Strengthening Antimicrobial Stewardship in the Internal Medicine Wards at Dr. George Mukhari Academic Hospital-An Interventional Study

A mini-dissertation submitted by

Johnson Mwebaze Nabyoma

In partial fulfilment of the requirements for the degree

Master of Science (Med) in Pharmacy

in the

Faculty of Health Sciences

(School of Health Care Sciences)

of the

University of Limpopo (Medunsa Campus)

Department of Pharmacy

Supervisor: Dr Moliehi Matlala
Co-supervisor: Prof A.G.S Gous

2015
DECLARATION

I declare that the dissertation hereby submitted to the University of Limpopo, Medunsa Campus, for the degree of Master of Science in Medicine (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.

______________________________
Nabyoma MJ (Mr)

______________________________
Date
DEDICATION

The work contained in this dissertation is dedicated to my family, especially my mother Mrs. Miria Rebecca Nankola, fiance' Angella Kaye Naddamba, for all the help you have accorded me throughout, my late father Mr. Sefatia John Nankola for the motivation and direction that you led me, now I can say you were absolutely right, my sisters Susan, Brenda, Daphne, Eunice and brothers Daniel, Derrick for the support.
TABLE OF CONTENTS

ACKNOWLEDGEMENTS ........................................................................................................... iv
LIST OF FIGURES .................................................................................................................... v
LIST OF TABLES ...................................................................................................................... vii
LIST OF APPENDICES ............................................................................................................ viii
ABBREVIATIONS AND ACRONYMS ...................................................................................... ix
ABSTRACT ............................................................................................................................... x

CHAPTER 1 INTRODUCTION .................................................................................................. 1
  1.1 INTRODUCTION .............................................................................................................. 1
  1.2 BACKGROUND AND RATIONALE FOR THE STUDY ..................................................... 1
  1.3 RESEARCH QUESTION .................................................................................................... 2
  1.4 AIM OF THE STUDY ......................................................................................................... 2
  1.5 OBJECTIVES OF THE STUDY ......................................................................................... 2
  1.6 IMPORTANCE OR SIGNIFICANCE OF THE STUDY ......................................................... 3
  1.7 SUMMARY ........................................................................................................................ 3

CHAPTER 2 LITERATURE REVIEW ......................................................................................... 4
  2.1 INTRODUCTION .............................................................................................................. 4
  2.2 ANTIMICROBIAL STEWARDSHIP .................................................................................... 4
  2.3 ANTIMICROBIAL RESISTANCES ......................................................................................... 7
  2.4 THE NEED TO STRENGTHEN ANTIBIOTIC STEWARDSHIP ........................................ 7
  2.5 INTRAVENOUS TO ORAL SWITCH ................................................................................... 7
  2.6 FOCUS ON INTENSIVE CARE UNITS AND HIGH CARE WARDS ................................ 8
  2.7 USE OF A SHORT COURSE OF ANTIMICROBIALS TO REDUCE UNNECESSARY EXPOSURE ...................................................................................................................... 8
  2.8 PROCALCITONIN USE TO INDICATE BACTERIAL REPLICATION IN CRITICALLY ILL ......................................................................................................................... 9
  2.9 ADHERENCE TO GUIDELINES ......................................................................................... 9
  2.10 ANTIMICROBIAL USE IN THE HOSPITALS .................................................................. 10
  2.11 SUMMARY .................................................................................................................... 11

CHAPTER 3 METHOD .............................................................................................................. 12
  3.1 INTRODUCTION .............................................................................................................. 12
CHAPTER 4 RESULTS AND DISCUSSION ................................................................. 18

4.1 INTRODUCTION ............................................................................. 18

4.2 STUDY POPULATION ................................................................... 18
  4.2.1 Prescriber demographics ...................................................... 18
  4.2.2 Patient files ......................................................................... 18

4.3 PHASE ONE: RESULTS ................................................................. 19
  4.3.1 Prescriber Questionnaire - Results ...................................... 19
  4.3.2 Phase 1 results (baseline) of antimicrobial use investigated by researcher using data capturing form ......................................................... 30

4.4 PHASE 2: INTERVENTIONS ............................................................. 38

4.5 COMPARISON OF ANTIMICOBIAL PRESCRIBING PATTERNS REVIEW FOR PHASE 1 AND PHASE 3 ................................................................. 40
  4.5.1 Most common diagnosis .......................................................... 40
  4.5.2 Antimicrobial use at DGM AH internal medicine wards ............... 41
  4.5.3 Defined daily doses of prescribed antimicrobials ......................... 42
  4.5.4 Route of administration of prescribed antimicrobials ................. 45
  4.5.5 Comparison of adherence to guidelines, missed doses and collection of specimen for microbiological culture in both the pre and post intervention study .................................................. 46
  4.5.6 Adherence to guidelines while treating any conditions ............... 47
  4.5.7 Missed doses of prescribed antimicrobials per patient file .......... 48
  4.5.8 Collection of specimen for culture ........................................... 48
  4.5.9 Comparison of isolated microorganisms from the samples taken in the pre- and post-intervention phases .................................................. 48
  4.5.10 Intravenous to oral switch ...................................................... 49
### 4.6 SUMMARY  ........................................................................................................50

### CHAPTER 5 CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS  .......... 52

#### 5.1 INTRODUCTION  ............................................................................................. 52

#### 5.2 CONCLUSION  .................................................................................................. 52

- 5.2.1 Updating of forms used for motivational antimicrobials and treatment guidelines  
- 5.2.2 Assessing the knowledge of prescribers about the existing antimicrobial stewardship strategies  
- 5.2.3 Introduce other strategies to improve antimicrobial stewardship  

#### 5.3 RECOMMENDATIONS  .................................................................................... 54

#### 5.4 LIMITATIONS OF THE STUDY  ....................................................................... 55

### REFERENCES  ........................................................................................................ 56

### APPENDICES  ......................................................................................................... 68
ACKNOWLEDGEMENTS

There is no beautiful work that comes out of a man single handily therefore I would like to acknowledge the following people for their tireless input in making this work appreciable;

- Mrs M Matlala my supervisor for her continued support and guidance during the study, for the knowledge she has imparted to me.
- Professor AGS Gous my co-supervisor for the knowledge and support throughout the study and for believing in me that I can make it.
- Dr Natalie Schellack my MSc lecturer for her continued support towards my development as a clinical pharmacist and her input into the study.
- Mrs Nikki Williamson for her continued help with excel while analysing data and the encouragement she always gave me.
- Mr Wandisile Grootboom for his pharmacy related advice at DGMAH, guidance on the various aspects of this research.
- The staff at microbiology, special thanks to Dr Bonnie Maloba and Brenda Ngcube for their input into the study.
- The patients who took part in the study at the internal medicine wards, if it was not for you, this study wouldn't have been a success.
- The physicians at the internal medicine wards for taking part in the study and providing such relevant information for the improvement of stewardship in the wards.
- Department of pharmacy, Medunsa campus for empowering me with the knowledge throughout the study, this has made a significant difference in my life.
- Friends and family for their support and encouragement, especially at times when the situations were tough; my beloved mother, Rebecca Miria Nankola, my two brothers Derrick and Daniel, my sisters, Susan, Brenda, Eunice, Daphne and their families, my fiancée Angela that without their continuous support and encouragement it would have been so difficult to accomplish this task.
LIST OF FIGURES

Figure 2.1: Antimicrobial stewardship strategies ................................................................. 4

Figure 4.1: Prescriber category ............................................................................................. 19

Figure 4.2: Protocols used while prescribing ....................................................................... 20

Figure 4.3: Refer to protocols when prescribing ................................................................. 21

Figure 4.4: Other resources used when prescribing ............................................................. 23

Figure 4.5: Training in guidelines, IV to Oral switch guidelines and satisfaction with guidelines ......................................................................................................................... 24

Figure 4.6: Infectious conditions for which prescribers said samples for a culture were collected .................................................................................................................................. 26

Figure 4.7: Turn around time for collected samples ............................................................ 28

Figure 4.8: De-escalation of antimicrobial therapy ............................................................. 29

Figure 4.9: Top 10 most common diagnosis in Phase 1 ....................................................... 30

Figure 4.10: Diagnosis based on body systems .................................................................. 31

Figure 4.11: The top 10 most prescribed antimicrobials in Phase one ............................... 32

Figure 4.12: Number of patients who missed doses in phase one .................................... 33

Figure 4.13: Route of administration of prescribed antimicrobials .................................. 33

Figure 4.14: Adherence to local guidelines ............................................................................ 34

Figure 4.15: Intravenous to oral switch .................................................................................. 36

Figure 4.16: Most common diagnosis both pre and post intervention phases .................. 40

Figure 4.17: Top 10 most used antimicrobials in DGMAH internal medicine wards ...... 41

Figure 4.18: Route of administration of prescribed antimicrobials .................................. 46

Figure 4.19: Adherence to guidelines, missed doses and collection of microbiological specimen for culture. ................................................................................................................. 47

Figure 4.20: Isolated microorganisms for the specimens collected .................................... 49
Figure 4.21: Comparison between Phase 1 and Phase 2 intravenous to oral switch for patients
LIST OF TABLES

Table 2.1: Explanation of the stewardship strategies ................................................. 6
Table 4.1: Type of sample taken for culture and respective outcome ...................... 35
Table 4.2: Isolated microorganism ............................................................................. 35
Table 4.3: DDD’s for phase one antimicrobial use results ........................................ 43
Table 4.4: DDDs for phase two antimicrobial use result .......................................... 44
# LIST OF APPENDICES

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix 1</td>
<td>Medunsa Research &amp; Ethics Committee Clearance Certificate</td>
<td>68</td>
</tr>
<tr>
<td>Appendix 2</td>
<td>Patient Identification Form</td>
<td>69</td>
</tr>
<tr>
<td>Appendix 3</td>
<td>Data Capturing Form</td>
<td>70</td>
</tr>
<tr>
<td>Appendix 4</td>
<td>Erythromycin Motivation Form</td>
<td>71</td>
</tr>
<tr>
<td>Appendix 5</td>
<td>Moxifloxacin Motivation Form</td>
<td>72</td>
</tr>
<tr>
<td>Appendix 6</td>
<td>DGMAH Antimicrobial Motivation Form</td>
<td>74</td>
</tr>
<tr>
<td>Appendix 7</td>
<td>IV to Oral Switch Guidelines</td>
<td>75</td>
</tr>
<tr>
<td>Appendix 8</td>
<td>Updated Treatment Guidelines</td>
<td>76</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>Acute coronary syndrome</td>
<td></td>
</tr>
<tr>
<td>ASP</td>
<td>Antimicrobial stewardship</td>
<td></td>
</tr>
<tr>
<td>ASP</td>
<td>Antibiotic Stewardship Programme</td>
<td></td>
</tr>
<tr>
<td>AV</td>
<td>Arterial ventricular</td>
<td></td>
</tr>
<tr>
<td>BPH</td>
<td>Benign prostate hyperplasia</td>
<td></td>
</tr>
<tr>
<td>BVF</td>
<td>Biventricular failure</td>
<td></td>
</tr>
<tr>
<td>CAP</td>
<td>Community acquired pneumonia</td>
<td></td>
</tr>
<tr>
<td>CCF</td>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>CMO</td>
<td>Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>COAD</td>
<td>Coronary artery disease</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
<td></td>
</tr>
<tr>
<td>DCMO</td>
<td>Dilated cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>DGMAH</td>
<td>Dr George Mukhari Academic Hospital</td>
<td></td>
</tr>
<tr>
<td>DM-2</td>
<td>Diabetes mellitus type 2</td>
<td></td>
</tr>
<tr>
<td>DKA</td>
<td>Diabetic Ketoacidosis</td>
<td></td>
</tr>
<tr>
<td>ESKD</td>
<td>End Stage Kidney Disease</td>
<td></td>
</tr>
<tr>
<td>HPTN</td>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
<td></td>
</tr>
<tr>
<td>IHD</td>
<td>Ischaemic Heart Disease</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
<td></td>
</tr>
<tr>
<td>LVF</td>
<td>Left Ventricular Failure</td>
<td></td>
</tr>
<tr>
<td>RHF</td>
<td>Right Heart Failure</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary Tract Infections</td>
<td></td>
</tr>
</tbody>
</table>
ABSTRACT

Background: Antimicrobial stewardship programs designed as to optimize the use of antimicrobials in different institutions are of no value if monitoring is not done to see the impact on antimicrobial use and antimicrobial resistance.

The aim of the research was to determine the impact of strengthening antimicrobial stewardship programme at Dr. George Mukhari academic hospital (DGMAH). The objectives were to determine the prescribers’ knowledge about the existing antimicrobial stewardship strategies already introduced in the internal medicine wards, to update the forms used for motivational antimicrobials at the internal medicine wards introduce strategies to strengthen antibiotic stewardship at internal medicine ward at DGMAH such as antimicrobial grand rounds and make recommendations based on the findings to improve antibiotic stewardship at the internal medicine wards at DGMAH.

Methods: This was a 3 phased prospective descriptive study running from June 2013 to August 2014 where data on antimicrobial use were collected both before and after interventions, the results were analysed and comparison, of both Phases 1 and Phase 3, and with previous studies in the internal medicine wards on antimicrobial stewardship was carried out. All adult patients admitted to the internal medicine wards and received antimicrobials during the study period were part of the study population. A questionnaire was administered to volunteering prescribers to determine their knowledge and awareness about the existence of antimicrobial stewardship programmes in the wards.

The results: Baseline results show that ceftriaxone and amoxicillin clavulanic acid were two of the most used antimicrobials. The prescribers did not have a formal treatment guide to follow when treating infectious conditions. The duration of antimicrobial therapy was longer in most patients than what would be acceptable based on literature, samples for cultures were not collected regularly therefore results were not used to guide antimicrobial use. There was also minimal intravenous to oral switch of antimicrobials, there was a decline in IV to oral switch when pre-intervention to post intervention results are compared. Erythromycin was the biggest pharmaceutical cost driver in this study as seen in the study by Bala, (2012). Ceftriaxone was also the most prescribed antimicrobial to amoxicillin and clavulanic acid as in the study by Grootboom, (2011).

Conclusion: Antibiotic prescribing and knowledge about the antibiotic policy were not up to standard, therefore, continued strengthening antimicrobial stewardship is necessary to optimize antimicrobial use in the internal medicine wards to reduce the emergence of
resistance to antimicrobials and reduce the cost of antimicrobial treatment. This can be done through introducing a ward pharmacist to emphasise the stewardship strategies that are in existence and enforce the new strategies that are introduced.

