

**PRESCRIBING PATTERNS OF ANTIMICROBIAL AGENTS FOR SURGICAL SITE
INFECTIONS AT 1 MILITARY HOSPITAL AND MANKWENG HOSPITAL.**

By

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DISSERTATION

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Declaration

I Mathobela Caswell Kwena Kedishi declare that the dissertation hereby submitted to the University of Limpopo for the degree Master in Pharmacy (Pharmacology) has not been previously submitted by me for a degree at this or any other University, that it is my own work in design and in execution and that all the materials contained therein have been duly acknowledge.

.....
Mathobela Caswell Kwena Kedishi

.....
Date

Dedication

I would like to dedicate this study to my mom and my late father who wanted the best out of me to become something in life through education, as they did not have an opportunity to be educated. I would also like to dedicate this study to my son and my brother Lethabo and Kgoadi respectively for them to live and to love studying. Take control of what people read, listen, and take control of what children learn at school you will be in power.

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Firstly, I would like to acknowledge the University of Limpopo Department of Pharmacy for allowing me to carry out this study through them. Prof N. Nyazema and Prof Y. Dambisya as my supervisor and co-supervisor respectively for guiding me through during the project and supporting me during the challenges encountered during the study. I would like to thank Dr. R. Lekalakala who had been very helpful during the study in extracting the data and convening feedback sessions. The infection control team from Mankweng Hospital played a key role in obtaining the data.

I would like to send my sincere gratitude to Brig General N. Maphaha and Col T. Mothabeng (assisting me in addressing merits of the study) for allowing me to carry out the study at 1 Military Hospital and supporting me in obtaining the clearance, collecting data and convening the feedback session. I would like to thank Maj E. Shihlangu who helped me with data extraction from the lab and Cpl K. Shanaaz who helped me in filtering the data from lab.

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Definition of terms

Antibiotic formulary- is a local policy document produced by a multi-professional team, usually in a hospital trust or primary commissioning group, combining best evidence and clinical judgment or a simple list of drugs available to a clinician (National Institute for Health and Clinical Excellence guidelines, 2008).

Antibiotics- are medicines used to treat infections or diseases caused by bacteria by inhibiting the growth of bacteria, or act by destroying the bacteria (Shiva et al. 2013).

Antibiotic prophylaxis- is the preoperative use of antibiotics to prevent the development of surgical site infections (National Institute for Health and Clinical Excellence Guidelines, 2008).

Antimicrobial agent- is an agent with effects of killing microorganism or suppressing their multiplication or growth (The Free Medical Dictionary).

Antimicrobial resistance- Antimicrobial resistance is the ability of a microorganism to grow or survive in the presence of an antimicrobial agent that is usually sufficient to inhibit or kill microorganisms of the same species (Shiva et al. 2013).

Broad-spectrum antibiotic- refers to an antibiotic that acts against a wide range of disease-causing bacteria; it acts against both Gram-positive and Gram-negative bacteria (The free encyclopedia on Broad-spectrum antibiotic).

Irrational use of drugs- is the administration of drugs for indications where their effectiveness has not been confirmed, disregard of restrictions and warnings against their use, and the use of drug combinations which do not increase the therapeutic effect but to the contrary increase the risk of adverse drug reactions (Woron et al. 2007).

Microorganism- is a microscopic organism, which may be a single cell or multi-cellular organisms e.g. bacteria, virus, fungi (The Free Encyclopedia on Microorganism).

Rational prescribing- appropriate medication for the right patient at the right dose and interval for the right duration moreover for the right condition (Kumar et al. 2010).

Surgical procedure- is a medical procedure involving an incision with instrument, performed to repair damage or arrest disease in order to improve bodily function or appearance in a living body (The Free Encyclopedia of Surgery).

Surgical site infection (SSI) - is an infection occurring within 30 days after operation if no implant is left in place or within one year if an implant is in place and the infection appears to be related to the operation and affecting either the incision or deep tissue at the operation site (Owens and Stoessel 2008).

Abbreviations and acronyms

AMR:	Antimicrobial Resistance
CDC:	Centers for disease Control and Prevention
CPE:	Carbapenemase-Producing Enterobacteriaceae
CPO:	Carbapenem-Producing Organisms
CRE:	Carbapenem-resistant-Enterobacteriaceae
DI:	Defence Intelligence
DTC:	Drug Therapeutic Committee
ECDC:	European Centre for Disease Prevention and Control
ERCP:	Endoscopic Retrograde Cholangiopancreatography
ESBLs:	Extended Spectrum B-Lactamase
ESGAP:	European Study Group of Antibiotic Policy
FIDSSA:	Federation of Infectious Diseases Societies of Southern Africa
GAO:	General Accounting Office
GISA:	Glycopeptide-intermediate <i>Staphylococcus aureus</i>
GOPD:	General Out-Patient Department
HI:	Health Information
IDSA:	Infectious Disease Society of America
KPCs:	<i>Klebsiella Pneumoniae</i> Carbapenemases
MHRC:	Military Health Research Committee
MRSA:	Methicillin-resistant <i>Staphylococcus aureus</i>
NDM-1:	New Delhi metallo-B-lactamase-1
NHLS:	National Health Laboratory Services.
NICE:	National Institute for Health and Clinical Excellence
PD:	Pharmacodynamics
PEG:	Percutaneous Endoscopic Gastrostomy
PK:	Pharmacokinetics
SAAGAR:	South Australian expert Advisory group of Antibiotics resistance
SAAHIP:	South African Association of Hospital and Institutional Pharmacist
SAMJ:	South African Medicinal Journal
SSI:	Surgical Site Infection

VISA: Vancomycin-intermediate *Staphylococcus aureus*
VRSA: Vancomycin-resistant *Staphylococcus aureus*
WHO: World Health Organization

Conferences and proceedings

Oral presentation

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2014, 'Antimicrobial resistance in military healthcare facilities and in-patient stewardship: Review', 35th conference of The Academic of Pharmaceutical Sciences, Nelson Mandela Metropolitan University.

Dambisya, Y., Mathobela C.K.K., Nyazema N.Z. 2015, 'If antimicrobial resistance is a problem in the public hospitals, what is the level in the military hospital worldwide in selected countries?' South African Association of Hospital and Institutional Pharmacists.

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2015, 'Prescribing patterns of antibiotics for surgical site infections in the Post-Natal ward at Mankweng hospital', University of Limpopo Research day.

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2016, 'Hygiene, emergence of superbugs, and quality use of antimicrobial agents in Mankweng Hospital and 1 Military Hospital' University of Limpopo Research day.

Feedback to hospitals- oral presentations

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2015, 'Prescribing patterns of antimicrobials for surgical site infections at 1 Military Hospital and Mankweng Hospital', Mankweng Hospital staff.

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2015, 'Prescribing patterns of antimicrobials for surgical site infections at 1 Military Hospital and Mankweng Hospital', 1 Military Hospital Heads of Departments.

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2015, 'Prescribing patterns of antimicrobials for surgical site infections at 1 Military Hospital and Mankweng Hospital', Polokwane Hospital Drug Therapeutic Committee (DTC).

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2016, 'Prescribing patterns of antimicrobials for surgical site infections at 1 Military Hospital and Mankweng Hospital', Department of Health Drug Therapeutic Committee (DTC).

Poster presentation

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2016, 'Antimicrobial stewardship and its implications for public health', University of Fort Hare, Public Health Association of South Africa.

Dambisya, Y., Mathobela, C.K.K., Nyazema, N.Z. 2016, 'Knowledge of antimicrobial pharmacokinetic-pharmacodynamics parameters is a must have: You have no choice', all Africa congress on pharmacology and pharmacy, Evidence in action, Johannesburg, South Africa.

Abstracts submitted for conferences

Group A: Oral presentations abstracts

Antimicrobial resistance in military healthcare facilities and in patient

Stewardship

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Purpose: In the 1940s, the widespread availability of penicillin and the subsequent discovery of streptomycin led to a dramatic reduction in illness and death from infectious diseases. Today, the extensive use of antimicrobial drugs has resulted in drug resistance that threatens to reverse the medical advances of the last seventy years. Preventing the spread of infection and microbial resistance is a battle being fought not just in civilian healthcare settings worldwide but in the military healthcare system as well. This year *Staphylococcus aureus* resistance in the African region has so far been reported to be between 12-80% in both civilian and military healthcare facilities. A review of several articles on the level of antimicrobial resistance worldwide in military healthcare facilities was carried out. The purpose of the review was to determine antimicrobial stewardship in these military healthcare facilities.

Methods: Searches for everything relevant to antimicrobial resistance, in healthcare facilities in general, and in military facilities in particular was carried out. The articles found, were then sorted out into a coherent view of the “state of the art” of antimicrobial resistance and antimicrobial stewardship.

Results: Between 1980 and 2002 in one of the military healthcare facility, of the 3920 gram negative strains that were isolated in Europe, antimicrobial resistance for some of gram negative such as *E. coli* increased by 9.2%, *Pseudomonas spp.* resistance increased by 8%, *Enterobacter spp.* resistance increased by 4%. In 2014 *Staphylococcus aureus* overall reported range of resistance in African region was between 12-80% in both military and government healthcare facilities. In Walter Reed Army Hospital, Washington DC, the frequency of aminoglycosides resistance among clinical bacteria isolates increased from less than 1% in 1976 to 13% of all isolates in later years. Macrolide resistance among *Streptococcus pneumoniae* isolates from various countries is severe, e.g. Hong Kong is 81%, and Japan is

71%. The rate of Methicillin resistance among *Staphylococcus aureus* is high in Japan at 71.6% and 73% in Hong Kong.

Conclusion: Although the rate of antimicrobial resistance increases in both military and government healthcare facilities, reviews indicated that there are no action plans taken about antimicrobial resistance. In United States of America, it was suggested that high priority must be given to strategies that limit the emergence and dissemination of organism's resistance to the important antimicrobials.

Keywords: Antimicrobial agents, antimicrobial resistance, microorganisms.

IF ANTIMICROBIAL RESISTANCE IS A PROBLEM IN THE PUBLIC HOSPITALS, WHAT IS ITS LEVEL IN THE MILITARY HOSPITALS WORLDWIDE IN SELECTED COUNTRIES?

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Caswell K. Mathobela, Norman Z. Nyazema, and Yoswa M. Dambisya

Background:

Drug-resistant pathogens are a growing menace to all people, regardless of age, gender, or socioeconomic background. They endanger people in affluent, industrial societies like the United States, as well as in less-developed nations. Examples of clinically important microbes that are rapidly developing resistance to available antimicrobials include bacteria that cause pneumonia, ear infections, and meningitis (e.g., *Streptococcus pneumoniae*), skin, bone, lung, and bloodstream infections (e.g., *Staphylococcus aureus*), urinary tract infections (e.g., *Escherichia coli*), foodborne infections (e.g., *Salmonella* or *E. coli* acquired from meat, eggs, nuts, fresh produce etc.), and infections transmitted in healthcare settings (e.g., *enterococci*, *Pseudomonas aeruginosa*, and *Klebsiella spp.*).

The costs of treating antimicrobial resistance infections place a significant burden on society, a burden that is likely to grow larger as the number of cases of drug-resistant illness increases. An investigation on the level of antimicrobial resistance in military hospitals in selected countries was carried out.

Objectives:

- To identify the severity of antimicrobial resistance in military hospitals in selected countries.

Method:

Several articles were reviewed from military hospitals in selected countries.

Results:

E. coli, *K. pneumoniae*, and *P. aeruginosa* appear to be 100%, 99.3%, and 92.7% respectively resistant to ampicillin. Furthermore *A. baumannii* and *Serratia spp.* were also 100% resistant to ampicillin. *C. ferundii* was also 100% resistant to piperacillin.

Conclusion:

The expectations are, Military hospitals are supposed to be taking the lead in preventing or minimizing antimicrobial resistance as quick recovery is expected from their members, moreover military hospitals are supposed to be the dressing point of government hospitals as they have more funds to be utilized for excellent services to be provided. With new multidrug-resistant microorganisms being disseminated in tandem with well-known older pathogens, the window of opportunity is rapidly closing: no action today, no cure tomorrow which leads us back to the antimicrobial era where we had no antimicrobial agents.

Keywords: Antimicrobial agents, antimicrobial resistance.

Prescribing patterns of antibiotics for surgical site infections in the post-natal ward at Mankweng Hospital.

University of Limpopo (Turfloop Campus), School of health care Sciences, Department of Pharmacy

Caswell K. Mathobela, Norman Z. Nyazema, and Yoswa M. Dambisya

Background:

Surgical site infections are the infections involving, subcutaneous tissue and organs opened or manipulated during an operation, occurring 30 days after the procedure or within one year if orthopaedic implant is in situ. When there is an infection, the most difficult decision to take is when not to give antimicrobials or when to stop antimicrobials. Rational use of antimicrobials is influenced by several factors, including fear of prescribers for patients demanding their antimicrobial of choice, lack of information, excessive and unnecessary antibiotics prescribing, incorrect dosage or route of administration, antibiotic prescribing for non-bacterial infections. It is against this background that study was carried at Mankweng District Hospital.

Objectives:

- To determine antibiotic prescription pattern at Mankweng Hospital
- To identify the most common microorganisms and their resistant patterns

Method:

The questionnaires were circulated among pharmacists, post-natal ward nurses and doctors. Questions asked were related to antibiotics usage and the use of the laboratory. Patient's data was also obtained from the medical records of women 18 years and above. 94 patients from the year 2011 were reviewed, 13 nurses and 6 doctors from Post-natal ward were given questionnaires.

Results:

Ampicillin 500mg IV was found to be the most commonly used antibiotic for prophylaxis and *Staphylococcus aureus* was the most resistant micro-organism. Amoxicillin, cloxacillin and

metronidazole were used post-operatively. Physicians working on the ward were found to be using different surgical guidelines.

Conclusion:

Same surgical guidelines must be used to avoid different prescribing patterns of antibiotics in post-natal ward at Mankweng Hospital.

Key words: Surgical site infection, antibiotics, microorganisms.

HYGIENE, EMERGENCE OF SUPERBUGS, AND QUALITY USE OF ANTIMICROBIAL AGENTS

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Introduction: Hand hygiene rates of 10-40% have been observed in even the best of the units in the developed countries. Acceptability of such compliance rates and justifications of intense antimicrobial usage under the umbrella of “empirical therapy” has underscored the importance of increasing hand hygiene compliance. In recent years, the WHO has accepted of hand hygiene as a global challenge. There are now monitoring tools available to assist in hand hygiene compliance which lead to decline in “empirical antimicrobial therapy” responsible for emergence of superbugs. The present sub-study was carried out to investigate hygiene practises and the emergence of superbugs in two public hospitals A & B.

Objectives:

- 1) To identify factors that discourages the proper hygiene practises.
- 2) To determine the prevalence of superbugs in relation to antimicrobial use in the two public hospitals.

Method: A situation analysis was carried out in two hospitals by examining medical records and interviews with health care providers including pathology laboratory personnel.

Results: The results obtained from the two hospitals showed that there was poor hand washing at A-31% and B-25%; poor theatre sterility at A-38% and B-25%; unhygienic/small environment at A-69% and B-25%; and inadequate aseptic technique at A-31% and B-55%. In the two hospitals, the superbugs identified were *E. coli* and *Klebsiella pneumoniae* which were 100% resistant to antibacterial agents available.

Conclusion: Proper hygiene practices in particular hand washing in the hospital must be adhered to and effectively monitored irrespective of whether there is an explicit infection control or not.

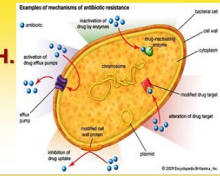
Keywords: Superbugs, antimicrobial, hygiene, empirical therapy.

Group B: Oral poster presentations



ANTIMICROBIAL STEWARDSHIP AND ITS IMPLICATIONS FOR PUBLIC HEALTH.

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INTRODUCTION

Antibiotic stewardship is concerned with the manner in which antimicrobial agents and antibiotics in particular are used. Absence and lack of adherence to surgical and empiric therapy guidelines, antibiotic policies have serious consequences to public health. It is against this background that a study was carried out at two tertiary institutions in Limpopo and Gauteng Provinces to investigate the state of antibiotic stewardship.

AIM OF THE STUDY

To investigate the prescribing pattern of antimicrobials for surgical site infections in Mankweng Hospital and 1 Military Hospital.

OBJECTIVES

- To identify the most prevalent microorganism on patients who developed surgical site infection,
- To identify which antimicrobials are used and their cost, and
- To determine the level of adherence to the use of antimicrobial guidelines.

METHOD

It was a retrospective study whereby 79 patient records from orthopaedic, surgical and gynaecology wards were critically reviewed. Structured interviews were carried out with doctors, pharmacists, nurses, and microbiologists followed by focus group discussions. Questions asked were related to antibiotics usage, the use of the laboratory facility, surgical guidelines, and antibiotic policy. From the patients' files microorganism found, antimicrobials given were recorded on the structured data collection tool. The resistant pattern was obtained from laboratory via infection control office, which guides prescribers which antibiotic to give, and which ones the microorganism are resistant to.

RESULTS AND DISCUSSION

Out of 79 patients given antibiotic therapy, 19% were readmitted with severe infections due to microorganism being resistant whereas the laboratory culture and sensitivity results stated which antibiotics to be used and not to be used. 73% patients were irrationally treated between 3 to 23 days with or without laboratory culture and sensitivity results. There appeared to be lack of appreciation among health-care professionals on antibiotic stewardship and its implication for public health.

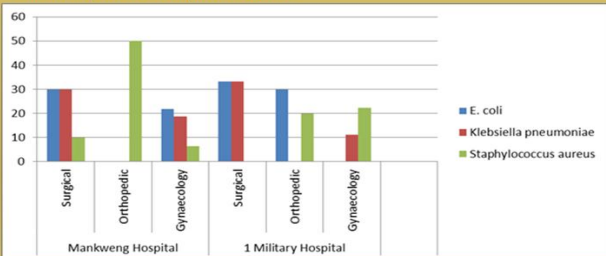


Fig 1: Most prevalent microorganisms

The most prevalent microorganism found were *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*, microorganisms of public concern. This is surprising because *E. coli* is found in the intestines but was found in orthopaedic ward. Therefore it was reasonable to assume lack of hygiene, an important aspect of antimicrobial stewardship, at the two hospitals. This is surprising as this is supposed to be practised all the time when dealing with infection control. Unfortunately this appeared to be the norm in public hospital as reported by Keeton (2016) in a newspaper that poor hand washing was the contributing factor.

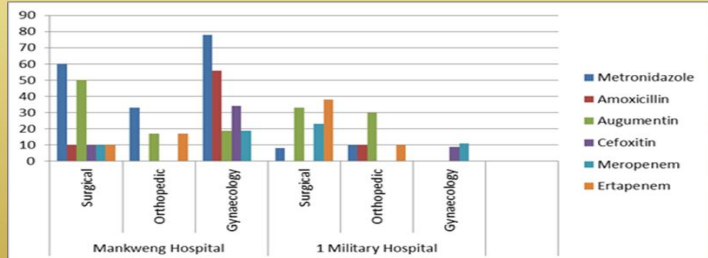


Fig 2: Mostly used antimicrobials

The mostly used antimicrobial was metronidazole, amoxicillin, and augmentin, cefoxitin, ertapenem, and meropenem, of which microorganisms more especially *E. coli* and *Klebsiella pneumoniae* developed resistant to almost all mostly used antimicrobials.

Mankweng Hospital (n=38)			1 Military Hospital (n=13)		
Surgical (n=7)	Orthopaedic (n=3)	Gynaecology (n=29)	Surgical (n=6)	Orthopaedic (n=7)	Gynaecology
R 2713.67	R 10624.41	R 2832.53	R 2861.19	R 985.44	R 658.52

Table 1. The average cost of irrationally used antimicrobials

It was found that R20675.76 was fruitlessly spent on irrational treatment on the antimicrobials given to the patients excluding other logistics costs.

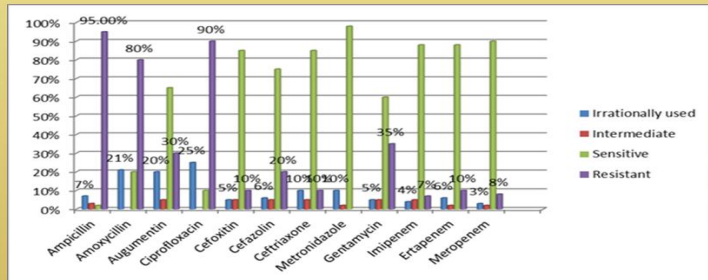


Fig 3: Resistant and sensitivity patterns.

Most of antimicrobials were irrationally used as per laboratory recommendations on which antimicrobial to give and which one not to give.

CONCLUSION

All health care workers should have key knowledge on antimicrobial stewardship which has a huge implication for public health. Absence of antimicrobial policies and their effective implementation are not good for antimicrobial stewardship which minimizes antimicrobial resistance.

RECOMMENDATIONS

Hygiene Hygiene Hygiene

ACKNOWLEDGEMENTS

I acknowledge University of Limpopo-Pharmacy Department, Department of Health-Mankweng Hospital, and Department of Defense-1 Military Hospital for providing access to carry out the study.

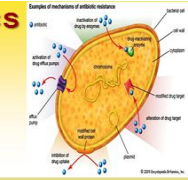
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KNOWLEDGE OF ANTIMICROBIAL PHARMACOKINETICS-PHARMACODYNAMICS PARAMETERS IS A MUST HAVE: YOU HAVE NO CHOICE.

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INTRODUCTION

The pharmacology of antimicrobial therapy can be divided into two distinct components namely pharmacokinetics (PK) and pharmacodynamics (PD). The pattern of antimicrobial activity over time is an important determinant of effective dosage regimens. MIC and MBCs the major two parameters are used to quantify the activity of an antibacterial drug against infecting pathogen in vitro. They are good predictors of the potency of the drug-organism interaction, but they do not provide any information on the time course of antimicrobial activity. This is important knowledge to have in controlling the emergence antimicrobial drug resistance. A study was carried out to investigate how much knowledge about antimicrobial agents was used in prescribing and dispensing in 1 Military Hospital and Mankweng Hospital.

AIM OF THE STUDY

The determine the level of knowledge on antimicrobial pharmacokinetics-pharmacodynamics parameters by pharmacist.

OBJECTIVE

- To determine the level of knowledge regarding pharmacokinetic and pharmacodynamics about β -lactam, fluoroquinolone, and carbapenems.

METHOD

It was a retrospective study whereby 79 medical records of patients who had had surgical site infection from orthopaedic, surgical and gynaecology wards were critically reviewed. Structured interviews were carried out with doctors, pharmacists, nurses, and microbiologists followed by focus group discussions. Questions asked were related to antibiotics usage, the use of the laboratory facility, surgical guidelines, and antibiotic policy. From the patients' files microorganism found, antimicrobials given were recorded on the structured data collection tool. The resistant pattern was obtained from laboratory via infection control office, which guides prescribers which antibiotic to give, and which ones the microorganism are resistant to.

RESULTS AND DISCUSSION

The most common microorganism identified were *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. *E. coli* and *Klebsiella pneumoniae* were found to be resistant to β -lactam, fluoroquinolone, and carbapenems, and *Staphylococcus aureus* was resistant to β -lactam.

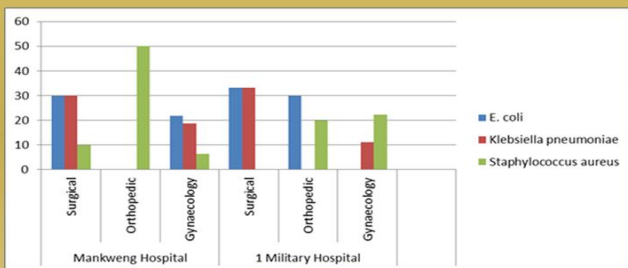


Figure 1: Mostly prevalent microorganisms

From the laboratory culture and sensitivity result, some microorganisms *E. coli* and *Klebsiella pneumoniae* in particular were found to be resistant to mostly used antimicrobials and pharmacists dispensed the very same antimicrobials prescribed irrationally. This appeared to be lack of knowledge on PK and PD from the pharmacists' side and prescribers, and causing the emergence of antimicrobial resistance.

