An Assessment of the need of Pharmaceutical Services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital

by

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Dissertation submitted in partial fulfilment of the requirements for the degree of

Master of Science (Medical) in Pharmacy

of the

University of Limpopo, South Africa

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June 2012
DECLARATION

I, Elmien Bronkhorst, hereby declare that the work on which this dissertation is based is original (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for any other degree at this or any other university.

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DEDICATION

This work is dedicated to my husband Pieter Bronkhorst, children Lohan and Elnieke and sister Lizette Smit who encouraged me through difficult periods and always believed in me when I could not see the way forward.
ACKNOWLEDGEMENTS

I would like to extend my sincere thanks to the following people without whom this work would not have been possible:

- **Dr Natalie Schellack**, my supervisor, for her positivity and inspiration. Her input in this work was invaluable.
- **Prof Andries Gous** for his clinical knowledge and experience.
- **Prof Jan Pretorius** for the opportunity to do this research in his department.
- **Patients** and their families who participated in the study.
- **Doctors and nurses** in the S-ICU of Steve Biko Hospital for receiving me into their unit with a positive attitude.
- **Lizette Smit** for her help with capturing the data and also assisting in editing and layout of the dissertation.
- **Lwando Kondlo** at the **Medical Research Council** for analyzing the data.
- **Friends and family** for their support.
- **Department of Pharmacy** for logistical support and assistance.
- **Department of Surgery** for logistical support and assistance.
DISSEMINATION OF FINDINGS

PODIUM PRESENTATION

NATIONAL CONFERENCE


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LIST OF ABBREVIATIONS

ACCP: American College of Clinical Pharmacy
APACHE: Acute Physiology and Chronic Health Evaluation
ASHP: American Society of Health-System Pharmacists
ATC: Anatomical Therapeutic Chemical classification system
CPAP: Continuous Positive Airway Pressure
CPIS: Clinical Pulmonary Infection Score
CRP: C-reactive Protein
DNA: Deoxyribonucleic acid
HCU: High Care Unit
ICU: Intensive Care Unit
MC&S: Microscopy culture and sensitivity
MIC: Minimum Inhibitory Concentration
MRSA: Methicillin-resistant *Staphylococcus aureus*
PC: Pharmaceutical Care
PPI: Proton pump Inhibitor
PSAP: Pharmaceutical Society of American Pharmacists
SASOCP: South African Society of Clinical Pharmacy
S-ICU: Surgical Intensive Care Unit
TDM: Therapeutic Drug Monitoring
VAP: Ventilator associated Pneumonia
WHO: World Health Organization
SUMMARY

The role of the pharmacist has evolved over the last two decades beyond the traditional functions of dispensing and stock control. The focus has shifted toward patient-oriented functions, in which the pharmacist assumes responsibility for the patient’s drug- and healthcare needs as well as the outcome of treatment.

The aim of this research was to assess the need for pharmaceutical care to the Surgical Intensive Care Unit of Steve Biko Hospital. The surgical and trauma ICU is a 12 bed unit to which the researcher rendered pharmaceutical care over an eight week period, from 14 February to 26 March 2011. Interventions to assess drug therapy and achieve definite outcomes to improve patients' quality of life were documented for 51 study patients according to the system developed by the American Society of Health-System Pharmacists (1992).

Of the 51 patients, 35 were male and 16 were female. The age of the patients ranged from 12 years to 86 years, with most patients admitted to the unit in the age groups 21 to 30 years, and 51 to 60 years. The patients’ estimated weights ranged from 40kg to 120kg with older patients, from age 41 upwards, weighing more. The average stay in the unit was 8.7 days, with the minimum stay for one patient being only one day, and the maximum stay for one patient was 26 days.

In the study, the HIV status of only 13 of the 51 patients was tested. Of the 13 patients, six were HIV positive, while seven tested negative. All the patients admitted to the unit were not tested for HIV, because they were not admitted to the unit for HIV-related causes, and test results would not have had an effect on their outcome.

Diagnoses encountered most frequently in the unit were trauma (21 patients), skeletal involvement or fractures (16 patients), infections or sepsis (15 patients) and gastro-intestinal bleeds (14 patients). In most cases more than one diagnosis applied to the same patient, since patients admitted with trauma also had skeletal or gastro-intestinal involvement.
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The medications prescribed most frequently were enoxaparin (49 patients), sucralfate (41 patients) and multivitamin syrup (47 patients); in accordance with the standard ward protocol for prophylactic regimens. The drug class most often used was the anti-infectives having 124 items prescribed during the study period. Of these, the broad spectrum antibiotics were used most frequently, e.g. piperacillin/tazobactam (22 patients), meropenem (11 patients) and imipenem (11 patients). An average of 12 medications was prescribed for each patient in the ward.

A total of 181 interventions were suggested for the 51 patients during the study period, of which 127 (70%) were accepted and implemented by the medical and nursing staff. The average number of interventions per patient ranged from 0 to 13 with a median of 3.5 interventions per patient. The four most frequent problem types were untreated medical conditions (15.5%), length or course of therapy inappropriate (13.8%), investigations indicated or outstanding (12.2%) and prescribed doses and dosing frequency appropriate (11%). Interventions were also made regularly to address system errors or non-compliance and factors hindering achievement of therapeutic effect.

The perceived need for pharmaceutical care by healthcare professionals in the S-ICU was measured by questionnaires before and after the study period. The feedback by staff regarding the pharmacist working in the ward was very positive. They appreciated the researchers input on ward rounds, as well as assistance with problems encountered with the pharmacy.

Of the total time spent in the ward, the researcher spent 28% of her time on patient evaluation. Ward rounds also took up a great deal of time (21.7%), since ward rounds were done with different members of the multidisciplinary team. Most interventions were suggested during ward rounds.

The costs saved during the study period were enough to justify the appointment of a pharmacist to the ward on a permanent basis, albeit for limited hours daily.

The researcher designed an antibiotic protocol for the unit. The protocol was designed according to international standards, and after discussion with the microbiologists, adapted for use in the specific unit.
In conclusion, the study results have demonstrated that a pharmacist’s contribution to patient care at ward level in a surgical ICU resulted in clinical outcomes that improved the patient’s quality of life. Drug-related problems were identified and addressed. Medical staff in the S-ICU accepted the pharmacist’s interventions and even welcomed her contribution to other ward functions, for instance managing medication and providing education.

Pharmaceutical care should be rendered on a permanent basis to the Surgical ICU and the pharmacist should increasingly become a key part of the multidisciplinary team, taking responsibility for patients’ medication needs.
1.1 The development of the pharmacist’s role

The pharmacy profession has experienced significant growth and development over the past 30 years. Pharmacy experienced three major periods of development namely the traditional, transitional and patient care stages (Hepler & Strand: 1990). Pharmacy entered the 20th century performing the social role of apothecary – preparing and selling medicinal drugs. Traditionally the pharmacist’s function was procuring, preparing and evaluating drug products. The main obligation was to ensure the drugs sold were pure, and to provide a good service to customers (Hepler & Strand: 1990).

The pharmaceutical industry took over the role of preparing drugs and the choice of therapeutic agents was passed on to the physician. The pharmacist’s role was constrained by being relegated to that of dispenser of pre-fabricated drugs (Hepler & Strand: 1990).

Clinical pharmacy practice was born in the mid 1960’s with a professional transition in which pharmacists sought self-actualization. The transitional stage saw pharmacists performing innovative and new functions to the profession. According to Hepler and Strand (1990), pharmacists should assume a professional responsibility for patient welfare in performing services like pharmacokinetic dosing, therapeutic monitoring and drug information.

Clinical pharmacy was defined in the 1960s in terms of functions. By the 1980s clinical pharmacy had evolved to mean the responsibility for patient care outcomes and had therefore been defined as the direct, responsible provision of medication-related care for achieving definite outcomes that improve a patient’s quality of life (American Society of Hospital Pharmacists: 1992).

Clinical pharmacy only started to emerge in the late 1980s in South-Africa (Summers: 1991).
1.2 Importance of the study

The study was conducted because a need for the provision of pharmaceutical services to the Surgical Intensive Care Unit of Steve Biko Academic hospital was identified by the head of the Surgical Department and the head of Critical Care, Prof Jan Pretorius. The study was done to measure the effect of having a pharmacist perform pharmaceutical care in the ICU setting. The results will provide insight to the specific services a clinical pharmacist can render in the ICU setting. The study will also give an indication of the time needed to perform these services in the ward.

1.3 Aim

The aim of the study was to determine the need for the provision of pharmaceutical care through the introduction of a ward-based clinical pharmacy service at the ICU and HCU of Steve Biko Academic Hospital.

1.4 Objectives of the study

The following objectives were formulated:

- To assist with the design and implementation of an antimicrobial ward protocol in the ICU and HCU
- To record and assess antimicrobial prescribing patterns in the ICU and HCU
- To describe and categorize the interventions performed by a pharmacist during the provision of pharmaceutical care
- To identify factors which limit the provision of pharmaceutical care and provide recommendations for future undertakings
- To assess the time spent on interventions performed by a pharmacist during the provision of pharmaceutical care
• To calculate the cost implication before and after pharmaceutical care interventions were made
• To determine if medical staff members in the ICU and HCU feel there is a need for a pharmacist to provide pharmaceutical services to the wards

1.5 Outline of the dissertation

In this study pharmaceutical care was rendered in order to document patient-centred interventions and to assess the need for a pharmacist working in a Surgical ICU. Pharmaceutical care includes the provision of effective, safe and cost effective drug therapy, as well as improving the patient’s quality of life. Several types of interventions were required, with the main focus being placed on antimicrobial therapy in the unit.