**Recommendations:** Continuous monitoring of antimicrobial stewardship strategies should be done to ensure that proper antimicrobial use is practiced in the wards.

Ensure that the pending strategies are finalised and introduced in the internal medicine wards since they were developed to address problems that were observed in the wards.

Continuous updating of all antimicrobial stewardship information included in the strategies should be done so that the prescribers can have no excuse of not using them.
Chapter 1: Introduction

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

This chapter will give an introduction to the research explaining in detail the key aspects of the research, the background and rationale of the study, research question, aim and objectives of the study and the significance of the study.

Antimicrobials are very special in a way that their activity is on microorganisms other than human targets, they act in more than one particular system of the body if required, are used in enormous amounts in either prophylaxis or treatment, but usually for a shorter period of time, and target more than one class of microorganisms therefore causing the emergence of resistance through processes such as gene transfer or cloning (Warren, 2004).

Hospitals remain a place of high antibiotic consumption due to the fact that infectious conditions still remain the highest cause of death in the entire world, therefore the focal point for interventions to improve antimicrobial prescribing (Owen & Ambrose, 2006). Resistance, lack of resources and increasing health care costs have led to the development of ideas on how to reduce health care costs while ensuring quality care for the patients and one of the strategies is antimicrobial stewardship (MacDougall, 2005).

Antimicrobial stewardship is the optimal selection of the dose and duration of an antimicrobial that brings about the best clinical outcome for the treatment or prevention of infection. While this is achieved, there should be minimal toxicity to the patient and reduced chances of subsequent resistance to the given antimicrobial developing (Bell, 2001).

There are a number of antimicrobial stewardship strategies that have been developed which can be categorised as either pre- prescription or post prescription interventions as tools for antimicrobial stewardship (Duguind & Cruikshank, 2012; Owen & Ambrose, 2006).

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Antimicrobial resistance has been on the increase over the years, yet the pipeline for new antimicrobials are drastically drying up after a few decades of antimicrobial use since their discovery. This has resulted in untreatable bacterial infections, yet antimicrobials have played a great role in the advancement of medical practice for decades, such as successful
outcomes of many surgical procedures, and immunosuppressive treatment which are somehow dependent on antibiotic prophylaxis and treatment of complications thus posing a serious threat to health care (MacGowan & Macnaughton, 2013)

Globally, there has been a gradual but growing increase in the number of isolates that are resistant to the available antimicrobials that they were previously sensitized. This has led to treatment options being limited and complicated. The rapidly emerging resistance is believed to be as a result of a multitude of reasons such as inadequate treatment, scale up of antibiotic use in hospitals, increased agricultural use of antimicrobials just to name a few. The emergence of resistance due to overuse or misuse of antimicrobials is not the only problem, but also the increased spread of resistant microorganisms in the community in which resistant strains of microorganisms were not seen earlier (Arias et al., 2009, DiazGransdos et al., 2008, Gould, 2009).

South African hospitals have also noticed a growing challenge with numerous types of pathogenic organisms such as vancomycin resistant *Staphylococcus aureus* and *Enterococcus faecium*, penicillin resistant *Streptococcus pneumoniae* and methicillin resistant *Staphylococcus aureus*. Some of these resistant strains of microorganisms have already been isolated in Dr George Mukhari Academic Hospital (DGMAH) and therefore the need to come up with interventions to curb the development and propagation of resistant microorganisms (Bala, 2013; Best care, 2011)

1.3 RESEARCH QUESTION

What is the impact of strengthening antibiotic stewardship in the internal medicine wards at DGMAH?

1.4 AIM OF THE STUDY

To measure the impact of strengthening antibiotic stewardship in the internal medicine wards at DGMAH

1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To determine the knowledge the prescribers have about the existing antimicrobial stewardship strategies already available in the internal medicine wards.
Chapter 1: Introduction

- To implement and educate clinicians in the internal medicine wards on the updated antibiotic protocols.
- To update the form used for motivational antimicrobials at the internal medicine wards and introduce it to the doctors and the pharmacy staff.
- Introduce other strategies to strengthen antibiotic stewardship at the internal medicine ward at DGMH.
- To assess antimicrobial use using the defined daily doses (DDD) as per WHO guidelines.
- Make recommendations based on the findings to improve antibiotic stewardship at the internal medicine wards at DGMAH in terms of new and existing antibiotic stewardship strategies.

1.6 IMPORTANCE OR SIGNIFICANCE OF THE STUDY

The most effective approach to improve antimicrobial use in hospitals is an organised antimicrobial management team under antimicrobial stewardship, with a systematic approach to optimising the use of antimicrobials; this in the long run reduces inappropriate antimicrobial use, improves patient outcomes and reduce adverse consequences of antimicrobial use such as antimicrobial resistance, toxicity and unnecessary costs (Owen, 2008). According to Drew et al, (2009), antimicrobial stewardship has been shown to decrease antimicrobial use and improve patient care along with infection control, hand hygiene and surveillance, preventing the emergence of antimicrobial resistance and decrease preventable healthcare associated infection. In DGMAH, previous researchers have shown the need for strengthening AS in the hospital to foster the effectiveness of the already existing strategies and to introduce other strategies (Dellit et al., 2007)

1.7 SUMMARY

In this chapter the background and rationale for the study was discussed, stating the aim of the study, which is strengthening antimicrobial stewardship in the internal medicine wards at DGMAH. The objectives of the study were highlighted. At the end of the chapter, the importance of the study was eluded. Chapter 2 will focus on literature review in line with the study.
2.1 INTRODUCTION

This chapter focuses on the various methods that have been used to strengthen antimicrobial stewardship in South Africa and around the world. Furthermore, factors that contribute to a successful antimicrobial stewardship team as well as key stakeholders in the successful establishment of an effective antimicrobial stewardship team. Antimicrobial stewardship strategies that were strengthened in the study will also be discussed in detail in this chapter.

2.2 ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship is defined as the optimal selection of the dose and duration of an antimicrobial that brings about the best clinical outcome for the treatment or prevention of infection. While this is achieved, there should be minimal toxicity to the patient and reduced chances of subsequent resistance developing (Bell, 2001; Vlieghe, 2009). There are a number of antimicrobial stewardship strategies that have been developed as shown below;

![Figure 2.1: Antimicrobial stewardship strategies](image-url)
Chapter 2: Literature Review

The above can be classified as either pre- or post-prescription interventions with pre-prescription interventions being prior approval of antimicrobial to be used, formulary restriction when prescribing antimicrobials, antimicrobial cycling in which different classes of antimicrobial are used in cycle to treat the same condition and educating the physicians and following guidelines developed for prophylaxis or treatment of infections. The post prescription interventions include intravenous to oral antimicrobial switch using approved guidelines, streamlining or de-escalations in cases where multiple antimicrobials were used initially pending microbiological investigations and results, pharmacodynamics dose optimisation, computer assisted programmes and prospective audits and feedback all aimed at reducing the development of resistance to antimicrobials (Ford, 2010). The study made use of both the pre-prescription and post prescription strategies in antimicrobial stewardship.

The Table 2.1 indicates the procedure, personnel involved, advantages and disadvantages of the different strategies involved in antimicrobial stewardship.
### Table 2.1: Explanation of the stewardship strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Procedure</th>
<th>Personnel Involved</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education and guidelines</strong></td>
<td>Creation of guidelines for antimicrobial use, group or individual education of clinicians by educators</td>
<td>Antimicrobial committee to create guidelines and educators, i.e. clinicians and pharmacists</td>
<td>May alter behaviour and avoids loss of prescriber autonomy</td>
<td>Passive education not always effective</td>
</tr>
<tr>
<td><strong>Formulary restriction</strong></td>
<td>Restrict dispensing of a targeted antimicrobial to approved indications</td>
<td>Antimicrobial committee to create guidelines. Personnel for approval include physicians, infectious disease fellows, clinical pharmacists</td>
<td>Provides direct control over antimicrobial use and done through individual education consultations</td>
<td>Perceived loss of autonomy for prescribers as there is a need for all-hour consultation</td>
</tr>
<tr>
<td><strong>Review and feedback</strong></td>
<td>A daily review of targeted antimicrobial appropriateness, and if not, then recommend an alternative therapy</td>
<td>Antimicrobial committee to create guidelines and personnel for review usually clinical pharmacists</td>
<td>Avoids loss of autonomy for prescribers and provides individual educational opportunities</td>
<td>Compliance with recommendations is voluntary</td>
</tr>
<tr>
<td><strong>Antimicrobial Cycling</strong></td>
<td>Scheduled rotation of antimicrobial prescribed in a hospital or unit</td>
<td>Antimicrobial committee creates a cycling protocol and personnel oversee adherence</td>
<td>May reduce resistance by changing selection pressure</td>
<td>Difficult to ensure adherence to cycling protocol and there are theoretical concerns about effectiveness</td>
</tr>
<tr>
<td><strong>Computer assistance</strong></td>
<td>Makes use of information technology to implement previous strategies, expert systems provide patient specific recommendations at the point of care</td>
<td>Antimicrobial committee to create rules for computer systems, personnel to help with an approval or review, which are physicians or pharmacists using computer programmes</td>
<td>It provides patient specific data when to most likely to take an impact at the point of care and this facilitates other strategies</td>
<td>Significant time and resource investment is needed to be able to implement sophisticated systems</td>
</tr>
</tbody>
</table>
2.3 ANTIMICROBIAL RESISTANCES

Due to misuse or overuse, there has been a gradual but growing increase in the number of isolates that are resistant to the available antimicrobials that they were previously sensitive and this has led to treatment options being limited and complicated. The rapidly emerging resistance is believed to be as a result of a multitude of reasons such as inadequate treatment, scale up of antimicrobials use in hospitals, increased agricultural use of antimicrobials, just to name a few. The emergence of resistance due to overuse/ misuse of antimicrobials is not the only problem, but also the increased spread of resistant microorganisms in the community in which resistant strains of microorganisms were not seen earlier (Arias et al., 2009; DiazGransdos et al., 2008; Gould, 2009).

Antimicrobial resistance is a significant worldwide problem involving all types of pathogens, namely; bacteria, fungi, viruses, mycobacteria and parasites (McGowan, 2012). For instance, one of the greatest threat among others is multi drug resistant tuberculosis (MDR) with an estimated half a million new cases annually in the United States of America (WHO, 2009).

2.4 THE NEED TO STRENGTHEN ANTIBIOTIC STEWARDSHIP

In a study done by Arnold et al., (2011) in the European Union, it was brought to light that antimicrobial stewardship strategies play a key role in improving antibiotic decision making in the best interest of the patient welfare and development of resistance (Smidt et al, 2014). In this study, a review of 24 reports believed to be of high quality between 1996-2010 proved that stewardship programmes can achieve a significant reduction in inappropriate antibiotic use to a percentage between 11-18%, including significant reduction in total antibiotic consumption, duration and inappropriate use of antimicrobials Some of the effective hospital based interventions that were identified by (Arnold et al, 2006; Delit, 2005; McGowan et al, 2011) to be of documented benefit in strengthening antibiotic stewardship in their study will be discussed below.

2.5 INTRAVENOUS TO ORAL SWITCH

The over use of intravenous antimicrobials is a worldwide problem and a big contributor to antimicrobial resistance globally. Switching therapy is a principle that can be applied to streamline antibiotic therapy, reducing on unnecessary and prolonged exposure to IV antimicrobials. The principle is that there is conversion of IV to oral therapy as the name suggested as soon as the patients are deemed clinically stable based on specific criteria
without compromising antimicrobial potency (Lior et al., 2014). This is a very important
decision for physicians to make as it determines the length of hospitalization therefore a
potential target for intervention (Holloway, 2011).

Timed switch from IV to oral antimicrobials does not accrue benefits only to the hospital, but
also to the patient in that it significantly improves patient care and decreases the risk of
infections, and reduces expenses associated with hospitalisation. This has been reflected in
studies, particularly those for patients with community acquired pneumonia (Omidvarl, 2001).
The lack of IV catheters improves patient comfort and mobility, reducing the incidence of bed
sores and thrombosis in such patients (Waele, 2010; Wang et al., 2014). The chances of
missing doses due to many reasons such as if the IV line is not in situ are significantly
reduced using antimicrobials for oral use such as fluoroquinolones, metronidazole,
clindamycin, fluconazole, azithromycin etc. (Harris, 2012).

2.6 FOCUS ON INTENSIVE CARE UNITS AND HIGH CARE WARDS

Nosocomial infections occur 5-7 times more in ICU than in general wards and are associated
with an increase in morbidity, mortality and a significant increase in the cost of treatment
(Yulung et al, 2000). These units are a breeding place for resistant microorganisms such as
carbapenemase-producing Klebsiella pneumoniae. (Snitikin et al., 2012). Also, there is
sometimes prolonged use of antimicrobials in patients who underwent surgery and yet the
prophylaxis given does not cover the most problematic organisms associated with resistance
in the wards. It is therefore important to have systems in place to deal with high antibiotic
use in these units to curb the increased emergence of resistant microorganisms. It has been
noted that physicians tend to continue prophylaxis or empiric treatment for longer than
required despite the availability of cultures and susceptibility results leading to the
development of very resistant microorganisms. It is important that the three day rule be
adhered to switch patients to narrow spectrum antimicrobials avoiding alteration in the host’s
normal flora and selection of resistant microorganisms (Smidt, 2014).