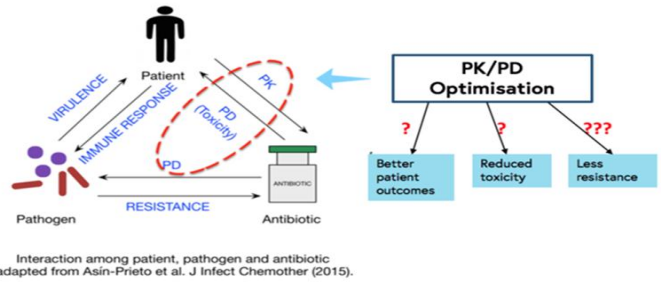


Figure 2: Interaction among patient, pathogen, and antimicrobial

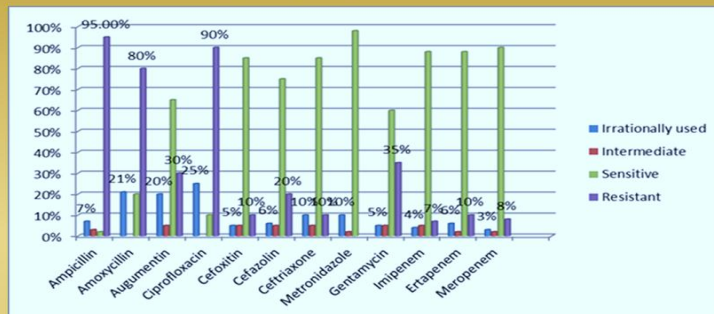


Figure 3: Resistant pattern of the mostly used antimicrobials

CONCLUSION

- In order to optimize the PK/PD of antibiotics, good basic knowledge about PK/PD in different patient population is necessary,
- It is important to keep in mind that PK/PD of antimicrobial may differ among new-borns, children, elderly, critically ill patients etc.
- It appeared there was antibiotic therapeutic anarchy and lack of detailed knowledge of pharmacokinetic-pharmacodynamics of antimicrobial agents and microbiological factors.
- Lack of utilization of laboratory test results appeared to contribute to resistance pattern.

RECOMMENDATIONS

- Laboratory culture and sensitivity results form part of pharmacokinetics when dealing with antimicrobials, therefore laboratory must be utilized adequately,
- Pharmacist must have knowledge on laboratory culture and sensitivity results, PK and PD in particular and be able to guide nor inform prescribers if they prescribed an antimicrobial which the microorganisms are resistant to.

ACKNOWLEDGEMENTS

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ABSTRACT

Introduction

Decades of injudicious antimicrobial prescribing and a disregard for basic infection practice have left the international community facing a return to the age of untreated bacterial infections, surgical site infections (SSI) in particular. SSIs are infections involving subcutaneous tissue and organs opened or manipulated during an operation, occurring 30 days after the procedure or within one year for orthopedic implant *in situ*. These infections are difficult to treat and are associated with substantially longer hospital stay, higher treatment costs, morbidity, and mortality particularly when the etiological agent is multidrug-resistant and continues to pose an important clinical challenge. When selecting an antimicrobial agent, it is better to have an idea of the microorganism you are dealing with than giving broad-spectrum antibiotic like ertapenem as cover for most bacteria. And this renders the narrow spectrum antibiotic obsolete and yet most of the broad spectrums antibiotics are expensive, as a result this will contribute to an exorbitant cost implications which are avoidable with rational use of antibiotics.

In light of the above the present study was carried out to investigate the prescribing pattern of antimicrobial agents for surgical site infections at 1 Military and Mankweng Hospitals.

The objectives of the study were to identify the most prevalent microorganism among patients who developed surgical site infection in orthopedic, surgical, and gynecology wards and their respective outpatient clinics at 1 Military Hospital and Mankweng Hospital: to identify which antimicrobials agents were prescribed and their unit cost; to determine the level of use of laboratory culture and sensitivity test results for the decision on which antimicrobial agent to be prescribed; to determine the level of adherence to surgical guidelines; and to identify factors contributing to surgical site infection.

Method

This was a qualitative and quantitative study whereby 79 patients' medical records from orthopedic, surgical and gynecology wards were critically reviewed. The study was conducted at 1 Military Hospital and Mankweng Hospital. It was retrospective and interventionist study. Structured interviews were carried out with doctors, pharmacists, nurses, and microbiologists followed by feedback sessions on the results. Questions asked were related to antimicrobial

agent usage, the use of the laboratory facility, surgical guidelines, and antibiotic policy. From the patient files, patients' demography, hospital stay, microorganisms found, culture and sensitivity test results, antimicrobial agents prescribed were recorded on the structured data collection tool. The resistant pattern was obtained from the laboratory via infection control office, which guided the prescribers. The data were then analyzed using Statistical software (STATA 9.0; StataCorp; College Station, TX). Descriptive (frequency distribution) and inferential (Chi-square) statistics methods were used to interpret the data at a p-value of <0.5 which was considered significant.

Results

Majority of the files examined were of female patients' (n=41) 52% particularly from gynecology ward. The most common microorganisms identified from the medical records were *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. *E. coli* and *K. pneumoniae* were found to be resistant to β -lactams, fluoroquinolone, and carbapenems while *S. aureus* was resistant to β -lactams. From the medical records from the two hospitals 19% of the patients were re-admitted due to surgical site re-infection. 73% of patients appeared to have been irrationally treated between 3 to 23 days with or without laboratory culture and sensitivity test results which in most cases appeared that the microorganisms were resistant to antimicrobial agent prescribed. The result showed that there were different views regarding common isolates, commonly used antimicrobial agent for prophylaxis and treatment by microbiologists, doctors and nurses.

Conclusion

It appeared that there was antimicrobial therapeutic anarchy and lack of detailed knowledge of pharmacokinetic-pharmacodynamics of antimicrobial agents and microbiological factors. Lack of utilization of laboratory test results appeared to contribute to resistance pattern. The laboratory plays a critical role in surveillance and in identifying the most common isolates and therefore results from the laboratory should always be taken into consideration when prescribing antimicrobial agents. This will assist in avoiding prescription of antimicrobial agents to which common isolates are resistant to. There is need for effective infection control and antibiotic policies at the two hospitals before anyone can encourage antimicrobial stewardship.

CHAPTER ONE: INTRODUCTION

Surgical site infections (SSI) are infections involving, subcutaneous tissue and organs opened or manipulated during an operation, occurring 30 days after the procedure or within one year if orthopedic implant is *in situ* (Owens and Stoessel, 2008). These infections are difficult to treat and are often associated with substantially longer hospital stay, higher treatment costs, morbidity, and mortality particularly when the etiological agent is multidrug-resistant and continues to pose an important clinical challenge (Fabiano et al., 2004).

SSI morbidity may cause long-term disabilities and mortality which contribute to 75 % of deaths among patients who developed SSI (Anderson et al., 2008). A study carried out by McGarry et al. (2004) showed that SSI in the elderly population caused a 2-fold increase in hospital charges, adding an extra \$41 000 to mean attributable charges per SSI. According to Cosgrove (2006) healthcare-associated infections constitute approximately 10% of hospitalization, and up to 75% of these are due to organism resistant to first-line antimicrobial therapy.

In developed countries, SSI incidence has been reduced by active surveillance systems (Brandt et al., 2006; Miliani et al., 2009), but unfortunately all over the world, microorganisms that are responsible for these SSIs are increasingly resistant to antimicrobials prescribed (Hadi et al., 2008). It was reported in US that the infection rate among patients varies with hospital setting, reflecting infection control practices as well as factors related to the agent, environment and the host (Fabiano et al., 2004). Studies of the epidemiology of SSI are confounded by the heterogeneous nature of these infections which varies widely between the procedures done, the surgeons, and between patients as shown in Table 1. SSI is an important complication of any surgery with varying micro-organisms and, the most prevalent micro-organisms on specific site of an infection vary (Owens and Stoessel, 2008).

When there is an infection, one of the most complex decisions to be taken by a surgeon, is when not to give antimicrobials and when to stop antimicrobials therapy (Kavita, 2011). Rational use of antimicrobials is influenced by several factors. These include fear by prescribers of patients demanding their antimicrobial of choice, self-prescribing, lack of information, excessive and unnecessary antibiotics prescribing, incorrect dosage or route of administration, antibiotic

prescribing for non-bacterial infections (Harbath et al., 2002). It has been posited that in order to promote rational use of antimicrobials, when a new drug is introduced to overcome resistance, it should be used only on the resistance strains, proved by culture and sensitivity tests (Kavita, 2011). This emphasizes the importance of laboratory diagnosis in the management of infection diagnosis.

Table 1: Types of surgical site infections (CDC, 2014).

Type of SSI	Description
Superficial incisional SSI	This infection occurs just in the area of the skin where the incision was made.
Deep incisional SSI	This infection occurs beneath the incision area in muscles and tissues surrounding the muscles.
Organ or space SSI	This type of infection can be in any area of the body other than the skin, muscles and surrounding tissues that was involved in the surgery. This includes body organs or a space between organs.

Antimicrobial agents have led to a dramatic change not only in the treatment of infectious diseases but also in the fate of mankind. Moreover, antimicrobial chemotherapy made remarkable advances, resulting in the overly optimistic view that infectious diseases would be conquered in the near future. However, in reality, emerging and re-emerging infectious diseases have left us facing a counter-charge from infections. These led to infections with drug resistant organisms remaining an important problem in clinical practice that is difficult to solve (Saga and Yamaguchi, 2009).

The key to controlling antimicrobial resistance is to prevent antimicrobial agent misuse or to use them rationally (Sintchenko et al., 2008). Prominent level of resistance (ranging from 50 to 100%) of microorganisms such as *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* to the commonly prescribed antibacterial agents such as ampicillin, co-trimoxazole, gentamycin, chloramphenicol and third generation cephalosporins such as ceftriaxone have been shown in studies carried out in developing countries (Mawalla et al., 2011).

If an inappropriate antimicrobial agent is chosen for the treatment of infection caused by resistant microorganisms, the therapy may not achieve a beneficial effect, and moreover, may lead to a worse prognosis. In addition, in a where multidrug-resistant organism have spread widely, there may be a limited choice of agents for antimicrobial therapy and the choice may result in high treatment cost (Saga and Yamaguchi, 2009).

It has been demonstrated that antimicrobials constitute approximately 20% of the drug market in Turkey (Turkish Pharmaceuticals Manufactures Association, 2000). According to Tunger et al. (2009), a high percentage between 40-60% of antimicrobial consumption in Turkey was reported to be unnecessary. In India, antimicrobial drugs being among the most commonly prescribed therapeutic agents, accounted for 30-50% of drug prescriptions. This is because there is a higher incidence of infections among adults leading to higher use of antimicrobial agent, contributing to an overall increase in healthcare costs, as well as potentially severe adverse drug reactions. Furthermore, monitoring and control of antimicrobial agent use is a growing concern as antimicrobial resistance is an emerging global problem yet prescribing practices lack uniformity (Sheefali et al., 2011).

Antimicrobial resistance is one of the world's most serious public health problems, the major cause of which is the incorrect, inappropriate, or irrational use of medicines. In addition, the problem is so serious that unless concerted action is taken worldwide we run the risk of returning to the pre-antibiotic era (Khor, 2005). Gould (2009) further elaborated that the problem cannot be prevented but its prevalence can be decreased. During the pre-antibiotic era, major surgery was impossible due to the risk of infection. Currently there are lots of antimicrobials that are prescribed in surgery, for example the most commonly prescribed are cefazolin and

amoxicillin. Whether there are guidelines or no guidelines, there are problems, in general with the way antimicrobial agents are prescribed (Khor, 2005).

Poor adherence to the guidelines for prevention of surgical site infection and for prescribing antimicrobials plays a significant role in causing surgical site infections. Prescribing patterns of antimicrobials without evidence of the prevalent micro-organism could contribute towards resistance of antimicrobials, and this could be alleviated by having a set-up which requires qualified staff who can be relied upon to take independent decisions on how to identify an isolate or which antibiotics are to be tested (Kavita, 2011).

When selecting an antimicrobial agent, it is necessary to have an idea of the microorganism you are dealing with, rather than giving broad-spectrum antibiotic like ertapenem as a cover for almost all unknown bacteria. And this renders the narrow spectrum antibiotic obsolete and not forgetting that most of the broad spectrums are expensive, as a result this will contribute to prohibitive costs and a bad image for hospital pharmacies that could be avoided (Kavita, 2011).

CHAPTER TWO: LITERATURE REVIEW

2.1 SSIs treatment, management, antimicrobial resistance, and Surgical procedure associated with SSIs and rates of infections

What SSIs are being addressed extensively in the Introduction. In spite of being carried out aseptically and following specific surgical techniques, there are classes of surgical procedures that are associated with SSIs (NICE, 2008). These are as follows:

- **Clean wound:** this is an incision, for example a breast biopsy in which no inflammation encountered, without a break in sterile technique, during which the respiratory, alimentary and genitourinary tracts are not entered. It is performed in elective, non-emergency, non-traumatic cases, (Bernard and Grandon, 2004). Joseph et al. (2008) explained that the risk of infection for this class is <5%.
- **Clean-contaminated wound:** it is an incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered for example appendectomy. According to Bernard and Grandon (2004), this has no evidence of infection at the time of surgery but involve operation on an internal organ. Ronald (1998) stipulated that the risk of infection is <10%.
- **Contaminated wound:** it is an incision undertaken during an operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract, or an incision in which acute, non-purulent inflammation is encountered. Open traumatic wounds that are more than 12-24 hours old also fall into the contaminated wound category. The risk of infection for the contaminated wound category according to Ronald (1998) is equivalent to 20%.
- **Dirty or infected wound:** it is an incision undertaken during an operation in which the viscera are perforated or when acute inflammation with pus is encountered during the operation (e.g. emergency surgery for faecal peritonitis), on traumatic wounds where treatment is delayed, and there is faecal contamination or devitalized tissue present. The risk of infection is 40% (Ronald, 1998).

In other studies patients that had undergone cholecystectomy, the SSI rate following laparoscopy procedures was reported to be 1.1%, compared with 4% following open procedures. Similarly, in patients with acute appendicitis, the SSI rate has been reported to be

2% with minimally invasive procedures and 8% with open procedures. The differences may be explained by several factors which include the smaller incision, earlier mobilization, less postoperative pain, better preservation of immune system function, and decreased use of central venous catheters (Boni et al., 2006).

In every health facility in general, there are recommended surgical guidelines. The Centers for Disease Control and Prevention (CDC) 2014 recommends steps that should be taken to prevent SSIs (Mangram et al., 1999) as illustrated in the guidelines below.

2.1.1 Prevention of SSIs

The following are steps recommended by CDC (Mangram et al., 1999):

Step A: Preoperative

Preparation of the patient

- 1) Where possible, remote infection are identified and treated, and postpone surgery until such infection have resolved,
- 2) The hair must not be removed around the operation site, unless if it will interfere with the operation,
- 3) If hair is removed, this should be done immediately before the operation, preferably with clippers,
- 4) Adequate control of blood glucose in diabetic patients (perioperative hyperglycemia must be avoided).
- 5) Encourage cessation of tobacco smoking,
- 6) Pre-operative blood products should not be withheld as a means of preventing SSIs,
- 7) Patients are required to shower or bath with an appropriate antiseptic agent on or at least the night before the operation. This reduces microorganisms that may be on the skin. In addition, the area around the incision site must be thoroughly washed and cleaned.

Hand/ forearm antiseptic for surgical team members

- 1) All efforts should be made to prevent cross-contamination from the surgical team to patients, for instance by keeping their nails short, performing surgical scrub for 2-5 minutes.
- 2) These should form part and parcel of postoperative incision care.

Management of infected or colonized surgical personnel

- 1) Any surgical team member who is colonized in general with infectious illness should be discouraged from performing any surgical procedures.
- 2) A well-defined policy should be developed concerning patient care responsibilities when personnel have potentially transmissible infectious conditions.

Antimicrobial prophylaxis

- 1) Antimicrobial prophylaxis is administered only when indicated and the agent is selected according to efficacy against most common pathogens associated with surgical procedures, and preferably from laboratory.

Step B: Intraoperative

According to the guidelines there should be Standard Operating Procedures specifically for the prevention of SSIs and generally part and parcel of infection control policy where surgical procedures are taking place that ought to be followed regarding;

- Ventilation of the theater,
- Cleaning and disinfection of environment surfaces,
- Microbiological sampling of operating theater environment surfaces or air,
- Sterilization of all surgical instruments according to published guidelines,
- Wearing of appropriate surgical attire when entering the operating theater.

Step C: Surveillance

- 1) Surveillance should be encouraged for both in-patients and out-patients. For inpatient care, case-finding (including re-admission), direct prospective observation, indirect prospective detection, or a combination of direct and indirect methods for the duration of hospitalization may be used. For outpatients, case-finding, a method that accommodates available resources and data needs should be used.

- 2) For each patient undergoing an operation chosen for surveillance, record those variables shown to be associated with increase SSI risk (e.g. surgical wound class, duration of operation, etc.),
- 3) Periodically calculate operation-specific SSI rates stratified by variables shown to be associated with increase SSI risk,
- 4) According to the guidelines, when all the data has been obtained, it is important to feedback data to concern.

According to Hold (2011), the surgeon plays a significant role in SSI to influence the outcomes, especially on procedure-related factors such as the duration of the surgery and preoperative wound contamination. The wound needs to be methodically and thoroughly cleaned and scrubbed before the scrub sister handles the patients as this dramatically decreases the bacterial load. Other factors playing a role in antimicrobial resistance are incomplete courses of antibiotic therapies and the unnecessary use of broader spectrum regiments (Van Schalkwyk, 2010). According to Owens and Stoessel (2008) pre-existing infections at sites remote to the operation site should be identified and treated, and if practicable elective surgery should be delayed until such infections have resolved as illustrated in the guidelines above. Preoperative strategies focus on controlling patient-related risk factors and appropriate hand/forearm antisepsis for surgical team members which is illustrated in the guidelines above (Owens and Stoessel, 2008).

Most SSIs are attributed to patient-related factors rather than procedure-related factors. In order to prevent SSI, strategies should be based both on reducing the risk of bacterial contamination and on improving the patient's defense against infection. This requires a bundle approach with attention to multiple patient-related and procedure-related risk factors (Dellinger et al., 2005 and Leaper et al., 2004). In a study analyzed by Dominioni et al. (2006) age and low serum albumin concentrations were identified as the most important patient-related factors contributing to SSI and the quality of surgical technique as an important procedure-related factor.

Antibiotic resistance is when a microorganism is no longer sensitive to antibiotic drug agents that were originally effective for treatment of infections caused by that particular microorganism; thus, the drug agent is now rendered ineffective against that microorganism (WHO, 2012).

Antibiotic resistance reduces the effectiveness of treatment, due to development of resistant mechanisms by the bacteria, thus patients remain infected for a longer time, increasing the risk of spreading resistant microorganisms to others (Bratzler et al., 2013).

Increased transmission of resistant microorganisms is caused by weak infection prevention and control practices, and a disregard of the guidelines thereof. Furthermore, this is particularly challenging in resource-limited settings with poor health infrastructure and a shortage of health-care staff. Inadequate laboratory capacity limits the ability to rapidly detect resistant microorganisms for prompt treatment and control measures (Struelens, 1998).

Although antimicrobial resistance is primarily a medical problem, the factors that influence the spread of resistance are ecological, epidemiological, cultural, social, and economic. Therefore patients, physicians, healthcare facilities and retailers from large pharmacies to local drug sellers have little motivation (economic or otherwise) to acknowledge the consequences of their use of antibiotics on others, especially future generations (Laxminarayan et al., 2007).

Assuming whatever guidelines there may be which are similar to guidelines as outlined by Mangram et al., (1999) there is still a need to make sure that antimicrobial agents are prescribed rationally.

2.1.2 Antimicrobial agent prophylaxis

The purpose of antimicrobial prophylaxis in surgical procedures is not to sterilize tissues but to reduce the colonization pressure of microorganisms introduced at the time of operation to a level that the patient's immune system is able to overcome (Van Schalkwyk, 2010). According to the American College of Obstetrics (2003) prophylaxis does not prevent infection caused by postoperative contamination. Antimicrobial prophylaxis is intended to prevent infection whereas treatment with antimicrobial is intended to resolve an established infection, typically requiring a longer course of therapy.

For a long time, antimicrobial prophylaxis has been beneficial in decreasing SSI rates; numerous guidelines have been published recommending one-dose of a narrow-spectrum

prophylactic antibiotic given just before surgical incision (Weed, 2003). It was recognized that very often surgeons do not comply with short courses of prophylactic antimicrobial agents or they use broad-spectrum antimicrobial agent. No one has demonstrated that an increase in adverse effects was seen using surgical prophylaxis for 24 hours (Quenon et al., 2004).

According to the National Institute for Health and Clinical Excellence (NICE) guidelines on surgical site infection (2008) antibiotic prophylaxis should be given to patients before clean surgery (involving the placement of prosthesis or implant), clean-contaminated, and contaminated surgery. In addition, the guidelines also recommend that antimicrobial prophylaxis should not routinely be prescribed for clean non-prosthetic uncomplicated surgery. It was further stipulated that antimicrobial treatment should be given in addition to prophylaxis to patients having surgery on a dirty or infected wound. The New York-Presbyterian Hospital guidelines on antimicrobial prophylaxis on surgical procedures (2009) stated that cephalosporins such as cefazolin are mostly prescribed as antimicrobial prophylaxis as illustrated in Table 2. In practice, Ong et al. (2008) in Singapore reported that the use of antimicrobial guidelines as far as prophylaxis is concerned was very infrequent and that there were no local or national guidelines.

The increasing trend toward resistant organism may undermine the effectiveness of existing recommendations for antimicrobial prophylaxis i.e. inappropriate choice, improper timing, and inadequate dose based on body mass index. Additionally, antimicrobial prophylaxis should be administered in accordance with evidence based standards and guidelines, and antibiotics should be discontinued within 24 hours after surgery end time and 48 hours for cardiac procedures (Fry, 2008).

Giving antimicrobial prophylaxis in the decisive period preoperatively decreases SSIs by 25%. Unfortunately, up to 40% of antimicrobial agents are given incorrectly in theatre, and many incentives and disincentives are used to try and improve compliance (Hold, 2011).

Table 2, 3, and 4 illustrate the recommendations for the use of antimicrobial prophylaxis in gynecology, surgical, and orthopedic wards.

Table 2: Prophylactic antibiotic recommendations for obstetrical procedures

(Van Schalkwyk et al., 2010)

Procedure	Antibiotic	Dosage
Emergency or elective caesarean Section (no labor, no rupture of Membranes) prior to incision	Cefazolin IV 15-60 min	1-2g IV
If penicillin allergic	Clindamycin OR Erythromycin	600mg IV 500mg IV
Repair third or fourth degree laceration	Cefotetan Cefoxitin	1g IV 1g IV
Operative vaginal delivery	none recommended	N/A
Manual removal placenta	none recommended	N/A
Postpartum dilatation and curettage	none recommended	N/A
Cerclage	none recommended	N/A

Before an agent is considered for use as a prophylactic antimicrobial, there must be evidence that it reduces or prevents postoperative infection, it must also be safe, inexpensive, and it must be effective against organisms likely to be encountered in the surgical procedure. For a number of procedures in obstetrics and gynecology, the use of prophylactic antibiotics has been shown to reduce infectious morbidity in a safe and cost-effective manner as shown in Table 2 (Van Schalkwyk, 2010).

Antimicrobial prophylaxis is primarily indicated in the elective procedures in which skin incisions are closed in the operating theatre. As shown in Table 6, the choice of antimicrobial prophylactic agent should be based on the pathogens most commonly associated with the procedure being performed (Owens and Stoessel, 2008). In practice, vancomycin is not recommended for routine prophylaxis, broad-spectrum beta-lactam agents (particularly cephalosporins) are most widely prescribed, with an agent such as metronidazole being added if necessary to provide cover against anaerobes as illustrated in Table 4 and 5 (Owens and Stoessel, 2008).

Table 3: Recommended prophylaxis for gastrointestinal procedures.

According to (South Australian expert Advisory Group on Antibiotic Resistance (SAAGAR), 2014).

Procedure	Antibiotic	Dose
Percutaneous Endoscopic Gastrostomy (PEG) insertion/revision.	Cefazolin	1g IV
Endoscopic Retrograde Cholangiopancreatography (ERCP), Only patients with a high risk of infection, (Known or suspected biliary obstruction, Biliary sepsis, pancreatic pseudocyst)	Ampicillin/Amoxicillin plus Gentamycin plus Metronidazole	2g IV 2mg/kg IV 500mg IV
All other procedures (with or without biopsy) -endoscopy -sigmoidoscopy -colonoscopy -sclerotherapy -oesophageal dilatation	Prophylaxis Not generally recommended*	
Post-Operative Care (Post-ERCP)		
Post-ERCP if biliary drainage is PO incomplete	Amoxicillin+clavulanate	875mg/125mg

In all other cases, post-operative antimicrobials are NOT indicated unless infection is confirmed or suspected, regardless of the presence of surgical drains. If infection is suspected according to SAAGAR (2014) modification of antimicrobial regimen should be modified as per clinical condition and microbiological results. It recommends Cefazolin 2g be given for patient's ≥ 80 kg.