Chapter 2 contains a review of the literature. Section 2.1 entails a discussion of the evolving concept of pharmaceutical care, the benefits of pharmaceutical care and pharmaceutical care specifically in South-Africa.

Section 2.2 involves a discussion on antimicrobial therapy and includes discussions on antimicrobial resistance patterns, as well as how to manage antibiotic drug resistance and the cost of antibiotic treatment.

Section 2.3 gives an outline on general functions a pharmacist performs at ward level, and the responsibility assumed by the pharmacist regarding the patient’s pharmacological needs.

The methods used for the provision of pharmaceutical care to the patients admitted to the ICU are discussed in Chapter 3.

Chapter 4 is a detailed report covering various results and discussions of results from the study, including the interventions performed and the cost-saving facilitated by the researcher.
Chapter 5 describes the outcome and conclusion of the study under various sections, e.g. pharmaceutical care, time spent in the unit, cost saving and needs assessment of nursing and medical staff. It also includes a discussion on the limitations of the study as well as recommendations for future investigative studies regarding certain aspects of the study.
CHAPTER 2: LITERATURE REVIEW

This chapter deals with an overview of existing research that has been conducted in the various fields, needed to conduct this study. Section 2.1 discusses the concept of pharmaceutical care in general, and the role a pharmacist can play in the Intensive Care Ward setting. Section 2.2 is an overview on antimicrobial use, concentrating on resistance to antibiotics and the rational use thereof. Section 2.3 gives an outline on general functions a pharmacist performs at ward level.

2.1 Pharmaceutical Care

2.1.1 The evolving concept of pharmaceutical care

The profession of pharmacy has experienced significant growth and development over the past 30 years. Pharmacy experienced three major periods of development namely the traditional, transitional and patient care stages. Pharmacy entered the 20th century performing the social role of apothecary – preparing and selling medicinal drugs. Traditionally the pharmacist’s function was procuring, preparing and evaluating drug products. His main obligation was to ensure the drugs he sold were pure, and to provide a good service to customers (Hepler & Strand: 1990).

The pharmaceutical industry took over the role of preparing drugs and the choice of therapeutic agents was passed on to the physician. The pharmacist’s role was constrained by being relegated to that of dispenser of pre-fabricated drugs (Hepler & Strand:1990).

Clinical pharmacy practice was born in the mid 1960’s with a professional transition in which pharmacists sought self-actualization. The transitional stage saw pharmacists performing innovative and new functions to the profession. Pharmacists can choose to keep up from a clinical care perspective, or they can fall behind by not keeping up to date on new scientific knowledge (Vanderberg:2002). According to Hepler and Strand (1990), pharmacists should assume a professional responsibility for patient welfare in
In 1987, at the “Pharmacy in the 21st century” conference, Dr Douglas Hepler presented his paper, co-authored by Prof L Strand, titled “Opportunities and Responsibilities in Pharmaceutical Care”. At the Hilton Head conference it was derived that pharmacy as a whole is inherently a clinical profession. It was not sufficient just to sell pharmaceutical products to the public. It became essential that the pharmacy profession focus upon outcomes that result from serving the drug-related needs of society.

According to the Minnesota-model, the first step for pharmaceutical care was to identify what a patient's drug-related needs were. These seven categories of drug-therapy problems include:
CHAPTER 2: LITERATURE REVIEW

- Need new drug therapy
- Unnecessary drug therapy
- Wrong drug therapy
- Dosage too low
- Adverse drug reaction
- Dosage too high
- Compliance problem

(Munroe, Dalmady-Israel:1998)

On the basis of drug-therapy problems, the Minnesota-model developed a tool to carry out pharmaceutical care. Pharmaceutical care must contain seven elements:

- Review all active medication
- Link each medication to an appropriate indication
- Assess actual or potential drug therapy problems
- Take action to resolve and or prevent drug therapy problems
- Establish a care plan with the patient to achieve desired therapeutic goals of each medical condition, drug therapy problem and plan for follow-up evaluation.
- Follow up with the patient to evaluate actual patient outcomes and status of the patient’s medical conditions.
- Document above elements in a readily retrievable billable fashion.

(Simpson: 1997)

The medicines management cycle was described by Bates, Spell & Cullen in 1995 (see Figure 2.2). This cycle explains the role of the pharmacist in the multidisciplinary team treating the patient. The doctor examines the patient, transfers his findings or information, makes the decision to prescribe therapy, and enters the order in the form of a prescription. The pharmacist review the order, validates the correctness thereof, supplies the medication and also
supplies information to the patient and to nursing staff. Nurses play a role in distributing and administering medication to the patient. Thereafter the doctor will again monitor the response.

The Medicines Management Cycle

DOCTORS

Transfer information

Decision to prescribe

Order entry

Review order

Supply medicine

Pharmacy

Supply information

Distribute

Administer

Monitor response

Patient

Nurses

Figure 2.2: The Medicines Management Cycle

2.1.2 Definition of Pharmaceutical Care

The first definition of pharmaceutical care was given by the clinical pharmacists of the United States in 1975 as: “... the care that a patient requires and receives which assures safe and rational drug usage...” (Mikeal et al:1975).

Although there are many definitions of pharmaceutical care, the definition by Hepler and Strand (Hepler & Strand:1990), has been described as the original definition. The definition of pharmaceutical care has been redefined by Strand (1997) as she stated that the definition of pharmaceutical care is "a practice in
which the practitioner takes responsibility for a patient’s drug related needs and holds him or herself accountable for meeting these needs.”

Strand went on to explain why pharmaceutical care was needed. Pharmacy is a profession A profession could only be justified fully if it contributed solutions to different unique sets of problems. Drug-related morbidity and mortality fulfilled that description, and rational prescribing was needed through pharmaceutical care. Contrary to what one might believe, rational prescribing does not necessarily reduce drug usage of the individual patient. In practice it has been found that about 20% of patients need additional drug therapy. She explains that the challenge of the pharmaceutical care practitioner was to ensure there was an indication for every item of drug therapy.

The International Pharmaceutical Federation added a significant amendment, defining pharmaceutical care as: “…the direct provision of medication-related care for the purpose of achieving definite outcomes that improve a patient’s quality of life” (Wiedenmayer, Summers, Mackle, Gous & Everhard:2006).

The definition of pharmaceutical care by the South African Society of Clinical Pharmacy (SASOCP), 2011 was adopted from the definition by the American College of Clinical Pharmacy (ACCP: 1993), which emphasizes patient care as one of the principal elements of pharmaceutical care, it goes on to explain that patient care involves more than just the pharmacist, but also the multidisciplinary team members. According to the ACCP, and now the SASCOP, pharmaceutical care is medicine-related. This means that the care that is directly provided to the patient to ensure definite outcomes. These outcomes are intended to improve the patient’s quality of life, and this requires that the provider accepts personal responsibility for the outcomes.

2.1.3 The benefits of pharmaceutical care

According to Van Mil (2004) two types of research were done in the field of pharmaceutical care. The first is a needs assessment that investigates the kind
of care given to a patient that may lead to interventions. The second type of research assesses the impact of the provision of pharmaceutical care, to see whether it actually makes a positive difference to the patients’ clinical, humanistic and economic outcomes. He concluded that it is difficult to prove that, without a doubt, pharmaceutical care is beneficial.

Breland (2007) stated that the care given by pharmacists to patients has various benefits, and pharmacists indeed help patients make the best use of their medicines. He emphasized that it is important for pharmacists to renew their commitment to patient-focused pharmaceutical care.

Interaction between the pharmacist and the patient is essential in assuring a relationship based on caring, trust, communication and mutual decision-making. These are all principles for providing effective pharmaceutical care (American Pharmacists Association: 2007).

The practice of pharmaceutical care has multiple benefits and various areas derive benefits from pharmacists providing this care (Begley: 2006). This includes, but is not limited to:

- The patient
- The health care team
- The facility/practice situation
- Pharmacists and pharmacy as a profession
- The healthcare system

### 2.1.4 Pharmaceutical Care in South Africa

The process of pharmacists monitoring medication on ward rounds has already been explored by Summers (1991). She noted that for pharmacists to evaluate drug therapy it is essential that they see the full patient picture and communicate effectively with other members of the health care team. To perform optimal
pharmaceutical care and build good communication with other members of the health-care team, hospital pharmacists must move out into the wards where drugs are administered and doctors’ rounds are done. Low staff levels and a lack of training in this area resulted in low pharmacist presence in a clinical capacity. In particular, a lack of the following functions was identified in South-Africa at that time:

- Therapeutic drug monitoring
- Adverse drug reaction monitoring
- In-service training for the nursing and medical staff
- Providing drug information
- Monitoring drug usage

In 2001 the Department of Health adopted and developed a Quality of care policy. This states that quality is the result of identifying discernible problems.

As part of its mission the South African Pharmacy Council (SAPC) stated that pharmacists, with their unique knowledge of medication have a responsibility towards the utilization of scientific knowledge in the proper use of medicines and the protection of the public against dangers that are inherent in the use of medicines. (SAPC: 2004)

Although the role of the pharmacist in South-Africa has evolved over the last decade, pharmacists need to be encouraged to take up their professional role as part of the healthcare team and fulfil their role as provider of patient care in South Africa.