2.7 USE OF A SHORT COURSE OF ANTIMICROBIALS TO REDUCE
UNNECESSARY EXPOSURE

Antimicrobial use should be limited to only a few days as long as the halt does not interfere
with patients’ clinical outcome in any way (Yankelevitz et al., 2010). It is important that the
correct initial empiric treatment is given to the patient as this directly influences clinical
improvement of the patient (Danyasz, 2006). Over treatment with antimicrobials increases
costs, adverse effects, the probability and danger of long periods of hospitalization, and
increase in the emergence of resistant organisms (Erdejic et al., 2004). Prolonged antimicrobial use has been associated with an increased risk of *Clostridium difficile* diarrhoea thus further increasing antimicrobial use to correct the problem. In surgery prophylaxis, many of the antimicrobials used are of less effect on many of the problematic microorganisms such as *Clostridium difficile*, methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant enterococci which are selected out by these antimicrobials and aggravate the problem of resistance especially when used for prolonged periods of time after surgery (Fatima et al., 1999)

2.8 PROCALCITONIN USE TO INDICATE BACTERIAL REPLICATION IN CRITICALLY ILL

Compared to other biomarkers such as C-reactive protein (CRP) and white blood cell count (WBC), procalcitonin is a very specific biomarker for bacterial infection because of its specificity for bacterial infection, the rapidity of its rise upon insult which is approximately 6 hours, the rapid decline once the immune system has been restored, and excellent correlation with the severity of illness and the lack of impact of anti-inflammatory and immunosuppressive states on its production (Tang et al., 2009). Clinically procalcitonin can be applied in the following settings:

a) Differentiating between bacterial and viral respiratory tract infection  
b) Determining antibiotic treatment length in respiratory infections  
c) Diagnosis, risk stratification, and monitoring of sepsis and septic shock  
d) Monitoring response to antimicrobial therapy  
e) Diagnosis of systemic secondary infection post-surgery, post-organ transplant, and in severe burns, multi-organ failure, and severe trauma

In a review by (Agarwal & Schwartz, 2011) in the use of procalcitonin in the intensive care unit, it was brought to light that procalcitonin guidance was associated with significantly reduced antimicrobial exposure in all five studies, length of ICU stay was significantly reduced, and a decrease in antimicrobial use was observed.

2.9 ADHERENCE TO GUIDELINES

Optimal dosing of antimicrobials taking into consideration the minimum inhibitory concentrations is paramount to successfully treat infections. This is achieved through the development of guidelines. A guideline is a written guidance on prevention or treatment of
specific infections and designed to improve the quality of prescribing (Drummond, 2006). This in the long run leads to improvement in the quality of prescribing and subsequently decreasing the resistance developing, reduction in cost and improvement of patient care. However, the success factor in achieving this is the level of adherence to the guidelines and recent reviews suggest that locally developed guidelines according to the hospitals’ microbial reports are more adhered to than nationally developed guidelines (Cantrell et al., 2011). These have the potential to increase chances of patients receiving effective treatment, there is less variations, there is clarity on the reason for certain treatments and improved patient safety. However, there has been some negative attributes to the use of guidelines such as evidence used to be erroneous, improper application of guidelines, out-dated guidelines (Richards et al, 2003).

There is a need for antibiotic interventions in developing countries, especially hospital based, antibiotic policies (Ganguly, 2011) and a hospital has reported positive outcomes as a result of adoption of antimicrobial guidelines at their hospital, where this was conducted (Metlay et al., 2003).

A study conducted in South Africa at a tertiary institution showed that as much as stewardship strategies can be implemented and made available, there is a need for a ward pharmacist to monitor and foster the use of strategies that are available in the wards for the physicians to follow (Best care, 2011). Presently there are antibiotic stewardship strategies that were introduced in DGMH that need to be strengthened so as to continue saving antimicrobials through rational antimicrobial use.

2.10 ANTIMICROBIAL USE IN THE HOSPITALS

The Defined Daily Dose (DDD) is defined as the assumed average maintenance dose per day for a drug for its indication in adult patients taken as a World Health Organization measure of drug utilization (Griffith, 2012; WHO, 2003) It is a unit of measurement and does not represent a recommended or prescribed daily dose (Sweilah et al., 2012). It is used to give a rough estimate of drug consumption, but not actually use since cost data do not adequately show antibiotic utilization (Best care, 2012).

DDD is used for the following:

- Comparing drug utilization.
- Evaluating long term tendencies in drug use.
- Assessing the impact of certain events on drug use.
• It is independent of price, currencies, package size and strength which enable the researcher to assess the changes in drug consumption and perform comparison between different population groups (Moodley et al, 2002; Olveira, 2009; WHO, 2003).

2.11 SUMMARY

This chapter focused on the literature reviewed in light of the study and highlighted areas pertaining to antimicrobial resistance, antimicrobial stewardship and the need to strengthen antimicrobial stewardship in order to attain optimal use of antimicrobials. The next chapter will focus on the methods used in conducting the study.
CHAPTER 3
METHOD

3.1 INTRODUCTION

This chapter presents the methods that were used in conducting the study, which include; the study design, the study site, sample selection including the inclusion and exclusion criteria, data collection instruments, and data entry and analysis.

3.2 BACKGROUND TO THE METHOD

The study was aimed at measuring the impact of strengthening antibiotic stewardship in the internal medicine wards at DGMAH. It also investigated the prescribers’ level of awareness about existing antimicrobial stewardship strategies. This was done in accordance with the objectives set out in chapter one and antimicrobial use was established in order to attach a cost of treatment per 100 patient days on antibiotic treatment.

3.3 STUDY DESIGN

This was a prospective and a descriptive intervention study, operational in nature, conducted in three phases. A quasi-experimental design was used, where the first phase of the study served as a reference point, to determine which of the predetermined strategies would need to be strengthened in the second phase. Phase 2 of the study was interventional where recommendations from the previous study (Bala, 2012) were also implemented and new strategies developed. Phase 3 involved assessments of the impact of the interventions carried out in Phase 2 on prescribing of antimicrobials by doctors. Phase 1 and Phase 3 involved the following;

- Reviewing of prescribing patterns

  Reviewing of prescribers' knowledge about existing antimicrobial stewardship strategies (Phase 1 only). To assess the knowledge of the prescribers about the already available antimicrobial stewardship strategies in Phase 1, a self-administered questionnaire was given to the doctors who had to sign a consent form.

- Monitoring of laboratory investigations/ infection markers to guide antibiotic therapy
Phase 2 was an intervention phase in which no data were collected rather presentations were made to doctors in the internal medicine wards about de-escalation, intravenous (IV) to oral switch guidelines, updated treatment guidelines and antibiotic stewardship (ABS) as a whole. The researcher also identified patients with special antibiotic needs and these were discussed during ward rounds, interventions were made if necessary for the better outcome of the patient in line with rational use of antimicrobials.

Phase 3 involved the collection of data to compare with the initial findings in Phase 1 of the study. The method of data collection in Phase 3 was similar to the data collected in Phase 1. Similar tools were used in the collection of both data sets except that prescriber knowledge was not assessed in Phase 3. The data collected included the following:

- Reviewing of prescribing patterns
- Monitoring of laboratory investigations/ infection markers to guide antibiotic therapy
- Using DDD’s to assess drug use in the internal medicine wards.

### 3.4 STUDY SITE

The research was conducted at Dr. George Mukhari Academic Hospital, a tertiary hospital in Ga-Rankuwa, attached to the University of Limpopo, Medunsa campus in Pretoria. There were six internal medicine wards selected for the study, accommodating both females and males in different wards with ward 36 as the admission ward. The wards were as follows:

- Adult male wards – ward 33 and 34
- Adult female wards - ward 37 and 38
- Admission ward for both males and females - ward 36

### 3.5 STUDY POPULATION

The target population for the study was all adult female and male patients admitted to the internal medicine wards at DGMAH and were prescribed an antimicrobial agent during the study period. It also included physicians in the internal medicine wards in order to assess their knowledge about existing antimicrobial stewardship strategies.
3.6 STUDY PERIOD

The study was conducted from June 2013 to September 2014. A pilot study was not conducted as the instruments that were used in the study had been previously tested. The baseline for the study commenced on 15th June 2013 and interventions were done as per the discussion in Section 4.4. Phase 3 was conducted from the 28 July 2014 to 30 September 2014.

3.7 SAMPLE SELECTION

Patient files in the entire study were selected by moving from bed to bed and those with antimicrobials prescribed irrespective of the diagnosis were considered for the study. Sampling continued until the sample size of 100 patient files was achieved. These 100 patients’ files were followed until when the patient was discharged or until when the antimicrobials were stopped. Phase 1 was the baseline and Phase 3 was to assess any improvement in antibiotic use and prescribing patterns after the interventions in Phase 2.

In Phase 2, patients with specific antibiotic therapy needs were identified by the researcher and considered first for ward rounds thereafter the types of interventions made on each round were noted. Presentations were made to the doctors on the highlighted antimicrobial strategies introduced or those that needed to be improved.

3.8 INCLUSION AND EXCLUSION CRITERIA

3.8.1 Inclusion criteria

For files to be considered for the study, they had to satisfy the following entry criteria;

They had to be from the internal medicine wards.

Had to have an antimicrobial prescribed for the chief complaint on admission.

The doctors had to be practising in the internal medicine wards.

3.8.2 Exclusion criteria

The exclusion criteria were as follows;

- All patients’ files in the internal medicine ward during the period of study that did not contain any antimicrobials prescribed.
• All the other doctors that were not working in the internal medicine wards during the entire study period.

3.9 DATA COLLECTION INSTRUMENTS

A pioneer study was done in the wards (Bala, 2012) and therefore the researcher adopted the relevant data collection instruments for this study to assess the impact the ASP strategies had, on the prescribing patterns in the internal medicine wards in an effort to combat the development of resistance and reduce the cost of antibiotic therapy in the wards.

3.9.1 Instrument 1 - Patient identification form (Refer to Appendix 2)

This form was intended to help the researcher identify the patient without compromising the confidentiality of the patient information in any way during the research period and post research. It had the patient name, hospital file number, ward number and a study number allocated by the researcher. This helped to identify the patients in the different wards while following them on a daily basis. It was also used by the supervisor or any other researcher to retrieve information during or after the study. The study number enabled the researcher to link a patient file with the data collection instrument. This information was not captured onto any computer; instead it was stored in a locked cupboard.

3.9.2 Instrument 2 - Data capturing form (Refer to Appendix 3)

The tool was used to measure and monitor antimicrobial stewardship at the internal medicine wards. The form included the following information; the study number, diagnosis, prescribed antimicrobials, maximum daily dose, microbiology results, duration of treatment, route of administration, adherence to treatment guidelines; number of days to switch from IV to oral antimicrobials, motivational antimicrobials prescribed, the number of days spent in the hospital and estimated cost of both antimicrobials and patient stay in the hospital. Only antimicrobials that the patient was being treated with were recorded on this form. Added antimicrobials were recorded and no other pharmacological agents that the patients would have been treated with for other morbidities during the study period were recorded.

3.10 DATA ENTRY AND ANALYSIS

All data collected was captured into an Excel spread sheet (Microsoft Excel® 2010). Verification of data and validity checks were done as part of data cleaning to ensure that the data was captured correctly. Data analysis was done in consultation with a statistician and
Chapter 3: Method

descriptive statistics were used to analyse the data which were appropriately presented in tables and graphs.

Data that did not comply with the guidelines were analysed in depth to find out the reason for the deviation from the guidelines. The comparisons were as follows:

Pre-intervention data on all scripts collectively were compared with post-intervention collective data on all scripts by means of comparison of the outcomes of the analysis of the data, done by the researcher using excel (Microsoft Excel® 2010) and such differences highlighted thereafter.

Adherence to treatment guidelines was assessed by comparing the prescribed treatment for a particular infection with the existing treatment guidelines.

The time taken for patients on IV antimicrobial to be switched to an oral antibiotic was determined and compared with guidelines and other clinical indicators for IV to oral switch.

The adherence to aseptic techniques was investigated and adherence would be indicated by the complete eradication of specimen cultured with non-pathological coagulase negative *Staphylococcus epidermidis* deemed not to be of clinical value in terms of the source of infection upon consultation with the attending physician and microbiological results

DDDs were calculated for both antimicrobial use in the pre and post intervention study and then compared.

Recommendations were made based on the findings to improve cost effectiveness and rational use of antimicrobials in the internal medicine wards at DGMAH.

3.11 RELIABILITY AND VALIDITY

The researcher recorded data from the patient files only ensuring that no alteration is made to the data obtained. A number was assigned to each patient file so that information from that file can be easily retrieved in the future for any other use by other researchers or supervisor. Information from the microbiology laboratory as pertains to the sensitivity and resistance patterns was not altered in any way by the researcher and will always be available at the microbiology laboratory thus accounting for the reliability of the information. Because all the information captured can be easily retrieved and yield the same results, this accounts for the reliability of the data.

Validity is defined as the extent to which a research is appropriately conducted which is linked to the sampling procedure, time, place and condition in which the research is
conducted (Graziano & Raulin, 1993). Data was only collected and captured by the researcher and no one else, ensuring that errors are avoided or minimised to the lowest level possible. Seasonal changes may have had an effect on infectious disease, therefore, since the study was not being conducted over the four seasons of the year, the researcher comported this in mind when analysing the data thus accounting for the validity and reliability of the data.

3.12 ETHICAL CONSIDERATIONS

Permission and approval to conduct this study was sought from the Medunsa Research Ethics Committee (MREC), DGMH Superintendent, and the head of department internal medicine. Permission was granted by MREC with issue of a clearance certificate; project number MREC/H/200/2013: PG (Appendix 1). The research was observational and did not interfere with patient therapy in any way, therefore an informed consent from the patient was deemed not necessary.

Confidentiality was maintained at all times with all the information that would nullify the confidentiality of the patient being kept in a locker. The patients that met the criteria for inclusion into the study were allocated a study number for the purpose of confidentiality and this is what was used in the data capturing process. A consent form was signed by the doctors who had accepted participation in phase one of research. This form was adopted from the Medunsa Research Ethics Committee (MREC).

3.13 SUMMARY

In this chapter, the method used in the research was discussed, giving a background to the method, information on the study design and study site. The chapter also gave detailed information about sample selection and data collection instruments used in the study and ended with a discussion of the ethics that were taken into consideration throughout the study period. In the next chapter, the results obtained during data collection are presented.
CHAPTER 4
RESULTS AND DISCUSSION

4.1 INTRODUCTION

The results of the data collected during the study will be presented in this chapter according to the phases in which the research the research was conducted. Phase 1’s results will deal with prescriber responses to a questionnaire assessing prescriber knowledge about antimicrobial policies and antimicrobial stewardship at DGMAH taken as baseline data for the study. The discussion will compare the results from the different phases of the study and those that were previously presented in the preceding study by Bala (2012) and any other studies related to antimicrobial stewardship.

4.2 STUDY POPULATION

4.2.1 Prescriber demographics

The prescribers at DGMAH internal medicine wards comprised of 36 registrars, 10 interns, 10 community service doctors and 18 consultants. Availability and convenience sampling was used in the research therefore some categories were not represented or may not be equally represented as a result, interns and registrars participated more in filling in the questionnaire which were administered in the wards. The researcher administered the questionnaire on 11 prescribers therefore the group did not represent any category of the prescribers in the internal medicine wards as it is just a number of prescribers who were present and willing to take part in answering the questionnaire at the time of the study.