SAAGAR (2014) recommended that a single dose of any prophylactic agent is sufficient for most procedures, however repeat intra-operative doses are advisable e.g. for prolonged surgery of >4 hours when a short-acting agent is used (e.g. ampicillin, cefazolin), or if major blood loss occurs, following fluid resuscitation as shown Table 3 and 4.

Table 4: Recommended prophylaxis for gastrointestinal surgery.

(South Australian expert Advisory Group on Antibiotic Resistance (SAAGAR), 2014).

Procedure	Antibiotic	Dose
Gastric/duodenal/esophageal (bypass, resection, ulcer oversew, oesophagectomy etc.)	Cefazolin	1g IV
Biliary (cholecystectomy etc.)	Cefazolin	1g IV
Colorectal (colon or small bowel resection, revision of anastomosis plus either or stoma, appendicectomy etc.)	Metronidazole Cefazolin or Gentamycin	500mg IV 1g IV 2mg/kg IV
Exploratory laparotomy/ division of adhesions	Cefazolin plus Metronidazole	1g IV 500mg IV
Hernia repair (with mesh insert)	Cefazolin	1g IV

Post-Operative care

Post-operative antimicrobial agents are NOT indicated unless infection is confirmed or suspected, regardless of the presence of surgical drains. If infection is suspected, consider modification of antibiotic regimen according to clinical condition and microbiology results. Cefazolin is given 2g for patients' ≥80kg.

Broad-spectrum beta-lactam agents (particularly cephalosporins) are mostly used in practice, with an agent such as metronidazole being added if necessary to provide cover against anaerobes and vancomycin is not recommended for routine prophylaxis as illustrated in Table 5 (Van Schalkwyk, 2010).

Table 5: Recommended prophylaxis for orthopedic surgery.

South Australian expert Advisory Group on Antibiotic Resistance (SAAGAR, 2014).

Procedure	Antibiotic	Dose
Internal fixation of hip fracture	Cefazolin	1g IV
Other internal fixation	Cefazolin	1g IV
Arthroscopic procedures and other clean procedures not involving foreign material (pin, plate etc.)	Prophylaxis NOT recommended	
Lower limb amputation	Cefazolin Plus Metronidazole then (post-operation) Cefazolin plus Metronidazole	1g IV 500mg IV 1g IV 500mg IV
Spinal procedures	Cefazolin	1g

Post-operative care

Post-operative antibiotics are NOT indicated unless infection is confirmed or suspected, regardless of the presence of surgical drains. If infection is suspected, consider modification of antibiotic regimen according to clinical condition and microbiology results.

Cefazolin 2g must be given to patients ≥ 80 kg and children <12 years: 25mg/kg up to 1g (Table 5). Cefazolin 1g post-operation must be given 8-hourly for 2 more doses (total 3 doses). Clindamycin should be prescribed for patients with Beta lactam allergies.

According to Olsen et al. (2008) in orthopedic procedures, vancomycin should be reserved for the treatment of life-threatening infections and can be prescribed in patients with suspected methicillin-resistant *S. aureus* (MRSA) colonization (>5 days hospitalization, previous ICU

admission, patients from nursing homes) as shown in Table 5. Fonseca et al. (2006) concluded that a one-dose antibiotic prophylaxis did not lead to an increase in rates of surgical site infection and brought a monthly savings of \$1980 considering cefazolin alone. The high compliance of one-dose prophylaxis was achieved through an educational intervention encouraged by the hospital director and administrative measures that reduced access to extra doses (Fonseca et al., 2006).

During post-operation, things can go wrong because of many factors; this will then require proper treatment and management of infections resulting in different sorts of prescribing patterns. Before this is done a clear understanding of the prevalence of common isolates of microorganisms that might result in SSI needs to be established. This can be done as surveillance as indicated earlier in the guidelines under step c.

In any setting, if adherence to surgical guidelines can be followed, SSIs would be minimized. This can be achieved through proper/rational use of antimicrobial agents starting from antimicrobial prophylaxis to treatment of infection. It is also therefore important to understand the prescribing patterns which assist in the adherence to antimicrobial stewardship. One of the aspects of antimicrobial stewardship is to understand the pharmacodynamics and pharmacokinetics of antimicrobial agents.

2.1.3 Prescribing practices of antimicrobial agents

It was discovered in the 19th century that microorganisms were responsible for infectious diseases contributing a substantial proportion to the burden of diseases (Saga and Yamaguchi, 2009). At that time, there was no treatment for infectious diseases. It was in 1928 that Fleming discovered an antibiotic called penicillin which inhibited the growth of *Staphylococcus aureus* bacterium commonly found in mucous membranes and the human skin. Returning from holiday, Fleming began to sort through petri dishes containing colonies of *Staphylococcus*, bacteria that cause boils, sore throats and abscesses. He noticed something unusual on one dish. It was dotted with colonies, save for one area where a blob of mold was growing. The zone immediately around the mold, which was later identified as a rare strain of *Penicillium notatum* which was clear, as if the mold had secreted something that inhibited bacterial growth (Brown,

2004). Only in 1940 did antibiotics become clinically useful in saving lives, in particular during the Second World War and from puerperal sepsis (Saga and Yamaguchi, 2009).

Antibacterial action generally falls within one of four mechanisms, three of which involve the inhibition or regulation of enzymes involved in cell wall synthesis, nucleic acid metabolism and repair, or protein synthesis, respectively and the fourth mechanism involves the disruption of membrane structure. Many of these cellular functions targeted by antibiotics are most active in multiplying cells as illustrated in Figure 1 (Mayaud et al., 2013). In addition to understanding mechanism of action (pharmacodynamics), it is also important for any prescriber to be familiar with pharmacokinetics of the agent to aid in antimicrobial prescribing practices. This was also highlighted in the editorial of (SAMJ, 2012).

Prescribing practices can be defined as the ability of the health professional to differentiate and discriminate among the various choices of drugs and to determine the ones that will be most beneficial to their patient (Sheefali et al., 2011). When antimicrobials are prescribed incorrectly in humans or in veterinary practice, for too short a time or too small a dose, at inadequate strengths, or for the wrong disease, bacteria are not killed and can pass on survival traits to even more bacteria. This will result in more severe infections, increased morbidity and even death. Observance of standards of medical treatment at all levels of healthcare delivery system should include medical audit of prescribing patterns. The medical audit seeks to evaluate, monitor, if possible, suggest modification in prescribing practices to make medical care rational and cost-effective (GAO, 2004).

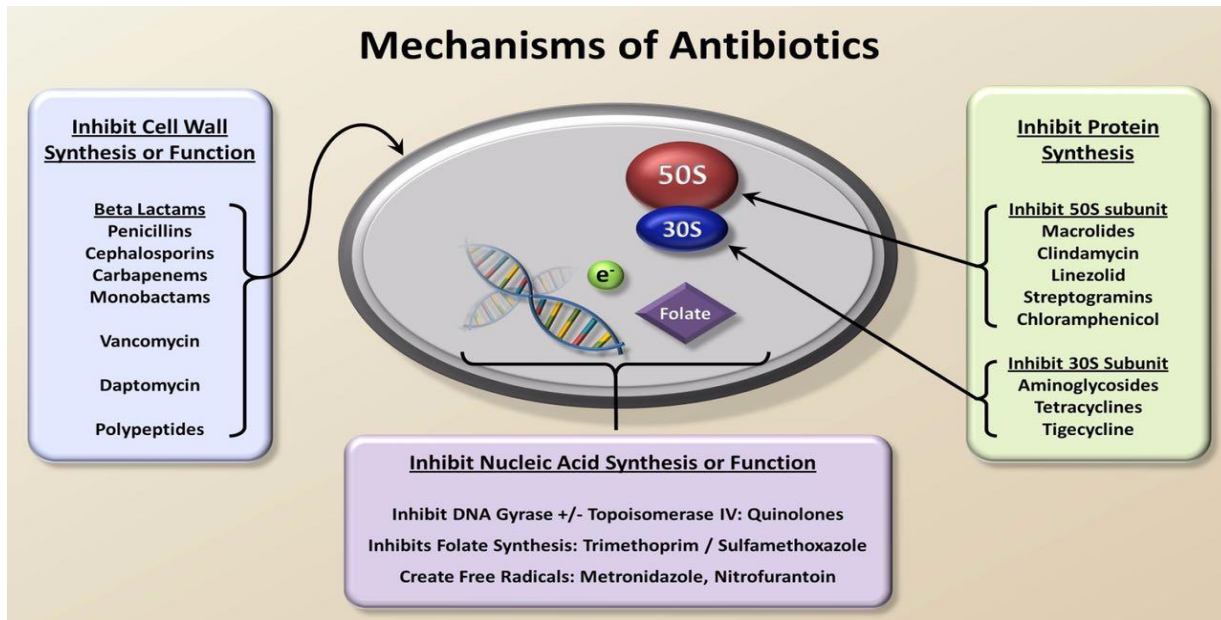


Figure 1: Mechanisms of action of antibiotics (Mayaud et al., 2013).

Kavita (2011) highlighted that some antimicrobials may show an *In vitro* sensitivity but do not reach the site of action e.g. aminoglycosides in meningitis. A remark made during WHO seminar in 2005 was that the major cause of irrational medicines usage, antimicrobial agents in particular, in developing countries was the unethical promotion of drugs by drug companies. Companies were said to practice double standards in marketing and labeling and gave incentives to doctors to use more medicines (Khor, 2005).

According to Ferguson (2004) antimicrobials are prescribed in one of the three categories:

- **Prophylactic therapy:** as mentioned earlier in the CDC guidelines is when administration is designed to prevent serious infection in a defined at-risk situation e.g. post-operation infection,
- **Empiric therapy:** is when a clinical syndrome that may be due to infection is managed before evidence confirming the presence of infection or its cause is available,
- **Direct therapy:** is when antibiotics are aimed at microorganisms which have been confirmed as the cause of an infection.

Empiric therapy

In antimicrobial empiric therapy, if the causative microorganisms are not known and where delay in initiating therapy would be life threatening or risk serious morbidity, antimicrobial therapy based on a clinically defined infection is justified. There are factors to be taken into consideration which include:

- Do not rush to treat;
- Collect the necessary specimens before commencing therapy;
- Cover all possible microbial causes;
- Try to attain synergy with different antimicrobial agents;
- Consider possible interaction with other drugs;
- Accuracy of diagnosis should be reviewed regularly and treatment altered/stopped when microbiological results become available; and
- Use less costly drugs where possible (The National Infection Prevention and Control policy and strategy, 2007).

For each of the above-mentioned therapies, there are principles that aim to minimize the use of antimicrobial agents and also ameliorate the selection of antimicrobial resistance (Ferguson, 2004). The assessment done by Tiley and Ferguson (2003) in hospital assessed patients after 24-48 hours of empiric therapy investigated if:

- Bacterial infection unlikely- then antimicrobial should be stopped,
- If microbiological evidence was available- the therapy had to be changed to directed therapy.

According to Burke et al. (2005) during surgery, an approach in using antimicrobials is that antimicrobials can be stopped once the surgery is finished and no further contamination of the wound is expected. If contamination does occur, continuation of a therapeutic course of antimicrobials is appropriate. Irrational use of antimicrobial agents might be hazardous instead of helping patients if not prescribed carefully and correctly. This includes effective communication between the laboratory and the clinicians resulting in random use of antimicrobials (Kavita, 2011). However, from the clinician's perspective, a rapid decision is needed to start antimicrobial therapy wherein the choice, duration, frequency, route and dosage, are not well thought out, even when there is enough time to do so.

According to the study done by Khade et al. (2013) in India, culture and sensitivity were not done in even a single case of antimicrobial recipients. Inappropriate antimicrobial doses were given to 37.64% cases while frequency of drug administration was inappropriate in 3.05% cases. In India, the following factors contributed to inappropriate prescribing; wrong choice of drug with doubtful efficacy or safety for the specific indication; drug misinformation; industry influenced marketing practices; lack of recognition of drug resistant strains; shortage of supplies of appropriate drugs; heavy workload; lack of laboratory facilities for cultures chiefly due to lack of funding (Khade et al., 2013).

In addition, as highlighted earlier in surgical guidelines, lack of guidelines in general contributes to improper antimicrobial prescription practices. The problem stems from a complex interplay of factors. These include insufficient training and supervision of healthcare personnel; lack of access to rapid diagnostic facilities to support treatment decisions; perverse economic incentives such as profit from both prescribing and dispensing; and inappropriate marketing of pharmaceuticals (Leung á, et al., 2011).

Togoobaatar (2010) reported that the absence of legislation regulating the quality and use of antimicrobials and poor enforcement efforts foster the unauthorized dispensing of antimicrobials by poorly trained personnel which can contribute to indiscriminate use. This is supported by the study carried out by Erbay (2003) who found that the percentage of irrational antimicrobial agents' use was between 40-60%.

Several studies cited above by Burke et al., 2005; Erbay, 2003; Ferguson, 2004; Kavita, 2011; Khade et al., 2013; Leung á, et al., 2011; The National Infection Prevention and Control policy and strategy, 2007; Tiley and Ferguson, 2003 and Togoobaatar, 2010 all point to the importance of laboratory culture and sensitivity test results which contribute to the general surveillance of the most common isolates in any situation.

2.1.4 Common isolates associated with SSIs

The predominant microorganisms present around the caudal aspect of the body are staphylococci, streptococci and corynebacteria with Gram-negative enteric bacteria potentiating the coverage use of cephalosporins or clavulanate-amoxicillin as appropriate for the bacterial

spectrum (Bray n. d.). Metronidazole is added if necessary to provide cover against anaerobes (Owens and Stoessel, 2008). Studies have shown that the most common bacterial isolates from SSI are *Staphylococcus aureus* and *Escherichia coli*, and their sources are from hospital environment and were documented to be endogenous and exogenous (Atata et al., 2010).

In a study carried out in Slovakia in the Central Military Hospital Ružomberok, ICU Gram-negative pathogens were the main problematic bacterial groups of strains in particular *Pseudomonas spp.* (Timko, 2004). *A. baumannii* was found to be the common nosocomial challenge in Egypt and has emerged as one of the important opportunistic pathogens in hospitalized patients throughout the world (Meyer et al., 2011). Whereas *Staphylococcus aureus* was the most prevalent microorganism with 30% causing SSI in USA as illustrated in Table 6. This is simply because most of the procedures involve skin cut where *staphylococcus aureus* is found (Horan et al., 2008). As mentioned earlier under classes of procedures it has been documented that procedures are associated with different pathogens as shown in Table 6 (Owens and Stoessel, 2008).

Table 6: Types of surgery and their related pathogens

Type of surgery	Common pathogens
Placement of graft, prosthesis or implant	<i>Staphylococcus aureus</i> ; CoNS
Cardiac	<i>S. aureus</i> ; CoNS
Neurosurgery	<i>S. aureus</i> ; CoNS
Breast	<i>S. aureus</i> ; CoNS
Ophthalmic	<i>S. aureus</i> ; CoNS; <i>streptococci</i> ; Gram-negative bacilli
Orthopedic	<i>S. aureus</i> ; CoNS; Gram-negative
Non-cardiothoracic	<i>S. aureus</i> ; CoNS; <i>Streptococcus pneumoniae</i> ; Gram-negative bacilli
Vascular	<i>S. aureus</i> ; CoNS
Appendectomy	Gram-negative bacilli; anaerobes
Biliary tract	Gram-negative bacilli; anaerobes
Colorectal	Gram-negative bacilli; anaerobes

Gastro duodenal	Gram-negative bacilli; streptococci; oropharyngeal anaerobes (e.g. peptostreptococci)
Head and neck	<i>S. aureus</i> ; streptococci; oropharyngeal anaerobes (e.g. peptostreptococci)
Obstetric and gynecological	Gram-negative bacilli; enterococci; Group B streptococci; anaerobes
Urological	gram-negative bacilli

CoNS, coagulase-negative staphylococci.

Some pathogens according to Owens and Stoessel (2008) are predominantly aerobes, particularly Gram-positive organisms such as *Staphylococci* and *Streptococci* and choice of agent should be based on the pathogens most commonly associated with the procedure being performed as shown in Table 6.

Mangram et al. (1999) outlined that the risk of SSI developing after microbial contamination of the surgical site will depend on the dose and virulence of the pathogen and the patient's level of resistance, according to the relationship:

$$\text{Risk of SSI} = \frac{\text{Dose of bacterial contamination} \times \text{virulence}}{\text{Resistance of patients}}$$

The risk of SSI is considered elevated when the level of contamination exceeds 10^5 organisms per gram of tissue, although levels of contamination doses may be required if foreign materials such as sutures is present (Mangram et al., 1999). According to the study done by Mohammadi-mehr and Feizabadi, (2011) *E. coli* and *Klebsiella pneumoniae* were the most common organisms involved in UTI and respiratory tract infection respectively. Moreover, with the study, the most frequent nosocomial infection was urinary tract infection (56.7%) followed by pneumonia (39%), primary septicemia (2.7%), surgical site infection (1.6%). According to the study done by Horan et al. (2008) in USA, organisms causing SSI from January 2006 to October 2007 were as shown in Table 7.

Table 7: Organisms and their prevalence's

<i>Staphylococcus aureus</i>	30%
Coagulase-negative <i>staphylococci</i>	13.7%
<i>Enterococcus spp.</i>	11.2%
<i>Escherichia coli</i>	9.6%
<i>Pseudomonas aeruginosa</i>	5.6%
<i>Enterobacter spp.</i>	4.2%
<i>Klebsiella pneumoniae</i>	3.0%
<i>Candida spp.</i>	2.0%
<i>Klebsiella oxytoca</i>	0.7%
<i>Acinetobacter baumannii</i>	0.6%

Hold (2011) found that *S. aureus* was responsible for 55% of all SSI, and of these, half were MRSA. Since there are different common isolates related to SSI or indeed any other microbial isolates, there are challenges and complications that result from common isolates being difficult to treat as they become resistant. For example, in the beginning penicillin was originally effective against gram positive organisms such as *S. aureus*. These microorganisms eventually became resistant which led eventually to the development of methicillin (Saga and Yamaguchi, 2009). To best understand and minimize SSIs and antimicrobial resistance, it is best to understand the origin of antimicrobials and the development of antimicrobial resistance.

2.1.5 Development of resistance

To better understand antimicrobial resistance, it is important to know the mechanisms of action of antimicrobial agents. Broadly, antimicrobial agents may be described as bacteriostatic which only inhibit the growth or multiplication of the bacteria giving immune system of the host time to clear them from the system, and bactericidal antimicrobial agents which kill the bacteria and therefore with or without a competent immune system of the host, the bacteria will be dead as shown in Figure 2 (Byarugaba et al., 2010). The mechanism of action of antimicrobial agents

can be characterized based on the structure of the bacteria or the function that is affected by the agents as illustrated in Figure 3. These include the following:

- Inhibition of the cell wall synthesis,
- Inhibition of ribosome function,
- Inhibition of nucleic acid synthesis,
- Inhibition of folate metabolism, and
- Inhibition of cell membrane function (Byarugaba et al., 2010).

Antimicrobial resistance is the ability of a microorganism to grow or survive in the presence of an antimicrobial agent that is usually sufficient to inhibit or kill microorganism of the same species. It is important because it is one of the greatest threats to modern health and we are facing a future without cures for infections. There is an emerging clinical crisis in human medicine because of antimicrobial resistance which makes infectious diseases harder to treat with antimicrobial agents (RUMA, 2014). According to United State General Accounting Office (GAO, 2004) bacteria can develop ways to fight off antimicrobial agents by: preventing antibiotics from reaching their target cells (e.g. reducing or changing the permeability of cell walls or pumping the drugs out of the cells); changing the structure of target cells or entirely replacing them; or producing enzymes that destroy antibiotics as illustrated in Figure 3.

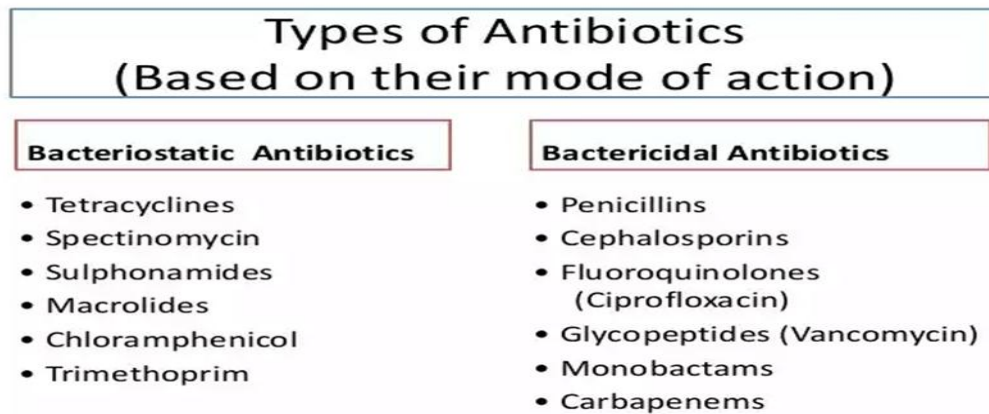


Figure 2: Bacteriostatic and bactericidal antimicrobial agents (Mayaud et al., 2013).

Casey and Pichichero (2005) showed that antimicrobial resistance leads to increased duration of the treatment, as long as antimicrobial guidelines are not followed (that depends upon the organism and antibiotic in question). The rational use of antimicrobial agents is likely to decrease rates of resistance, reduce cost, and have better outcomes leading to fewer complications.

Antimicrobial resistance is a growing threat to the control of infectious diseases globally. It was further stipulated by Casey and Pinchichero (2005) that lethal organisms once thought to be on the decline are re-emerging with resistance to commonly prescribed antimicrobials. Resistance makes infections such as surgical site infections, more difficult to treat, leading to poorer outcomes and increasing numbers of deaths (Casey and Pichichero, 2005). In Barcelona, evidence suggested that poultry or pork may be a possible source of quinolone-resistant *E. coli* in the community where 26% of children were found to be fecal carriers of these organisms despite apparently never having been exposed to quinolones (Steinke and Davey, 2001).

Penicillin was originally effective against Gram-positive organisms such *S. aureus*, later to address penicillin-resistant *S. aureus* which produced the penicillin-hydrolysing enzyme penicillinase, methicillin was developed, four years after penicillin started to be mass-produced; it was one of the earlier bacteria in which penicillin resistance was found in 1947, and methicillin became the antibiotic of choice. Methicillin was then replaced by oxacillin due to significant kidney toxicity. In 1961 in Britain, Methicillin-Resistant Staphylococcus Aureus (MRSA) was firstly detected. It is now common in hospitals, and was responsible for 37% of fatal cases of sepsis in UK in 1999, up from 4% in 1991. In the 2003 half of *S. aureus* infections in the US were resistant to penicillin, methicillin, tetracycline and erythromycin (Casey and Pichichero, 2005).

Mechanisms of being resistant

- **(A) Chromosomal mutations:**
 1. Reduced permeability.
 2. Enhanced efflux
 3. Enzymatic inactivation (beta-lactamase)
 4. Alteration of drug target
 5. Loss of enzymes involved in drug activation
- **(B) Plasmid or transposon mediated:**

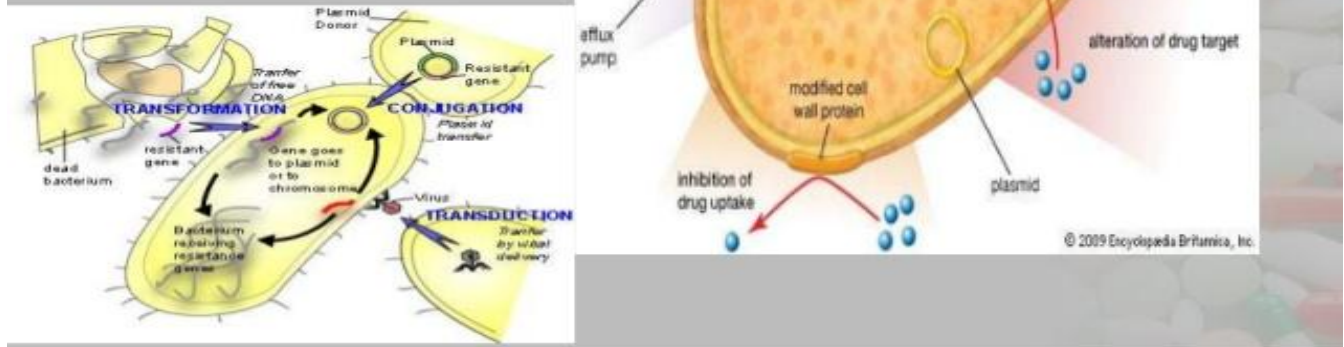


Figure 3: Illustration of how antimicrobial agents are rendered ineffective or antimicrobial resistant (Byarugaba et al., 2010).