2.2 Antimicrobials

2.2.1 Introduction

Antimicrobials are chemical agents that kill or inhibit the growth of microorganisms. The first antibiotic, namely penicillin, was discovered by accident by Alexander Fleming in 1929. In modern medicine, antimicrobials provide the most dramatic examples of the advances of modern medicine and are among the most commonly prescribed medications in the world. They are used to treat infectious
diseases and for prophylaxis of infection. Approximately 30% of hospital admissions in the United States can be blamed on infectious diseases and it is estimated that one in ten hospitalized patients will acquire an infection after admission. Increased infection rates have resulted in escalating morbidity and mortality, leading to substantial economic cost. These costs are primarily associated with extended lengths of stay that often include additional diagnostic and therapeutic interventions (Martin & Estrada: 2010).

2.2.2 Mechanism of action of antimicrobials

Antibiotics target specific sites that are unique to bacteria or fungi and its mechanism of action differs for different classes of antibiotics (Chambers & Deck: 2009).

- **Target the synthesis of the bacterial cell wall**

  The cell wall is a rigid outer layer that surrounds the cytoplasmic membrane of bacterial cells. It maintains the shape of the cell and prevents cell lysis. β-lactam antibiotics, e.g. penicillins and cephalosporins contain a four-member beta-lactam ring, which targets the bacterial enzymes that are responsible for the meshwork that keeps the cell wall intact. Penicillin binding proteins catalyze the transpeptidase reaction that removes the terminal alanine to form a crosslink with a nearby peptide, which gives cell walls its structural rigidity. They are active against bacteria that are actively synthesizing the cell wall. When the cell wall is disrupted they cause lysis and cell death. Penicillins and cephalosporins are bactericidal only if cells are actively growing and synthesizing cell wall.

  Other antibiotics that target the cell wall are the glycopeptides (vancomycin and teicoplanin). Other than the beta-lactams, they do not target the enzymes, but inhibit cell wall synthesis by binding to the D-Ala-D-Ala terminus of nascent peptidoglycan pentapeptide. This inhibits transglycosylase, preventing further
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elongation of peptidoglycan and cross-linking. Although beta-lactams and vancomycin act at the same site, they can be used together because of their slightly different mechanisms of action (Chambers & Deck: 2009).

- **Target protein synthesis**
  Prokaryotic (bacterial) cells have ribonucleic acid (RNA) and ribosomes different from those of eukaryotic (human) cells. These cells can be targeted by antibiotics without being harmful to humans. Classes of drugs that inhibit protein synthesis include chloramphenicol that inhibits the peptidyltransferase step of protein synthesis; the macrolides (e.g. erythromycin and azithromycin), that inhibit protein synthesis because aminoacyl translocation reactions and the formation of initiation complexes are blocked; Tetracycline, aminoglycosides, streptogramins and oxazolidinones inhibit protein synthesis by preventing formation of the ribosome complex that initiates protein synthesis. (Chambers & Deck: 2009).

- **Inhibit deoxyribonucleic acid (DNA) replication and repair**
  Fluoroquinolones inhibit DNA topoisomerase II (also known as DNA gyrase). Inhibition of DNA gyrase prevents the relaxation of positively supercoiled DNA that is required for normal transcription and replication. Inhibition of topoisomerase IV interferes with separation of replicated chromosomal DNA into the respective daughter cells during cell division. (Chambers & Deck: 2009).

- **Inhibit folic acid synthesis**
  Susceptible microorganisms require extracellular PABA in order to form dihydrofolic acid, an essential step in the production of purines and the synthesis of nucleic acids. Sulfonamides are structural analogs of PABA that competitively inhibit dihydropteroate synthase by reversibly blocking folic acid synthesis. (Chambers & Deck: 2009).
2.2.3 Antimicrobial resistance, consequences and management of resistance

Drug resistance happens when the maximum level of antibiotic that can be tolerated by the host (human) does not inhibit the growth of microorganisms (Mycek, Harvey & Champe: 1997). Microorganisms have the ability to adapt to their environment and thus overcome the effects of antibiotics (Chambers & Deck: 2009).

Microorganisms have several mechanisms to regain resistance to antimicrobial organisms.

- **Reducing the intracellular concentration of the antibiotic**
  Bacterial cells can achieve this in several ways. They can reduce the permeability of their outer cell membrane, therefore reducing the amount of antibiotic that enters the bacteria. An example is the lack of a porin (a hollow membrane) on the membrane of *Pseudomonas aeruginosa*, making it resistant to imipenem. They can reduce the uptake of the antibiotic across the cytoplasmic membrane, e.g. *Staphylococcus aureus* that is resistant to aminoglycoside antibiotics. Gram negative organisms also may produce an efflux pump, which consists of cytoplasmic and periplasmic protein components, the efficiently transport some beta-lactam antibiotics from the periplasm back across the outer membrane. (Chambers & Deck:2009).

- **Inactivation of antibiotic by the bacteria**
  Bacteria can inactivate antibiotics by producing inactivation enzymes. These enzymes hydrolyse the beta-lactam ring that is present in penicillins, cephalosporins, monobactams and carbapenems. An example is the production of beta-lactamases by gram-negative organisms like beta-lactamases of *Pseudomonas aeruginosa* or carbapenemases of *Klebsiella pneumoniae*. Gram positive organisms like *Staphylococcus aureus* are relatively narrow in substrate specificity and will hydrolyze penicillins but not cephalosporins. More than 300 beta-lactamases have been identified.
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Other enzymes modify the structure of the antibiotic, e.g. aminoglycosides are modified by some enzymes produced by both gram-negative and gram-positive antibiotics, rendering them incapable of interrupting protein synthesis. (Chambers & Deck:2009).

- The antibiotic target site can be modified by mutation
  The mutation of bacterial cells reduces the affinity of the antibiotic for the target site. An example is the alteration of the penicillin binding proteins (PBP’s) that makes Streptococcus pneumoniae, Neisseria meningitidis and Enterococcus faecium resistant to penicillins. Resistance to fluoroquinolone therapy is due to one or more point mutations in the quinolone binding region of the target enzyme or to a change in the permeability of the organism. (Chambers & Deck:2009).

- Bacteria can eliminate their target site.
  Bacteria that eliminate their target site develop new metabolic pathways that bypass the original target. Absence of the proper channel or down-regulation of its production can prevent or greatly reduce drug entry into the cell. Strains of enterococci have used this method to gain resistance to vancomycin, by modification of the D-Ala-D-Ala terminus of nascent peptidoglycan pentapeptide (Chambers & Deck:2009).

Genetic mutations can also be transferred from one organism to another. Resistance can thus be transferred from one organism to another. Organisms mutate in order to enable themselves to better withstand hostile environments. In the case of antibiotics, they mutate in order to protect themselves from the effects of antibiotics. Plasmids or transposons (extra chromosomal genetic material) will transfer the gene mutations from one cell to another. They move from cell to cell by different processes. They can move by conjugation, where genetic material is transferred between bacteria in direct contact with one another. They can also do it by transduction, where viruses transfer small
amounts of bacterial DNA from one bacterium to another. The last way is by transformation where the bacteria incorporate a naked DNA from the environment that codes for resistance into its genome.

The causes of antimicrobial resistance are multifactorial. Ultimately, exposure of bacteria to antimicrobial agents that previously were active against the organism, leads to resistance.

In the ICU, antibiotic resistance among a few organisms produced widespread effects in almost all patients. The so-called ESKAPE organisms (Enterococcus spp., Staphylococcus aureus, Klebsiella spp., Acinetobacterspp., Pseudomonas aeruginosa, Enterobacterspp.) account for most of the hospital acquired infections in ICU. Rapidly increasing infection rates from vancomycin-resistant enterococci (VRE), methicillin-resistant S. aureus, fluoroquinolone-resistant P. aeruginosa and third-generation cephalosporin-resistant K. pneumonia and Enterobacter spp. have been reported.

There is a positive link between the use of antibiotics and resistance. According to an article released by Homer, Ritchie-Dunham, Rabbino, Puente, Jorgensen & Hendricks (no date), various investigators have demonstrated the association between antibiotic use and resistance. The association is still under discussion, but experts agree that the high and unnecessary use of antimicrobials causes the problem (Homer, et al: no date).

2.2.4 Examples of common and important resistant organisms

2.2.4.1 Methicillin-resistant Staphylococcus aureus

First reported in 1961 and became a major hospital and community pathogen in the 1990s. It is one of the organisms most resistant to antibiotics.

Risk factors for the development of MRSA:

- Old age
- Exposure to carriers of MRSA
- Hospitalization, especially to ICU
CHAPTER 2: LITERATURE REVIEW

- Invasive procedures
- Long hospital stays
- Previous prolonged antibiotic use
- Persistent wounds
- Intravenous lines or catheters

(Dickinson, 2000)

2.2.4.2 ESKAPE resistance

*Enterococcus*
Resistance among enterococci to commonly used therapeutic agents has become commonplace in the ICU. Most *E. faecium* strains are multidrug resistant with high-level resistance to penicillin and ampicillin, and to gentamicin. Resistance in *E. faecium* usually results from changes in penicillin-binding proteins. In a nationwide surveillance study in the US between 1995 and 2002, enterococci were the third most common cause of nosocomial bloodstream infection, and high-level vancomycin resistance was present in 60% of *E. faecium* strains (Martin & Estrada:2010).