4.2.2 Patient files

The study included files of both male and female patients admitted in the internal medicine wards that were receiving antimicrobial agents. In both phase 1 and phase 3 a total of 100 patient files were reviewed prospectively to determine the antimicrobial use practices in the internal medicine wards. The results of Phase 1 and Phase 3 were compared to determine whether there was any impact on prescribing made by the interventions made in Phase 2.
4.3 PHASE ONE: RESULTS

4.3.1 Prescriber Questionnaire - Results

A self-administered questionnaire containing 11 questions was administered to 11 prescribers by the researcher. The responses to the questions from the prescribers are discussed below.

4.3.1.1. Prescriber category

The distribution of the prescribers in internal medicine is presented in Figure 4.1

![Pie chart showing prescriber category distribution]

**Figure 4.1: Prescriber category**

Five respondents were interns (46%) three were registrars (27%) and one each (9%) for community service doctors, medical officer and consultants or specialist.

This was consistent with the study by Bala, (2012) in which five interns also participated in answering the questionnaire. This can be attributed to the fact that interns are referred to as "house keepers" in the wards therefore readily available and based on availability and convenience sampling that was employed in the study, it was easier to find interns in the wards at all the time than the other categories of prescribers. However, this was not the case with the registrars as there was a 50% drop in this category of respondents compared to Bala, (2012) findings. This could have been due to the fact that at the time of phase 1 of the study the registrars were in their assessment period therefore were not readily available in the wards. This could have had an impact on the total number of respondents being low as well as many were not in the wards. A study by Von Holdt, (2006) showed that staff shortages and management failures in public hospitals have compromised the quality of
patient care in South African hospitals. Another study by Minnar, (2007) about the level of satisfaction by nurses in the Witwatersrand showed a high level of dissatisfaction with work load among nurses which could be the same case with prescribers that they are not interested in being in the wards and thus taking part in extra ward activities such as research.

4.3.1.2. Antimicrobial protocols used in the internal medicine wards

Figure 4.2 indicates the antimicrobial protocols used by prescribers on individual choice in the internal medicine wards as indicated on the questionnaire.

Figure 4.2: Protocols used while prescribing

Key: COPD- Chronic obstructive pulmonary disease, CKF- Chronic kidney failure, ARF- Acute renal failure.

The list of the above protocols was obtained from the antimicrobial protocols existing at the internal medicine wards. Since the list of protocols was born from the internal medicine department, the prescribers were expected to be aware of their existence. The most common protocol known to the prescribers (11) (100%) was for the management of community acquired pneumonia (CAP), followed by acute meningitis (8) (72%) and chronic meningitis (5) (62%). All the other protocols were proportionately known to the prescribers at
about (50%) except for the protocol for the management of dialysis post chronic kidney failure or acute renal failure and amoebic liver abscesses with only one respondent being aware of their existence. These results were consistent with findings in the study by Bala (2012) in which (13) 100% of the prescribers who responded were also aware of CAP protocols, and meningitis, and the least known being the protocol on the management of amoebic liver abscesses, hemodialysis related sepsis and dialysis for CKF / ARF. According to Moehring et al., (2012), antimicrobial protocols form part of a successful ASP since they are an integral part of the pre-prescription interventions involved in a successful ASP leading to optimization of antimicrobial use decreasing the incidence of infection with multidrug resistant organisms and the emergence of drug resistance. It is therefore important for the prescribers to be 100% aware of the different protocols available to them in the internal medicine wards so that this helps in guiding treatment which will in the end help foster ASP thus reducing resistance.

4.3.1.3. **Referring to a protocol when prescribing**

With respect to referring to any protocol when prescribing, 9 (82%) of the respondents said that they referred to at least one protocol when prescribing and 2 (18%) said they rarely referred to any protocol when prescribing as shown in Figure 4.3. In the study by Bala (2012), it was found that 5 (45%) prescribers sometimes referred to a protocol, 3 (27%) referred to a protocol all the time, 1 (9%) said they rarely and 2 (18%) never referred to any protocol when prescribing. In a study by Okae, (2010) in Ghana indicated that 74% of prescribers used protocols while prescribing antimicrobials.

![Figure 4.3: Refer to protocols when prescribing.](image)
The use of protocols might be influenced by the presence of other resources that the prescribers use. Among the reasons that all the 11 prescribers gave for not referring to any protocol was that they were not readily available (4 prescribers), they were not regularly updated (6 prescribers) and that some of the conditions that the patients presented with were not catered for in some of the local references (5 prescribers) such as the standard treatment guidelines (STG/EML) for South Africa. In a study conducted by Essack et al., (2005) in KwaZulu Natal to determine antimicrobial use and resistance in the state hospitals, it was evident that the bacteria varied from hospital to hospital and that a general guideline for all hospitals such as is with the STG/EDL may not cater or be appropriate for all conditions in some facilities especially with the world being a global village, aiding the quick transmission of infectious conditions from one place to another, therefore the need to use other kinds of protocols in such incidences while treating some of the infectious conditions.

4.3.1.4. Other resources used when prescribing antimicrobials

Fifty five percent of the prescribers indicated that they used the standard treatment guidelines (STG) hospital level or the essential medicines list (EML), five (45%) used the South African medicines formulary (SAMF) and three (27%) used the DGMAH guidelines while three (27%) were using other sources such as Medscape and other local and international journals when prescribing as shown in Figure 4.4. Comparing these results with those from the study by Bala (2012), it was noted that the most used source was SAMF with a count of seven (64%) while the other, namely STG/EML, DGMAH guidelines and others, e.g. Medscape had the least use with three (27%), two (18%) and two (18%) respondents respectively and therefore an inconsistency noted in the resources that the prescribers use in the internal medicine wards while prescribing.
The reason for the use of other resources might be because of the lack of definite protocols for the most common infectious conditions in the wards as noted earlier, the lack of duly updated protocols and advancement in technology which has led to the availability of up to date information from all over the world in a handset therefore ease of use (Okae, 2010). Another factor would be the lack of proper training of some staff on the use of the already available protocols therefore leading to the use of resources that they feel comfortable using while prescribing (Sellman, 2004).

**4.3.1.5. Training in policy guidelines, IV to Oral switch guidelines and satisfaction with guidelines**

For proper use of guidelines by the intended population, there needs to be proper training to introduce the intended guidelines (Vancelik et al., 2007). The prescribers were assessed on whether they had been trained on policy guidelines present in the internal medicine wards. The results are shown in Figure 4.5 (i).
4.3.1.6. **Training in the guidelines for the management of infectious diseases**

Only five (46%) of the prescribers indicated that they had been trained about local guidelines. There was an improvement compared to the study by Bala (2012) in which only two (18%) had indicated they underwent training on local protocols. The increase in the number of respondents could be attributed to Bala’s training of the internal medicine staff about the guidelines or the development of a better introductory programme for the new staff joining the internal medicine wards. In a study conducted by Zuber (2011), even when guidelines are in place for prescribers, investment into policy guideline, regulations and pre-service education is required for sustainable provision of quality services following the accepted guidelines.

4.3.1.7. **Satisfaction with policy guidelines**

Of the 11 respondents, seven said they were satisfied with the guidelines that they were making use of them. Four were not satisfied with the guidelines developed for internal medicine as seen in Figure 4.5-(ii) above. Some of the reasons the prescribers gave for the dissatisfaction were that some of the guidelines specifically the local internal medicine guidelines were not standardized and upgraded regularly; therefore the use of other guidelines to supplement the local guidelines with a result that prescriptions differed from one prescriber to another since each prescriber used a preferable guideline. Five prescribers said that the current internal medicine protocols were out-dated therefore did not have the
latest information to address specific patient problems encountered time to time. Three prescribers said they were not user friendly as they did not give alternatives to therapy in case an agent was out of stock in the pharmacy yet therapeutic interchange by pharmacists is not allowed by law (Bothma, 2011) while this would help in making sure that the patient receives adequate treatment in accordance with the guidelines even when the prescribed item is out of stock from the pharmacy. This would help reduce patient waiting time and unnecessary send backs to the prescribers. Therapeutic interchange is defined as the dispensing of a drug that is therapeutically equivalent to but chemically different from the originally prescribed drug by a physician or other authorized prescriber, usually in the same pharmacologic class though may differ in pharmacokinetic properties, possess a different mechanism of action, adverse-reaction, toxicity, and drug interaction profiles (Bothma, 2011). In most cases, the interchanged drugs have close similarity in efficacy and safety profiles (Gray, 2004). Lastly seven prescribers said that the internal medicine guidelines did not have all the conditions that the patients may present with therefore the prescribers were forced to refer to other guidelines.

4.3.1.8. Awareness of IV to oral switch guidelines

One of the biggest drivers of antimicrobial costs is intravenously administered antimicrobials according to previous study (Bala, 2012). IV to oral switch guidelines were developed and implemented in the wards through presentation and posters were put up in the internal medicine wards by Bala, (2012). This study investigated if the prescribers in the wards were aware of the presence of these guidelines in the wards and the results are shown in Figure 4.5-(iii) above.

The majority of the respondents were aware of the existence of the guidelines with eight respondents as seen above and three respondents did not know anything about the guidelines. Eight of the 11 respondents were aware of the already introduced IV to oral switch guidelines, though they did not fully follow the guidelines. The reasons given for this by the prescribers were as follows; two prescriber indicated that the normal practice in the wards required longer treatment duration, especially for conditions such as meningitis. Other respondents said that some physicians were not allowed to change therapy since the patient therapy was initiated by specialists who were in most cases not readily available in the wards to confirm the switch.

Antimicrobial therapy review was meant to be done on a daily basis to ascertain if the patient still needed the antibiotic, but this was not always possible because of shortage of staff in
Chapter 4: Results and Discussion

the internal medicine wards therefore attention was given to other issues other than reviewing antimicrobial therapy

Some of the physicians were not comfortable with switching from IV to oral antimicrobials as they believed oral antimicrobials do not give the same effect as the IV formulation.

4.3.1.9. Specimen collection by prescribers

When treating infections, it is important that prescribers start antimicrobial therapy as soon as possible but very important is tailoring pharmacologic therapy to the microorganisms that are responsible for the infection through streamlining therapy upon collection of culture at an appropriate time. Obtaining culture before initiating therapy is emphasised and is important for identification of the microorganism and thus improves patient care. (Baddour et al., 2005; Dellinger et al., 2004; Rojo 2006)

The prescribers were asked to indicate the medical conditions for which specimens were normally sent to the laboratory for culture and sensitivity and the results are shown in the figure 4.6.

![Figure 4.6: Infectious conditions for which prescribers said samples for a culture were collected.](image)

**Figure 4.6:** Infectious conditions for which prescribers said samples for a culture were collected.

Figure 4.6 shows that the conditions for which samples for analysis were collected varied, with meningitis being the condition most investigated at (36%). This was consistent with
previous findings by Bala (2012) in terms of the most investigated conditions which are meningitis (73%), followed by sepsis (27%) and moderately tuberculosis and infective endocarditis at (18%) and the others the least investigated There was a decline in the occurrence of samples collected for culture and sensitivity investigation when compared to results by Bala (2012). This can be linked to the lack of proper guidelines as earlier discussed to highlight to the prescribers the process to be followed when treating particular conditions in the internal medicine wards, as well as the difference in the guidelines used in the internal medicine wards. Berild et al., (2005) in their study about the use of culture to narrow therapy reported that adjustment of therapy after culture helps reduce the cost of antimicrobial therapy. A study conducted by Schlueter et al., (2010) on practice patterns of de-escalation in culture negative healthcare associated pneumonia show that there are benefits of taking samples for culture and de-escalating as this leads to reduced hospital stay, lower hospital costs and lower mortality rates. De Bush et al., (2014) eluded that the use of guidelines based on the local ecology of disease has an advantage as they are based on surveillance except when dealing with multi-drug resistant microorganisms.

4.3.1.10. Aseptic techniques while taking samples

One of the important aspects of collecting samples for culture is avoidance of specimen contamination through ensuring aseptic techniques are followed (Dreyer, 2012). Results from Phase 1 showed that 11 (100%) respondents indicated that they followed aseptic techniques when taking samples for analysis. A study conducted by (Van der Heijden et al., 2011) shows that 87% of randomly selected coagulase negative staphylococcus cultures were contaminated. A study by Ehjie et al., (2011) in a national hospital in Abuja revealed that contamination of samples is unavoidable but should be within acceptable limits otherwise appropriate measures should be put in place e.g. by giving proper instructions to prescribers taking specimens and processing specimen within two hours of collection or stored in preservatives or refrigerated. There is need to set a benchmark contamination rate so as to enhance its use as a quality indicator in sample processing. Other measures put to light by Hall and Lynmann, (2006) include skin preparation since 20% of skin commensal can survive disinfectants, adequate culture bottle preparation since the rubber stopper is not always sterile, the use of two needles one for pricking and the other when transferring samples, although single needle use is the most preferable with the current HIV/AIDS burden and lastly obtaining cultures percutaneous instead of using vascular catheters by the phlebotomy team.
4.3.1.11. Turnaround time for laboratory results from collected samples

The prescribers were asked how long it normally took for the results for the specimen collected to come back from the microbiology laboratory. Governments and insurance companies are increasingly concerned with savings and cost-effectiveness in view of the rapidly escalating cost of health care. On the other hand, health care professionals want to know whether their efforts are achieving their intended goals and the patient wants to be able to receive and select the best possible quality health care (WHO, 2010). The results are shown in Figure 4.7.

![Figure 4.7: Turn around time for collected samples](image)

Quality assurance programmes including programmes for laboratories are now regularly conducted in various countries, relying on laboratories to isolate and identify bacterial pathogens. This must be done within the shortest time possible. In seven public hospitals in Malaysia, the mean turnaround time was between one to seven days. This is acceptable in third world countries as the methods involved do not allow for fast processing of cultures (Lim et al., 1992).

The turnaround time at DGMAH was mostly about 48 hours from the time of sample collection to the time the prescribers would receive the results according to the findings given in their responses, four prescribers said that sometimes turnaround time was within 120 hours and one said within 24 hours. A study by Butler –Wu et al., (2011) on optimisation of pre-prosthetic culture for diagnosis of Propionibacterium acnes prosthetic joint infection shows that the longer cultures take, the more likely it is to recover non clinically important isolated for specific bacteria such as P. acnes in joint infection if incubated for more than 13 days. This has a direct effect on the outcome of therapy. Davies, (2003) outlines that
automated liquid culture system together with molecular techniques decreased the time required for culture, identification and antimicrobial susceptibility testing of *Mycobacterium tuberculosis*. Similar techniques can be used to further reduce the time needed for turnaround of collecting samples.