Because *S. aureus* was resistant to penicillin, methicillin, tetracycline and erythromycin, this left vancomycin as the only effective agent at that time in 2003, and strains with intermediate levels of resistance, termed glycopeptide-intermediate *S. aureus* (GISA) or Vancomycin-intermediate *S. aureus* (VISA), began appearing in the late 1990s. A new class of antimicrobial agents, Oxazolidinones in particular became available in 1990, and the first commercially available Oxazolidinone, Linezolid was comparable to Vancomycin in effectiveness against MRSA (Casey and Pichichero, 2005). Strains of *E. coli* became resistant to multiple fluoroquinolone antibiotics in 1993 (Albrich, Monnet and Harbarth, 2004). In 2002, a strain with complete resistance to Vancomycin named Vancomycin-resistant *S. aureus* (VRSA) appeared in the United States (Casey and Pichichero, 2005). A limited number of new antimicrobial agents currently in development that have antimicrobial activity (e.g. doripenem) against multidrug-resistant gram-negative bacteria have developed resistance of which makes the emergence of multidrug resistance is looming (Paterson, 2006).

The relationship between antimicrobial resistance and prescribing patterns is that antimicrobial treatment is likely to influence colonization with resistant bacteria in two ways: firstly, by promoting mutation of bacteria, and secondly by facilitating the persistence of drug-resistant strains that are already present in the normal flora. However, colonization with drug-resistant bacteria may occur independently of antibiotic exposure either by acquisition of drug-resistant bacteria or dissemination of genetic determinants through contact with other individuals, or by spontaneous mutation of drug-sensitive bacteria to drug-resistant bacteria (Steinke and Davey, 2001).

Surveillance in general, is fundamental as indicated earlier in identifying common resistant isolates. It is an important strategy for antimicrobial resistance (AMR) containment, providing the data required to locate an AMR problem, monitor its growth, transmission and direction of travel, and determines the impact of interventions intended to contain it. Collective action is required in order to produce effective surveillance systems because; the barriers to establishing a surveillance system are high, particularly for poorer nations, given the larger initial investment required; surveillance produces benefits for other countries which an individual nation does not account for in deciding whether to invest in a surveillance system; and a global system requires compatible data of adequate quality (Smith and Coast, 2002).

Linezolid-resistant *S. aureus* was reported in 2001 (Casey and Pichichero, 2005). According to (Adegoke, 2010) other studies showed elevated levels of *S. aureus* resistance which was found among commonly used antibiotics like ampicillin, co-trimoxazole, and tetracycline in both Gram-positive and Gram-negative bacteria. The Centre for Disease Control and Prevention (CDC) witnessed a dramatic increase in infection due to Carbapenemase-producing Enterobacteriaceae (CPE) in the past decade with associated poor outcomes for infected patients (CDC, 2009).

According to Lautenbach (2014) in the past decade there has been a drastic increase in the several types of antimicrobial-resistant gram-negative bacteria, including extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae, Carbapenem-resistant Enterobacteriaceae, and multidrug-resistant strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Infections due to these organisms have been associated with significantly worse clinical

outcomes, with mortality rates up to four times higher than infections caused by susceptible strains (Ben-David, 2012).

Falagas et al. (2011) stated that what makes the emergence of multidrug-resistant gram-negative organisms uniquely compelling is the fact that few antimicrobial agents currently exist for treatment of these infections (e.g. polymyxins, and tigecycline). Both morbidity and mortality are increased in infections caused by Methicillin-resistant *Staphylococcus aureus*, vancomycin resistant enterococcus, and extended-spectrum beta-lactamase-producing organism, as they may be more virulent and are more difficult to treat because therapeutic options are limited (Van Schalkwyk, 2010).

According to Cunha (2008) some irrational use of antimicrobial agents has been proved to increase resistance in the ICU setting if prescribed for prolonged periods or regular on all patients. In addition, ceftazidime and ciprofloxacin (and to a lesser extent, other quinolones) increase the prevalence of Methicillin-resistance in staphylococci. Macrolide resistance is of particular concern because this class of antimicrobial agents is often prescribed for prophylaxis and treatment of individuals who are allergic to penicillin (Meyer et al., 2011).

Infections caused by multidrug-resistant staphylococci (methicillin- and vancomycin-resistant *Staphylococcus aureus*) and gram-negative bacilli, may drastically diminish the efficacy of antimicrobial therapy (Paterson, 2006). Linden et al. (2003) identified infection due to multidrug-resistant *Pseudomonas aeruginosa* in 23 liver transplant recipients treated between January 1996 and February 2003 at University of Pittsburgh Medical Center and for whom Colistin was the only treatment option. According to CDC (2004), infection with multidrug-resistant *A. baumannii* has been identified in patients at military hospitals where service members injured in Afghanistan, Iraq, or Kuwait were treated. Quale et al. (2003) described the clonal emergence of carbapenem-resistant *A. baumannii* in 15 hospitals in the New York metropolitan area, a finding that clearly indicates the potential for hospital-to-hospital transfer of resistant organisms. The above studies demonstrate the importance of surveillance.

Table 8: Proportion of resistance to different antimicrobial agents among gram negative bacteria isolated from patient at 3 army hospitals. (Mohammadi-mehr and Feizabadi, 2011)

Antibiotics	<i>E.coli</i> N (%)	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>A. baumannii</i>	<i>P. mirabilis</i>	<i>C. ferundii</i>
Imipenem	1(1.6)	2(3.4)	4(16.66)	7(41.2)	1(12.5)	0(0.0)
Ampicillin	53(88.33)	57(98.3)	22(91.66)	17(100)	8(100)	5(100)
Trimethoprim						
Sulphamethoxazole	35(58.33)	37(63.8)	21(87.5)	14(82.4)	6(75.0)	4(80.0)
Ciprofloxacin	36(60.0)	37(63.8)	6(25.0)	9(52.9)	1(12.5)	3(60.0)
Cefotaxime	36(60.0)	48(82.8)	16(66.7)	17(100)	5(62.5)	3(60.0)
Cetazidime	37(61.7)	48(82.8)	10(41.7)	16(94.1)	2(25.0)	2(40.0)
Piperacillin	45(75.0)	50(86.2)	10(41.7)	15(88.2)	5(62.5)	5(100)
Amikacin	7(11.7)	34(58.6)	16(66.7)	13(76.5)	2(25.0)	1(20.0)
Ceftriaxone	36(60.0)	45(77.6)	14(58.3)	17(100)	3(37.5)	2(40.0)
Gentamycin	19(31.7)	29(50.0)	6(25.0)	13(76.5)	4(50.0)	2(40.0)

Mohammadi-mehr and Feizabadi (2011) indicated in their study, high rate of resistance to third generation cephalosporins (of which cephalosporins are highly being prescribed in Iran due to their low side effects) was observed among isolates of *E. coli* and *K. pneumoniae*. In addition, production of ESBLs was found in 46.6% of isolates of both organisms, and 38% of Gram negative bacteria. Bacteria other than *E. coli* and *K. pneumoniae* also showed resistance to beta-lactam containing antibiotics and all isolates of *Acinetobacter baumannii* were resistant to ampicillin, cefotaxime and ceftriaxone (100%) as shown in Table 8. U.S. military personnel deployed in the Middle East and Afghanistan have been threatened by antimicrobial resistant strains of bacteria from combat-and non-combat-related infections caused by these highly resistant pathogens (Meyer et al., 2011). *Acinetobacter baumannii-calcoaceticus complex*, *Pseudomonas aeruginosa*, *K. pneumoniae* and *E. coli* are common pathogens, but, compared to past wars, the acquisition of multidrug-resistant isolates appears to have significantly increased (Akers et al., 2009).

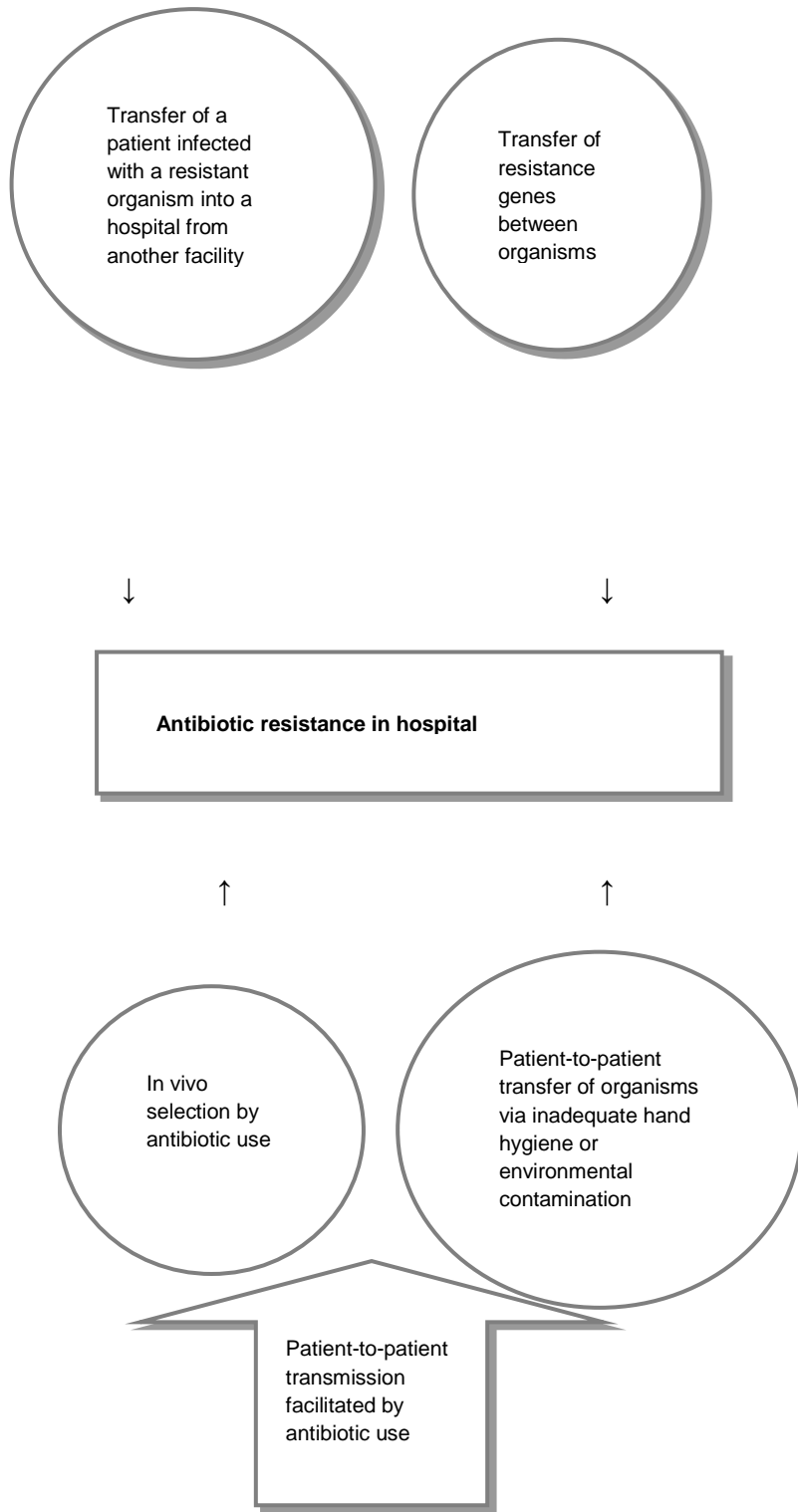


Figure 4: How antimicrobial-resistant organisms enter hospitals (Paterson, 2006).

Figure 4 shows a little understanding and appreciated phenomenon of how antimicrobial resistant organisms enter hospitals e.g. when the patient is transferred from another health facility, from patient to patient of different or same organisms due non hygiene practices and patient to patient facilitated antimicrobial agent use (Paterson (2006).

2.1.6 Challenges and complications posed by SSIs and antimicrobial resistance

Although antimicrobial resistance has been noted in nearly all microorganisms, a unique and immediate threat has been posed by multidrug resistance among Gram-negative bacteria (Lautenbach, 2014). Few antimicrobial agents currently exist for treatment of these Gram-negative microorganisms. Clinical cases in which an affecting organism is effectively resistant to all available antimicrobial agents are increasingly common (Banerjee et al., 2013). Infectious Disease Society of America [(IDSA), 2011] said that the complexity of this issue is lack of new agents' active against these organisms which should be developed.

Antimicrobial resistance in hospital represents not only a medical but also an economic problem. In addition, it makes several cheaper and narrow-spectrum antibiotics unusable, leading to longer hospitalization. As a result, the patient will be prescribed more efficient but expensive antimicrobial agent. For example, cephalosporins consumption was observed to have increased at a central military hospital in Slovakia from 2001 to 2004 (Timko, 2004).

In orthopedic procedures, infections can be a potentially devastating complication often requiring multiple procedures to achieve cure and occasionally ending up in amputations. A patient with a surgical site infection has a five times higher risk of being readmitted to hospital, 60% higher chances of spending time in an ICU and is twice as likely to die compared to patients without SSI (Eastl and SnyckersII, 2011).

According Sunday Times of South Africa (2016: 6) ten million people could die every year from 2050 onwards unless sweeping global changes are agreed to tackle increasing resistance to antimicrobial agents, which can turn common ailments into killers. O' Neill when asked by British government to chair the review, noted that one million people in South Africa had died of antimicrobial resistance since the review started in mid-2014 (Times, 2016:6).

The prevalence of surgical site infections on patients raises the cost due to prolonged hospitalization, additional diagnostic tests, therapeutic antibiotic treatment, overloading health workers with more patients admitted, and rarely re-operation (Urban, 2006). The study done by Reichman and Greenberg (2009) on studies examining the cost of SSIs revealed a mean increase of 115% for the cost of care of patient with an SSI as compared with non-infected control subjects.

The length of hospital stay in U.S.A by patients who developed SSIs was extended by 9.7 days, and increased the cost by \$20.842 (US dollars) per admission, this amount to hospital cost exceeding \$900 million, with hospital readmission due to SSI accounting for an additional \$700 million in health care spending (de Lissovoy et al., 2009). Eastl and SnyckersII (2011) outlined the fact that postoperative infections also have significant economic impact, requiring on average 12 days extra hospitalization and costing more than \$5 038.

The broad-spectrum antimicrobial agents being mostly prescribed to alleviate the resistance problem, and for covering for nosocomial pathogens (e.g. *P. aeruginosa*) do not further reduce SSI risk and instead may increase the cost of therapy and promote bacterial resistance (Joseph et al., 2008).

In the European Union, according to European Centre for Disease Prevention and Control (ECDC), about 25 000 patients die each year from infections caused by selected multidrug-resistant bacteria and the associated costs are estimated at about 1.5 billion euros per year (European Centre for Disease Prevention and Control, 2009). According to Owens and Stoessel (2008) cost estimation from the literature include orthopedic with 59 match pairs: median total direct cost of hospitalizations per infected patient was \$24,344, as compared with \$6,636 per uninfected patient. Adjusting the costs by hospitals and clinics pressured infection control specialists to decrease antimicrobial usage due to concerns with antimicrobial resistance. Later the procedures were reviewed in hospitals and clinics to adjust their budgets due to increasing health care costs (Fonseca et al., 2006).

There are better ways that have been adopted in different parts of the world to minimize SSIs and antimicrobial resistance, as outlined in section 2.1.7.

2.1.7 Workable solutions in improving antimicrobial use, minimizing antimicrobial resistance and SSIs

The detection of problems with use of AMD in health centers is the first step in evaluating the underlying causes and taking suitable remedial actions (Sheefali et al., 2011). The following three important points should be taken into consideration when establishing rational use of antimicrobials, namely efficacy, safety, and low cost of an antimicrobial (Ozkurt et al., 2005). There are four types of interventional strategies to improve drug use namely: educational, managerial, financial and regulatory. In addition, Gyssens and Meer (2001) stipulated that these strategies should include education, control of the hospital formulary, written justification forms, automatic stop order on going utilization review, restriction, required consultation, control of laboratory susceptibility testing, and limitation of contact time between physician and pharmaceutical representatives.

In 2003 in Turkey, there was an antibiotic restriction policy that was developed by the Ministry of Health and it was applied to decrease the antibiotic usage and particularly the economic burden of antibiotic. According to that new policy, prescriptions of the parentally-administered broad-spectrum and expensive antibiotics were limited and their use required approval from an infectious disease specialist (Tunger et al., 2009). Implementation of antibiotic stewardship is needed for hospitals to practice within antibiotic protocol/ policy to ensure best utilization of antibiotics (Hold, 2011), this is the responsible use of a critical and threatened health resource, antibiotics in particular which we depend on to prevent and treat infectious diseases (Brink et al., 2006). Antibiotic stewardship implies not only appropriate clinical decision-making for individual patients, but a perspective that:

- Maximizes the overall benefits,
- Minimizes adverse events related to antibiotic therapy, and most importantly,
- Delays the onset of widespread microbial resistance to commonly prescribed antimicrobial agents (Brink et al., 2006).

Adherence to both treatment and prophylaxis guidelines likely assists in reducing infection and antibiotic resistance (Van Schalkwyk, 2010). The hypothesis given by Fonseca et al. (2006) in US was that the SSI rate would not increase when fewer antimicrobial agents are prescribed, with intend to demonstrate that by comparing SSI data collected by in-hospital surveillance and

post-discharge surveillance before and after implementing the program. It was concluded by Bantar et al. (2003) that surveillance for SSI is a standard procedure in many hospitals which identifies the commonest prevailing microorganisms, of which the US has a countrywide surveillance system.

According to Owens and Stoessel (2008), CDC guidelines recommend that incision that have been closed by primary intention should be protected by sterile dressing for 24-48hrs, and that personnel should use sterile technique when changing dressing on any kind of skin incision. Reporting appropriate data and surveillance of SSIs have been shown to be effective components of strategies to reduce SSI risk. Moreover, according to CDC guidelines, it is recommended that both direct (based on observation of the surgical site by appropriate medical personnel) and indirect (based on retrospective review of patients' record and discussions with clinical staff) methods should be used to document the incidence of SSIs associated with specific procedures and that these data should be reported back to the surgical team (Owens and Stoessel, 2008).

Public health care professionals should join hands with microbiologists and primary health care workers to tackle epidemics in the community (Bhattacharya, 2010) and drug resistant being a major health problem, it requires a range of interventions and multidisciplinary teams approach of doctors, pharmacist, microbiologists, and nurses (Ndihokubwayo et al., 2013). It was further explained that this kind of set-up requires highly qualified technical staff who can be relied upon to take independent decisions regarding how to identify an isolate or which antimicrobials are to be tested. For instances, that this frees the clinical microbiologist to take the reports to the bedside and offer solutions to the clinicians (Bhattacharya, 2010).

WHO in 2001 published the WHO global strategy on containment of antimicrobial resistance along with a series of recommendations aimed at enabling countries to define and implement national policies in response to antimicrobial resistance (WHO, 2001). In 2005 World Health Assembly resolution on antimicrobial resistance cautioned about the slow progress and called for the rational use of antimicrobial agents by providers and consumers. Thus, the essential strategic interventions to control antimicrobial resistance have been known for some time. So far, however, national and global responses according to WHO have been inadequate (Leung á,

2011). According Keuleyan (2001) an antibiotic restriction policy combined with or without other strategies showed that an antibiotic policy provides a decrease of consumption and thus the cost of the drugs.

According to Timko (2004) surveillance of bacterial resistance is a key element in understanding the size of the problem. Furthermore, the substantial number of existing networks for resistance surveillance needs to be coordinated and the results should become available. Excellent quality local data provide basis for national and international surveillance and are necessary to help doctors to choose appropriate antimicrobials and to detect local epidemics of resistant bacteria surveillance at a local level (Timko, 2004).

We need to know what we are treating and to be able to de-escalate from broad-spectrum empiric therapy to targeted narrow-spectrum antimicrobials that are less likely to lead to resistance. It was further concluded that taking appropriate cultures from sterile sites is therefore a key component of rational prescribing and a practice that is sorely lacking at all levels of healthcare in South Africa (SAMJ, 2012). Furthermore, irrational prescribing pattern can be avoided by formulating essential drug list for the region as per the prevalent microorganism and educating the erring doctors (Khade et al., 2013).

Although Tiley and Ferguson (2003) realized that, improving antimicrobial prescribing in hospital practice is a complex challenge to infectious disease, microbiology, and pharmacy services, therefore added elements of successful hospital programs which included:

- Active involvement of clinicians in the development and dissemination of consensus, evidence-based guidelines for antimicrobial use,
- Regular monitoring of antimicrobial usage and drug usage evaluation with feedback to prescribers,
- Clinical decision support systems and other aids such as treatment cards or hand-held computerized guidelines,
- Formulary control of certain broad-spectrum antimicrobial agents so as to reduce indiscriminate use,
- Use of infectious disease consultancy services for advice in the management of complex cases,

- Improvements in the use of diagnostic technology and microbiology to provide more specific diagnosis of infective syndromes.

Incentives are being put forward in surgical procedures if targets are met with the Pay for Performance (P4P) is now in operation in several countries (Tiley and Ferguson, 2003). This was implemented as a motivation if antibiotic is given timeously, and a warm patient is brought back to normoglycaemic at the end of the operation, then financial rewards are paid out. But in South Africa disincentives are now in operation because medical aids are refusing to reimburse for iatrogenic hospital-acquired infections (Hold, 2011).

Having reviewed the prevalence of SSIs and antimicrobial resistance in other countries, it is equally important to know the current stage of SSIs and antimicrobial resistance in South Africa.

2.2 South African situational analysis

According to Suleman and Meyer (2012), South Africa had not yet implemented nationally standardized hospital infection and antimicrobial resistance surveillance system or fully translated available antimicrobial resistance surveillance data into policy. Up to today in 2017 it would appear that things have not changed if Sunday Times (Keeton, 2016) articles that appeared in media are anything to go by. There appeared to be problems and contradictory messages coming out from the public sector with regard to infection which has been reported in the media. For example, a physician from Charlotte Maxeke Johannesburg Academic Hospital indicated that patients going in for elective surgeries were increasingly exposed to resistant infections. It has also been reported that in Gauteng Province about 1500 people contracted hospital-acquired infections in Provincial Hospitals from 2012 to 2014 and 20 of these people died. Elective procedures where this infection are being seen include knee or hip replacement (Keeton, 2016:9). This contradiction that is coming out from public sector implies that whatever control measures in place are not effective. These control measures include infection control policy, antimicrobial policy, empirical therapy policy, hand washing, screening of patients when referred to other hospitals, and antimicrobial stewardship. Interestingly the report goes on to say that the good news was that academic, public, and private hospitals were at the forefront of

infection control in South African in taking certain steps. These steps included early detection and surveillance to try to ensure superbugs were under control (Keeton, 2016:9).

Unfortunately, there appeared to be contradictory messages coming out from the public sector. For example, elective procedures where hospital infections being seen included infections associated with knee or hip replacement (Keeton, 2016:9). Four years earlier in 2012, according to South Africa Medical Journal emergence in South Africa of bacteria carrying the highly mobile New Delhi metallo-B-lactamase-1 (NDM-1) gene, which had been associated with rapid spread of carbapenem-resistant-Enterobacteriaceae (CRE), and *Klebsiella pneumoniae* carbapenemases (KPCs) were reported to be going to cause a profound effect on the lives of patients and on the health services (SAMJ, 2012). The rise of CRE does not occur as a result of the injudicious use of carbapenems alone, but due to misuse and overuse of all antimicrobials (Brink et al., 2012).

As mention above, South African hospitals are still currently battling with a growing emergence of microorganisms which are resistant to routine antimicrobial therapy. According to Brink et al. (2006) the following challenges were being faced in certain areas of South Africa and one wonders whether ten years later the situation has changed or not:

- Vancomycin-resistant *Staphylococcus aureus* and *Enterococcus faecium*,
- Penicillin-resistant *Streptococcus pneumoniae*,
- Methicillin-Resistant *Staphylococcus Aureus* (MRSA),
- Third-generation cephalosporins-resistant *E. coli* and *Klebsiella pneumoniae*,
- Carbapenem-resistant *Klebsiella pneumoniae*, *Enterobacter spp.* and *Pseudomonas aeruginosa*,
- Glycopeptide-resistant *Enterococci*
- Multi-drug resistant *Mycobacterium tuberculosis*, *Acinetobacter baumannii*, *E. coli*, and *Pseudomonas aeruginosa*.

South African Medical Journal (2012) mentioned that it is difficult to treat Gram-positive bacteria resistant with antimicrobial agent as there are limited choices of antimicrobial agents and they are expensive. Duse (2012) during the address for South African Association of Hospital and Institutional Pharmacist (SAAHIP) concluded that “Appropriate antibiotic use depends on

understanding the pathogen, the host and the antimicrobial agents and their appropriate use of antimicrobial agents is one of the main tools in preventing resistance development. The studies made by Ntsama et al. (2013) showed that in Central African Republic 18% of prevalence of SSIs was reported and 12% in South Africa and 11.4% was reported in Ethiopia (Amenu et al., 2011).