*Staphylococcus aureus*
Methicillin-resistance in *S. aureus* traditionally observed only in the hospital environment has spread to the community setting in the past decade. Community acquired MRSA is genetically distinct from hospital-acquired MRSA strains; it produces a cytotoxin that is uncommon in hospital acquired strains (Martin & Estrada:2010).

*Klebsiella* spp.
B-lactamase-mediated resistance was the driver of resistance rising almost 10-fold among *K. pneumonia*. Carbapenemase-mediated resistance is also becoming more prominent, especially *K. Pneumoniae* carbapenemase (KPC)
enzymes. The KPC enzymes hydrolyze all β-lactam antibiotics including penicillins, cephalosporins and aztreonam (Martin & Estrada:2010).

**Acinetobacter** spp.
In the United States, *Acinetobacter* spp. is a common cause of nosocomial infections. *Acinetobacter* infections are increasing worldwide, since the involvement of the USA military in operations in Iraq and Afghanistan, numerous injured soldiers and civilians have been infected or colonized with *Acinetobacter*.
Risk factors associated with poor outcomes after *Acinetobacter* infections include elevated APACHE II scores, underlying chronic disease, mechanical ventilation, multiple trauma and previous antimicrobial exposure. Because the resistance patterns shown by *Acinetobacter* spp. are changing, antibiotic selection is challenging (Martin & Estrada:2010).

**Pseudomonas aeruginosa**
The proportion of multidrug-resistant *P. aeruginosa* rose 3-fold between 1993 and 2002. Fluoroquinolone resistance mechanisms in *P. aeruginosa* include over expression of non-substrate-specific efflux pumps and mutations of the topoisomerase target site. Patients infected with fluoroquinolone-resistant strains of *P. aeruginosa* had longer illness and higher mortality rates compared with patients infected with susceptible strains (Martin & Estrada:2010).

**Enterobacter** spp
*Enterobacter* spp. are intrinsically resistant to aminopenicillins, cefazolin and cefoxitin because of the production of constitutive chromosomal AmpC β-lactamases, which hydrolyze cephalosporins. Exposure of *Enterobacter* organisms to third-generation cephalosporins may select for mutant strains associated with the hyper production of AmpC- β-actamase (Martin & Estrada:2010).
2.2.5 Antimicrobial use

Antibiotics and vaccines are undoubtedly among the most significant discoveries in human history. Their use has saved countless lives from once-lethal infections. Unfortunately, antibiotics are also the only drugs in which widespread use decreases their utility. Possibly more unsettling than the increase in antibiotic resistance, is the decrease in antibiotic research and development. As of 2009, no new classes of antibiotics were in late-stage development, and only 16 antibiotics are in late stage development at all (McCoy, Toussant & Gallagher:2011).

Twenty five million pounds of antibiotics are produced each year for human consumption and are administered to 30-50% of hospitalized patients; non-hospitalized patients receive 160 million courses of antibiotics. All the while, studies and surveys suggest that as much as 50% of all antimicrobial use is inappropriate (Owens, Fraser& Stogsdill:2004a).

2.2.6 The role of the pharmacist in antibiotic stewardship

The term antimicrobial stewardship is defined as the optimal selection, dosage and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance (as stated by the Interagency Task Force for Antimicrobial Resistance) (Owens, Gilles & Stogsdill:2004b).

An increasing percentage of institutionally acquired infections are attributed to antimicrobial-resistant organisms. Recommendations for preventing and reducing antimicrobial resistance in hospitals stress the importance of improving antimicrobial use, referred to as antimicrobial stewardship.

The use of the term antimicrobial stewardship programme implies a multidisciplinary, programmatic, prospective, interventional approach to optimizing the use of antimicrobial agents. The pharmacist can play a role in concurrent review with feedback to the prescriber (Weller & Jamieson:2004).
An overall reduction in the use of antimicrobial agents will affect resistance patterns. Pharmacists can play a role by educating providers and the public, implementing guidelines and providing audit and feedback activities (Hobdy-Henderson:1999).

2.2.7 Cost of antibiotic treatment

In a study by Kopp, et al. (2007) the potential cost avoidance through interventions done during patient care rounds and chart reviews was measured and found to be most likely to achieve an impact on cost avoidance. Their conclusion was that both patient care rounds and chart-review activities were associated with potential cost avoidance.

While pharmacist interventions in the ward are aimed at improving the quality of life of patients, the cost-saving involved in streamlining therapy and discontinuing unnecessary medication, modifying the route of administration or reducing the length of use of antimicrobial therapy was significant. It was difficult however, to measure the impact of interventions on length of hospital stay, in-hospital mortality or re-admissions (McMullin, Hennenfent, Ritchie, Huey, Lonergan, Schaiff, Tonn & Bailey:1999).

2.2.8 Rational antimicrobial drug use

Central to the argument for promoting good antimicrobial stewardship is the growing concern about antimicrobial resistance and patient safety. The availability of antibiotics has facilitated increasingly complex care and, not surprisingly, microbial resistance to antibiotics has been identified as one of the greatest threats to human health. A return to the "pre-antibiotic" era would render many routine infections untreatable and would seriously affect current practice in surgery, intensive care and other services through major increases in morbidity and mortality. “New antibiotic development is lacking. The time to act is now, before we lose antibiotics for good”. (Gottlieb & Nimmo:2011)
2.2.9 Managing antibiotic drug resistance

Antibiotic resistance appears to be an inevitable problem. An increasing percentage of infections are attributed to antimicrobial resistant organisms. Antibiotics are administered to 30-50% of hospitalized patients; non-hospitalized patients receive 160 million courses of antibiotics per annum. All the while, studies and surveys suggest that as much as 50% of all antimicrobial use is inappropriate (Centers for Disease Control and Prevention: 1992).

The keynote address at the Antimicrobial Resistance Summit 2011 was given by Professor Otto Cars, and he made an urgent call to action as antibiotic resistance is an emerging threat to public health. He highlighted that the key factor contributing to the alarming resistance trend in bacteria is the indiscriminate use of antibiotics (Gottlieb & Nimmo: 2011).

2.2.9.1 Antibiotic guidelines and protocols

Antibiotic guidelines and protocols have been shown to limit unnecessary antibiotic use and therefore improve antibiotic susceptibility patterns (Raymond, Pelletier, Sawyer: 2002). Antibiotic practice guidelines or protocols have emerged as potentially effective means of both avoiding unnecessary antibiotic administration and increasing the effectiveness of prescribed antibiotics. Their use has also been associated with stable antibiotic susceptibility patterns for both Gram-positive and Gram-negative bacteria, possibly as a result of promoting antimicrobial heterogeneity and specific endpoints for antibiotic discontinuation (Kollef: 2005).

One way in which these guidelines limit the unnecessary use of antimicrobial agents is by recommending that therapy be modified when initial empiric broad-spectrum antibiotics are prescribed and the culture results reveal that more narrow-spectrum antibiotics can be employed.
2.2.9.2 Hospital formulary restrictions

Restricted use of specific antibiotics or antibiotic classes from the hospital formulary has been employed as a strategy to reduce the occurrence of antibiotic resistance and antimicrobial costs. Such an approach has been shown to achieve reductions in pharmacy expenses and in adverse drug reactions from the restricted drugs. To date it has been difficult to demonstrate that restricted hospital formularies are effective in curbing the overall emergence of antibiotic resistance among bacterial species. This may be due in large part to methodological problems. Their use has however been successful in specific outbreaks of infection with antibiotic-resistant bacteria (Kollef:2005).

2.2.9.3 Use of narrow spectrum antibiotics

Several investigations suggest that infections such as community acquired pneumonia can usually be successfully treated with narrow-spectrum antibiotic agents, especially if the infection is not life-threatening. Similarly, the avoidance of broad-spectrum antibiotics and the reintroduction of narrow-spectrum agents along with infection control practices have been successful in reducing the occurrence of Clostridium difficile infections. Initial empiric treatment with broad-spectrum agents is however usually necessary to treat ICU patients until culture results become available (Kollef:2005).

2.2.9.4 Combination antibiotic therapy

No convincing data exists to validate the hypothesis of combination therapy for nosocomial infections. The use of monotherapy with beta-lactam antibiotics for the definitive treatment of neutropenic fever and severe sepsis is recommended. However, empiric combination therapy directed against high-risk pathogens such as P. aeruginosa should be encouraged until the results of antimicrobial susceptibility become available. Such an approach to empiric treatment can
increase the likelihood of providing appropriate initial antimicrobial therapy with improved outcomes (Kollef: 2005).

2.2.9.5 Antibiotic heterogeneity

Antibiotic heterogeneity is also known as antibiotic rotation. The concept has been suggested as a potential strategy for reducing the emergence of antimicrobial resistance. In theory, a class of antibiotics or a specific antibiotic drug is withdrawn from use for a defined period of time and reintroduced at a later point in time in an attempt to limit bacterial resistance to the cycled antimicrobial agents. This offers the potential for antibiotic classes to be used that possess greater overall activity against the predominant ICU pathogens, resulting in more effective treatment of nosocomial infections. Antibiotic cycling is one method of achieving antimicrobial heterogeneity. Other methods include mixing of antibiotic classes, scheduled changes of antibiotic classes and the rotation of antibiotics (Kollef: 2006).

Figure 2.3 shows strategies for achieving antibiotic heterogeneity.

