethoxazole had the highest resistance, making it ineffective in most infections followed by penicillins and cephalosporins respectively and this may be linked to their frequent use. No resistance against vancomycin was reported during the study period. Sample collection technique should be reviewed especially in the surgical wards. The hospital’s pharmacy and therapeutics committee can use these results to update the outdated antimicrobial policy and use them to draw a draft to formulate an antimicrobial policy for the surgical wards, and update existing protocols.

6.5 LESSONS LEARNED
The lessons learnt is that through my recommendations, I can increase the availability of existing policies by making sure that each prescriber has a personal copy, make sure that the policies are regularly updated as per local prevalence and standard treatment guidelines, train the prescribers on the changes made, strengthen the pharmaceutics therapeutic committee. Prevalence and susceptibility patterns change over time, it is important to liaise with the microbiology department in order to review these patterns over time so that changes to policies can be amended. The lesson on the importance of antibiotic policies, the necessity to regularly update them and steps to follow were highlighted in this research. The role of clinical pharmacists as champion team member of the antimicrobial stewardship programme was emphasised.
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## APPENDICES

### Appendix 1: Data collection questionnaire

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<th>ANTIMICROBIAL POLICY AVAILABLE?</th>
<th>LAST DATE OF REVIEW</th>
<th>ANTIMICROBIAL POLICY IN ACCORDANCE WITH THE LATEST GUIDELINES (EML)</th>
<th>PROTOCOL RELEVANT TO CURRENT FREQUENT ORGANISMS AND SUSCEPTIBILITIES SEEN IN THE HOSPITAL</th>
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Appendix 2: Prevalence and susceptibilities in different wards

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<th>BACTERIAL STRAIN</th>
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Appendices

Appendix 3: Letter of intent

Dear Mr Madonsela
Dr George Mukhari Academic Hospital

Letter of intent to conduct a prospective, quantitative descriptive study at Doctor George Mukhari Academic Hospital

My Name is Tumelo M. Modau, a post-graduate student at the Department of Pharmacy, Sefako Makgatho Health Sciences University. As part of the requirements for my post-graduate qualification, I am required to conduct research. I am here by requesting to conduct a study in the hospital wards and at the National Health Laboratory Services of Dr George Mukhari Academic Hospital. I am enrolled for an MSc (Med) in Pharmacy at Sefako Makgatho Health Sciences University.

Attached please find the proposal for the study entitled: “The availability of recent antimicrobial policies in different wards/units at Doctor George Mukhari Academic Hospital, Gauteng Province.”

The proposal will be submitted to the School of Health Care Sciences and the Sefako Makgatho Health Sciences University Research and Ethics committee (SMUREC).

The aim of the study is:
To investigate the availability of recent antimicrobial policies in the different units/wards of Dr George Mukhari Academic Hospital, Gauteng Province.

The objectives are:
- To investigate the availability of antimicrobial policies in the hospital and review existing policies.
- To examine the frequent susceptibilities and resistance patterns.
Appendices

- To evaluate the antimicrobial policies according to the Essential Medicines List (EML), and frequent susceptibilities and resistance patterns seen at the hospital.

Kind regards,

Mr T.M. Modau
Academic Intern
Department of Pharmacy
Sefako Makgatho Health Sciences University
012 521 3286
Cc E. Bronkhorst, Prof AGS Gous
Appendices

Appendix 4: SMUREC Clearance Certificate

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

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

APPROVAL NOTICE - NEW APPLICATION

04 June 2015
Mr TM Modau
Department of Pharmacy
P.O Box 218
Medunsa, 0204

MEETING: 05/2015
SMUREC Ethics Reference Number: SMUREC/H127/2015: PG

The New Application received on 25 May 2015, was reviewed by members of Sefako Makgatho University Research Ethics Committee on 04 June 2015 and was approved on 04 June 2015.

Title: The availability of recent antibiotic policies in different wards units at Dr George Mukhari Academic Hospital, Gauteng Province
Researcher: Mr TM Modau
Supervisor: Prof AGS Gous
Co-supervisor: Mrs E Bonekhoetl
Hospital Superintendent: Dr NC Holm
Department: Pharmacy
School: Health Care Sciences
Degree: Masters in Pharmacy

Please note the following information about your approved research protocol:


Please remember to use your protocol number (SMUREC/H127/2015: PG) on any documents or correspondence with the REC concerning your research protocol.

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

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

International Organization (IORG0004319), Institutional Review Board (IRB000095122), Federal Wide Assurance (FWA00005419)
Expiry date: 11 October 2016 and NHREC No: REC 210408-003

Sincerely

[Signature]
PROF GA OGBUNUJO
CHAIRPERSON SMUREC

[Stamp]