2.3 PURPOSE OF STUDY

2.3.1 Problem statement

Surgical Site Infection (SSI) with varying microorganisms is an important complication of any surgery. The literature shows that the most prevalent microorganisms vary from site of an infection to another (Owens and Stoessel, 2008). There are guidelines in dealing with these microorganisms as per treatment is concerned. Poor adherence to the guidelines for prevention of surgical site infection and for prescribing antimicrobials plays an important role in causing surgical site infections. Prescribing patterns of antimicrobials without evidence of the prevalent micro-organism could contribute towards resistance of antimicrobials, and this could be alleviated by having a healthcare set-up which constitutes qualified personnel who can be relied upon to take independent decisions regarding identification of common isolates and which antimicrobial agents are to be prescribed (Kavita, 2011). When selecting an antimicrobial agent, it is best to have an idea of the microorganism you are dealing with than giving broad-spectrum antimicrobial agents e.g. ertapenem as cover for most bacteria. These could lead to other antimicrobial agents expiring in the pharmacies and the fact that most of the broad spectrums are expensive, this will have a negative cost implication (Kavita, 2011). Surgical site infection and irrational use of antibiotics pose a health risk to the community and our, observations suggested that broad-spectrum antimicrobial agents are mostly prescribed in the two study institutions hence the motivations for the study as there were no studies done to determine the prescribing patterns of antimicrobials and prevalence of surgical site infections in those institutions. According to Leung á (2011) new multidrug-resistant microorganism are being disseminated in tandem with well-known older pathogens, therefore the window of opportunity is rapidly closing: no action today, no cure tomorrow.

2.3.2 Aim of the study

To investigate the prescribing pattern of antimicrobial agents for surgical site infections at 1 Military and Mankweng Hospitals.

2.3.3 Research questions

Regarding surgical site infections in orthopedic, surgical, and gynecology departments at 1 Military and Mankweng Hospital:

- What are the prescribing patterns of antimicrobials for surgical site infections?

2.3.4 Objectives

- To identify the most prevalent microorganism isolated from surgical site infections in orthopedic, surgical, and gynecology wards and their outpatient clinics at 1 Military and Mankweng Hospital,
- To identify which antimicrobials agent were mostly prescribed and their unit cost,
- To determine the level of use of laboratory culture and sensitivity test results for the decision on which antimicrobial agent to be prescribed,
- To determine the level of adherence to the use of antimicrobial guidelines.

2.3.5 Significance of the study

As mentioned in problem statement, irrational use of antimicrobial agents poses a threat to patients care due to emerging multidrug resistant organisms. The study findings will contribute to the body of knowledge in determining health policies on antimicrobial agents use. The drug therapeutic committees could improve the alignment of hospital formularies to suit the recommendations from the laboratory based surveillance. This will improve patients' healthcare, benefit and improve the knowledge of health care professionals, improve healthcare services and ultimately patients' outcome. The study aims at contributing to improving patient safety by assessing the prevalence of SSI and determining the risk factors influencing SSI. Minimizing the usage or using antibiotics appropriately and minimizing surgical site infections will minimize the cost on budget of antibiotics; shorten hospital stay, and alleviate work load on health workers.

CHAPTER THREE: METHODOLOGY

3.1 Study design and settings

The study used both qualitative and quantitative methodological approaches. It was retrospective and also interventionist conducted at the two hospitals, at 1 Military Hospital and Mankweng Hospital.

1 Military Hospital is located on Voortreker Road, Thaba Tshwane in Pretoria. It is a referral hospital for all the military hospitals and sickbays in South Africa. It also a Referral (level four) for all United Nations hospitals in peace keeping mission countries. The hospital also provides health services to the presidency and members of parliament. It has 400 beds.

Mankweng Hospital is a tertiary hospital located in Mankweng near University of Limpopo (Turfloop Campus) on Houtborsdorp route in Limpopo Province. It has 509 beds providing referral services for regional and district hospitals in Limpopo Province and 21 (fixed clinics) and 3 mobile clinics giving primary health care services to Mamabolo, Mothiba, Dikgale and Molepo areas.

3.2 Data collection

3.2.1 Medical records examination

A total of 550 medical records from the two hospitals were examined from the following wards orthopaedic, surgical, and gynaecology wards for a period February 2015 until February 2016 inclusive. These were records of patients who developed surgical site infections while in the hospitals, after discharge, and when they did their follow up at their respective clinics within the hospitals as out-patients coming back for review.

At Mankweng Hospital, a weekly sepsis report was obtained from the National Health Laboratory Services (NHLS) via the infection control office. Each sepsis report had the patient's name, ward, and laboratory number. A total of 300 were examined. After having obtained clearance from the Department of Health, Limpopo Province, and permission at the hospital, the permission to access the records via NHLS intranet was granted. The laboratory number was used to access the hospital number of all patients who had developed sepsis in all the wards

within the hospital. From the sepsis list, the records of all patients in study wards were then identified and retrieved.

After retrieving 300 medical records from 48 files of patients who had developed SSI at Mankweng Hospital, the following information was obtained:

- Demographic data (age, gender).
- The admission and discharge summary. The information obtained here would then allow determining the hospital stay.
- The patients' consent forms that was signed by the patients before procedures were performed, to get information on antimicrobial agent prescribed.
- The laboratory culture and sensitivity test results. If not there, the patient's sepsis report was used. This was used to obtain the information of the nature of the microorganisms identified.
- Information on antimicrobial agents prescribed to treat patient with SSIs and route of administration.
- The discharge treatment summary. This was for the purpose of determining what antimicrobial treatment the patient was discharged on.

On the other hand, at 1 Military Hospital upon granting of permission to have access to medical records, the surgical codes for sepsis cases were retrieved from each Head of Department. To get medical records of the retrieved codes from the Health Information system, Hospital Chief Executive Officer (CEO) and the pharmacy manager had to sign a requisition form. Unfortunately, the information obtained via this route was not useful for the study. Instead all the records of wound swabs and blood samples that had been sent from the study wards were requested from the laboratory. With the aid of infection control office at the hospital, all the records of patients that had developed sepsis were retrieved. A total number of 250 medical records were examined. Out of 250 medical records, 31 medical records of patients who developed SSIs from the study wards were then treated in same manner as at Mankweng Hospital.

3.2.2 Interviews

A questionnaire that was developed as shown in appendix A was piloted among health care providers involved in infection control at the hospital. This was subsequently administered to health care professional included in the study.

All physicians at Mankweng Hospital (n=8) and 28 at 1 Military Hospital working in the three study wards following a presentation of the study at one of their meetings, were presented with the results found. The questionnaire included questions related to:

- The presence or absence of surgical guidelines,
- If any, whether these were South African guidelines or other countries guidelines,
- Surgical procedures that were most commonly performed,
- Usage of culture and sensitivity laboratory test results,
- Physicians' guide to prescribing the antimicrobial agents,
- The impact of surgical infection on re-admission, and
- Factors contributing to surgical site infections.

At one of their meetings, 12 pharmacists at Mankweng Hospital and 8 at 1 Military Hospital following the presentation of the study working were recruited. A piloted questionnaire was administered among them. The questionnaire included questions related to:

- Rational use of antimicrobials versus the diagnosis in the three study wards,
- The most ordered antimicrobial from the study wards, and
- Poly pharmacy of antimicrobial agents and its justification.

A presentation of the study was done at Mankweng Hospital to 13 nurses and 29 at 1 Military Hospital working in the three study wards. Due to nurses working shifts (day and night shift); questionnaires were given to the operational managers (with explanation, purpose and objectives of the study) to distribute among the nursing personnel working at night and were

collected back from operational managers the following day. A piloted questionnaire was administered among them. The questionnaire asked questions related to:

- The most commonly prescribed antimicrobial agents in the study wards and how they were administered,
- Their views regarding prescription of antimicrobial agents' relevance to diagnosis,
- The most common causative microorganisms of surgical site infections, and
- To their views regarding factors contributing to surgical site infection.

A separate meeting was organised with 4 microbiologists at Mankweng Hospital and 5 at 1 Military Hospital. Again, with them the purpose of the study was presented and a questionnaire was administered among them. The questionnaire asked questions related to:

- The most prevalent microorganisms identified in the three study wards,
- The most common sensitivity tests carried out,
- Their views on pressure-points regarding turn-around time,
- The implication of the pressure-point on turn-around time, and
- Their views on the usage of the laboratory culture and sensitivity test results in the prescribing of antimicrobial agents.

In addition to the meeting with microbiologists a site visit at the laboratory at 1 Military Hospital was organized to observe to techniques used for culture and sensitivity tests.

3.2.3 Feedback sessions to the hospitals

3.2.3.1 Polokwane-Mankweng Hospital Complex

At Mankweng Hospital with the assistance of National Health Laboratory Services (NHLS) clinical microbiologist, a feedback session of the study results was organised through the office of the clinical manager. The session was chaired by both the pathologist and the clinical manager. All relevant health care personnel including pharmacy personnel, nursing personnel, infection control personnel, environmental health personnel, specialist physicians, and

laboratory personnel were invited to attend the interactive session. The presentation was about rational use of antimicrobial agents, usage of laboratory culture and sensitivity test results by prescribers when prescribing antimicrobial agents for SSI in particular. Some of the physicians mentioned that the reasons why in most cases they do not utilize laboratory culture and sensitivity test results, is because the laboratory turn-around time was too long to be waiting for in order to initiate antimicrobial therapy. Because Polokwane and Mankweng Hospitals form a hospital complex and that there is an inter-movement particularly of prescribers and that the Drug Therapeutic Committee (DTC) meetings are held at Polokwane Hospital, a similar feedback session was organised at 1 Military Hospital.

3.2.3.2 1 Military Hospital

A power point presentation of the results from 1 Military Hospital was presented at a session attended by all clinical head specialists of different categories within the hospital. The session was organized with the assistance of the hospital CEO who presided over the meeting.

3.2.3.3 Desk top study

Documents related to budget allocation at Mankweng Hospital were examined.

3.3 Data analysis

The data collected using quantitative method were analyzed using Statistical software (STATA 9.0; StataCorp; College Station, TX). Descriptive (frequency distribution) and inferential (Chi-square) statistics methods were used to interpret the data at a *p-value* of >0.5 which was considered significant.

3.4 Ethical consideration

Approval was obtained from School of Health Sciences Research Ethics Committee, and ethics clearance was obtained from Sefako Makgato University (the former MEDUNSA) Research Ethics Committee (SMUREC) Ref No: SMUREC/HS/02/2015: PG.

Mankweng Hospital

With the clearance from SMUREC permission was granted by the Department of Health (Limpopo Province) Ref: 4/2/2 which was valid for 3 years period from 10/03/2015. The permission from the department of health was submitted to Mankweng Hospital and also

permission was granted Ref: S5/3/1/2. Approvals were taken to different heads of department for questionnaires to be filled.

1 Military Hospital

The clearance from SMUREC was submitted to 1 Military Hospital Research Ethics Committee (1MHREC) and approval was obtained Ref: 1MH/302/6/02.05.2015. All the clearances and a supporting letter from the hospital Officer Commanding (OC) were both submitted to Defence counter Intelligence (DI) division at 1 Military Hospital and approval was obtained. All were submitted to Health Information (HI) to pull the records as the records are electronically stored. HI declined the request and demanded the approval from DI (National). Approval was obtained from DI (National) with conditions Ref: DI/DDS/R/202/3/7. The approval from DI was then taken to OC of 1 Military Hospital. Both the OC and the pharmacy manager wrote a motivation, with all the clearances to pull the data from HI. The request was again submitted to HI which subsequently informed different heads of departments in order to have access to the records.

Patients' records

Upon obtaining clearance from different authorities to access the medical records, the medical records were treated with confidentiality, anonymously, and unlinked with the patients.

Prescribers and dispensers

From the medical records, the findings whether right or unethical practices by doctors were identified, the names of the prescribers were kept confidential, anonymous, and unlinked. Also from medical records, the findings whether right or wrong dispensing practices were identified, the names of the pharmacist were kept confidential, anonymous, and unlinked.

Nurses

Closed care of the patients is in most cases done by nurses in terms of giving them their frequent prescribed medications, even though there were some missed doses; the names of the nurses were kept confidential, anonymous, and unlinked.

3.5 Limitations

1 Military Hospital

- Health Information (HI) system not allowing the researcher to have patient's identification, for in case if there was some missing information or confirmation of data. The researcher relied on the HI personnel to pull the data and sometimes they filter some important data that would be useful in the study.
- No information or records of sepsis cases sent to infection control as the infection control department as the core centre to oversee all sepsis cases within the hospital.
- One code was used when the patient goes to theatre and also when the patient develops sepsis. Therefore, it was very difficult for one to pull the records of patients who had developed SSI out of the list of patients who were operated.

Mankweng Hospital

- There was incomplete information in the medical records. For example, lack of electronic record keeping would let whoever captured the information to make sure is complete during capturing.
- For a very long time, the Infection Control Department did not have a monitoring tool to monitor the sepsis.

3.6 Bias

A self-made questionnaire which was developed and adjusted based on the medical records examination. The questionnaire contained demographic data, ward, utilization of the laboratory, antimicrobial agents give and discharged on, duration stayed in the hospital utilization of surgical guidelines.

3.7 Reliability and validity

The content reliability and validity of the questionnaire was established by opinions of people involved in the study and infection control at one of the hospitals who eventually adopted the tool for their evaluation within the hospital. A pilot study was done with members who were not taking part in the study.

CHAPTER FOUR: RESULTS

Prevalent microorganism on patients who developed infection

A total of 79 patients' files out of 550 were reviewed for the study. Of these, 61% (48/79) were from Mankweng Hospital and 39% (31/79) from 1 Military Hospital.

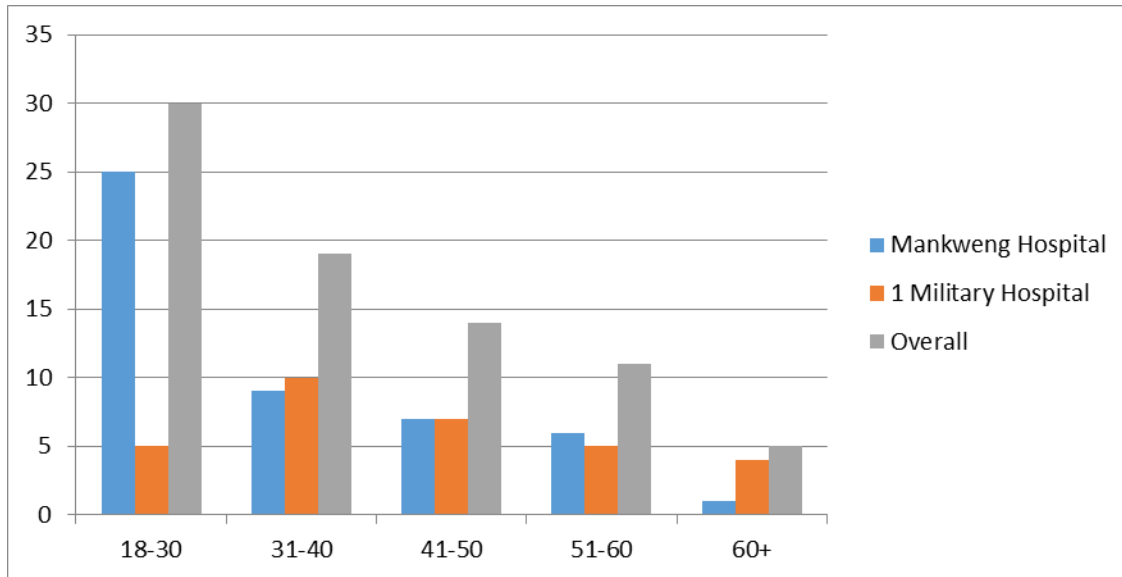


Figure 5: Age distribution.

Overall, as seen in Figure 5 a greater proportion of patients 38% were in the age group of 18-30 years, followed by 24% patients in the age group of 31-40 years as shown in Figure 5. Most of these patients were from gynecology ward. There were relatively more patients in the age range of 31-40 and 60+ in 1 Military Hospital. There were relatively equal percentages patients in the age group of 41-50 in both hospitals.

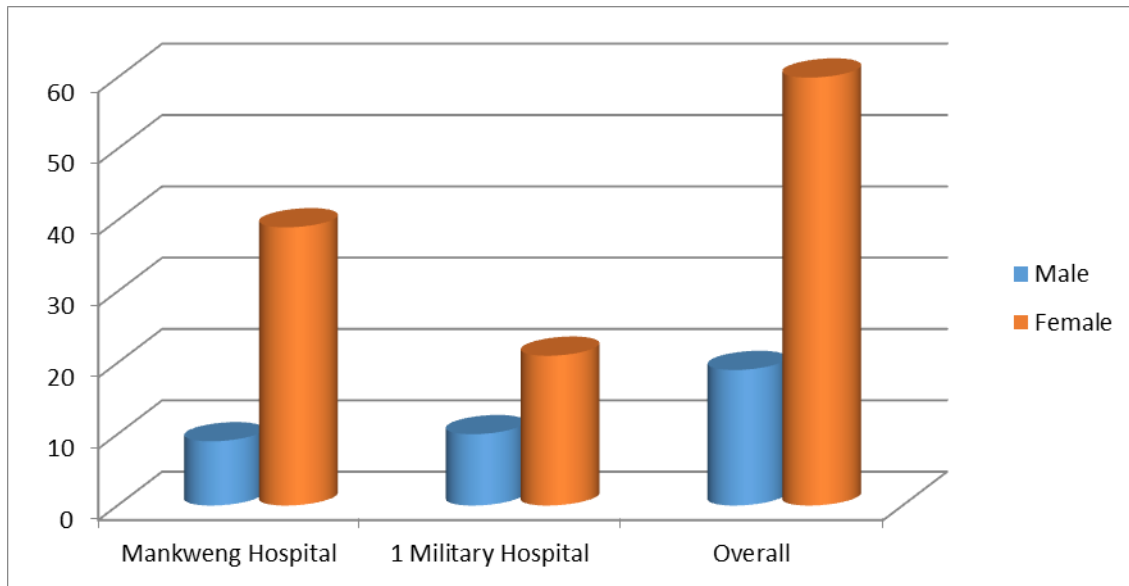


Figure 6: Gender relation with n=79.

As shown in Figure 6, there were relatively more female patients than male patients in both hospitals. More than two-thirds (76%) of the patients were female and only (24%) were male as shown in Figure 6.

Table 9: Demographic profile of the patients by facilities and wards

		Sample (n=79)	Mankweng Hospital (n=48)			1 Military Hospital (n=31)		
			Surgical (n=10)	Orthopedic (n=6)	Gynecology (n=32)	Surgical (n=12)	Orthopedic (n=10)	Gynecology (n=9)
Age	18-30	30(38%)	3	1	21	3	0	2
	30-40	19(24%)	3	0	6	4	1	5
	41-50	14(18%)	2	2	3	3	3	1
	51-60	11(14%)	2	2	2	2	2	1
	>60	5(6%)	0	1	0	0	4	0
Gender	Female	60(76%)	6	1	32	7	5	9
	Male	19(24%)	4	5	0	5	5	

P=0.5339

As indicated in Figure 5 and Figure 6, Table 9 shows in greater detail of gender and age distribution per ward at the two institutions.

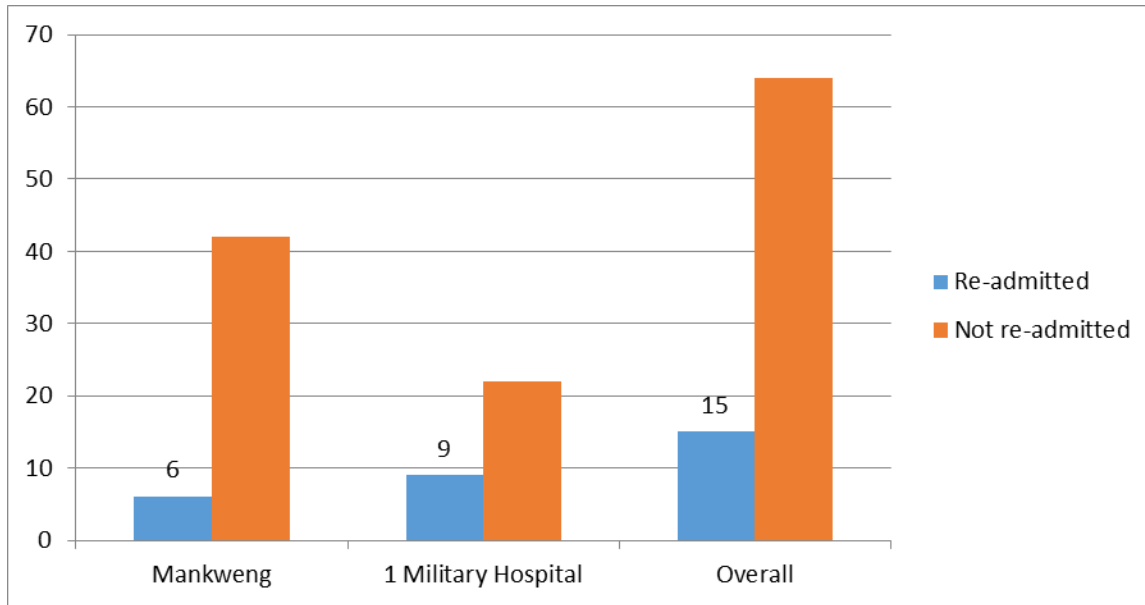


Figure 7: Re-admission pattern.

Out of the patients who developed surgical site infections, fifteen (15) patients (19%) out of 79 patients in both hospitals were re-admitted as illustrated in Figure 7. In Mankweng Hospital six (6) patients were re-admitted out of forty eight (48) patients, whereas in 1 Military Hospital nine (9) out of thirty-one (31) were re-admitted.

Table 10: Length of hospital stay, re-admission and number of days before culture and sensitivity tests

		Sample (n=79)	Mankweng Hospital (n=48)			1 Military Hospital (n=31)		
			Surgical (n=10)	Orthopedic (n=6)	Gynecology (n=32)	Surgical (n=12)	Orthopedic (n=10)	Gynecology (n=9)
No. of days admitted			23	11	9	21	23	16
Patient re-admitted	Yes	15(19%)	3	0	3	6	2	1
	No	64(81%)	7	6	29	6	8	8
No. of days before culture and sensitivity tests	0	9(11%)	1	0	8	0	0	0
	1-2	28(35%)	4	3	10	4	4	3
	3-4	11(14%)	0	2	3	2	3	1
	5-6	8(10%)	2	0	2	2	0	2
	7+	23(29%)	3	1	9	4	3	3

$p=0.5339$

The number of days which patients stayed in hospital ranged from 9 days to 23 days. The length of hospital stays also included the number of days patients were re-admitted. The table shows that culture and sensitivity test were done on majority of patients had stayed for a day or two in the hospital.