1. Antibiotic cycling or antibiotic rotation: A fixed temporal pattern for the predominant use of antibiotic class or classes, followed by their repeated removal and reintroduction over time.

   \[ Q \rightarrow CE \rightarrow B \rightarrow Q \rightarrow CE \rightarrow B \]

2. Scheduled antibiotic changes: A predetermined and scheduled change in the predominant antimicrobial agent employed. Changes in the antibiotic classes employed are often based on changing patterns of antimicrobial sensitivities and are not simply time based.

   \[ CE \rightarrow CA \rightarrow CE \rightarrow B \]

3. Antibiotic mixing: A strategy whereby all or most available antimicrobial classes are employed to minimize undue pressure for the emergence of resistance from having a single or limited number of antibiotic classes available.

   \[ CE + CA + B + Q \rightarrow CE + CA + B + Q \]

*Figure 2.3. Strategies for achieving antibiotic heterogeneity.* Each arrow denotes a unit of time. B: β-lactam; CA: carbapenem; CE: cephalosporin; Q: quinolone (Kollef: 2006)
2.2.9.6 Optimizing pharmacokinetic/ pharmacodynamics principles

Antibiotic concentrations that are sub lethal can promote the emergence of resistant pathogens. Optimization of antibiotic regimens on the basis of pharmacokinetic/pharmacodynamics principles could play a role in the reduction of antibiotic resistance. The duration of time that the serum drug concentration remains above the minimum inhibitory concentration of the antibiotic enhances the bacterial eradication with beta-lactams, carbapenems, monobactams, glycopeptides and oxazolidinones. Frequent dosing, prolonged infusion times or continuous infusions can increase the duration of time that the serum drug concentration remains above the minimum inhibitory concentration of the antibiotic and can improve clinical and microbiological cure rates (Kollef:2005).

The incidences of sepsis have mortality rates of 30% for mild to moderate sepsis and up to 82% for severe sepsis and septic shock. The new paradigm for treating sepsis is: “Get it right the first time”. Sepsis can have an effect on plasma antibiotic concentrations, by increasing capillary leaking, or decreasing clearance of drug (As shown in Figure 2.4). Although many intensive care patients have normal or decreased clearance of drugs (right side of figure), some with the pathophysiological changes of sepsis, such as increased cardiac output and increased volume of distribution, have low plasma drug concentrations.
These pharmacokinetic/pharmacodynamic difficulties can be overcome by keeping the minimum inhibitory concentration (MIC) higher than 4-5 times the MIC for longer than 60% of the time. This can be done by giving continuous or prolonged administrations. In the absence of any post-antibiotic effect, the plasma concentration of a β-lactam antibiotic should exceed the MIC for the respective organism for 100% of the dosing interval (Lipman & Boots:2009).

According to Lipman and Boots, (2009), the new paradigm for antibiotic treatment, particularly of nosocomial infections is:

- Cover all (or certainly most) organism initially – *get it right the first time*;
- Give large doses to prevent underdosing – *hit hard up front*;
- Avoid low doses of antibiotics, which predispose to resistance; and
- With a few exceptions, and provided there is source control, recognize it is seldom necessary to give more than a 5-7 day course (Lipman & Boots:2009).
2.3 Functions of the clinical pharmacist at ward level

Although antibiotic stewardship plays a huge part of the role of the clinical pharmacist, it does not make up the entire role of the clinical pharmacist. The practice of pharmaceutical care involves the pharmacist applying knowledge to promote the well-being of the public. It has three components, namely:

- Philosophy of pharmaceutical care practice
  The philosophy of practice defines what the practitioner should do, guided by rules, roles, relationships and responsibilities. Specific to pharmaceutical care, the philosophy of practice describes the approach that will be taken to meet the patient’s needs. The pharmacist identifies drug therapy problems, resolves them and prevents new problems in order to promote positive patient outcomes. These actions require the existence of a relationship so that effective communication between the pharmacist and the patient, and the pharmacist and the doctor may take place. The pharmacist must engage in the patient care process in order to provide a service. (Cipolle, Strand & Morley:1998)

- Patient care process
  The patient care process focus on the patient’s drug related needs. The process has three major steps: 1) Assessment of the patient’s needs 2) Constructing a care plan 3) Conducting a follow-up and evaluating patient progress.

Patients are central to the provision of pharmaceutical care. While pharmaceutical care can encompass pharmacy services such as patient counselling, drug utilization reviews and therapeutic drug monitoring, the delivery of pharmaceutical care demands that each patient's wishes, preferences and needs are determined. The pharmacist must then make a commitment to continue that care. (Cipolle et al.:1998)
• Practice management system
  This step includes follow-up evaluation of the patient. It is the practitioner's responsibility to follow up and document what actually happened to the patient. The purposes of evaluation are to determine progress towards the set goals of therapy. (Cipolle et al.:1998)

2.3.1 Specific functions of a clinical pharmacist at intensive care level

According to Schellack & Gous (2011) critical care pharmacy has become an essential part of the intensive care unit setting in the US. They have identified the following functions as essential in the delivering of pharmaceutical care to the intensive care unit:

• Providing in-service training to medical residents and the nursing staff.
• Monitoring drug usage.
• Providing drug information.
• Monitoring pharmacokinetic parameters.
  (Schellack & Gous:2011)

Pharmaceutical care is outcome oriented. The rationale behind pharmaceutical care is that drug related morbidity and mortality are serious problems to patients, which can be prevented by providing pharmaceutical care.

Working directly with the patient, this involves the pharmacist performing an assessment of the patient’s therapy and drug-related needs, which includes the identification of drug-related problems, e.g. drug interactions, side-effects and appropriate dosages of medication.

In conclusion the pharmacist can play a role in a variety of activities to improve the patient’s quality of clinical outcomes. (Cipolle, et al., 1998)
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The aim of the study was to determine the need for the provision of pharmaceutical care from the pharmacist in the ICU of Steve Biko Academic Hospital. Objectives included the design of an antimicrobial ward protocol, the description of interventions performed by the pharmacist as well as the time spent on these interventions, as have been described in Chapter 1. The overall aim of the study was to document procedures and outcomes of pharmaceutical care rendered in the Surgical ICU (S-ICU) of Steve Biko Hospital.

Pharmaceutical care was rendered during a specific study period by the researcher to the S-ICU and findings of clinical data, interventions and outcomes were documented in a standard format suggested by the American Society of Health System Pharmacists (ASHP:1992). A needs assessment was done with the nurses (before and after the study) and doctors (after the study) working in the unit to obtain feedback from medical staff on the quality of pharmaceutical care provided.

The time spent on different functions performed by the clinical pharmacist working in the ward setting was recorded on a time sheet.

3.1 Study Design

The design of the study was descriptive quantitative. This was in the form of an operational research study which included indicators of programme success, such as improving the quality of services and adding new services components. Data were collected prospectively daily for eight weeks. Quantitative aspects included patient demographics, clinical data, the number of interventions per patient, time spent, types of interventions, the cost of antimicrobials prescribed and resistance patterns. The study had a cross-sectional design. A needs assessment questionnaire was administered to the medical and nursing staff before and after the study. Open-ended questions were asked to justify yes and no responses.
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3.2 Study-site

The study was conducted in the S-ICU and HCU of Steve Biko Academic Hospital. The researcher worked in the units and documented data from the patients identified in the sample in these units.

3.3 Sample population

The sample population included all the patients that were admitted to the ICU and these patients were followed to the HCU during the study period. The ICU consists of 12 beds, with a patient turnover of about 50 patients per month. The average patient stay in the ICU varied between 4 – 10 days. The HCU consists of 16 beds, half of which are occupied by surgical patients. The ward’s patient turnover is about 100 patients per month, with an average stay of two days.

Initially the sample size was calculated, but when the study commenced, all patients admitted to the Surgical Intensive Care Unit were enrolled.

The sample population consisted of all the patients admitted to the ICU during the study period. All permanent nursing staff working day shift in the ward, registrars and consultants working in the ward were included to complete the questionnaires to determine their feedback.

3.4 Designing the Antimicrobial Protocol

One of the objectives of the study was to design and implement an antimicrobial ward protocol for the surgical ICU. The regular surgical procedures, availability of antibiotics and resistant patterns were documented. This information and international standards were incorporated to compile an antimicrobial protocol. The first drafts of the protocol was evaluated by a microbiologist and then adapted according to his recommendations, thereafter it was also approved by the head of the unit.
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3.5 Rendering of Pharmaceutical Care

Pharmaceutical care was rendered to all the patients of the S-ICU on a daily basis. The researcher evaluated patient prescriptions and clinical data on a daily basis, making the necessary interventions and documenting interventions and outcomes of interventions on the pharmaceutical care data sheets.

Figure 3.1 depicts the study algorithm. Pharmaceutical care rounds were done and interventions performed by writing on the patients bed-letters, or discussing them with doctors on ward rounds. The interventions and whether they were successful or unsuccessful were recorded on the pharmaceutical care forms.

The time spent on interventions and other ward functions were also recorded on the time sheet of the researcher.
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Figure 3.1: Study Algorithm

Ward rounds in the ICU and High Care Ward

Pharmaceutical care rounds

Record interventions on standardized data collection form (Appendix 2)

The interventions were made by:
- Writing in the bed letter and/or
- Ward round and/or
- Direct discussion with consultant or registrar

Intervention successful

Intervention unsuccessful

Time spent

- Pharmaceutical care
- Ward rounds with doctors
- Meetings
- Weekly staff lectures

Recorded on timesheet

- Information requests from doctors/nurses
- Request for consultation with patient

Address requests for consultations with patients by rendering pharmaceutical care

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3.6 Study period

The study was conducted daily over an eight week period, (250 hours), every day from 7H00 to 15H00 except weekends and public holidays.