### 4.3.1.12. De-escalation of antimicrobial therapy

Most of the patients admitted with life threatening infections are treated empirically globally, but upon culture and isolation of the causative microorganism or upon definite diagnosis, (Wang et al., 2014). De-escalation is paramount in these patients to avoid unwanted exposure to antimicrobials, which would lead to resistance and prolonged hospital stay which exposes the patient to the risk of infection and increased cost of treating the patient (De Bus et al 2014). The results of the study are shown in Figure 4.8 below and are as follows; seven of the prescribers rarely de-escalated antimicrobial therapy, one indicated that he de-escalated all the time and three did not know what de-escalation meant. The lack of de-escalation impacts on antimicrobial use, the total hospital expenditure on antimicrobials as well as propagating the development of resistant microorganisms driven by unnecessary exposure of bacteria to antimicrobials. The emergence of resistant microorganisms according to Davies, (2003) does not only affect an individual, hospital or region, but affects the entire world as resistant microorganism spread at a very rapid rate on the concept of the world being a global village where one can easily move from one place to another within hours and in this case carrying different strains of microorganisms from one place to another. The results are shown in the figure 4.8;

![De-escalate antimicrobial therapy](image-url)

**Figure 4.8: De-escalation of antimicrobial therapy**
4.3.2 Phase 1 results (baseline) of antimicrobial use investigated by researcher using data capturing form

These were results from Phase 1 which is also termed as the baseline results. A hundred patients were selected using convenience sampling and reviewed by the researcher looking at diagnosis, investigations and treatment. The findings were used to help guide the interventions that the researcher was to implement the internal medicine wards of DGMAH.

4.3.2.1. Top 10 most common diagnosis

The figure 4.9 shows the ten most common diagnoses among the hundred patients that were reviewed by the researcher.

![Figure 4.9: Top 10 most common diagnosis in Phase 1](image)

Key DKA- Diabetic keto acidosis, COAD - Coronary artery disease, DM2- Diabetes mellitus type 2

In order to summarise this data, the 10 most common diagnoses were identified. In Phase 1 of the study, pneumonia (19) and meningitis (13) were the most common diagnosis as depicted in figure 4.9. The two main diagnoses were commodities, either retroviral disease (RVD) or tuberculosis (TB) and patients with RVD usually presented with pneumonia or meningitis or TB, of which treatment for RVD and TB will not be discussed in this study. This is consistent with other studies such as the one by Tlali (2005) conducted in the internal medicine wards at DGMAH over a period of five months that revealed similar results as this
study in which pneumonia, meningitis and TB were the most common conditions diagnosed among RVD positive patients as expected. Similarly, in a study conducted by (Ellis, 2013) of health care cost and utilisation project in the united states showed pneumonia as the most common diagnosis in the year 2010. In another study conducted by Grootboom, (2010) in the internal medicine wards to at DGMAH to determine the prescribing pattern in adult patients with meningitis also revealed that pneumonia and meningitis as the most common diagnosis especially among patients with RVD. Though CAP incidence in South Africa is unknown, in the United States the incidence is about five to six cases per 1000 person years (Metlay et al 2003). In South Africa, it is one of the leading causes of mortality (Nyamande, 2013), especially in patients with existing commodities such as RVD.

4.3.2.2. **Diagnosis based on body systems**

Figure 4.10 presents diagnosis based on the body systems and is discussed in detail;

![Diagram](image)

**Figure 4.10: Diagnosis based on body systems**

Most of the diagnoses were of cardiovascular origin (28%), then the respiratory system (25%) and central nervous system at (21%). Sixteen per cent constituted other diagnoses such as diarrhoea, cough, and bronchitis among others. A patient could have more than one diagnosis therefore the \( n=104 \).
4.3.2.3. **The top 10 most prescribed antimicrobials**

The top ten most prescribed antimicrobials are shown in the Figure 4.11.

![Prescribed Antibiotics](image)

**Figure 4.11: The top 10 most prescribed antimicrobials in Phase one**

The most prescribed are ceftriaxone (33), followed by cefuroxime (31) and amoxicillin clavulanic acid (20). Tlali, (2005) in a study conducted in the internal medicine wards at DGMAH found cefuroxime as the most prescribed antimicrobial. It was still in high use and erythromycin (16) was fourth prescribed. There was a reduction in the usage of erythromycin compared to the results obtained by Tlali, (2005) and Bala, (2012) and can be attributed to the use of azithromycin in its place. When compared to the results obtained by Bala, (2012) in a study about antimicrobial stewardship in the internal medicine wards at DGMAH, ceftriaxone was the most prescribed antimicrobial as is in the results of Phase 1 of this study.

4.3.2.4. **Missed doses in phase one**

Figure 4.12 presents the results on the number of missed doses in phase one of the study.
Figure 4.12: Number of patients who missed doses in phase one

In the Phase 1, at least 42% of the patients seen by the researcher missed a dose or more of the prescribed antimicrobial agent. The reasons were either the medication was out of stock or there was failure in the provision of such medication by the health care provider.

4.3.2.5. Route of administration of prescribed antimicrobials

The prescribed antimicrobials had various routes of administration and will be discussed as shown in Figure 4.13.

Figure 4.13: Route of administration of prescribed antimicrobials
Assessment of the routes of administration of the prescribed antimicrobials revealed that 38% of it was intravenous, 46% of the patients received both intravenous and oral antimicrobials and 16% received only oral antimicrobials. In the study by Bala, (2012), 41% of patients who received erythromycin intravenously had other drugs given orally, 31% had intravenous erythromycin and other intravenous drugs given and 31% of them receiving oral erythromycin alone.

4.3.2.6. Adherence to local guidelines

The results of prescriber adherence to both local and other guidelines are shown in the Figure 4.14.

![Figure 4.14: Adherence to local guidelines](image)

When adherence to the local guidelines by the prescribers was assessed, it was found that 39% of the prescriptions were in line with at least one of the local guideline and 61% were not based on any local guideline. In a study conducted in Kwazulu Natal by Parry, (2009) to assess adherence to antihypertensive guidelines had similar results where the rate of adherence to local South African guidelines was 45%. The World Health Organisation in (2008) also assessed drug use in South Africa and found that 86% of prescriptions were as per the guidelines. Similarly Engelbrecht, (2010) in a study to adhere to the medicine code list in primary health care, military clinics in Gauteng found that 89% of prescriptions were according to at least one resource. In this case it is clear that following guidelines in the internal medicine wards when prescribing was not up to date with every prescriber as seen with treatment for CAP where ceftriaxone was the preferred agent over cefuroxime, but still its use remained minimal as seen from the drug usage results STG/EML (2012).
4.3.2.7. **Isolated microorganisms**

The results presented in Table 4.1 give the distribution of the samples that were collected with the highest being blood cultures at 12 times (37%) of which three were positive (25%) samples, followed by sputum cultures at five times (15%) and four were positive at (80%)

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>No of collections</th>
<th>No of negative results</th>
<th>No positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture</td>
<td>12</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Sputum</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Urine</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pus</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Plural fluid</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Throat swabs</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Rectal swab</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 4.1: **Type of sample taken for culture and respective outcome**

Table 4.2 presents the isolated microorganisms for the patients in the baseline study showing the area from which the specimen was collected and the number of times a particular microorganism was isolated.

Table 4.2  **Isolated microorganism**

<table>
<thead>
<tr>
<th>Microorganism isolated</th>
<th>Number of times</th>
<th>Specimen collected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>1</td>
<td>Sputum</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2</td>
<td>Pus</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
<td>Throat swabs</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>3</td>
<td>Sputum</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>1</td>
<td>Pus</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>1</td>
<td>Rectal swab</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>2</td>
<td>Urine sample</td>
</tr>
<tr>
<td>Coagulase negative staphylococcus aureus</td>
<td>3</td>
<td>Blood culture</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>1</td>
<td>Throat swabs</td>
</tr>
</tbody>
</table>
Chapter 4: Results and Discussion

Of the 32 samples taken, 38% were blood samples, 18% were throat swabs, 15% were sputum samples, 12% for pleural fluid, nine percent for pus and six percent for urine samples. Of the total samples 16 (50%) were positive as follows; four were of *Klebsiella pneumonia* as the most common isolate, this was followed by three of CONS and three for *Cryptococcus neoformans*. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were isolated in two samples respectively. The least isolated were *Streptococcus pneumonia* and *Candida albicans*. Most of the samples were taken from patients who had meningitis and pneumonia and with reference to the most common diagnosis discussed above, the expectation would have been more cultures to have been done since meningitis and pneumonia would frequently require an antimicrobial agent and therefore investigation needed to be done. The isolated organism did not point towards the most common diagnosis in the wards. The STG/EML 2012 suggest a blood culture or lumbar puncture for patients diagnosed with meningitis with other co-morbidities or without co-morbidities respectively (Tunkel et al., 2004). The South African guidelines for management of meningitis also highlight the importance of investigations such as blood culture and lumbar puncture where feasible and if not contraindicated (Boyles et al., 2013).

4.3.2.8. **Intravenous to oral switch**

The need for intravenous to oral switch was identified by Bala, (2012), a study about antimicrobial stewardship in the internal medicine wards at DGMAH. Guidelines were developed in the form of a poster by Bala, (2012) and introduced in the wards. The same guidelines in a poster form were used in this study to evaluate the awareness with the respective outcome as shown in the Figure 4.15;
Chapter 4: Results and Discussion

In the baseline study, all 100 patients received an intravenous antimicrobial during their stay in the hospital and the patient file review showed that only 34% of the patient had been successfully switched from intravenous to an oral antimicrobial. The average number of days taken to switch from IV to oral therapy was 14 days. Compared to a study by Cyrus & James, (2014) investigating IV to oral switch in which their average day on IV before switching to oral route was about 7 days, it took longer for the prescribers in this study to perform IV to oral switch.

The results from Phase 1 were analysed and an evaluation of the effectiveness of the existing stewardship strategies was done. As result interventions were developed to address shortcomings identified in Phase 1 of the study.
4.4 PHASE 2: INTERVENTIONS

The intervention phase of the study was carried out over four months from 01/05/2014 to 30/09/2014. Delit et al., (2007) highlights the various methods used to strengthen antimicrobial stewardship, which includes, among others, appropriate selection of an antimicrobial, dosing route, and appropriate duration of therapy as well as intravenous to oral switch. The researcher enforced these on the patient’s bedside through reviewing patient files.

The interventions that were implemented included:

Reinforcing intravenous to oral switch of antimicrobials using the existing guidelines, and extent of intravenous to oral switch and ways to strengthen it were developed by the researcher. The researcher moved from patient to patient assessing for the need to switch any antimicrobial to oral and if found, this was discussed with the prescribers in the wards but the decision to switch still remained the responsibility of the attending prescriber. Documentation of each patient where an intervention was made was recorded.

Updating the antimicrobial guidelines (Appendix 8) for the commonly encountered conditions in the internal medicine wards at DGMAH, previously developed by Bala, 2012 using comments from the various factions of internal medicine and microbiology were implemented by the researcher and the antimicrobial guidelines further distributed to consultants and registrars in the internal medicine department for comment, the researcher also used the already existing antimicrobial motivation forms to evaluate what information needed to be changed. Consultations were made with microbiology, pharmacy and internal medicine departments for input into the information that was deemed important and that needed to change. These recommendations were used to update all the information on the already existing forms as well as formulating the new motivation forms. The completed forms were again reviewed for correctness before being presented to the hospital pharmaceutical and therapeutics committee. Antibiotic restriction has been effective in reducing cost of therapy and excessive empiric use of broad spectrum antimicrobials (Weinstein, 2001). A study on the effectiveness of prior authorization in the Unites States revealed a 32% decrease in parenteral antimicrobial cost and an increase in sensitivity to beta lactam antimicrobials by bacterial isolates (Reed et al., 2012). It is therefore of advantage to have some antimicrobials on the motivational list. The following were the forms that were updated or developed;

- Erythromycin IVI see Appendix 4
Chapter 4: Results and Discussion

- Moxifloxacin IVI and oral see Appendix 5
- DGMAH antibiotic motivation form see Appendix 6

Updating of various forms used for motivational antimicrobials and development of motivational forms for those antimicrobials that needed control such as moxifloxacin, at DGMAH, updating of by Bala, (2012) the previously developed IV to oral switch guidelines (Appendix 7) and treatment guidelines from the previous study.
4.5 COMPARISON OF ANTIMICOBIAL PRESCRIBING PATTERNS REVIEW FOR PHASE 1 AND PHASE 3

4.5.1 Most common diagnosis

The Figure 4.16 presents data from both Phase 1 and Phase 3 of the study and will be used to assess the impact of the interventions that were done in the internal medicine wards in Phase 2. The total number of patients per phase was 100 but some of the patients had more than one diagnosis therefore the n>100 in the figure below.

In the pre- and post-intervention results, the top 10 most common diagnoses are presented below;

Pneumonia was the most frequent diagnosis in both the pre- and post-intervention phases of the studies with 19 (18%) and 28 (23%) times respectively. Meningitis was the second most encountered diagnosis in both the pre and post intervention study as illustrated by Figure 4.16.

![Figure 4.16: Most common diagnosis both pre and post intervention phases](image)

When the results from both phases were compared, it was evident that there were more patients with diagnosed with pneumonia in the post-intervention phase than in the pre-intervention phase. The other two conditions in which the diagnoses were more in the post-intervention study were acute confusion state and biventricular failure. When compared with the results from Bala, (2012), it can be noted that meningitis and pneumonia were still the
most common diagnosis. The diagnosis of pneumonia and meningitis were not the only diagnosis of these patients had, RVD was the other comorbidity as is with worldwide studies). The results by Tlali, (2005) in a study at internal medicine wards at DGMAH also showed a similar pattern of diagnosis. Similarly a study in the internal medicine wards in 2010 by Grootboom to determine prescribing patterns also revealed that the most common diagnoses in the internal medicine wards are meningitis and pneumonia among others. Van de Beek et al., (2012) says that meningitis is one of the killers in developing countries in that about a fifth of people with the disease die. He estimates that 0.6 to 4 per 100 0000 patients per year have bacterial meningitis

### 4.5.2 Antimicrobial use at DGMAH internal medicine wards

Analysis of the pre and post intervention data gave the following as the top 10 most prescribed antimicrobials as shown in Figure 4.17.