Table 11: Distribution of microorganisms from patients' records

	Sample (n=79)	Mankweng Hospital (n=48)			Military Hospital (n=31)		
		Surgical (n=10)	Orthopedic (n=6)	Gynecology (n=32)	Surgical (n=12)	Orthopedic (n=10)	Gynecology (n=9)
<i>E. coli</i>	21.5%	30.0%	-	21.9%	33.3%	30.0%	-
<i>Klebsiella pneumonia</i>	17.7%	30.0%	-	18.8%	33.3%	-	11.1%
<i>Staphylococcus aureus</i>	12.7%	10.0%	50.0%	6.3%	-	20.0%	22.3%
<i>Enterobacter cloacae</i>	10.1%	-	-	15.6%	16.7%	-	11.1%
<i>Proteus mirabilis</i>	5.1%	-	33.3%	6.3%	-	-	-
<i>Acinetobacter species</i>	3.8%	10.0%	16.7%	-	-	10.0%	-
<i>Pantoea agglomerans</i>	3.8%	-	-	6.3%	-	-	11.1%
<i>Citrobacter freundii</i>	2.5%	-	-	6.3%	-	-	-
<i>Morganella morganii</i>	2.6%	-	-	6.3%	-	-	-
<i>Staphylococcus haemol</i>	2.5%	-	-	3.1%	-	-	11.1%
<i>Streptococcus group A</i>	2.5%	-	-	3.1%	-	-	11.1%
Other	15.2%	20.0%	-	6%	16.7%	40.0%	22.2%

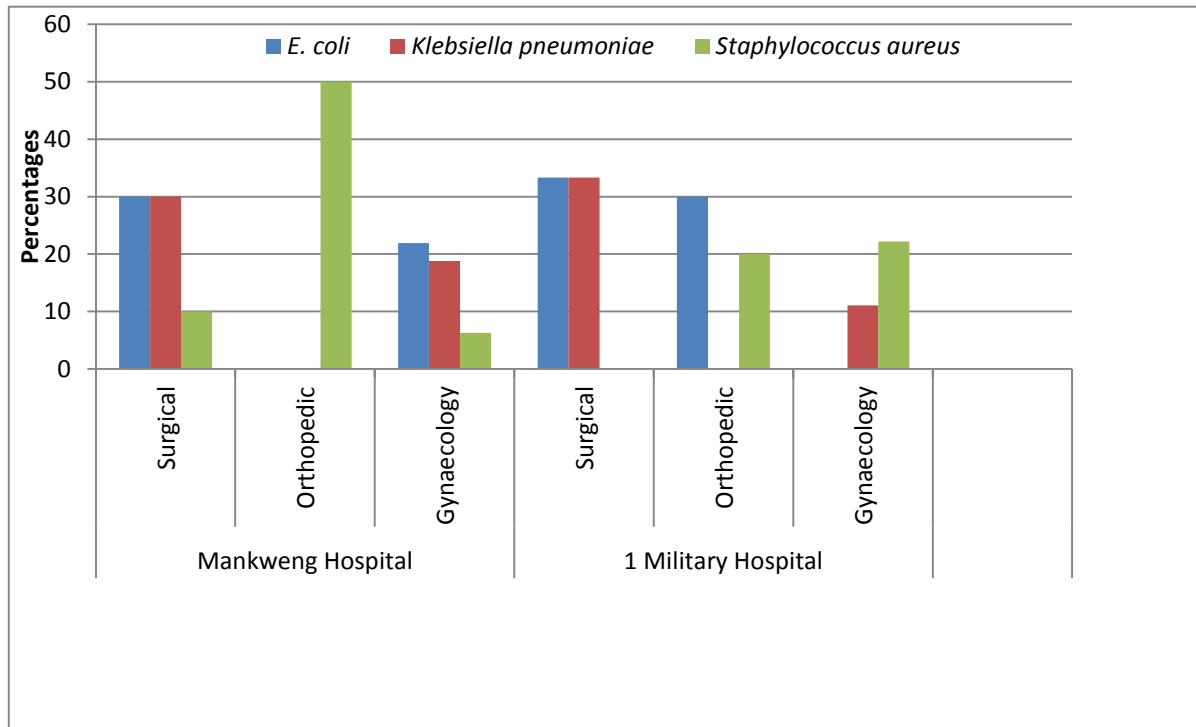


Figure 8: Most prevalent microorganisms

Table 11 and Figure 8 show the most prevalent microorganisms and less prevalent microorganisms. In overall, the most common prevalent microorganisms were *E. coli* (22%), *Klebsiella pneumoniae* (18%), *Staphylococcus aureus* (12.7%), *Enterobacter cloacae* (10.1%) and *Proteus mirabilis* (5.1%) as illustrated in Table 11. In Surgical wards at both Mankweng Hospital and 1 Military Hospital, *E. coli* and *Klebsiella pneumoniae* were the most prevalent microorganisms with 30% and 33% respectively. As can be seen from the table the only difference between these wards was that *Staphylococcus aureus* and *Acinetobacter spp.* were found at Mankweng Hospital and *Enterobacter cloacae* at 1 Military Hospital.

In orthopedic wards, *Staphylococcus aureus* was the most prevalent 50% at Mankweng Hospital and 20% at 1 Military Hospital. These were followed by *Proteus mirabilis* with 33% at Mankweng Hospital which was none at 1 Military Hospital. At 1 Military Hospital, the most prevalent found microorganism were specified under other microorganism which contributed 40% in orthopedic ward followed by 30% of *E. coli*. In Gynecology wards, at Mankweng Hospital *E. coli* and *Klebsiella pneumoniae* were the highest found prevalent microorganisms with 21.9% and 18.8% respectively, of which at 1 Military Hospital the *E. coli* was absent and *Klebsiella*

pneumoniae was at 11.1%. The most prevalent microorganism found in gynecology at 1 Military Hospital was *Staphylococcus aureus* with 22.3%.

Table 12: Distribution of microorganisms according to nurses' perceptions

	Sample (n=42)	Mankweng Hospital (n=13)		Military Hospital (n=29)	
		No	%	No	%
<i>Streptococcus Spp.</i>	23(55%)	9	69	14	48
<i>Klebsiella pneumoniae</i>	10(24%)	4	31	6	21
<i>Staphylococcus aureus</i>	35(83%)	12	92	23	79
<i>E. coli</i>	22(52%)	4	31	18	62
<i>Candida albicans</i>	7(17%)	-	-	7	24
<i>Pseudomonas</i>	5(12%)	-	-	5	17

According to nurses, overall, *Staphylococcus aureus* 83%, *Streptococcus* 55% and *E. coli* 52% were the most commonly identified microorganisms responsible for SSI. At Mankweng Hospital and 1 Military Hospital nurses were of the view that *Staphylococcus aureus* with 92% and 79% was the most prevalent microorganism.

Table 13: Distribution of microorganisms perceived by laboratory medical technologists.

Microorganisms	Sample (n=9)	Mankweng Hospital (n=4)			Military Hospital (n=5)		
		Surgical	Orthopedic	Gynecology	Surgical	Orthopedic	Gynecology
<i>E. coli</i>	6(67%)	1	1	1		3	
<i>Staphylococcus aureus</i>	6(67%)	1	1		4		
<i>Klebsiella pneumoniae</i>	5(56%)	1	1	1	1		1
<i>Hemolytic streptococci</i>	1(11%)	1					
<i>Proteus spp.</i>	1(11%)		1				
<i>Candida spp.</i>	2(22%)			2			
<i>Bacillus cereus</i>	1(11%)					1	
<i>Streptococcus</i>	1(11%)					1	
<i>Proteus mirabilis</i>	2(22%)						2
<i>Enterobacter faecalis</i>	1(11%)						1
<i>Acinetobacter baumannii.</i>	1(11%)						1

According to microbiologists as shown in Table 13 illustrates the most common prevalent microorganisms responsible for SSI was *E. coli* 67%, *Staphylococcus aureus* 67% and *Klebsiella pneumonia* 56%.

Table 14: Total number of antimicrobial agents prescribed postoperative per patients

	Mankweng Hospital		Military Hospital		Total	
	No	%	No	%	No	%
None	1	2	5	16	6	8
One drug	7	15	13	42	20	25
Two drugs	18	38	8	26	26	33
Three drugs	22	45	5	16	27	34
Total	48		31		79	

Table 14 shows the number of antimicrobials agents prescribed post-operatively per patients. On average patients received at least one antimicrobial agent. The table also gives an indication of poly pharmacy.

Table 15: Antimicrobial agents' rate of prescription postoperative from patients' files

	Mankweng Hospital				1 Military Hospital			
	Gynecology (n=32)	Orthopedics (n=6)	Surgery (n=10)	Prescription rates (n=48)	Gynecology (n=15)	Orthopedics (n=6)	Surgery (n=10)	Prescription rate (n=31)
Metronidazole	78%	33%	60%	69%		10%	8%	6%
Amoxicillin	56%	0%	10%	40%		10%		3%
Augumentin	19%	17%	50%	25%		30%	33%	23%
Cefoxitin	34%	0%	10%	25%				
Meropenem	19%		10%	25%	11%		23%	34%
Ceftriaxone	16%	17%	40%	21%	11%			3%
Cloxacillin	6%	67%	20%	17%		20%		6%
Ertapenem		17%	10%	9%		10%	38%	20%
Ampicillin	9%			6%				
Gentamycin	6%			4%	11%	10%	8%	10%
Chloramex			10%	2%				
Ciprofloxacin	3%		10%	2%		30%	17%	16%
Co-trimoxazole	3%			2%	11%	20%		10%
Doxycycline's	3%			2%				
Erythromycin	3%			2%			17%	10%
Imipenem			10%	2%				
Cefuroxime						10%	8%	6%
Cefazolin							8%	3%
Clarithromycin							8%	3%

Table 15 shows at Mankweng Hospital metronidazole appeared 69% of all patients' files indicating that it had been prescribed. The table also shows that metronidazole was prescribed more in gynecology ward at 78% and 60% in surgical ward. At 1 Military Hospital, the most commonly prescribe antimicrobial agent as seen from the table was meropenem at 34% compared to 25% at Mankweng Hospital. At Mankweng Hospital the second commonly prescribed antimicrobial agent was amoxicillin at 40% with more prescription again from gynecology ward while at 1 Military Hospital was augumentin at 23% with most prescriptions from surgical ward at 33%. Augumentin prescriptions at Mankweng Hospital were equal to those of cefoxitin and meropenem at 25% and again in general these were prescriptions from

gynecology ward. Ertapenem which is another carbapenem like meropenem was extensively prescribed at 1 Military Hospital particularly in the surgical ward. At Mankweng Hospital Cloxacillin was prescribed at 67% in the orthopedic ward. Cefazolin was only used at 1 Military Hospital in surgical ward. A summary of most commonly prescribed antimicrobial agents is given in Figure 9.

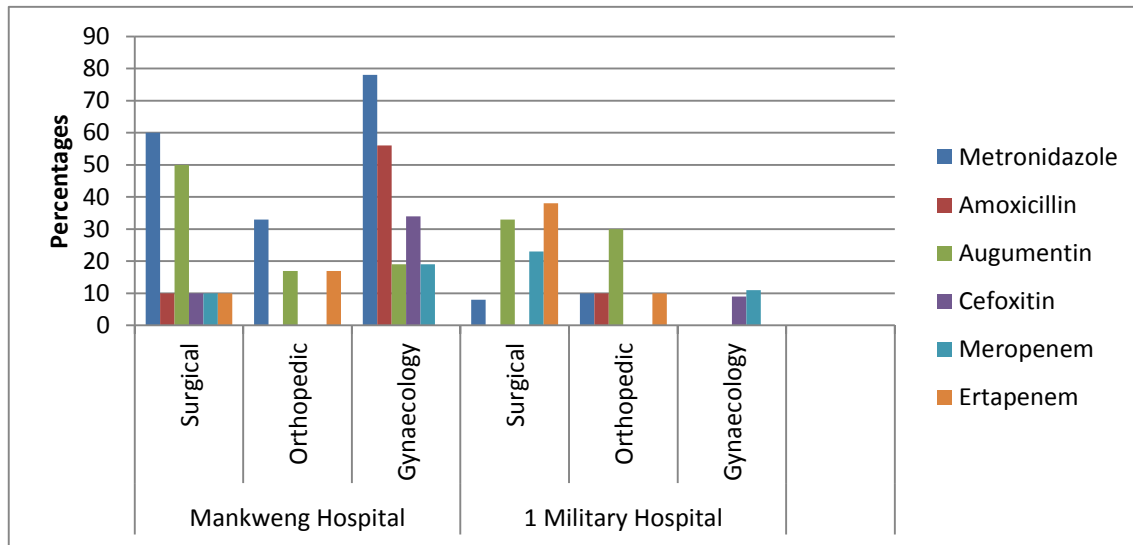


Figure 9: Mostly prescribed antimicrobials agents

Table 16: Commonly issued antimicrobial agents perceived by pharmacists for SSI patients

	Mankweng Hospital (n=12)		1 Military Hospital (n=8)	
	No	%	No	%
Amoxicillin	10	83	4	50
Augumentin	7	58	5	63
Cefoxitin	3	25	3	38
Ceftriaxone	3	25	2	25
Imipenem	1	8	3	38
Meropenem	1	8	4	50
Metronidazole	7	58	4	50
Ampicillin	3	25	2	25
Cefazolin	0	0	1	13
Ertapenem	0	0	3	38
Gentamycin	2	17	1	13
Cefuroxime	0	0	3	38
Ciprofloxacin	3	25	2	25
Cloxacillin	6	50	2	25
Erythromycin	1	8	1	13
Teiplanin	0	0	1	13

Table 16 shows that the most prescribed antimicrobial agents according to the views of the pharmacist who took part in the feedback meeting at Mankweng Hospital were amoxicillin (83%), augumentin (58%), metronidazole (58%) and cloxacillin (50%). At a similar meeting at 1 Military Hospital, the pharmacists' perceptions on mostly prescribed antimicrobial agent were augumentin (63%), amoxicillin (50%) and metronidazole (50%).

Table 17: Commonly administered antimicrobial agents perceived by nurses to SSI patients

	Mankweng Hospital (n=13)		Military Hospital (n=29)		Sample (n=42)	
	No	%	No	%	No	%
Metronidazole	13	100	14	48	27	64
Augumentin	5	38	15	52	20	48
Meropenem	-	-	16	55	16	38
Imipenem	-	-	14	48	14	33
Ampicillin	10	77	3	10	13	31
Cefazolin			12	41	12	29
Cefoxitin	9	69	-	-	9	21
Cefuroxime	-	-	7	24	7	17
Cloxacillin	4	31	2	7	6	14
Gentamycin	-	-	5	17	5	12
Penicillin	-	-	4	14	4	10
Vancomycin	-	-	3	10	3	7
Clindamycin	-	-	3	10	3	7
Amikacin	-	-	2	7	2	5
Ciprofloxacin	-	-	1	3	1	2
Targocid	-	-	1	3	1	2
Co-trimoxazole	-	-	1	3	1	2
Amoxicillin	1	8	-	-	1	2

All nurses in Mankweng Hospital reported that metronidazole 100%, ampicillin (77%), and cefoxitin (69%) were the most commonly prescribed antimicrobial agent as shown in Table 17. %, while at Military Hospital, meropenem (55%), augumentin (52%), metronidazole (48%) and imipenem (48%) were the most commonly prescribed antimicrobial agents. Interestingly amoxicillin was viewed to be least prescribed and yet in Table 16 according to the pharmacist it was the most at Mankweng Hospital.

Table 18: Commonly used antimicrobial agents in particular antibacterial agents for culture and sensitivity tests according to laboratory personnel

	Sample (n=9)	Mankweng Hospital (n=4)		Military Hospital (n=5)	
	No	No	%	No	%
Ampicillin	4(44%)	2	50	2	40
Augumentin	6(67%)	2	50	4	80
Cefazolin	2(22%)	1	25	1	20
Penicillin	2(22%)	1	25	1	
Co-trimoxazole	1(11%)	1	25		
Cefuroxime	3(33%)	2	50	1	20
Amoxicillin	2(22%)	1	25	1	20
Gentamycin	2(22%)	1	25	1	20
Ciprofloxacin	1(11%)	1	25		
Meropenem	1(11%)			1	20
Imipenem	1(11%)			1	20
Colistin	1(11%)			1	20

In general, the most used antimicrobial agents used for culture and sensitivity tests were penicillins and cephalosporins. Colistin and carbapenems were tested at 1 Military Hospital as shown in Table 18.

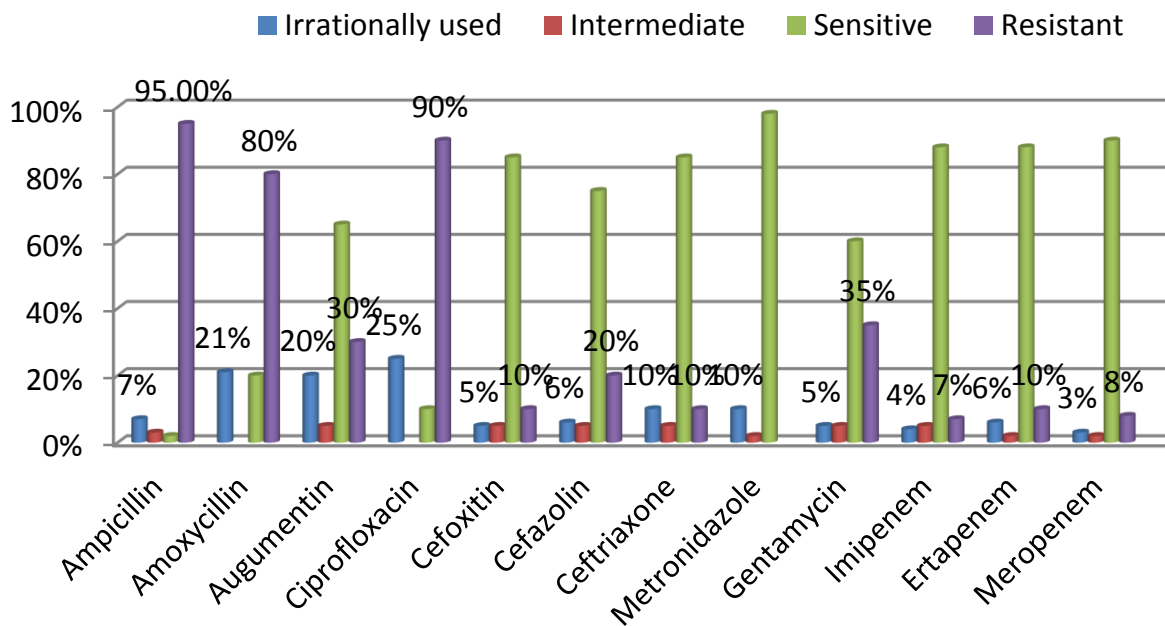


Figure 10: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents.

The figure above is showing how prescribing pattern was related to culture and sensitivity tests results in the patients' medical record. To illustrate, the laboratory found that 95% microorganisms tested were resistant to ampicillin. Only 2% microorganisms tested were sensitive to ampicillin. 7% of the prescriptions were of ampicillin. During the feedback session one of the specialist physician in pediatric ward mention that ampicillin is still a good drug of choice in their ward, although it was also shown on the results that most of microorganisms were resistant to ampicillin.

Table 19: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in gynecology ward at 1 Military Hospital, n=7.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to	Antibiotics given	Antibiotics given	Antibiotics discharged	Days irrationally used
Staphylococcus aureus	Candida albicans	Clindamycin	Ampicillin	Penicillin	Erythromycin	Ceftriaxone	Meropenem	Ampicillin*	Amoxicillin*	Augumentin	11
Staphylococcus aureus	Haemolytic streptococci	Ampicillin	Co-trimoxazole	Gentamycin	Penicillin	Augumentin	Ceftriaxone	Co-trimoxazole*	Meropenem	None	8
Klebsiella pneumoniae	E. coli	Amoxicillin	Augumentin	Cefazolin	Ciprofloxacin	Meropenem	Cefoxitin	Augumentin*	Metronidazole	None	5
Enterococcus faecalis		Erythromycin	Amoxicillin	Ampicillin		Meropenem	Augumentin	Amoxicillin*	Metronidazole	None	5
Enterococcus cloacae		Augumentin	Cefoxitin	Cefazolin	Amoxicillin	Meropenem	Levofloxacin	Augumentin*	Metronidazole	None	4
Streptococcus group		Erythromycin	Penicillin	Ampicillin	Clindamycin	Vancomycin	Linezolid	Gentamycin	Doxycycline	None	8
Pantoea agglomerans		Augumentin	Cefazolin	Ceftriaxone	Imipenem	Meropenem	Tobramycin	Augumentin*		None	6

In gynecology ward at 1 Military Hospital, most of the microorganisms found to be resistant to mostly prescribed antimicrobials were among others *S. aureus*, *K. pneumoniae* and *Enterococcus spp.* The above-mentioned microorganisms were resistant to among others amoxicillin, augumentin. As indicated in the Table 19, for example, *Klebsiella pneumoniae* and *E. coli* were isolated from laboratory and it was recommended that they were found to be resistant to amoxicillin, augumentin, cefazolin, and ciprofloxacin. Be it that they were resistant to those microorganisms, augumentin was yet given for 5 days. The mostly prescribed antimicrobial agents were irrationally prescribed between 4 to 11 days.

Table 20: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in orthopedic ward at 1 Military Hospital, n=7.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to	Antibiotics given	Antibiotics given	Antibiotics discharged	Days irrationally used
Corynebacterium Spp.		Co-trimoxazole				Augmentin	Meropenem	Co-trimoxazole*	Augumentin	Augumentin	5
Acinetobacter Spp.	Klebsiella pneumoniae	Co-trimoxazole	Augumentin	Ampicillin	Penicillin	Ertapenem	Meropenem	Co-trimoxazole*	Ertapenem	Augumentin*	4
E. coli		Amoxicillin	Augumentin	Ampicillin		(Colistin)	Meropenem	Amoxicillin*	Augumentin*	Augumentin*	14
Staphylococci	Staphylococcus epidermidis	Co-trimoxazole	Erythromycin	Augumentin	Penicillin	Ertapenem	Meropenem	Augumentin*		Augumentin*	11
Pantoea Spp.	Staphylococcus epidermidis	Ceftriaxone	Ampicillin	Augumentin	Gentamycin	Ertapenem	Meropenem	Augumentin*	Gentamycin*	None	9
E. coli	Staphylococcus aureus	Amoxicillin	Ampicillin	Augumentin	Ceftriaxone	Ciprofloxacin	Ertapenem	Augumentin*		Augumentin*	8
Streptococci Spp.	Proteus mirabilis	Amikacin	Gentamycin	Ciprofloxacin	Tobramycin	Augumentin	Meropenem	Ertapenem	Erythromycin	Ciprofloxacin*	7

The most prevalent microorganisms found in the ward were *Corynebacterium Spp.*, *Acinetobacter Spp.*, *E. coli*, *Staphylococci*, *Pantonea Spp.* etc. The most prescribed antimicrobial agents which were irrationally prescribed between 4 to 14 days were augumentin, amoxicillin and co-trimoxazole as indicated in Table 20.

Table 21: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in surgical ward at 1 Military Hospital, n=6.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to	Antibiotics given	Antibiotics given	Antibiotics discharged	Days irrationally used
Klebsiella pneumoniae & Pseudomonas aeruginosa	Candida albicans	Meropenem	Imipenem	Erythromycin	Vancomycin	(Colistin)	Ceftriaxone	Meropenem*	Erythromycin*	None	8
E. coli	Citrobacter freundii	Gentamycin	Augumentin	Ciprofloxacin	Ampicillin	Meropenem	Vancomycin	Gentamycin*	Cefazolin	None	3
Enterobacter Spp.	Proteus mirabilis	Augumentin	Cefoxitin	Cefotaxime	Ceftazidime	Meropenem	Ertapenem	Augumentin*		Augumentin*	21
Enterobacter Spp.	Proteus mirabilis	Augumentin	Cefoxitin	Ceftriaxone		Meropenem	Ertapenem	Augumentin*	Ertapenem	Augumentin*	6
Pseudomonas Spp.		Ciprofloxacin	Piperacillin	Imipenem		Meropenem	Gentamycin	Augumentin	Ciprofloxacin*	Ciprofloxacin*	14
E. coli	Augumentin prophylaxis*	Augumentin	Ampicillin	Ceftriaxone	Ciprofloxacin	Ertapenem	Gentamycin	Augumentin*	Metronidazole	Augumentin*	14

The most commonly found microorganisms were *Klebsiella pneumoniae*, *E. coli*, *Enterobacter Spp.*, *Proteus mirabilis*, and *Pseudomonas Spp.* The most irrationally used antimicrobial agent was Augmentin, for example *Klebsiella pneumoniae* and *Candida albicans* were isolated and were found to be resistant to meropenem, imipenem, erythromycin and vancomycin, and were sensitive to colistin, and ceftriaxone as shown in Table 21. Being the situation meropenem which microorganisms were resistant to was administered irrationally to the patient for 8 days.

Table 22: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in surgical ward at Mankweng Hospital, n=6.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to	Antibiotics given	Antibiotics given	Antibiotics discharged	Days irrationally used
Pseudomonas Spp.		Ciprofloxacin	Piperacillin	Imipenem		Meropenem	Gentamycin	Augumentin	Ciprofloxacin*	Ciprofloxacin*	14
E. coli	Augumentin prophylaxis*	Augumentin	Ampicillin	Ceftriaxone	Ciprofloxacin	Ertapenem	Gentamycin	Augumentin*	Metronidazole	Augumentin*	14
E. coli		Amoxicillin	Cefazolin	Ciprofloxacin	Augumentin	Cefoxitin	Meropenem	Augumentin*	Ceftriaxone	None	5
Klebsiella pneumoniae		Ampicillin	Augumentin	Amoxicillin	Ceftriaxone	Cefoxitin	Gentamycin	Cloxacillin	Ceftriaxone*	None	16
Pseudomonas aeruginosa		Imipenem	Meropenem			Ciprofloxacin	Gentamycin	Meropenem*		Ciprofloxacin	14
Acinetobacter Spp.		Ciprofloxacin	Ceftriaxone	Imipenem	Meropenem	Colistin	Gentamycin	Ciprofloxacin*	Imipenem*	Ciprofloxacin*	23

The Table 22 above shows the microorganisms which were isolated e.g. *E. coli*, *K. pneumoniae* etc. These microorganisms were resistant to some antimicrobial agents e.g. imipenem and the very same antimicrobial agent were irrationally administered to the patient for 23 days.