3.7 Data collection instruments

3.7.1 Questionnaire for registered nursing and medical staff

A questionnaire was completed by the doctors (only post-study) and registered nurses working at the ICU before and after the study. This was used to determine whether the medical staff members can benefit from education and medicine information provided by a pharmacist. The questionnaire contained open ended questions with instructions to justify yes and no response. Figure 3.2 shows an example of the questionnaire. The full questionnaires are available as Appendix 3 & 4.

Doctor’s Details

Rank: ___ Registrar _______________________

Questions

1. Do you feel there is a need for a pharmacist to routinely visit the ICU and High Care wards?
   Yes: ☐
   No: ☐
   Comment: ____________________________________________________________

Figure 3.2: Example of Doctor’s questionnaire

3.7.2 Pharmaceutical Care form

Pharmaceutical care forms that were used in the study as tools for capturing data were adapted from the Clinical Skills program: Advancing pharmaceutical care (American Society of Hospital Pharmacists;1992). The forms were adapted to fit
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this particular study. The *Pharmacist’s Patient Database Forms* were expanded and the *Pharmacist’s Care Plan* and *Monitoring Worksheet* were combined (See Appendix 1).

The forms were successfully used by UL Medunsa-Campus under-graduate and postgraduate students (Untiedt:2003; Schellack:2008). Each form contained a *Pharmacist’s Patient Database Form* that documents patient demographic and administrative information. The patient’s medical history and current medical problems were documented to assist with evaluating the patient’s progress. This section of the form gave an overview of the patient’s history of illness, including the medication the patient used prior to admission.

Another section of the form provided space to fill in the patient’s current drug therapy. Drugs and doses of the patient’s current medication were recorded in this section. There was also space to document each dose that was administered. When the drug was discontinued, a cross was put across the last block.

The patient’s laboratory information, like urea and electrolytes, full blood count, liver function tests and microbiological data were recorded in the section provided. Vital signs were also recorded in this section.

For the purpose of this study, the standardized pharmaceutical care form was modified slightly to capture detailed information on antimicrobial use and microorganisms cultured. This was done to address objectives 1 and 2. Data included the sample tested, the organism isolated and the sensitivity of isolated organism. Microbiology data and susceptibility profiles of organisms were not always readily available from the laboratory, and it was often time consuming to obtain these values. Figure 3.3 shows an example of the adjusted antimicrobial data sheet.

The antimicrobials prescribed and the cost implication of prescribed drug was also monitored.
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#### PHARMACIST’S PATIENT DATABASE FORMS

**MICROBIOLOGY**

<table>
<thead>
<tr>
<th>Date</th>
<th>Sample</th>
<th>Organism</th>
<th>Day Cultured</th>
<th>Sensitivity</th>
<th>Diagnosis</th>
<th>Antimicrobial Rx</th>
<th>Cost Implication</th>
<th>Intervention made</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011/04/07</td>
<td>Blood Culture</td>
<td>E.coli</td>
<td>3</td>
<td>Co-amoxyclov</td>
<td>Sepsis</td>
<td>Co-amoxyclov 1.2g 8h iv</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Figure 3.3: Microbiology data sheet*

*Drug Therapy Assessment Worksheet* addressed potential and actual problems with the patient’s therapy. There were 27 different types of possible problems that could arise with the patient’s therapy and they were grouped into eleven categories. If a problem existed with the patient’s therapy, it was coded as “1”. If more information was required to determine if a problem existed, it was coded as “2”. If no problem existed with therapy, it was coded as “3”.

Problems that had been identified in the *Drug Therapy Assessment Worksheet* were transcribed in the Drug Therapy Problem List. In this section of the form, problems were briefly described and the proposed pharmaceutical care problems were written on the *Pharmacist’s Care Plan Monitoring Worksheet*. The original documents have two separated documents e.g., *Pharmacist Care Plan* and *Monitoring Worksheet* which we have combined into one document. Outcomes of interventions were also written here with a brief explanation of how the outcome was achieved or why outcome was not achieved. An intervention was considered to be successful if the recommendation made was accepted by the
prescriber, and considered not successful if the recommendation was not accepted.

### 3.7.3 Times spent on intervention

The *Pharmacist’s time spent in ward* form was designed (see Appendix 2) to estimate the time it took the pharmacist to evaluate all the ward patients’ prescriptions and make relevant interventions. The form had space to note the date, the time started in the ward and the number of patients assessed, and the time finished with ward round. An average time spent per patient could then be calculated. Figure 3.4 shows an example of the time sheet.

<table>
<thead>
<tr>
<th>Pharmacist’s Time Spent in the Ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date: <strong>23/03/2011</strong>________________</td>
</tr>
<tr>
<td>Start time: <strong><strong>07:00</strong></strong>___________</td>
</tr>
<tr>
<td>Number of patients present in ward: <strong><strong>9</strong></strong>_____________</td>
</tr>
<tr>
<td>Time spent per patient: ___35________________________min</td>
</tr>
<tr>
<td>Time spent per pharmaceutical care intervention: ____15________________________min</td>
</tr>
</tbody>
</table>

*Figure 3.4: Pharmacist’s time spent in the ward*

### 3.7.4 Pilot Study

During the pilot study the researcher introduced herself to the staff in the ward and familiarized herself with the ward routine. During this time, she evaluated the antibiotic forms used already in the ward, and ascertains that the data needed to complete the data collection forms could be obtained from ward documentation.
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3.8 Data analysis

As a preliminary analysis, a summary of the descriptive statistics was produced; this included frequencies and percentages for categorical data, such as gender, type of surgery; continuous variable such as age was summarized using mean, median and standard deviation.

3.9 Reliability and Validity

Reliability and validity of the data collection instruments as discussed in Section 3.6 were tested during the pilot study. Changes were made accordingly. However these instruments have been standardized by the American Society of Hospital Pharmacists in 1992 and have been tested in a South African context by Untied in 2003 and Schellack in 2008.

3.10 Bias

Due to the nature of the study; a descriptive operational study; in which the researcher measured interventions made in the study population, it is recognized that bias may have been introduced. However some element of this was controlled due to the nature of the interventions. The researcher did not work on her own but in a multi-disciplinary team, and all interventions were approved by either the treating physician or another member of the health care team (depending on the type of intervention). The clinical supervisor had approved or declined all clinical interventions made.

3.11 Ethical considerations

Permission to conduct the study was obtained from the Chief Executive Officer (CEO) at Steve Biko Hospital (Appendix 5) and from Prof Pretorius Head of the Department of Critical Care (Appendix 6). Ethical approval was obtained from the University of Limpopo (Medunsa Campus) Research, Ethics and Publications
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Committee and from the University of Pretoria’s Ethics Committee. The certificates of approval are attached as Appendix 7 and 8. No direct alterations were made to the patients’ therapy without consultation with the treating physician. The researcher researched the different therapy options before making an informed decision on suggestions to make in a consultation with the treating physician, the physician then decided upon the best treatment option for the patient.

Patient confidentiality was strictly maintained at all times during the research project. Each study participant received a specifically allocated study number, under which data were recorded anonymously.

Informed consent to participate in the study was obtained from each patient, or a legal guardian or family member in cases where patients could not respond themselves. All of the nursing staff, as well as the doctors who participated in the questionnaires also received an information letter and signed a consent form (although some chose to stay anonymous) (Appendix 9, 10, 11 and 12).
CHAPTER 4: RESULTS AND DISCUSSION

The findings of the study are presented and discussed in this chapter. Since the study was operational, the results are in some instances presented as a discussion only. The study provides results on pharmaceutical care rendered to the unit, including patient demographics, use of medication and interventions performed. Other results also include the time spent on different ward functions as well as the experience and expectations of nursing and medical staff of having a pharmacist present in the ward.

4.1 Pharmaceutical Care

4.1.1 Patient Demographics

During the study period, a total of 78 patients were admitted to the Surgical Intensive Care Unit of Steve Biko Academic Hospital (Ward Statistics: 2011). The ward occupancy during the study period was 87%, (Ward Statistics: 2011) with 64 patients transferred to other wards, 11 patients died and three were still admitted to the ward when pharmaceutical services ended. A number of 51 patients (n=51; 65.3%) were included in the study. The reason for not seeing 100% of the patients was that the researcher only worked from Mondays to Fridays, thus patients admitted over weekends or on public holidays, and transferred to other wards could not be seen. The demographics of the 51 study patients will be described hereafter.
4.1.1.1 Gender

Of the 51 study patients, 35 were male and 16 were female (68.63%:31.37%). This gives a ratio of male: female of 2.18:1, which is not a reflection of the general population. According to the mid-year population estimates of Statistics South-Africa, the male to female ratio for South-Africa is 0.94:1. Figure 4.1 depicts the number of male and female patients as admitted to the Surgical ICU.

(Statistics, South-Africa:2011)

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**Figure 4.1: Gender of Patients in the Surgical ICU**
4.1.1.2 Age

The average age of the patients was 44.92 years, with a minimum age of 12 years and a maximum age of 86 years. One patient’s age was unknown (the patient was involved in a pedestrian accident which left him unconscious, and he was admitted without identification). Most patients admitted to the unit were between the ages of 21 and 30 years, and 51 to 60 years of age.