![Figure 4.17: Top 10 most used antimicrobials in DGMAH internal medicine wards](image)

When the results of the two phases were compared, it was noted that the use of ceftriaxone in both pre- and post-intervention phases were comparable. The dissimilar trend was one of amoxicillin/clavulanic acid which was the most prescribed antimicrobial in the post-intervention phase. This was also shown in a study that evaluated prescribing practices in public hospitals in Asia by Mollahaliloglu et al., (2013) in which the most commonly
prescribed antimicrobials were the beta lactams. The findings in this study are consistent with findings by Bala, (2012) in which ceftriaxone was the most prescribed antimicrobial and on the contrary, to the findings by Tlali, (2005) who conducted a study on antimicrobial usage in the internal medicine wards and found that cefuroxime was the most used antimicrobial. It is however important to note as well that the number of times ceftriaxone was prescribed reduced from 45 times as seen in the study by Bala, (2012) to 33 times in the pre-intervention study, yet the expectation would have been an increase due to the change in guidelines for treatment of pneumonia according to the STG/ EML (2012), which replaced cefuroxime with ceftriaxone as first line for CAP. This may be due to the fact that the most prevalent condition had not changed in the two study periods, but reduced in incidence due to seasonal changes or rather the prescribing patterns had slightly changed for those conditions treated with ceftriaxone. Another antimicrobial that appeared in the top 10 in the post-intervention phase of this study was piperacillin and tazobactam which was never used in the pre-intervention study. The use of ciprofloxacin in the post intervention phase was half that in the pre intervention phase. Azithromycin use was more in the post-intervention phase due to the change in guidelines from using erythromycin to azithromycin. There were no significant changes in the usage of metronidazole and cefuroxime in both the pre- and post-intervention phases.

4.5.3 Defined daily doses of prescribed antimicrobials

In the 1960’s Engel and Siderius did pioneering work in the field of drug utilisation at the WHO regional office for Europe between 1966-1967 in six European countries and showed great differences in drug use in between population groups. The study was then followed by a symposium in Oslo, in 1969 organised by the WHO regional office in Europe and there it was agreed that internationally accepted classification system needed to be born so as to cater for drug consumption studies. It was here that an internationally accepted technical unit of measurement called the defined daily dose for drug utilisation studies was born (WHO, 2013). This method was therefore adopted since it is an internationally accepted tool, to be used in drug utilisation studies in this study as shown in Table 4.3;
Table 4.3: DDD's for Phase 1 antimicrobial use results

<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>DAYS OF THERAPY</th>
<th>TOTAL QUANTITY DISPENSED</th>
<th>COST CHARGED</th>
<th>WHO DDD</th>
<th>WHO DDD UNIT</th>
<th>DDD USED</th>
<th>DDD/100 PATIENTS DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>9</td>
<td>4.5</td>
<td>27.5</td>
<td>1</td>
<td>g</td>
<td>4.5</td>
<td>50.0</td>
</tr>
<tr>
<td>Amoxycillin+clavulanic acid</td>
<td>146</td>
<td>525.6</td>
<td>5146.5</td>
<td>3</td>
<td>g</td>
<td>175.2</td>
<td>120.0</td>
</tr>
<tr>
<td>Amoxycillin+clavulanic acid PO</td>
<td>15</td>
<td>28.1</td>
<td>653.4</td>
<td>1</td>
<td>g</td>
<td>28.1</td>
<td>187.5</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>59</td>
<td>2950.0</td>
<td>2157.6</td>
<td>35</td>
<td>mg</td>
<td>84.3</td>
<td>142.8</td>
</tr>
<tr>
<td>Benzyl penicillin</td>
<td>38</td>
<td>349.4</td>
<td>767.7</td>
<td>3.6</td>
<td>g</td>
<td>97.1</td>
<td>255.4</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>274</td>
<td>1022</td>
<td>13375.5</td>
<td>2</td>
<td>g</td>
<td>511.0</td>
<td>186.5</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>224</td>
<td>857.2</td>
<td>11516.3</td>
<td>3</td>
<td>g</td>
<td>285.7</td>
<td>127.5</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>42</td>
<td>37</td>
<td>86.7</td>
<td>0.5</td>
<td>g</td>
<td>74.0</td>
<td>176.2</td>
</tr>
<tr>
<td>Ciprofloxacin p.o</td>
<td>42</td>
<td>44.5</td>
<td>45.9</td>
<td>1</td>
<td>g</td>
<td>44.5</td>
<td>105.9</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>7</td>
<td>7.0</td>
<td>33.9</td>
<td>0.5</td>
<td>g</td>
<td>14.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>12</td>
<td>28.8</td>
<td>632.6</td>
<td>1.2</td>
<td>g</td>
<td>24.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>25</td>
<td>90</td>
<td>1535.4</td>
<td>2</td>
<td>g</td>
<td>45.0</td>
<td>180.0</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>14</td>
<td>2.8</td>
<td>5.6</td>
<td>0.1</td>
<td>g</td>
<td>28.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>112</td>
<td>222.8</td>
<td>39241.0</td>
<td>1</td>
<td>g</td>
<td>222.8</td>
<td>198.9</td>
</tr>
<tr>
<td>Erythromycin oral</td>
<td>38</td>
<td>76.0</td>
<td>309.1</td>
<td>1</td>
<td>g</td>
<td>76.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Fluloxacin</td>
<td>12</td>
<td>12</td>
<td>19.9</td>
<td>2</td>
<td>g</td>
<td>6.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>127</td>
<td>91.2</td>
<td>1613.9</td>
<td>0.2</td>
<td>g</td>
<td>456.0</td>
<td>359.1</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>70</td>
<td>104.1</td>
<td>7166.9</td>
<td>1.5</td>
<td>g</td>
<td>69.4</td>
<td>99.1</td>
</tr>
<tr>
<td>Metronidazole p.o</td>
<td>76</td>
<td>7.6</td>
<td>15.4</td>
<td>2</td>
<td>g</td>
<td>3.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>9</td>
<td>4.5</td>
<td>24.8</td>
<td>1</td>
<td>g</td>
<td>4.5</td>
<td>50.0</td>
</tr>
<tr>
<td>Trimethoprim + sulphamethoxazole</td>
<td>121</td>
<td>378</td>
<td>114.5</td>
<td>4</td>
<td>4UD</td>
<td>94.5</td>
<td>78.1</td>
</tr>
<tr>
<td>Trimethoprim + sulphamethoxazole ivi</td>
<td>32</td>
<td>112</td>
<td>540.8</td>
<td>4</td>
<td>4UD</td>
<td>28.0</td>
<td>87.5</td>
</tr>
</tbody>
</table>

Key: UD-UNIT DOSES
<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>DAY OF THERAPY</th>
<th>TOTAL QUANTITY DISPENSED</th>
<th>TOTAL COST CHARGED</th>
<th>WHO DDD</th>
<th>WHO DDD UNIT</th>
<th>DDD</th>
<th>DDD/100 PATIENTS DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin+clavulanic acid</td>
<td>311</td>
<td>1086.0</td>
<td>10831.4</td>
<td>3</td>
<td>g</td>
<td>362.0</td>
<td>116.4</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>25</td>
<td>1250.0</td>
<td>914.3</td>
<td>35</td>
<td>mg</td>
<td>35.7</td>
<td>142.9</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>96</td>
<td>58.5</td>
<td>739.2</td>
<td>0.3</td>
<td>g</td>
<td>195.0</td>
<td>203.1</td>
</tr>
<tr>
<td>Benzyl penicillin</td>
<td>29</td>
<td>355.2</td>
<td>44.4</td>
<td>3.6</td>
<td>g</td>
<td>98.7</td>
<td>340.2</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>24</td>
<td>48.0</td>
<td>194.9</td>
<td>4</td>
<td>g</td>
<td>12.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>256</td>
<td>922.0</td>
<td>11853.0</td>
<td>3</td>
<td>g</td>
<td>307.3</td>
<td>120.1</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>208</td>
<td>758.3</td>
<td>9734.4</td>
<td>2</td>
<td>g</td>
<td>379.1</td>
<td>182.3</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>26</td>
<td>20.8</td>
<td>3273.9</td>
<td>0.5</td>
<td>g</td>
<td>41.6</td>
<td>160.0</td>
</tr>
<tr>
<td>Ciprofloxacin oral</td>
<td>5</td>
<td>5.0</td>
<td>5.2</td>
<td>1</td>
<td>g</td>
<td>5.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>47</td>
<td>188.0</td>
<td>3207.3</td>
<td>2</td>
<td>g</td>
<td>94.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Doxycycline oral</td>
<td>5</td>
<td>1.0</td>
<td>2.0</td>
<td>0.1</td>
<td>g</td>
<td>10.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>79</td>
<td>158.0</td>
<td>23329.2</td>
<td>1</td>
<td>g</td>
<td>158.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Erythromycin oral</td>
<td>37</td>
<td>69.0</td>
<td>216.8</td>
<td>1</td>
<td>g</td>
<td>69.0</td>
<td>186.5</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>23</td>
<td>13.6</td>
<td>75.7</td>
<td>0.2</td>
<td>g</td>
<td>68.0</td>
<td>295.7</td>
</tr>
<tr>
<td>Fluconazole oral</td>
<td>8</td>
<td>10.0</td>
<td>44.5</td>
<td>0.2</td>
<td>g</td>
<td>50.0</td>
<td>625.0</td>
</tr>
<tr>
<td>Imipenem</td>
<td>8</td>
<td>12.0</td>
<td>995.5</td>
<td>2</td>
<td>g</td>
<td>6.0</td>
<td>75.0</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>35</td>
<td>52.5</td>
<td>3742.1</td>
<td>1.5</td>
<td>g</td>
<td>35.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Piperacillin + Tazobactam</td>
<td>26</td>
<td>264.6</td>
<td>14905.8</td>
<td>14</td>
<td>g</td>
<td>18.9</td>
<td>72.7</td>
</tr>
<tr>
<td>Procaine Penicillin</td>
<td>16</td>
<td>230.4</td>
<td>215.0</td>
<td>0.6</td>
<td>g</td>
<td>384.0</td>
<td>2400.0</td>
</tr>
<tr>
<td>Trimethoprim+ sulphamethoxazole oral</td>
<td>9</td>
<td>18.0</td>
<td>46.8</td>
<td>4</td>
<td>4 UD</td>
<td>4.5</td>
<td>50.0</td>
</tr>
</tbody>
</table>

Key: UD-UNIT DOSES
The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. (WHOCC)

The rate of antimicrobial use in the hospital in DDDs is shown in Table 4.3 and Table 4.4 representing drug use in both the pre-and post-intervention phases respectively. Based on the findings, ceftriaxone and fluconazole were the most used antimicrobials followed by cefuroxime and erythromycin respectively as shown by their respective defined daily doses per day in the respective tables in Phase 1 of the study.

When compared with Phase 1 results it is seen that amoxicillin / clavulanic acid, cefuroxime, ciprofloxacin and procaine penicillin were the most used antimicrobials. This can be due to the following among other reasons;

- Change in the conditions commonly seen in the wards probably due to seasonal changes.
- Rotation of prescribers who may prefer to use other agents compared to what the prescribers in phase one used.

The advancement of new information concerning the treatment of these commonly encountered conditions as is expected to be with ceftriaxone due to the changes in the treatment guidelines where ceftriaxone became the first choice over cefuroxime in the treatment of pneumonia. This was not reflected with the DDD as still amoxicillin came out top. This was however seen with the change to using azithromycin instead of erythromycin for CAP.

It is also important to note that amikacin and flucloxacillin in Phase 1 were under dosed as in the case the DDDs being below that of the WHO unlike in Phase 2 the doses seem to be within normal range. It is, however, important to note that the overall DDDs used both in Phase 1 and Phase 2 were comparable.

4.5.4 Route of administration of prescribed antimicrobials

Most of the prescribed antimicrobials in the pre-and post-intervention studies per patient file were both IV and oral. About 37 patient files per 100 on average had only IV antimicrobials prescribed for both the pre- and post-intervention phases. There was no patient file with only oral antimicrobials in the post-intervention study while 16 patient files from the pre-intervention study had only an oral antimicrobial prescribed. In the previous study by Bala, (2012), at least 69% patients had their medicines administered via the intravenous route with an oral agent prescribed, 55% had only an intravenous medicine prescribed. The change
can be attributed to the change in the prescribers in the wards due to rotation of interns between the different wards. However, the data in this study and the previous studies were collected at approximately the same time, meaning no environmental changes might have played a big role in the prescribing of these antimicrobials. Refer to the figure 4.18.

Figure 4.18: Route of administration of prescribed antimicrobials

4.5.5 Comparison of adherence to guidelines, missed doses and collection of specimen for microbiological culture in both the pre and post intervention study

A comparison of the results for adherence to guidelines, missed doses and collection of specimen for culture in the pre- and post-intervention study were done according to the results presented in the Figure 4.19.
4.5.6 Adherence to guidelines while treating any conditions

In the pre-intervention study results, about 61% of the prescribed antimicrobials were, according to at least one of the protocols used in South Africa such as the local hospital protocols or the STG/ EML with an improvement in the post-intervention results to about 70% of all prescribed antimicrobials. This was because not only the local hospital guidelines were used, but other guidelines available for treatment of a particular diagnosis as mentioned by six prescribers. In the United States in a study by Shih et al., (2011) (Molyneux, about the adherence of physicians to the centre for disease control and prevention, treatment guidelines in the US emergency department visits with a diagnosis of pelvic inflammatory disease showed a 30.5% adherence to these guidelines. In a study done in India in Ujjain by Pathak et al to assess adherence to treatment guidelines in children up to 12 years in Ujjaine with diarrhoea showed a 1% adherence to guidelines. It can therefore be said that it is an international problem for prescribers not to adhere to guidelines. Interventions such as the one done in Kenya in a study by Zurovac et al., (2011) in which Kenyan prescribers were reminded via mobile text to improve adherence to malaria guidelines saw an improvement of 23% in adherence to malaria guidelines immediately and up to 25% in six months.
4.5.7 Missed doses of prescribed antimicrobials per patient file

Of all the prescribed antimicrobials in the pre-intervention study, almost 42 per cent of the patients had missed a dose or more of the antimicrobials prescribed. There was an improvement post-intervention with only 24% having at least one antimicrobial dose missed. One factor to consider would have been out of stock items such as erythromycin IV, which was out of stock due to the proposed change by the Gauteng PTC from using erythromycin IV to using azithromycin which is a cheaper option. This was because Gauteng was one of the highest users of erythromycin IV. The presence of the researcher in the ward following up on antimicrobial administration would also have played a role in the results seen.