Table 23: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in orthopedic ward at Mankweng Hospital, n=3.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to 2	Antibiotics given	Antibiotics given	Antibiotics discharged	Days irrationally used
Proteus mirabilis	Cefazolin prophylaxis*	Ampicillin	Cefazolin	Ceftriaxone		Meropenem	Cefoxitin	Cloxacillin	Metronidazole	Cloxacillin	1
Acinetobacter Spp.		Ceftriaxone	Meropenem	Ertapenem	Ciprofloxacin	Colistin	Gentamycin	Ertapenem*	Cloxacillin	Cloxacillin	10
Staphylococci Spp.	Staphylococcus aureus	Augumentin	Co-trimoxazole	Erythromycin		Meropenem	Ertapenem	Augumentin*		Augumentin*	11

Table 23 shows cefazolin being given as a prophylaxis. *Proteus mirabilis* was isolated and was found to be resistant to cefazolin which was given as a prophylaxis.

Table 24: The relationship between culture and sensitivity tests and prescribing pattern of antimicrobial agents in gynecology ward at Mankweng Hospital, n=29.

Microorganism found	Microorganism found	Resistant to	Resistant to	Resistant to	Resistant to	Sensitive to	Sensitive to	Antibiotics given	Antibiotics given	Antibiotics discharged	Days Irrationally used
Klebsiella pneumoniae		Amoxicillin	Ampicillin			Meropenem	Augmentin	Amoxicillin*	Metronidazole	Amoxicillin*/Metronidazole	3
Klebsiella pneumoniae	E. coli	Amoxicillin	Augmentin	Cefazolin	Ciprofloxacin	Meropenem	Cefoxitin	Amoxicillin*	Augmentin & metronidazole	None	5
Staphylococcus aureus		Amoxicillin	Ampicillin	Gentamycin	Co-trimoxazole	Ciprofloxacin	Cloxacillin	Amoxicillin *	Metronidazole	None	2
Klebsiella pneumoniae	Cefazolin prophylaxis*	Amoxicillin	Ampicillin	Cefazolin	Gentamycin	Augmentin	Cefoxitin	Amoxicillin*	Metronidazole	Amoxicillin*	9
Staphylococci Spp	E. coli	Amoxicillin	Augmentin	Ampicillin	Co-trimoxazole	Cefazolin	Meropenem	Amoxicillin*	Metronidazole	None	3
Morganella morganii		Amoxicillin	Augmentin	Ampicillin	Cefoxitin	Ertapenem	Imipenem	Ampicillin*	Metronidazole	Amoxicillin*/Metronidazole	4
Klebsiella pneumoniae		Amoxicillin	Ampicillin	Co-trimoxazole		Ceftriaxone	Meropenem	Amoxicillin*	Cefoxitin	Amoxicillin*/Metronidazole	7
Proteus mirabilis	Ampicillin prophylaxis*	Nitrofurantion	Co-trimoxazole	Ampicillin		Augmentin	Imipenem	Ampicillin*		None	1
Klebsiella pneumoniae		Amoxicillin	Augmentin	Tazobactam	Cefuroxime	Ciprofloxacin	Imipenem	Amoxicillin*	Metronidazole	None	6
Enterobacter cloacae		Amoxicillin	Augmentin	Ampicillin		Colistin	Meropenem	None	None	None	-
E. coli		Amoxicillin	Augmentin	Ampicillin	Ciprofloxacin	Cefoxitin	Amikacin	Amoxicillin*	Cloxacillin	None	8
Citrobacter freundii	Klebsiella oxytoca	Amoxicillin	Ampicillin	Cefoxitin	Ciprofloxacin	Meropenem	Imipenem	Cefoxitin*	Metronidazole	Cloxacillin & Metronidazole	4
Klebsiella pneumoniae	Cefazolin prophylaxis*	Meropenem	Ampicillin	Cefoxitin	Cefazolin	Augmentin	Gentamycin	Cefoxitin*	Meropenem	Amoxicillin*	8
Enterobacter cloacae		Augmentin	Amoxicillin	Cefoxitin	Cefazolin	Meropenem	Levofloxacin	Augmentin*	Metronidazole	None	4
Enterobacter cloacae	Augmentin prophylaxis	Augmentin	Amoxicillin	Cefoxitin	Ceftriaxone	Meropenem	Imipenem	Augmentin*		None	9
Pantoea agglomerans		Amoxicillin	Piperacillin	Ampicillin	Co-trimoxazole	Augmentin	Cefazolin	Amoxicillin*	Cefoxitin	Amoxicillin*	9
Klebsiella oxytoca	Cefazolin prophylaxis	Amoxicillin	Cefazolin	Ceftriaxone	Cefoxitin	Augmentin	Meropenem	Amoxicillin*	Cefoxitin*	None	3
E. coli		Amoxicillin	Cefazolin	Ampicillin	Ciprofloxacin	Augmentin	Meropenem	Amoxicillin*	Ampicillin*	None	4
Enterobacter cloacae	Cefazolin prophylaxis	Augmentin	Amoxicillin	Ampicillin	Cefazolin	Meropenem	Co-trimoxazole	Amoxicillin*	Ampicillin*	None	5
E. coli		Amoxicillin	Ceftriaxone	Cefazolin	Ampicillin	Augmentin	Cefoxitin	Ceftriaxone*	Metronidazole	Amoxicillin*	8
Pantoea agglomerans		Augmentin	Cefazolin	Ceftriaxone	Imipenem	Meropenem	Tobramycin	Augmentin*		None	6
Citrobacter freundii		Augmentin	Cefoxitin	Amoxicillin	Ampicillin	Meropenem	Gentamycin	Cefoxitin*	Metronidazole	Amoxicillin*	10
E. coli		Augmentin	Cefazolin	Amoxicillin	Ampicillin	Meropenem	Cefoxitin	Augmentin*	Metronidazole	Augmentin*	8
E. coli		Augmentin	Ampicillin	Cefazolin	Gentamycin	Meropenem	Levofloxacin	Amoxicillin*	Metronidazole	Amoxicillin*/Metronidazole	8
E. coli		Augmentin	Ampicillin			Augmentin	Cefazolin	Amoxicillin*	Cefoxitin	Amoxicillin*/Metronidazole	9
Morganella morganii		Augmentin	Amoxicillin	Ceftriaxone	Ampicillin	Meropenem	Gentamycin	Amoxicillin*	Metronidazole	Amoxicillin*/Metronidazole	12
Serratia odorifera		Amoxicillin	Ampicillin	Cefazolin	Piperacillin	Augmentin	Cefoxitin	Metronidazole		Amoxicillin* & Metronidazole	7
Enterobacter cloacae		Amoxicillin	Ampicillin	Cefoxitin		Ceftriaxone	Meropenem	Amoxicillin*	Cefoxitin*	Amoxicillin* & Metronidazole	11
Staphylococcus haemolyticus		Ampicillin	Co-trimoxazole	Gentamycin	Piperacillin	Augmentin	Ceftriaxone	Co-trimoxazole*	Gentamycin*	None	8

In this ward, there were microorganisms which were isolated, among others were *Morganella morganii*, *Proteus mirabilis* etc. They were found to be resistant to augumentin, and ampicillin respectively. Ampicillin was given as a prophylaxis and augumentin as a post treatment as shown in Table 24.

Table 25: The summary of cost implications due to irrational prescribing of antimicrobial agents at the two hospitals.

Mankweng Hospital (n=38)			1 Military Hospital (n=13)		
Surgical (n=7)	Orthopedic (n=3)	Gynecology (n=29)	Surgical (n=6)	Orthopedic (n=7)	Gynecology
R 2713.67	R 10624.41	R 2832.53	R 2861.19	R 985.44	R 658.52

At Mankweng Hospital, orthopedic ward appeared to have incurred highest cost R10624.41 which was due to irrational prescribing of antimicrobial agents, followed by gynecology ward with R2832.53 and lastly surgical ward with R2713.67 as shown in Table 25. At 1 Military Hospital, surgical ward had incurred highest cost R2861.19 which was due irrational prescribing of antimicrobial agents, followed by orthopedic ward with R985.44, and gynecology ward with R658.52.

According to the 2013/2014 budget of Pharmacy department at Mankweng Hospital, R5, 442 960.00 was allocated to Pharmacy Department by Department of Health in Limpopo, of which R2, 778 200.00 was consumed by commonly prescribed top ten antimicrobial agents which constitute 51% of the total budget. This was from 01/04/2013 to 31/03/2014 (The Pharmacy manager at Mankweng Hospital, 2014).

Table 26: Responses from pharmacists regarding questions on diagnosis, poly pharmacy and consumption

		Sample (n=20)		Mankweng Hospital (n=12)		Military Hospital (n=8)		p-values
		No	%	No	%	No	%	
1. Were antimicrobial agents prescribed according to the diagnosis?	Yes	15	75	10	83	5	63	0.347
	No	5	25	2	17	3	38	
2. Is more than one antimicrobial agent always prescribed?	Yes	20	100	12	100	8	100	-
	No	0	0	0	0	0	0	
3. Is poly pharmacy always justified?	Yes	13	65	9	75	4	50	0.356
	No	7	35	3	25	4	50	
4. Rank the wards according to consumption	Surgical	16	80	11	92	5	63	0.049
	Orthopedic	3	15	0	0	3	37	
	Gynecology	1	5	1	8	0	0	

Most of the pharmacists agreed that the antimicrobial agents prescribed were relevant to the diagnosis. Regarding poly pharmacy, pharmacists' perceptions seem to be equally divided in terms of being justified or not. The above table seems to suggest that according to pharmacists' perception, the surgical wards at the two hospitals consumed more antimicrobial agents than the other two wards. This seems to contrast with information contained in Table 15.

Table 27: Responses to questionnaires by laboratory personnel regarding techniques used, pressure points and their implications

		Mankweng Hospital (n=4)		1 Military Hospital (n=5)	
		No	%	No	%
1. What sensitive test do you carried-out?	Automated Vitek	4	100	5	100
	Kirby Bauer	1	25	3	75
	API	3	75		
2. What are the pressure points on turn-around time?	Samples coming late to lab	4	100		
	Samples incorrectly labeled	3	36	4	50
3. What are the implications of the pressure points?	Clinician get result late	3	75	4	80
4. How regular are laboratory results used?	Often	3	75	1	20
	Less often	1	25	4	80

The above table shows that they were several techniques used to carry out the culture and sensitivity tests and the automated one being the most commonly used. Generally, the highest-pressure point was as a result of samples coming incorrectly labeled, however at Mankweng Hospital samples were said to be coming very late to the lab. According to microbiologists the implications of the pressure points resulted in clinicians getting their results very late. Interestingly, laboratory personnel generally were saying the opposite of each the other. In the feedback session at 1 Military Hospital the pathologist then mentioned that physicians sent wrong samples to laboratory i.e. swabs instead of blood samples, moreover they do not do follow-ups. In Mankweng hospital during the feedback session the pathologist then mentioned that physicians have access to NHLS intranet to view the patients' laboratory culture and sensitivity test results to start therapy than waiting for laboratory personnel to bring the hard copy to the ward before therapy can be started. Moreover, physicians sent wrong samples to laboratory i.e. swabs instead of blood samples, moreover they do not do follow-ups.

Table 28: Responses from doctors on questions regarding the use of surgical guidelines and laboratory culture and sensitivity results

		Mankweng Hospital (n=8)		1 Military Hospital (n=28)		p-values
		No	%	No	%	
1. Are there surgical guidelines?	Yes	5	63	17	61	1.000
	No	3	38	11	39	
2. Which guidelines?	South African	5	63	12	43	<0.001
	Other country's	3	38	-	-	
	Other			15	54	
3. Lab result used to prescribe antimicrobial agents	None	-	-	-	-	0.548
	Less often	6	75	14	50	
	Often	2	25	13	46	
	Very Often		0	1	4	

At the two hospitals from the table, doctors indicate that were surgical guidelines mainly South African but also some from other countries. Generally, the above table seems to indicate that results from the laboratory were less often used. The answers to question 3 from doctors seem to suggest that doctors do get the results from the lab but they do not use them (Table 27). During the feedback session at 1 Military Hospital some of the physicians mentioned that the reasons why in most cases they do not utilize laboratory culture and sensitivity test results, is because the laboratory turn-around time was too long to be waiting for to initiate antimicrobial

therapy. Some of the physicians acknowledged that things were not done in a proper way in as far as antimicrobial agents are concerned. Gynecology specialist also mentioned that they outsource some procedures from neighboring government hospitals. In Mankweng Hospital during the feedback session some of the physicians mentioned that the reasons why in most cases they do not utilize laboratory culture and sensitivity test results, is because the laboratory turn-around time was too long to be waiting for.

Table 29: Factors contributing to surgical site infection as perceived by nurses in general

		Sample (n=36)		Mankweng Hospital (n=16)		Military Hospital (n=20)	
		No	%	No	%	No	%
Factors that contribute to surgical site infection	Co-morbidities	12	33	5	31	7	35
	Poor wound care	25	69	7	44	18	90
	Immune-compromised patients	8	22	2	13	6	30
	Poor Hygiene	7	19	2	13	5	25
	Inadequate aseptic technique	16	44	5	31	11	55
	Poor Nutrition	1	3	1	6		
	Poor theatre sterility	11	14	6	38	5	25
	Poor hand washing	10	14	5	31	5	25
	Unhygienic/small environment	16	19	11	69	5	25
	Long surgical procedure	3	8			3	15

Table 29 above indicates that the major contributing factors were poor wound care, inadequate aseptic technique, co-morbidities, immune-compromised patients and poor hygiene as perceived by nurses in general. One of the ICU specialist mentioned during the feedback session that they do not need soap dispenser in their ward, and that maintenance personnel can come erect it to other wards where it is needed.

Table 30: Types of operations performed at Mankweng Hospital

Type of operation performed	Gynecology	Orthopedic	Surgical	Total
Below knee amputation	0	0	3	3
CT abdomen laparotomy	0	0	1	1
Caesarean section	20	0	0	20
Debridement	0	1	0	1
Debridement of soft tissue	0	0	1	1
Debridement of wound	0	0	1	1
Debridement or removal of womb	1	0	0	1
Explorative laparotomy	2	0	1	3
Incision and drainage	0	1	0	1
Laparotomy and biopsy	2	0	0	2
Left limb debridement	0	0	1	1
Open reduction fracture	0	1	0	1
Percutaneous drainage	0	0	2	2
Previous caesarean section	1	0	0	1
Re-joint patella tension	0	1	0	1
Skin graft	0	0	1	1
Tibia debridement	0	1	0	1
Total abdominal hysterectomy	6	0	0	6
Total	32	6	10	48

In gynecology ward, there were 20 cases of sepsis from caesarean section operation, 6 cases of sepsis from total abdominal hysterectomy, 4 cases of sepsis from explorative laparotomy and biopsy. In surgical ward 3 cases of sepsis were from below knee amputation, 2 from percutaneous drainage as illustrated in Table 31.

Tablet 31: Types of operations performed at 1 Military Hospital

Type of operation performed	Gynecology	Orthopedic	Surgical	Total
Below knee amputation	0	0	1	1
Caesarean section	2	0	0	2
Debridement	0	1	0	1
Debridement of wound	0	1	0	1
Destruct lesion of skull	0	1	0	1
Exploratory laparotomy	1	0	0	1
Hernia repair	0	0	1	1
Laparotomy	0	0	3	3
Laparotomy and biopsy	1	0	0	1
Laparotomy and left tissue	0	0	1	1
Laparotomy cholecystectomy	0	0	2	2
Laparotomy	0	0	1	1
Left reverse shoulder	0	1	0	1
Left thumb excision	0	1	0	1
Open reduction intern	0	1	0	1
Percutaneous drainage	0	0	1	1
Re-laparotomy	1	0	0	1
Removal of hardware	0	1	0	1
Right knee aspiration	0	1	0	1
Thoracotomy	0	0	1	1
Total abdominal hysterectomy	4	0	0	4
Total hip replacement	0	2	0	2
Unspecified	0	0	1	1
Total	9	10	12	31

At 1 Military Hospital, the most performed operations in gynecology ward were total abdominal hysterectomy with 4 cases, followed by caesarean section with 2 cases. In orthopedic ward, the most performed operations were total hip replacement with 2 cases, followed by debridement, debridement of wound, destruct lesion of skull, left reverse shoulder, left thumb excision, percutaneous drainage, and thoracotomy all with one-one cases. In surgical ward, the most performed operations were laparotomy with 3 cases, followed by laparotomy cholecystectomy with 2 cases and the rest of the cases were one-one cases as shown in Table 32.

CHAPTER FIVE: DISCUSSION

From the results obtained women constituted the largest number of patients (76%) who developed Surgical Site Infection (SSI). This was not surprising because most procedures that were done were caesarean sections were most of the SSI were found.

From the results, there were relatively more female patients than male patients in both hospitals as illustrated in Figure 6. As shown in Figure 6 women constituted of 32 patients from Mankweng Hospital and 9 patients from 1 Military Hospital and most were from gynecology wards. The results showed that there were more SSI in gynecology wards of patients between the ages of 18-30 which is a child bearing age most likely to undergo caesarean section hence possible SSI as shown in Figure 5. SSI would not be expected to be very high after caesarean section because this is regarded as a clean procedure and one would expect risk of infection to be less than 5% with judicious antimicrobial prophylaxis use (Joseph et al., 2008). Indeed, this was the case as shown in Table 32 and 33 that 43% of women had undergone caesarean section in addition to 13% of women who had undergone total abdominal hysterectomy. Surprisingly if the procedures carried out in gynecology ward at Mankweng Hospital were clean procedure, how come the most prevalent microorganisms were *E. coli* (22%), *Klebsiella pneumoniae* (18%), and *Enterobacter cloacae* (16%)?

During the feedback session nurses and microbiologists agreed that from the community, the most prevalent microorganism was *Staphylococcus aureus* and not *E. coli* as was seen in the patients' medical records. It would be reasonable to assume that infection control policy at both hospitals would be difficult to implement as patients' medical records, nurses, and microbiologists' perceptions are not in agreement. Microbiologists and infections control teams should be the ones knowing the most prevalence of microbial isolates because they are regarded as the champions of surveillance.

Surveillance would mean case-finding including re-admission which was on average 7% at both hospitals, use of direct prospective observation, indirect prospective detection or a combination of direct and indirect method for the duration of hospitalization (Mangram et al., 1999). As the contradictions seen in Table 15, 17, 18, 26, 27, and 28, this information from surveillance as part of infection control and if doctors, nurses, microbiologist, and pharmacists in a health facility are communicating with each other would assist in the selection, ordering, and stocking of

antimicrobial agents for prophylaxis and treatment according to efficacy as determined by the laboratory against most common pathogens associated with any surgical procedure. The present study showed that the most commonly prescribed antimicrobial agents for prophylaxis at both hospitals were amoxicillin-clavulanate, cefazolin, and ampicillin. From the results obtained the most common isolates identified were resistant to amoxicillin-clavulanate, cefazolin, and ampicillin table resistant and sensitivity. This is not surprising as seen in the results table guidelines that 39% of prescribers did not have surgical guidelines.

The results seen in Table 11 and Figure 8 regarding the orthopedic ward at 1 Military Hospital were disturbing because of the high prevalence of *E. coli* at 30%. It was also found at that level of prevalence in surgical and gynecology wards as illustrated in Table 11 and Figure 8. There are many different types of *E. coli* bacteria, most of which are carried harmlessly in the gut. These strains of *E. coli* make up a significant and necessary proportion of the natural flora in the gut of people and most animals. When strains of *E. coli* are outside of their normal habitat of the gut, they can cause serious infections, several of which can be fatal (WHO, 2011). Therefore, one can get an *E. coli* infection by coming into contact with the feces, or stool, of humans or animals. It is the common cause of SSIs, especially those following operations on the abdomen where it is often found mixed with other gut bacteria. Entry of *E. coli* into the body can be as a result of drinking water or eating food that has been contaminated by feces. It should be considered unlikely for its prevalence to be so high in orthopedic ward and even in gynecology where the gut is not perforated, but high in general surgical ward.

The prevention *E. coli* infection includes among others:

- Washing hands or use an antibacterial hand rub after you have had any physical contact with a patient – whether the patient has diarrhea or not.
- Encouraging patients to wash their hands after using the toilet, as well as before and after eating.
- Avoiding prescribing broad-spectrum antimicrobial agents, which affect the natural flora of the gut and select for the resistant strains (WHO, 2011).

These are general guiding principles of infection control policy in any health facility.

Infection control policy

The purpose of the policy is to set minimum national standards for the effective prevention and management of health care associated infections, so that hazards associated with biological agents are minimized for patients, visitors and health care personnel in health care establishments (The National Infection Prevention and Control policy and strategy, 2007).

The policy's objectives are:

1. To encourage and improve effective prevention and management of health care associated infections for the public health care sector. In the two hospitals prevalence of *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* would not be at the level observed during the study if there was an effectively implemented infection control policy. In fact, it was interesting to hear during the feedback when an ICU specialist recommended that they do not need soap dispenser in their ward and it could be erected in other wards. This could also be understood as an indication of the absence of standardized guidelines as shown in Table 28.
2. To prevent and minimize environment hazards associated with microbes for all in and outpatients, health care workers and visitors to health care institutions;
3. To optimize infection prevention and control programmes and resources in health care settings. During the study, one of the data gathering instruments was adopted by infection control department in one of the hospitals. This was an indication that there was no activity related to infection control. In fact, this was further supported by why the nurses thought *Staphylococcus aureus* was the most prevalent microorganism instead of *E. coli* as shown in Table 12.
4. Controlling and minimization transmission of and colonization by resistant organisms were nonexistent at the two hospitals if the results from prescribing patterns for prophylaxis and treatment were anything to go by. For example, *E. coli* and *Klebsiella pneumoniae* from the laboratory results were found to be resistant to amoxicillin and ampicillin and yet they were prescribed for prophylaxis and for post-operative treatment as it is shown in Table 24 and Figure 10. This was irrational. It then resulted in some patients to be re-admitted as it is shown in Figure 7 and staying longer in the hospitals shown in Table 10. If they had been any effective surveillance, as part of the infection

control policy antimicrobial agents would have been prescribed rationally against *E. coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* (prevalence of 22%, 18%, and 13% respectively).

5. To improve infection control surveillance. If there had been surveillance of microorganism at the two hospitals, the prevalence of *Klebsiella pneumoniae* which was the second highest prevalent microorganisms would have been less.

Klebsiella pneumoniae just like *E. coli* can also be found inside the intestines. The infections are typically nosocomial. It is spread through direct person-to-person contact, such as when someone with contaminated hands touches a surgical site. This critical issue of hygiene has been highlighted before in the thesis. Taking antimicrobial agent over a long course of time can also increase a person's risk of getting a *Klebsiella* infection (Bennington-Castro, 2017). Taking antimicrobial agents should not be the case in a situation where there is an effective antimicrobial policy which among other things would give guidelines on poly pharmacy.

Antimicrobial policy

According World Health Organization (WHO) antimicrobial policy its primary aim is to minimize the morbidity and mortality due to antimicrobial-resistant infection; and to preserve the effectiveness of antimicrobial agents in the treatment and prevention of communicable diseases. From the results obtained preservation of effective antimicrobial agents to be used in SSI would be difficult at both Mankweng Hospital and 1 Military Hospital where health professional nurses and pharmacist in particular had different perception regarding antimicrobial pattern e.g. Table 16 and 17. Pharmacists generally had an impression that where there was an infection, the correct antimicrobial agent was prescribed as shown in Table 26, even though the doctors indeed admitted that laboratory culture and sensitivity test results were less often used to prescribe antimicrobial agent as shown in Table 28. The WHO further states that antimicrobial policy is essential for prophylaxis, empirical and definitive therapy. Antimicrobial policy is based on several factors. These include spectrum of antimicrobial agent activity, pharmacokinetics/ pharmacodynamics of these medicines, adverse effects, costs, special needs of individual patient groups, and potential to select resistance (WHO, 2011). In addition, if there are surgical guidelines for prophylaxis as reviewed in section 2.1.2 supported by antimicrobial policy, cefazolin would have been prescribed extensively.