In a study done by Wunsch, Angus, Harrison, Linde-Zwirble & Rowan (2007) on the different demographic data on ICU admissions in the USA and UK, the patient age distribution was similar in the two countries, with a slightly higher mean age in the US (60.4 years) than the UK (57.4 years). Proportionally, there were twice as many patients aged 85 years and older in the US ICU’s than in the UK ICU. The mean age of patients in the S-ICU of Steve Biko was 44.92 years, which is lower than that of the US and UK.

Figure 4.2 depicts the distribution of age in the S-ICU.

Figure 4.2: Age of patients admitted to the Surgical ICU
4.1.1.3 Weight

Most of the patients in the ward were not actually weighed, so an estimation of the patient’s weight was made in those cases. The average weight of the patients was 77.72 kg, with a minimum estimated weight of 40kg and a maximum estimated weight of 120kg. Three patients' weight could not be established because they were unconscious when admitted and could not be weighed. The older patients, for age 41 upwards tended to weigh more than the younger patients.

The inability to weight patients is not unique to the study site and is a challenge in most ICUs due to the lack of weighing beds and or the severity of patients. It is important that the clinical pharmacist is aware this practice can create challenges, as the estimation of weight is most often not accurate and can differ from actual weight by as much as 20kg. This can have an influence on medication dosages and may result in patients being over- or under dosed (Henderson, Robinson & Roland:2006).

4.1.1.4 Duration of hospital stay and outcomes

The average stay of the patients in the intensive care unit was 8.705 (SD = 8.1223) days, with a minimum stay of one day, and a maximum stay of 46 days. It was the objective to have patients stay as short as possible, to prevent nosocomial infections. Older patients had a longer average stay in the unit than younger patients. According to Wunsch, et al. (2007), older patients do not necessarily have a longer ICU stay, and that the duration of ICU stay is rather influenced by the patient's APACHE II score on admission to the unit. APACHE is the Acute Physiology And Chronic Health Evaluation score which provides an estimate of ICU mortality based on a number of laboratory values and patient signs taking both acute and chronic disease into account.
Only one patient had a hospital stay of 46 days, which was considerably longer than the average of 8.7 days. A standard deviation of 8.1223 indicates that 95% of the patients stayed between 0.6 and 16.8 days. The patient with a stay of only one day was admitted to the ward after an aortic bypass. The patient recovered well and was stable enough to transfer to the cardiac unit immediately, so as to minimize infection risk.

Figure 4.3: Age, weight and days in hospital according to gender

Figure 4.3 depicts the average age, weight and days in ICU according to gender. Male patients had a greater age, higher weight and slightly longer stay in ICU than female patients.

According to Wunsch, et al. (2007), patients’ weight, age or gender does not necessarily influence their stay in ICU, but that the duration of ICU stay is rather influenced by the patient’s APACHE II score on admission to the unit. The patient’s medical history, existing chronic conditions and also the length of hospital admission before admission to the ICU may also play a role.
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4.1.1.5 The reason for discharge

The reasons for discharge from the S-ICU are shown in Table 4.1.

Table 4.1. Reason for discharge from the ward

<table>
<thead>
<tr>
<th>Reason for discharge</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient died</td>
<td>8</td>
<td>15.69</td>
</tr>
<tr>
<td>Still in ward – pharmaceutical care ended</td>
<td>3</td>
<td>5.88</td>
</tr>
<tr>
<td>Transfer patient to ward/High Care</td>
<td>36</td>
<td>70.59</td>
</tr>
<tr>
<td>Transfer to Neuro ICU</td>
<td>3</td>
<td>5.88</td>
</tr>
<tr>
<td>Transfer to plastic surgery</td>
<td>1</td>
<td>1.96</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>100.00</td>
</tr>
</tbody>
</table>

A total of eight patients (n=51) died in the ward during the study period, mostly from septic shock, but one patient also died from cardiac arrest. Most patients (36) were transferred from the ICU to the High Care Unit (where pharmaceutical care rounds were also done), where they stayed an average of two days before they were transferred to general wards. Patients with head injuries were primarily admitted to the Surgical ICU because the Neuro ICU did not have available beds, and were transferred to the Neuro ICU as soon as beds became available. The patient with burn wounds was transferred to the plastic surgery ward for skin grafting to be done. When the study period was completed, three patients for whom pharmaceutical care was commenced were still admitted to the S-ICU, and pharmaceutical care could not be continued.

4.1.1.4 Alcohol and Tobacco use

Of the 51 patients seen in the Surgical ICU, nine indicated that they used alcohol, while 42 indicated no use of alcohol. Fifteen patients indicated that they used tobacco, while 36 indicated that they do not use tobacco, or the
information was not indicated on the patient’s file on admission. This information could not be obtained for all patients, as they were unconscious or sedated while in the ward. More males than females used tobacco (11:4) and more males than females used alcohol (9:7). These figures may however not be an accurate reflection of the reality, as not all of the patients were able to give information on alcohol and tobacco use. The reason for this is that patients were admitted in an unconscious state, or patients were sedated while in the ward, and family members were not always available to give information.

Smoking and hazardous alcohol drinking are the most frequent lifestyle risk factors that can influence the outcome after surgery (Tonnesen, Nielsen, Lauritzen& Moller:2009). The incidence of smoking is about 30% (in line with what was indicated in the study population) and the incidence of drinking is 7-49% for general surgical populations undergoing elective procedures and 14-38% for emergency procedures in the western world. The incidence is often higher in the ICU setting than in the general population (Tonnesen, et al.:2009).

The most common perioperative complications related to smoking are impaired wound and tissue healing and wound infections (Tonnesen, et al.:2009). Of the patients in this study who used tobacco, one had an ischemic cardiac incident in the unit, two of the six patients who had free flap operations, and smoked, died. Interestingly, three patients with bleeding gastric ulcers also used tobacco and alcohol.

4.1.1.5 HIV Status

Of all the study patients, 13 patients’ HIV status was known. Of the 13 patients, six were HIV positive, while seven were negative. The information was obtained by the nursing staff when admitting the patient to the ward, or when a patient was tested while admitted to the ward. The remaining 38 patients’ HIV status was unknown by themselves, and they were not tested while admitted to the
CHAPTER 4: RESULTS AND DISCUSSION

According to references, (Bhangwanjee, Muckart, Jeena & Moodley:1997) the routine HIV testing of patients in a surgical ICU does not make a difference to the outcome of treatment. Of the six patients that were HIV positive, three was previously on antiretroviral treatment, while two were initiated on treatment and one patient did not want her status disclosed. The HIV-positive patients were all female, while the HIV-negative patients were five male and two female. Of the patients with unknown status 30 were male and eight female. According to the midyear estimates of Statistics South-Africa (2011), the estimated overall HIV prevalence rate is approximately 10.6%. An estimated 16.6% of the adult population aged 15-49 years is HIV positive. The 11.1% positive patients in the Surgical ICU is thus not a true reflection of the population. (Statistics, South-Africa:2011)

In a study done in a surgical ICU in Kwa-Zulu Natal, SA, it was concluded that there was no difference in mortality between HIV positive and HIV negative patients, as they were admitted for procedures not relating to HIV. However, morbidity was higher in the HIV positive group. According to the study, HIV patients had significantly higher incidences of organ failure (71%:49%) and a higher incidence of septic shock (38%:15%). Their HIV status also did not influence their duration of stay in the surgical ICU (Bhagwanjee ,et al.:1997).

4.1.2 Diagnoses

Diagnoses were obtained from the patients' bed letters, as noted by the treating physicians. A total number of 72 diagnoses were recorded for the 51 patients. It is to be noted that more than one diagnosis may apply to a single patient. The median number of diagnoses was 1.21 per patient. The diagnoses per affected system are categorized in Table 4.2.
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Table 4.2: Number of diagnosis per system

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients (n=51)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine-metabolic</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>GIT</td>
<td>14</td>
<td>27%</td>
</tr>
<tr>
<td>Renal</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Infectious</td>
<td>15</td>
<td>29%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>Skeletal</td>
<td>16</td>
<td>31%</td>
</tr>
<tr>
<td>Trauma</td>
<td>21</td>
<td>41%</td>
</tr>
<tr>
<td>Reproductive system</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Tumor excision</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>Head injury</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Skin</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Note that in most cases, more than one diagnosis applied to the same patient (n=72)*

Since the unit is the Surgical Intensive Care Unit (also known as the surgical and trauma ICU), the diagnoses most commonly encountered in the unit, were trauma (21 patients; n=51). This included gun-shot wounds and motor vehicle accidents. The patients’ injuries ranged from fractures, soft tissue laceration and abdominal wounds obtained from gun shots or blunt force trauma. Most patients admitted with trauma also had skeletal or gastro-intestinal involvement.

The GI tract (14 patients; n=51) was also a common diagnosis, with most patients admitted post general surgery. Differential diagnoses included upper gastro-intestinal bleeds, ruptured spleen and colon perforation.

The diagnosis of infection (15 patients; n=51) was made secondary to the admission diagnosis in 14 of the 15 cases. This included ventilator-associated pneumonia (VAP), as well as septic wounds (surgical and orthopaedic in origin). One medical patient was admitted to the unit with pneumonia, since the Medical Intensive Care Unit (M-ICU) was full.
In a study by Weissman (1997), the admission diagnosis was compared to the diagnosis of patients on admission to the ICU. It was found that the reason for admission to the ICU was frequently a secondary diagnosis. Nosocomial pneumonia is one of the most common diagnosis made in surgical ICU’s and is common in patients undergoing mechanical ventilation (Cunha:2008). Sepsis and septic shock also contribute to the most common diagnoses in ICU. These diagnoses can all be included under the “infectious” diagnosis.