4.5.8 Collection of specimen for culture

The pre-intervention study revealed that only 32% of patients' files reviewed prospectively had a culture collected for analysis; the rest were just treated empirically with either one or a combination of antimicrobials. After the interventions, there was an improvement to about 45%. This can be attributed to a number of factors such as the presence of a pharmacist in the wards who would have had an influence on the number of samples taken, the rotation of some of the interns as well as a medical officer from other departments that could have been already aware of the practice of taking cultures wherever an infectious condition is encountered. However, coagulase negative *Staphylococcus epidermidis* (CONS) was isolated three times out of the 19 (16%) positive cultures, despite the assertion that aseptic techniques were being followed by the prescribers since they seemed to be aware of it as highlighted in the prescriber questionnaire results. This calls for more investigations to be done to find out the reasons for the isolation of CONS and if noninfectious therefore a contaminant in the samples, relevant measure to be put in place to help reduce the incidence.

4.5.9 Comparison of isolated microorganisms from the samples taken in the pre- and post-intervention phases

The results of the isolated microorganisms for both the pre intervention and the post intervention phase are presented as shown in the Figure 4.20.
Chapter 4: Results and Discussion

Figure 4.20: Isolated microorganisms for the specimens collected

In the pre-intervention study, a total number of 19 isolates were made and 19 isolates in the post-intervention study from the 100 patient files reviewed in each of the study. Seven of the samples taken did not have any culture isolated in the post-intervention study and 28 in the pre-intervention study therefore antimicrobials were not indicated in these patients after culture yet therapy was continued any way. Coagulase negative Staphylococcus aureus was the most isolated organism in the post intervention study and the second most isolated to Klebsiella pneumoniae in the pre-intervention study. The isolated microorganism CONS were consistent with results from the previous study by Bala (2012) in which CONS still was one of the most isolated microorganisms. This was speculated to be as a result of not following aseptic techniques while collecting samples. These results therefore appeal to the need to re-enforce aseptic techniques regularly to avoid sample contamination.

4.5.10 Intravenous to oral switch

Many of the patients admitted to hospital for severe infection and require IV therapy initially can be switched to oral therapy within two to three days upon initiation of an antibiotic provided that they are clinically improving and can tolerate an oral formulation (Van Niekerk,
2012; Chang-Ro et al., 2013). Figure 4.21 below shows the results from the data collected for both pre- and post-intervention phase for IV to oral switch.

![Figure 4.21: Comparison between Phase 1 and Phase 2 intravenous to oral switch for patients](image)

An IV to oral switch guideline was developed by Bala, 2012 in his study on antimicrobial stewardship and implemented, however, continued strengthening of this practice needed to be in place in order to have improved adherence (Boyles et al., 2013).

Successful switching from an IV to oral agent of antimicrobial is dependent on a number of factors such as microbiological culture, availability of equal potent antimicrobials and the ability of the patient to take oral medication. In the pre-intervention phase, there were 34 patients in which IV to oral switch was done as opposed to the 14 patients that were switched in the post-intervention phase. A drop in the number of patients that were successfully switched was noted and this could have been due to the increased use of ceftriaxone (which does not have an oral equivalent), it was also noted that the physicians were not comfortable with switching patients who were deemed to be too ill.

### 4.6 SUMMARY

This chapter presented and discussed all the results obtained in the study, according to the objectives of the study and were compared with results from the previous study and
published literature, both locally and internationally as well as unpublished studies that were conducted in the internal medicine wards at DGMAH. The results from prescriber questionnaire were compared with those obtained in the study by Bala, (2012) and results of Phase 1 (baseline) were compared with those obtained in Phase 3 (after intervention) where the similarities and differences were compared and discussed in detail

The next chapter will present the conclusion, recommendations and limitation of this study based on the results discussed above.
CHAPTER 5

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

5.1 INTRODUCTION

In this chapter, the conclusion of the results in Chapter 4 will be presented and based on the findings, recommendations for practice and further research will be offered. The chapter also presents the limitations encountered or observed while conducting the study.

5.2 CONCLUSION

The study comprised of both male and female adult patients admitted in the internal medicine wards and there were no particular format in which the patients were selected according to gender, but only on the basis of treatment with an antimicrobial agent. The physicians who participated in the research did not represent any particular percentage of prescribers but were selected according to availability. The conclusions will be based on the objectives of the study as follows;

5.2.1 Updating of forms used for motivational antimicrobials and treatment guidelines

Forms used for motivational antimicrobials and treatment guidelines were updated and presented to the PTC for review and implementation. This was not successfully done due to time constraints and the delay in PTC making decisions on the adoption process.

Regular update to the guidelines should be done as one of the main reasons why the prescribers did not use of the available guidelines is that they are not updated at all.

Updating of motivation forms was aimed at providing a better control of antimicrobials including those that are controlled but this was not achieved because the forms were not implemented. There is need for inter departmental participation in the implementation of these updated forms.

Intravenous to oral switch guidelines were introduced by Bala, (2012) in his study and were strengthened in this study. The motivational forms were also meant to further augment IV to oral switch with the already introduced IV to oral switch charts in the wards. In order to achieve a 100% IV to oral switch of all patients who are legible for switching. The successful
achievement of that will need a full time ward based pharmacist emphasizing the switching of eligible patients at all times.

Adherence to a treatment guideline saw an improvement in the post-intervention phase due to the fact that the presence of the researcher in the wards looking at the prescribed regimens against the primary diagnosis and discussing the findings with the prescribers in the wards thus an improvement in the use of preferred guidelines for a particular infection by the prescribers.

Specimens were supposed to be collected for culture before initiation of an antimicrobial agent. This was emphasised by the researcher in the wards to the physicians on a one on one basis and saw a positive responses as seen in the results with an improvement in the number of samples taken though not that significant therefore the need to emphasise collection for samples for culture more to achieve a better outcome in the forthcoming studies.

The isolation of CONS was seen in this study as was in the previous study by Bala, (2012), this require continued assessment and emphasising of aseptic techniques while taking samples for culture. Further investigation also needs to be done in order to find out if the CONS isolated in pathological or a normal commensal and appropriate measure put in place.

The number of missed doses dropped in the post-intervention study when compared to the pre-intervention study due to the presence of the researcher in the wards who continually documented and investigated causes of the patients missing doses. It can be further emphasised that there is a need for a ward based pharmacist to enforce this in the wards.

5.2.2 Assessing the knowledge of prescribers about the existing antimicrobial stewardship strategies

There is need to make sure all prescribers in the internal medicine wards are aware of the existing antimicrobial stewardship strategies despite the rotations they undertake. This can be achieved through incorporation of these strategies into the orientation programme that the department has for all new prescribers in the wards as well as at least quarterly presentations to the internal medicine staff in meeting about these strategies other than a once off presentation.
5.2.3 **Introduce other strategies to improve antimicrobial stewardship**

The researcher tried to introduce other strategies to further improve antimicrobial stewardship such as antimicrobial grand round. This was not implemented successfully due to the lack of enough human resource to cater for the needs that would arise after introduction therefore a thorough preparation is needed to enable a successful implementation of antimicrobial grand round.

In ward bed presentations were done on a one on one basis whenever chance arose on IV to oral switch guidelines, antimicrobial de-escalation, missed doses and the proposed treatment guidelines which saw an improvement in some of these areas.

The study has brought to light that there is a need to emphasise IV to oral switch of prescribed antimicrobials, accepted standard treatment protocols for the most common infectious conditions in the internal medicine wards and motivational forms for controlled antimicrobials through updating and implementing them and the establishment of a full time pharmacist to monitor stewardship in the internal medicine wards. Documentation should be done to show the impact of a ward pharmacist in the internal medicine wards on a daily basis.

5.3 **RECOMMENDATIONS**

- More enforcement of the existing antimicrobial stewardship strategies needs to be done, to ensure that physicians follow the guidelines through the introduction of a ward pharmacist to at least emphasise and monitor progress on a daily basis so that there is a cumulative change. Reynolds et al., (2008) states that effective strategies include education based on proper understanding of existing beliefs and investment in improved surveillance, in this case the pharmacist in the ward will keep surveillance of all the progress made in improving antimicrobial use in the wards.

- The proposed IV to oral switch guidelines and the antimicrobial motivation form should be presented in the form of a pocket book so that it is readily available to physicians.

- Updated guidelines should be implemented and then a roll out of the updated guidelines should include all the prescribers in internal medicine department so that assimilation of the guidelines into the daily prescribing by prescribers is enhanced.
• The antimicrobial guidelines should be updated and presented to the internal medicine wards to increase awareness of the prescribers’ about the updates. The changes should be acceptable to all the physicians in the internal medicine wards.

5.4 LIMITATIONS OF THE STUDY

The limitations that were observed during the study include the following:

• The study was conducted in the internal medicine wards which are not a representation of the whole hospital, therefore any recommendations cannot be generalised.

• The prescribers who took part in the study were inclined towards interns. Effort should be made in the coming studies so that prescribers who may not be in the wards but wish to take part in the study are given an opportunity to do so by making the questionnaires readily available to them in their time of convenience.

• Only patients who had their files on the bed and had an antimicrobial prescribed were included in the study, meanwhile there might have been patients with antimicrobials prescribed that were not in the wards at the time the study was conducted therefore missed to be included in the study.

• Antimicrobial rounds were meant to be introduced but the lack of enough staff and the lack of cooperation from some of the departments led to their failure.
REFERENCES


Danysz, KZ. 2006. The investigation of antimicrobial prescribing patterns at Themba hospital, Kabokweni. Available at ul.netd.ac.za/bitstream/10386/397/1/Danysz%20Dissertation%20FINAL.pdf


References

https://www.accp.com/docs/positions/guidelines/Pharm2511_ACCP-TherapIntchg.pdf
accessed 23/11/2014


Grootboom, WM. 2010. Prescribing patterns in adult patients with meningitis in internal medicine wards, Dr.George Mukhari Hospital. Dissertation (Masters) Medunsa.

Hall, KK. Lyman. 2006. Updated review of blood culture contamination. Available at http://cmr.asm.org/content/19/4/788. Accessed 10/12/201


Mollahaliloglu, S. Alkan, A. Donertas, B. Ozgulcu, S. Akici, A. 2013. Assessment of antibiotic prescribing at different hospitals and primary health care facilities. Available at http://ac.els-cdn.com/S1319016412000941/1-s2.0-S1319016412000941-main.pdf?_tid=3e4c7b06-5e9b-11e4-ae6d-00000aab06b&acdnat=1414498338_7cc78cc40e0aa226c02520c1904c7213 Accessed 29/10/2014


Sooruth, U. 2013. The use of Standard Treatment Guidelines and Essential Medicines List by registered nurses at primary health care clinics in the uMgungundlovu district, South Africa. Available at


References


Zuber, A. McCarthy, CF. Verani, AR. Msidi, E. Johnson, C. 2011. A Survey of Nurse-initiated and -Managed Antiretroviral Therapy (NIMART) in Practice, Education, Policy, and

Appendix 1: Medunsa Research & Ethics Committee Clearance Certificate

MEETING: 07/2013
PROJECT NUMBER: MREC/H/2013: PG

Title: Strengthening antimicrobial stewardship in the internal medicine ward at Dr George Mukhari Academic Hospital. An interventional study

Researcher: Mr JM Nabwana
Co-supervisor: Prof AGS Gaus
Hospital Superintendent: Dr J Roberts (Dr George Mukhari Academic Hospital)
Department: Pharmacy
School: Health Care Science
Degree: MSc (Med) Pharmacy

DECISION OF THE COMMITTEE:
MREC approved the project.

DATE: 05 September 2013

Note:
(i) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.
(ii) The budget for the research will be considered separately from the protocol. PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.
Appendices

Appendix 2: Patient Identification Form

## PATIENT IDENTIFICATION FORM

<table>
<thead>
<tr>
<th>Study number</th>
<th>Patient names</th>
<th>Hospital number</th>
<th>Ward#</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>006</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>015</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>016</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>017</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>018</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>019</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>020</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>021</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>022</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>023</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>024</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>025</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>026</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>027</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>028</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>029</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendices

Appendix 3: Data Capturing Form

Diagnosis: ...........................................................................................................................................

Microbiological specimen collected: ........................................................................................................

Status ....................................................................................................................................................

Organism isolated.................. … Days to switch to Oral antibiotic.................................................

<table>
<thead>
<tr>
<th>Duration of therapy in days</th>
</tr>
</thead>
<tbody>
<tr>
<td>(√ = administration)</td>
</tr>
</tbody>
</table>

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>
# Appendix 4: Erythromycin Motivation Form

**MOTIVATION FOR THE USE OF ERYTHROMYCIN IVI AT DR. GEORGE MUKHARI ACADEMIC HOSPITAL**

*(To be attached to the prescription)*

<table>
<thead>
<tr>
<th>PATIENT INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAME:</td>
</tr>
<tr>
<td>GT number:</td>
</tr>
<tr>
<td>Ward:</td>
</tr>
</tbody>
</table>

**Diagnosis and duration of therapy**

*(To be hand written by prescriber)*

<table>
<thead>
<tr>
<th>Is the patient on any oral medication</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

**Reason/s for IVI route:**

1. Critically ill patient and cannot swallow
2. Patient cannot tolerate oral formulation

**Clinician’s Name & Qualification**

**Signature**

**Phone No/ Ext**

**PHARMACY USE**

QUANTITY ISSUED…………………………………………………………………………………………………………………………..

PHARMACIST'S NAME……………………………………SIGNATURE…………………………DATE………...
Appendices

Appendix 5: Moxifloxacin Motivation Form

MOTIVATION FOR THE USE OF MOXIFLOXACIN AT DR GEORGE MUKHARI ACADEMIC HOSPITAL

To be attached to the prescription

Available dosage forms: Moxifloxacin 400mg IVI and Moxifloxacin 400mg oral

<table>
<thead>
<tr>
<th>PATIENT INFORMATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NAME:</td>
<td>DATE:</td>
</tr>
<tr>
<td>GT number:</td>
<td>Age:</td>
</tr>
<tr>
<td>Ward:</td>
<td>Gender:</td>
</tr>
</tbody>
</table>
### Appendices

**DIAGNOSIS (tick appropriate one)**

<table>
<thead>
<tr>
<th>A. BRONCHOECTASIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
</tr>
</tbody>
</table>

1. Patient allergic to penicillin |
   - Moxifloxacin 400mg orally (10 days)

<table>
<thead>
<tr>
<th>B. COMMUNITY ACQUIRED PNEUMONIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
</tr>
</tbody>
</table>

1. Un complicated/severe pneumonia with Penicillin allergy |
   - Moxifloxacin 400mg orally

<table>
<thead>
<tr>
<th>C. MDR TUBERCULOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
</tr>
</tbody>
</table>

1. Intensive phase (guided by TB culture) |
   - Moxifloxacin 400mg (6 months)

2. Continuous phase |
   - Moxifloxacin 400mg (18 months)

Dose and duration of therapy
(To be hand written by prescriber)

Clinician’s name, Qualification

Signature

Phone No/ Ext

---

**PHARMACY USE**

QUANTITY ISSUED..............................................................................................................................