From the results obtained in particular when *Klebsiella pneumoniae* was treated as indicated in Table 24 it was quite clear that at the two hospitals there were no antimicrobial policies. It appeared from the results that broad-spectrum antibacterial agents were commonly prescribed as indicated in Table 15 and Figure 9 e.g. amoxicillin, augumentin, meropenem etc. Meropenem is reserved for ICU patients in some hospitals settings. In addition, if there was antimicrobial policy, given that the most prevalent microorganism was *E. coli* and *Klebsiella pneumoniae*, there was no justification for extensive at 78% use of metronidazole as seen in Table15 and Figure 9. Furthermore, if there has been antimicrobial policy at each hospital, ampicillin and amoxicillin which encourage production of Beta-lactamases by the bacteria, carbapenems and cephalosporins which encourage production of Carbapenemases by the bacteria thereby reducing susceptibility of bacteria to all these agents, would not have been allowed. This kind of prescribing patterns demonstrated how the prescribers were not aware of MCR-1 gene transfer in *E. coli* and *K. pneumoniae*.

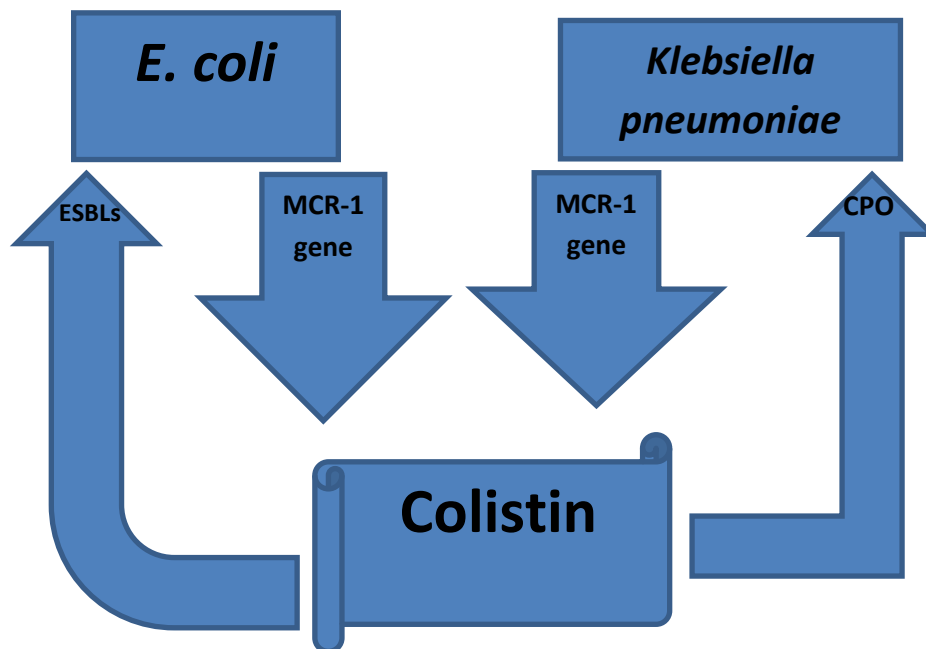


Figure 11: The relationship between *E. coli* and *Klebsiella pneumoniae*

These two microorganisms *E. coli* and *Klebsiella pneumoniae* are the once responsible for Carbapenems Resistant Enterobacteriaceae (CRE) or Carbapenems Producing Organisms (CPO) and Extended Spectrum B-lactamase (ESBLs). Extended spectrum beta-lactamases are

defined as enzymes produced by certain bacteria that are able to hydrolyze extended spectrum cephalosporin. Literature shows that there is a rise of extended spectrum beta-lactamase (ESBL)-producing bacteria and subsequently Carbapenemase-resistant strains, leaving colistin as the sole antimicrobial agent in the armamentarium for *E. coli*, *K. pneumoniae*, and *S aureus* SSI. This is an antimicrobial agent that was discovered in the 1960s, unfortunately with a high toxicity profile. In addition to toxic effects, colistin due to an emerging resistance, renders some patients untreatable and is still a drug which is unregistered in South Africa, but appeared to be readily available in some hospitals. In South Africa, the recent identification and subsequent spread of New Delhi Metallo-beta-lactamase-1 (NDM-1) (Brink et al., 2012) and *Klebsiella pneumoniae* Carbapenemase (KPCs)-Producing Enterobacteriaceae has been reported to signify the latest 'super-bugs' to threaten public health (FIDSSA, 2017). These explain the rising of NDM-1 infections that were reported in literature (Keeton, 2016). The non-response of the most common isolates identified to colistin is explained diagrammatically in Figure 11. The discussion above of infection control policy, antimicrobial policy, and the results obtained serve to illustrate the importance of clinical governance of antimicrobial prescribing i.e. antimicrobial stewardship.

Antimicrobial stewardship

Antimicrobial stewardship as indicated in the literature implies not only appropriate clinical decision-making for individual patients, but a perspective that:

- Maximizes the overall benefits;
- Minimizes adverse events related to antimicrobial therapy, and most importantly;
- Delays the onset of widespread microbial resistance to commonly prescribed antimicrobial.

Its goals are:

- To stabilize or decrease in the number of resistant organisms encountered over time;
- A reduction in organism resistance rates/ emergence of new resistant organisms (Brink et al., 2006).

Even though some aspects of clinical governance have been touched upon earlier, it is however important to go into a little bit more detail regarding personal hygiene hand washing in particular

as an important factor in clinical governance. This was an important factor identified during the study as responsible for SSI as illustrated in Table 28.

Hand washing

One of the contributing factors of infection was poor hand washing in both hospitals at 31% in Mankweng Hospital and 25% in 1 Military Hospital. This is surprising as this is supposed to be practice all the time when dealing with infections. It appeared that it's a norm in public hospitals as reported by Keeton (2016) in a newspaper article that poor hand washing was the contributing factor. This led to the patient spreading the CRE and ultimately the patient died because both the nurse and the doctor did not wash their hands. Hand hygiene rates of 10-40% have been observed in even the best of the units in the developed countries. Acceptability of such compliance rates and justifications of intense antimicrobial usage under the umbrella of "empirical therapy" has underscored the importance of increasing hand hygiene compliance. In recent years, the WHO has accepted of hand hygiene as a global challenge. There are now monitoring tools available to assist in hand hygiene compliance which lead to decline in "empirical antimicrobial therapy" responsible for emergence of superbugs (WHO, 2011). Most of the precautionary measures to prevent cross-infection recommend washing hands frequently more especially when dealing with infections. Maintenance of aseptic technique indirectly applies to the importance of inter-hospital transfers

From the results obtained at 1 Military Hospital one can conclude that some of the infections from gynecology ward could be due to the fact that there was poor screening.

Screening of patients for inter-hospital transfer

Screening patients should be considered for routine admission when transferring patients from one hospital to another. Patients who have specific risk factors should be screened under the following situations which include:

- Patients with unhealed wounds or broken skin;
- Elevated risk patients' groups- ICU high dependency;
- Selective pre-operative patients e.g. joint replacement etc.;
- History of MRSA infection;
- Frequent hospital admission with the last 12 months;

- Transfer from another acute care facility particularly one known to have a high MRSA prevalence e.g. tertiary hospitals; and
- Patients with indwelling medical devices; and patients with a high prevalence of community strains e.g. indigenous population.

This screening is very important aspect in preventing infections particularly where hospitals outsource. Outsourcing other procedures due to lack of resources from one hospital to another hospital is a problem when dealing with infections if screening of patients is not adhered to because microorganisms differ from environment to environment. During the feedback of results at 1 Military Hospital it was found that, due to lack of resources the hospital was outsourcing for procedure like caesarean section, total abdominal hysterectomy etc. as indicated in Table 32. It can be argued that the public hospitals involved in outsourcing by 1 Military Hospital had higher SSI prevalence. One could have expected screening of patients before or after inter-hospital transfer. As discussed earlier regarding the development of superbugs, it would have been important for 1 Military Hospital to have clearly stated procedures that are followed regarding screening of patients for inter-hospital transfers. In general screening of patients for inter and intra hospital transfer is important for the surveillance for nosocomial infections such as SSI; for rational use antimicrobial agents; reduction of the emergent of resistant pathogens; and unacceptable pharmaco-economic consequences. These pharmaco-economic consequences include:

1. Unnecessary hospital stay as shown in Table 9 which show that it was 300\$ for SSI patient per day. The amount excludes treatment cost.
2. An increase in irrational use of antimicrobial agents. As indicated in Table 21 for example where *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were isolated and found to be resistant to meropenem yet meropenem was given to the patient for 8 days. Table 21 illustrated total cost incurred through irrational use of antimicrobial agents in three wards studied.

CHAPTER SIX: CONCLUSION AND RECOMMENDATION

6.1 Conclusion

From the results obtained the indications were that there was antibiotic therapeutic anarchy and lack of detailed knowledge of pharmacokinetic-pharmacodynamics of antimicrobial agents and microbiological factors. Lack of utilization of laboratory test results appeared to contribute to irrational use of antimicrobial agents leading antimicrobial resistance. The laboratory plays a critical role in surveillance and identifying the most common isolates and therefore results from the laboratory should always be taken into consideration when prescribing antimicrobial agents. This will assist in avoiding prescription of antimicrobial agents to which common isolates are resistant to. Although the rate of antimicrobial resistance increases in both military and government healthcare facilities, reviews indicated that there are no action plans taken about antimicrobial resistance and this had a negative cost implications. From the results obtained it appeared that different surgical guidelines were in use. Therefore, surgical guidelines must be used to avoid different prescribing patterns of antibiotics in the ward.

In order to optimize the pharmacokinetics (PK) and pharmacodynamics (PD) of antimicrobial agents, good basic knowledge by both pharmacist and prescribers about PK/PD in different patient population is necessary. This requires pharmacist with these knowledge to form part of the ward round team. From the mere fact that one of the data gathering instrument was found to be useful at Mankweng Hospital it can be concluded that prior to the study, there had not been effective implementation of the infection control. While at 1 Military Hospital the reaction from ICU specialist could also be an indication that there was no effective implementation of infection control. There is need for effective infection control and antibiotic policies at the two hospitals before anyone can encourage antimicrobial stewardship. It takes a team to eradicate antimicrobial resistant e.g. doctors, pharmacists, nurses, and microbiologists to join hands working together.

6.2 Recommendations

1. In every hospital setting, the situation should be conducive for surveillance to identify the areas of concerns and to improve were necessary. This appeared not be the case at the

two hospitals. The study carried out in the three wards should also be done as many hospitals as possible.

2. Surveillance in general, is fundamental as indicated earlier in identifying common isolates. It is an important strategy for antimicrobial resistant (AMR) containment, providing the data required to locate an AMR problem. This requires accurate and consistent data capturing for example SSIs which surely can be done electronically instead of manually.
3. A future study should be carried out at the hospitals including all wards to determine the extent of the problem in order to come up with a more comprehensive antimicrobial stewardship programme. Antimicrobial stewardship includes antimicrobial policy-this takes care of rational prescribing; infection control which will take care of general hygiene e.g. hand washing.

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APPENDICES

Appendix A: Demographics and culture and sensitivity tests results

	Patient A						
Ward	Surgical ward <input type="checkbox"/>		Orthopedic ward <input type="checkbox"/>		Gynecology ward <input type="checkbox"/>		
Type of operation performed							
Population parameters	Age	18-30	31-40	41-50	51-60	60+	
	Gender	Male <input type="checkbox"/>	Female <input type="checkbox"/>				
Antibiotics given post operation?	1.						
	2.						
	3.						
	4.						
	5.						
	6.						
Wound swabs/blood samples send to the laboratory?	Yes <input type="checkbox"/>	No <input type="checkbox"/>					
Microorganisms found?	1.						
	2.						
	3.						
	4.						
	5.						
Microorganism resistant to which antimicrobial?	1.						
	2.						
	3.						
	4.						
	5.						
	6.						

Appendix B: Patient's clinical therapy in the hospitals

1. Date of admission:
2. Date of discharge.....
3. Surgical site infection (SSI):
 - i. Preoperative diagnosis:
 - ii. Site of infection:
 - iii. Duration from admission to operation.....(hours/days)
 - iv. Antibiotic chemoprophylaxis given preoperative:
 - a)
 - b)
 - v. Antibiotics used postoperative:
 - vi. SSI detected on how many days postoperative:
4. Length of hospital stay before index culture:
5. Antibiotics used post-operatively before index culture taken
 - i. Type..... Duration..... days
 - ii. Type..... Duration.....days
 - iii. Type..... Duration.....days
6. Outcome:
 - (a) Improved and discharged..... days in hospital stay.
7. Antimicrobials discharged on:
 - I.
 - II.
 - III.

IV.

V.

8. Cost of the antibiotics use:

Appendix C: Tool for Pharmacists

Are the antimicrobials dispensed from surgical, orthopedic and gynecology ward rational to the diagnosis?	Yes <input type="checkbox"/>	No <input type="checkbox"/>	
For stores Pharmacists/ Ward services: what are the most ordered antimicrobials in surgical, orthopedic and gynecology ward?	1. 2. 3. 4. 5.		
For dispensing Pharmacist: from surgical, orthopedic and gynecology ward prescriptions, Is there poly pharmacy of more than one antimicrobial?	Yes <input type="checkbox"/>	No <input type="checkbox"/>	
If <u>Yes</u> in above question, was it justified or unjustified?	Justified <input type="checkbox"/>	unjustified <input type="checkbox"/>	
Elaborate on both answers		
Between the three departments/ wards, which one consumes more of the drug budgets on antimicrobials than others?	Surgical ward <input type="checkbox"/>	Orthopedic ward <input type="checkbox"/>	Gynecology ward <input type="checkbox"/>

Appendix D: Tool for Surgeons and Medical officers

1. Are there any surgical guidelines?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2. If <u>Yes</u> in question 1, is it South African guidelines or other country's guidelines?	South African guidelines. <input type="checkbox"/>	Other country's guidelines. Specify.....
3. If <u>NO</u> , how are surgical procedures performed?	
4. Were the laboratory tests results used to prescribe the antimicrobial?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
5. If <u>No</u> in question 4, what guided the prescriber to prescribe the antimicrobial?	1. 2. 3.	
6. Do patients who report for follow-ups and who develop surgical site infection get re-admitted?	Yes <input type="checkbox"/> Why?	No <input type="checkbox"/> Why?
7. In your opinion, what factors would contribute surgical site infection?	1. 2. 3. 4. 5. 6.	
Beside pressure points, how often do you result from the Lab used in prescribing antibiotics?	1. None <input type="checkbox"/> 2. Less often <input type="checkbox"/> 3. Often <input type="checkbox"/> 4. Very often <input type="checkbox"/>	


Appendix E: Tool for nurses

<p>What are the most commonly used antimicrobials for patients with surgical site infection in your ward?</p>	<p>1. 2. 3. 4.</p>	
<p>How are they administered?</p>	<p>Right time</p>	<p>Right dosage</p>
	<p>Right route</p>	<p>Right frequency</p>
<p>What are the most commonly causative microorganisms of surgical site infection?</p>	<p>1. 2. 3. 4. 5.</p>	
<p>In your opinion, what factors would contribute to surgical site infection?</p>	<p>1. 2. 3. 4.</p>	
<p>Do you think that the antibiotics are prescribed correctly for the diagnosis?</p>	<p>Yes <input type="checkbox"/></p>	<p>No <input type="checkbox"/></p>

Appendix F: Tool for laboratory personnel

Ward	Surgical	Orthopedic	Gynecology
What are the most prevalent microorganisms identified?	1. 2. 3. 4.	1. 2. 3. 4.	1. 2. 3. 4.
What are the most common sensitivity tests do you carry out (methods)?	1. 2. 3. 4.	1. 2. 3. 4.	1. 2. 3. 4.
Which antibiotics do you test for the microorganisms and which ones are resistant to?	1. 2. 3. 4.	1. 2. 3. 4.	1. 2. 3. 4.
What are the pressure points on turn-around time?	1. 2. 3. 4.		
What are the implications of the pressure points turn-around time?	1. 2. 3. 4.		
In your own opinion, how often are the results from the Lab used in prescribing antibiotics?	5. None <input type="checkbox"/> 6. Less often <input type="checkbox"/> 7. Often <input type="checkbox"/> 8. Very often <input type="checkbox"/>		

Appendix G: Clearance from the Sefako Makgato University



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

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

APPROVAL NOTICE - NEW APPLICATION

12 February 2015

Mr CC Mathobela
University of Limpopo
Department of Pharmacy

MEETING: 01/2015

SMUREC Ethics Reference Number: SMUREC/HS/02/2015: PG

Title: Prescribing patterns of antimicrobials for surgical site infection at 1 Military Hospital and Mankweng Hospital

Researcher: Mr CC Mathobela

Supervisor: Prof N Nyazema

Co-supervisor: Prof Y Dambisya

Department: Pharmacy

Degree: Masters in Pharmacy (Pharmacology)

The New Application received on 06 November 2014, feedback received on 12 February 2015 was reviewed by members of Sefako Makgato University Research Ethics Committee on 12 February 2015 and was approved on 12 February 2015.

Please note the following information about your approved research protocol:

Protocol Approval Period: 12 February 2015 – 12 February 2016

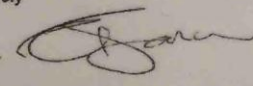
Please remember to use your protocol number (SMUREC/HS/02/2015: PG) on any documents or correspondence with the REC concerning your research protocol.

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


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

International Organisation (IORG0004319), Institutional Review Board (IRB00005122), Federal Wide Assurance (FWA00009419)
Expiry date: 11 October 2016 and NHREC No: REC 210408-003

Sincerely

PP. 

PROF GA OGUNBANJO
CHAIRPERSON SMUREC



SEFAKO MAKGATHO
HEALTH SCIENCES UNIVERSITY
SMU Research Ethics Committee
Chairperson

Date: 12/02/2015

Members of the Interim Council
Prof O Shisana (Chairperson), Ms SA Mchunu, Mr P Slack, Dr N Simelela, Prof AM Segone, Dr E van Staden

Appendix H: Clearance from 1 Military Hospital Research Ethics Committee

RESTRICTED

1MH/302/6/02.05.2015



sa military health service
Department:
Defence
REPUBLIC OF SOUTH AFRICA

Tel: 012 314 0013
Facsimile: 012 314 0623
Enquiries: Prof / Lt Col M.K. Baker

1 Military Hospital
Private Bag X1026
Thaba Tshwane
0143
17 July 2015

CLINICAL TRIAL APPROVAL: "PRESCRIBING PATTERNS OF ANTIMICROBIALS FOR SURGICAL SITE INFECTIONS AT 1 MILITARY HOSPITAL AND MANKWENG HOSPITAL."

1. The 1 Military Hospital Research Ethics Committee (1MHREC) registered in South Africa with the National Health Research Ethics Council (NHREC) (REC-111208-019-RA) adhering to GCP/ICH and SA Clinical Trial guidelines, evaluated the above-mentioned protocol and additional documents.
2. The following members approved the study:
 - a. Lt Col M.K. Baker: Neurologist, male, chairman 1 MHREC.
 - b. Lt Col C.S.J. Duvenage: Specialist physician, female, member 1 MHREC.
 - c. Lt Col D. Mahapa: Dermatologist, female, member 1 MHREC.
 - d. Lt Col A.D. Moselane: Urologist, male, member 1 MHREC.
 - e. Lt Col E.J. Venter: Periodontist, male, member 1 MHREC.
 - f. Lt Col S. Hassim: Doctor, male, member 1 MHREC.
 - g. Maj M.L. Kekana: Specialist physician, female, member 1 MHREC.
 - h. DR T.J. Marè: Advocate, independent of the organization, male, member 1 MHREC.
 - i. Mrs. C. Jackson: Layperson, independent of the organization, female, member 1 MHREC.
3. The following documents were evaluated:
 - a. Study proposal dated April 2015
 - b. Appendix A: Culture and sensitivity results
 - c. Appendix B: Patient's clinical demographics
 - d. Appendix C: Tool for pharmacists
 - e. Appendix D: Tool for Surgeons and Medical officers
 - f. Appendix E: Tool for nurses
 - g. Letter from statistician dated 09.01.2015
 - h. Curriculum Vitaes' Capt. CC Mathobela, Prof NZ Nyazema
 - i. Informed Consent
4. The recommendations are: The study was ethically approved on 22 July 2014. The principal investigator, Capt CC Mathobela, will be supervised by

Health Worriers Serving the Brave
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1MH/302/6/02.05.2015

Prof N.Z. Nyazema. Report backs are to be made to the 1MHREC six monthly, in the event of any serious adverse events and on completion or termination of the study. Should publications result from the study the relevant manuscripts will also need to be approved by Military Counter Intelligence.

5. The 1 MHREC wishes you success with the study.



(M.K BAKER)

**CHAIRMAN 1 MILITARY HOSPITAL RESEARCH ETHICS COMMITTEE:
LT COL / PROF**

DIST

For Action

Capt. CC Mathobela

Health Worriers Serving the Brave
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Appendix I: Clearance from Defence Intelligence

RESTRICTED



Defence Intelligence

Department:
Defence
REPUBLIC OF SOUTH AFRICA

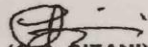
DI/DDS/R/202/3/7

Telephone: (012) 315-0216
Fax: (012) 326-3246
Enquiries: Brig Gen M. Sizani

Defence Intelligence
Private Bag X367
Pretoria
0001
19 August 2015

AUTHORITY TO CONDUCT RESEARCH IN THE DEPARTMENT OF DEFENCE (DOD): CAPT C.C. MATHOBELA

1. Request letter 1MH/302/6/02.05.2015 dd 17 July 2015 has reference.
2. Approval is hereby granted from a security perspective to Capt C.C. Mathobela to conduct research in the DOD on the topic entitled "**Prescribing Patterns of Antimicrobials for Surgical Site Infections at 1Military Hospital and Mankweng Hospital**" as a prerequisite for an attainment of a Masters Degree in Pharmacology with the University of Limpopo as requested.
3. On completion the final research product must be submitted to Defence Intelligence (DI), Sub-Division Counter Intelligence (SDCI) for security scrutiny before it is released to any entity outside the DOD.
4. For your attention.


(G.S. SIZANI)

**CHIEF DIRECTOR COUNTER INTELLIGENCE: MAJ GEN
KS/KS (Capt C.C. Mathobela)**

DSTR

For Action

OC 1Military Hospital

(Attention: Capt C.C. Mathobela)

Internal


File: DI/DDS/R/202/3/7



Lahloha le Baphesetho: Umphelelo wasekwenkweni. Kqomo ye Tshirafetso. ISebe lesiKhuselo. Department of Defence. Nqobiso we Tshirafetso. Umphelelo wezokuhlala. Nqobiso ye eza-Mandlalo. Lahloha le Tshirafetso. Department van Verdediging. UThixo le Baphesetho

RESTRICTED

Appendix J: Permission from Department of Health-Limpopo Province

**LIMPOPO**
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Latif Shamila Ref:4/2/2

Mathobela CC
Sefako Makgatho Health Sciences University
Ga-Rankuwa

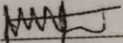
Greetings,

RE: Prescribing patterns of antimicrobials for surgical site infection at 1 Military Hospital and Mankweng Hospitals.

The above matter refers.

1. Permission to conduct the above mentioned study is hereby granted.
2. Kindly be informed that:-
 - Research must be loaded on the NHRD site (<http://nhrd.hst.org.za>) by the researcher.
 - Further arrangement should be made with the targeted institutions.
 - In the course of your study there should be no action that disrupts the services.
 - After completion of the study, a copy should be submitted to the Department to serve as a resource.
 - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
 - The above approval is valid for a 3 year period.
 - If the proposal has been amended, a new approval should be sought from the Department of Health.

Your cooperation will be highly appreciated.




P Head of Department

Date 10/03/2015

18 College Street, Polokwane, 0700, Private Bag x9302, POLOLKWANE, 0700
Tel: (015) 293 6000, Fax: (015) 293 6211/20 Website: <http://www.limpopo.gov.za>

The heartland of Southern Africa – development is about people

Appendix K: Permission from Mankweng Hospital

 **LIMPOPO**
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

MANKWENG HOSPITAL

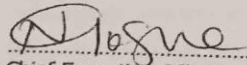
Ref: S5/3/1/2
Enq: Makola M.M
From: HR Utilization and Capacity Development
Date: 26 March 2015
To: Mathobela C.C
Sefako Makgatho Health Science University
Ga-Rankuwa

Department Of Health Mankweng Hospital Receive: <i>Makola</i> 2015 -03- 26 Circle No. 109 Tel: 015 239 1010 LIMPOPO PROVINCE

PERMISSION TO CONDUCT RESEARCH AT MANKWENG HOSPITAL: MATHOBELA C.C

1. The above matter has reference.
2. This is to confirm that Mathobela C.C has been granted permission to conduct research on " Prescribing patterns of antimicrobials for surgical site infection at 1 Military Hospital and Mankweng Hospital".
3. He will be conducting research as from Friday, 01 May 2015 to Friday, 30 October 2015 .
4. Attached please find his application letter, Ethics Committee approval (Sefako Makgatho Health Science University), approval letter from Provincial Office and Research proposal.

Thanking you in advance


.....
Chief Executive Officer

2015/3/26
Date