PHARMACIST'S NAME...........................................................SIGNATURE........................................DATE..............
Appendix 6: DGMAH Antimicrobial Motivation Form

Please attach this form to patients treatment card

This form is to be used for ordering any of the intravenous / intra muscular antimicrobials listed below. Due to antibiotic stewardship and cost it was decided by the antibiotic committee with the support of the management that these antimicrobials will only be issued by the pharmacy on the approval of the Head of department or senior consultant in the prescribing department.

<table>
<thead>
<tr>
<th>ANTIVIRALS</th>
<th>Acyclovir</th>
<th>Ganciclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycopeptides:</td>
<td>Vancomycin</td>
<td></td>
</tr>
<tr>
<td>Carbapenems:</td>
<td>Meropenem</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Cephalosporins:</td>
<td>Cefotaxime</td>
<td>Ceftazidime</td>
</tr>
<tr>
<td></td>
<td>Cepeime</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>Aminoglycosides:</td>
<td>Tobramycin</td>
<td></td>
</tr>
<tr>
<td>Linsosamides:</td>
<td>Clindamycin</td>
<td></td>
</tr>
<tr>
<td>Sulphonamides + trimethoprim:</td>
<td>Co-trimoxazole</td>
<td></td>
</tr>
<tr>
<td>Penicillins:</td>
<td>Amoxicillin + clavulanic acid</td>
<td>Piperacillin &amp; Tazobactam</td>
</tr>
<tr>
<td>Fluoroquinolones:</td>
<td>Ciprofloxacin</td>
<td></td>
</tr>
<tr>
<td>Rifamycin derivative:</td>
<td>Rifampicin</td>
<td></td>
</tr>
<tr>
<td>ANTIFUNGALS:</td>
<td>Polynes:</td>
<td>Amphotericin B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE**

1. This form should be accompanied by culture results showing sensitivity to the requested antibiotic except for bacterial meningitis.

2. Motivation is not needed for first 3 days of therapy in the following wards; ICU, NICU and admission ward in internal medicine (Ward 36).

**PATIENT NAME.................................................... Hosp No....................................DATE.............**

**ISOLATED MICROORGANISM/S..........................................................**

**DRUG..........................................................DOSAGE..........................................................**

**PROPOSED DURATION OF THERAPY..........................................................**

**PRESCRIBING OFFICER’S SIGNATURE....................................................**

**APPROVEDBY**

(HOD or Senior Consultant)..........................................................SIGNATURE...................................................

**PHARMACY USE**

**PHARMACIST’S NAME..........................................................SIGNATURE.............................................DATE..............**
Appendices

Appendix 7: IV to Oral Switch Guidelines

IVO TO ORAL SWITCH GUIDELINE (2012)

REASONS FOR CONTINUING WITH IV THERAPY

- Patient is unable to swallow, unconscious or sedated
- Patient has severe nausea, vomiting, diarrhoea, short bowel syndrome, GI obstruction, mal-absorptive syndrome or loss of access
- Patient has active gastrointestinal bleeding
- Patient has continuous tube feedings that cannot be interrupted
- The required medication is known to be bad to enteral nutrition formulas (e.g., Intralipid 10% Divalent cations)
- Patient has experienced severe sepsis within the last 72 hours
- Severely immunosuppressed patients
- Neutropenic patients
- High risk patients or have deep seated infections which require IV antimicrobials to guarantee sufficient drug levels at the site of action e.g.: S. aureus bacteraemia
- Meninigitis
- Necrotising fasciitis
- Severe cellulitis & soft tissue infections e.g., group A streptococcal infections
- Intra-abdominal abscesses
- Liver abscesses
- Infective endocarditis
- Legrene pneumonia
- Exacerbations of cystic fibrosis
- Malnourished patients
- Inadequately drained abscesses
- Empyema
- Infections of implants/prostheses
- Osteomyelitis
- Septic arthritis

REASONS FOR SWITCHING

- There is clinical improvement
- Signs and symptoms of infection are improving e.g., fever, white cell count, CRP, PCT etc.
- Patient is able to eat a regular or modified diet
- Patient is able to receive enteral nutrition via the oral, gastric or other enteral tube
- Patient is able to receive other scheduled medications by the oral route
- The oral route is not compromised e.g. by vomiting, severe diarrhoea, mal-absorptive disorder, swallowing problems or unconscious
- Patient does not meet any of the exclusion criteria

Continue IV therapy and review for switching criteria every 24 hours.

Does the patient meet the above criteria for switching?

Y

N

Use the table to select the appropriate oral agent to switch to.

<table>
<thead>
<tr>
<th>IV agents</th>
<th>ORAL agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin 500mg – 3 x 4 hourly</td>
<td>Amoxicillin 500mg – 1 x 8 hourly</td>
</tr>
<tr>
<td>Ampicillin 1.5g – 2 x 4 hourly</td>
<td>Ampicillin 500mg – 1 x 4 hourly</td>
</tr>
<tr>
<td>Co-amoxicillin 1.25g x 4 hourly</td>
<td>Co-amoxicillin 500mg x 4 hourly Co-amoxicillin 750mg + Amoxicillin 500mg</td>
</tr>
<tr>
<td>Ceftriaxone 500mg – 1 x 8 hourly</td>
<td>Ceftriaxone 500mg x 4 hourly</td>
</tr>
<tr>
<td>Gentamicin 75mg x 1 or 1.5g 6 hourly</td>
<td>Gentamicin 500mg x 8 hourly</td>
</tr>
<tr>
<td>Ciprofloxacin 500mg x 12 hourly</td>
<td>Ciprofloxacin 500mg x 8 hourly</td>
</tr>
<tr>
<td>Cefuroxime 500mg x 8 hourly 24 hourly PJP prophylaxis, 900mg x 2 hourly in acute infections and 1000mg x 2 hourly in PJP treatment for 21 days</td>
<td>Cefuroxime 500mg x 8 hourly 24 hourly PJP prophylaxis, 900mg x 2 hourly in acute infections and 1000mg x 2 hourly in PJP treatment for 21 days</td>
</tr>
<tr>
<td>Ciprofloxacin 400mg x 12 hourly</td>
<td>Ciprofloxacin 500mg x 12 hourly</td>
</tr>
<tr>
<td>Ceftazidime 1g x 4 hourly (maximum 12g daily)</td>
<td>Ceftazidime 500mg x 12 hourly</td>
</tr>
<tr>
<td>Ambisone 15mg x 12 hourly</td>
<td>Ambisone 15mg x 12 hourly</td>
</tr>
<tr>
<td>Gentamycin 1mg x 12 hourly (in 6-hourly Enoxacin in combination with a penicillin)</td>
<td>Gentamycin 500mg x 12 hourly</td>
</tr>
<tr>
<td>Metronidazole 500mg x 8 hourly</td>
<td>Metronidazole 500mg x 8 hourly</td>
</tr>
<tr>
<td>Erythromycin 1g x 8 hourly</td>
<td>Erythromycin 500mg x 8 hourly</td>
</tr>
</tbody>
</table>

RESOURCE
1. INTRODUCTION

Antimicrobial stewardship involves the optimal selection, dosage and duration of an antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance. (Owen et al. 2004). One of the essential strategies used in antimicrobial stewardship programmes is provision of guidelines for antimicrobial prescribing in the form if antimicrobial guidelines. It’s a pre-prescription strategy which greatly impact antimicrobial prescribing when implemented and followed accurately. The upsurge of antimicrobial resistance over the years is a great threat to the patient management, especially in hospital settings. The overuse coupled with irrational use of antimicrobials has been noted amongst the contributing factors to this development of resistance. It’s therefore important to note that providing guidelines for antimicrobial prescribing is pivotal in preventing this problem.

NB. Microbiological specimens should be collected before initiation of empiric therapy or antimicrobial treatment.

2. PURPOSE

The guidelines are intended to assist clinicians in quick decision making regarding treatment plans for their patients. They are intended for adult patients managed in a hospital setting and based on local and commonest infectious disease treatment guidelines, sensitivity patterns and evidence based literature.

3. MENINGITIS

3.1 Acute bacterial meningitis

This is a medical emergency, blood culture together with CSF (if their intracranial pressure is not raised) should be collected and empirical therapy should be started immediately.

NB: Do not await results before initiating empirical therapy

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested empirical therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>N. meningitidis</td>
<td>Ceftriaxone 2g IV q12h for 2 weeks</td>
<td>Cefotaxime 3g IV q6h for 2 weeks</td>
</tr>
<tr>
<td>H. influenzae</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.2 Chronic meningitis

Past medical history is very important in aiding the diagnosis process. Blood culture should be done for both bacteria and tuberculosis. Also, CSF should be obtained for investigating Cryptococcus, syphilis and tuberculosis.

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. tuberculosis, Brucella, T. pallidum, Cryptococcus, Toxoplasmosis, Enterovirus, Histoplasmosis</td>
<td>Treat pathogen after confirming the diagnosis. Give empiric therapy as above.</td>
<td>Treatment based on the isolated organism.</td>
</tr>
</tbody>
</table>

3.1.2 Cryptococcal meningitis

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. neoformans</td>
<td>Amphotericin B IV 1mg/kg/day for 6-8 weeks plus fluconazole 800mg/ day for 2 weeks. Followed by Fluconazole 400mg daily Orally for 2 months then 200mg/ day 12 months or longer until CD4 count &gt; 200cell/ul taken 6 months apart.</td>
<td>Fluconazole 1200mg daily IV or Oral for 10 weeks after a minimum of 2-4 weeks of amphotericin B therapy and patient not tolerant any more.</td>
</tr>
</tbody>
</table>

NB. Continue maintenance therapy until CD4-T lymphocyte count > 200cells/ul for 6 months.

3.2.2 Tubercular meningitis

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. tuberculosis</td>
<td>Use standard combination tuberculosis therapy for 9-12 months. Add pyridoxine</td>
<td>Not available</td>
</tr>
</tbody>
</table>
Appendices

| 25mg/day for INH. |

3.3 Other organisms e.g. viruses etc.

<table>
<thead>
<tr>
<th>Common pathogens</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes simples virus,</td>
<td>Acyclovir 10mg/kg / day for 21 days until PCR is negative</td>
<td>Other not approved for use</td>
</tr>
</tbody>
</table>

4. PNEUMONIA

4.1 Community acquired pneumonia in an HIV negative patient

4.1.1 Community acquired pneumonia in patients who are admitted without co-morbidities and are less than 65 years

<table>
<thead>
<tr>
<th>Common pathogens</th>
<th>Suggested therapy (MILD CASES)</th>
<th>Alternative therapy (SEVERE CASES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae</td>
<td>Amoxicillin 1g q8h Oral for 5-7 days / cefuroxime 500mg bd (or Higher)</td>
<td>Amoxicillin/Clavulanic acid 875mg or Cefuroxime 750mg q8h. In penicillin allergy give Ofloxacin 400 or Moxifloxacin 400 bd (confirm)</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>if poor response after 48-72 hours add Doxycycline 200mg Oral immediately followed by 100mg twice daily for 14 days or Erythromycin 500mg Oral q6h for 14 days</td>
<td>If poor response after 48-72 hours add the same agents as for mild cases in the second column</td>
</tr>
<tr>
<td>S. aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical pathogens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legionella spp. (falls under other not atypical)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.1.2 Community acquired pneumonia in patients who are admitted with co-morbidities and are above 65 years (e.g. COPD, diabetes mellitus, renal disease, cardiac failure etc.)

<table>
<thead>
<tr>
<th>Common pathogens</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same community pathogens</td>
<td>Amoxicillin/Clavulanic acid</td>
<td>if allergic to penicillin give</td>
</tr>
</tbody>
</table>
4.1.3 Community acquired pneumonia in prisons and old age homes.

<table>
<thead>
<tr>
<th>Common pathogens</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em>, <em>Mycoplasma pneumoniae</em>, <em>Chlamydia spp</em>, <em>Legionella</em>, <em>Coxiella burnetti</em>, <em>Staphylococcus aureus</em></td>
<td>Benzyl penicillin 2 million units q6h plus metronidazole, 400mg q8h orally plus Amikacin 15mg/kg/day for 5 days. Follow with amoxicillin 500mg q8h plus metronidazole oral 400mg q8h</td>
<td>Clindamycin IV 600mg q8h</td>
</tr>
</tbody>
</table>

4.1.4 Community acquired pneumonia and HIV infection

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis jiroveci</em> (PCP)</td>
<td>Co-trimoxazole 160/800 oral q6h for 21 days followed by 160/800 oral daily for at least 6 months and until CD4 count increases to greater than 200 cells/mm³ if one is on HAART or give it lifelong if they are not on HAART</td>
<td>Dapsone 100mg Oral q24h (in case of allergy)</td>
</tr>
</tbody>
</table>

Key: HAART, Highly active antiretroviral therapy

4.1.5 Mycobacteria avium pneumonia

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. avium complex</em></td>
<td>Ofloxacin/Ciprofloxacin</td>
<td>Alt Rx Pg 53 antibiotic</td>
</tr>
</tbody>
</table>
### 4.2 Hospital /ventilator acquired pneumonia

<table>
<thead>
<tr>
<th>Common pathogen/s</th>
<th>Suggested therapy</th>
<th>Alternative therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em> (especially MRSA) Enterobacteriaceae <em>P. aeruginosa</em> Acinetobacter spp</td>
<td>Piperacillin/tazobactam 4.5g q8h Plus or minus Vancomycin if MRSA is suspected</td>
<td>Cefepime 2g q8h or Ertapenem 1g q24h or ciprofloxacin 400mg q8h or Levofloxacin 500mg q12h (for sensitive <em>S. aureus</em>) or 750mg q24h or Imipenem 500mg IV q6h or Meropenem IV 1g q8h</td>
</tr>
</tbody>
</table>

5. REFERENCES


Appendices