4.1.3 Medication according to ATC Standard classification

In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are divided in groups at five different levels and fourteen main groups (WHO Collaborating Centre for Drug Statistics Methodology). The main purpose of the ATC system is as a tool for presenting drug utilization statistics with the aim of improving drug use. The system has been used since the early 1970’s in drug utilization studies for national and international comparisons of drug utilization (WHO ATC/DDD Index:2011).

The ATC system is divided in fourteen main groups which include:

- A= Alimentary tract and metabolism
- B= Blood and blood forming organs
- C= Cardiovascular system
- D= Dermatologicals
- G= Genito-urinary system and sex hormones
- H= Systemic hormonal preparations
- J= Antiinfectives for systemic use
- L= Antineoplastic and immunomodulating agents
- M= Musculo-skeletal system
- N= Nervous system
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- P= Antiparasitic products
- R= Respiratory system
- S= Sensory organs
- V= Various

Table 4.3 contains the medications used in the S-ICU according to the ATC codes and also the frequency of medications used. The complete classification can be seen in Appendix 13, but in Table 4.4 only the most frequent used medication in each system is listed. In the S-ICU the medication used is mostly representative of the alimentary tract, cardiovascular system and anti-infectives for systemic use.

The diagnosis (discussed in Section 4.2) can be linked to the use of medication. The diagnosis of trauma made up 41% of all the diagnosis in the S-ICU. All of these patients received enoxaparin as prophylactic treatment for thromboembolisms. Infections, which made up 29% of the diagnosis, resulted in the anti-infective medication being the class used mostly in the S-ICU.

Table 4.3: Medication used according to ATC classification

<table>
<thead>
<tr>
<th>Organ system</th>
<th>ATC code</th>
<th>International propriety name</th>
<th>Frequency of medication used</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alimentary tract &amp; metabolism</td>
<td>A11A</td>
<td>Multi-vitamins</td>
<td>47</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>A02BX02</td>
<td>Sucralfate</td>
<td>41</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>A02BA02</td>
<td>Pantoprazole</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>A03FA01</td>
<td>Metoclopramide</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>A06AD11</td>
<td>Lactulose</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>A02BA01</td>
<td>Cimetidine</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Blood and blood forming organs</td>
<td>B01AB06</td>
<td>Enoxaparin sodium</td>
<td>49</td>
<td>1</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>C03CA01</td>
<td>Furosemide</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>C09AA04</td>
<td>Perindopril</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>C10AA01</td>
<td>Simvastatin</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>C01CA06</td>
<td>Phenylephrine</td>
<td>5</td>
<td>17</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Code</th>
<th>Medication</th>
<th>Quantity</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>C01BD01</td>
<td>Amiodarone</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>H02AB09</td>
<td>Hydrocortizone systemic</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>D06BA01</td>
<td>Silver sulfadiazine</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>H01BB02</td>
<td>Oxytocin</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>J01CR05</td>
<td>Piperacillin/tazobactam</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>J01DA04</td>
<td>Cefazolin</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>J01CR02</td>
<td>Co-amoxyclov</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>J01DH02</td>
<td>Meropenem</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>J01DH51</td>
<td>Imipenem</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>J01FA01</td>
<td>Erythromycin</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>J02AC01</td>
<td>Fluconazole</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>M01AB05</td>
<td>Diclofenac</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>M03AC03</td>
<td>Vecuronium bromide</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>N02AG01</td>
<td>Morphine</td>
<td>38</td>
<td>4</td>
</tr>
<tr>
<td>N05CD08</td>
<td>Midazolam</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>N02BE01</td>
<td>Paracetamol oral</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td>N05AD01</td>
<td>Haloperidol</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>N03AG01</td>
<td>Valproic acid</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>N03AB02</td>
<td>Phenytoin</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>P01AB01</td>
<td>Metronidazole</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>R03AA01</td>
<td>Adrenaline</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>R03BB01</td>
<td>Ipratropium bromide/Fenoterol</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>V03AF01</td>
<td>Mesna</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>V06B</td>
<td>Dipeptivan</td>
<td>5</td>
<td>17</td>
</tr>
</tbody>
</table>

Anti-infectives is the class of medication second most frequently used (n=124 items) in the S-ICU, and this correlates with the diagnoses of ventilator-associated pneumonia, sepsis or septic shock that were most prevalent in the S-ICU. The alimentary tract is the most used class (n=174 items), but includes multivitamin supplementation and sucralfate used routinely as part of the ward protocol. The class used least in the S-ICU was the musculo-skeletal system. Vecuronium was prescribed only to one patient, to keep him paralyzed, since he...
was ventilated with two ventilators. Vecuronium is administered to facilitate mechanical ventilation, but prolonged use is not advised since neuromuscular paralysis lasting up to seven days may occur after the termination of long term administration (Segredo, Caldwell, Matthay, Sharma, Greunke & Miller:1992).

### 4.1.4 Medicine usage

A total of 579 items were prescribed to 51 patients in the eight weeks of the study. One patient received 26 different medications (the most) and one patient received only four medications (the least). An average of 12 medications was prescribed to each patient in the ward.

In a study done by Biswal, Mishra, Malhotra, Puri & Pandhi (2006) in India, the mean number of drugs at the time of admission to the intensive care unit were 5.3, it increased to 12.9 on the first day and 22.2 during the entire stay. In this study, more than 50% of the average number of drugs prescribed was antibiotics.

A study done in 2004 by Hartmann, Junger, Brammen, Rohrig, Klasen, Quinzio, Benson & Hempelmann, shows that antibiotics were used most frequently as treatment in the S-ICU. Of these antibiotics, the cephalosporins were used 39.9% of the time, and for a shorter period than three days. Other medications used most frequently were the standard preventive drugs e.g. sucralfate and enoxaparin.

Dasta (1986) described antibiotics as the drug class most used in the ICU setting. Patients in the Surgical ICU with an average stay of three days averaged with 7.6 drugs per visit.

From these studies it can be derived that the longer a patient stays in ICU, the more medication will be prescribed.

Figure 4.4 depicts the number of medications prescribed to each patient related to their length of stay in the ICU. The x-axis depicts the patient number. For
example, patient number 25 had an ICU-stay of 13 days, and 14 different medications were prescribed to him. This shows that the longer the patient stayed in the ICU, the more medications were prescribed.

![Graph showing the number of medications related to the length of ICU stay]

**Figure 4.4: The number of medication related to the length of ICU stay**

The medications used most frequently are shown in Table 4.4. Table 4.4 presents the nine medications used most often in the S-ICU, as can be seen by the lack of antibiotics on the list. A great many of these medications are used in the ICU not to treat a specific condition, but rather as prophylaxis against complications that can be encountered in ICU. Examples are enoxaparin for prophylaxis of post-operative deep vein thrombosis, or sucralfate for prophylaxis of stress ulcer formation.
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Table 4.4: Frequency of Medication used in the SICU

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number of patients (n=51)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin injection</td>
<td>49</td>
<td>96%</td>
</tr>
<tr>
<td>Multi-vitamin supplement syrup</td>
<td>47</td>
<td>92%</td>
</tr>
<tr>
<td>Sucralfate suspension</td>
<td>41</td>
<td>80%</td>
</tr>
<tr>
<td>Morphine infusion</td>
<td>38</td>
<td>74%</td>
</tr>
<tr>
<td>Midazolam infusion</td>
<td>32</td>
<td>62%</td>
</tr>
<tr>
<td>Paracetamol tablets</td>
<td>28</td>
<td>54%</td>
</tr>
<tr>
<td>Pantoprazole injection/infusion</td>
<td>18</td>
<td>35%</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam injection/infusion</td>
<td>16</td>
<td>31%</td>
</tr>
<tr>
<td>Metoclopramide injection</td>
<td>14</td>
<td>27%</td>
</tr>
</tbody>
</table>

Enoxaparin was used in 96% of the patients, for prevention of clotting. This also included the three patients that were treated with enoxaparin for embolisms. International guidelines state that deep vein thrombosis prophylaxis should be administered to surgical patients, especially for orthopaedic surgery, but also for patients undergoing large abdominal surgery (Nurmohamed, Verhaeghe, Haas, Iriatte, Vogel, Van Rij, Prentice & Ten Cate:1995).

The recommended dose for prophylaxis of DVT in orthopaedic patients (including hip- and knee-replacement surgery) is enoxaparin 40mg daily for 7-10 days, and can be continued for three weeks following initial phase of thromboprophylaxis. For abdominal surgery patients the recommended dose is enoxaparin 40mg daily, initiated two hours prior to surgery, and continued for 7-10 days after surgery (Nurmohamed, et al.:1995).

Most patients admitted into the intensive care unit are in need of sedation therapy. In the S-ICU of Steve Biko Hospital, the Ramsay Sedation Scale was used to administer midazolam and morphine(Ramsay, Savege, Simpson & Goodwin:1974).
The effective management of pain, anxiety and sleep (hypnosis) are the major aims of a sedation therapy regimen. The Ramsay Sedation Scale was designed as a test of rousability. The RSS scores sedation at six different levels. The patient is scored as follows:

Table 4.5: Ramsay Sedation Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Patient rousability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Patient is anxious and agitated/restless, or both</td>
</tr>
<tr>
<td>2</td>
<td>Patient is co-operative, oriented and tranquil</td>
</tr>
<tr>
<td>3</td>
<td>Patient responds to commands only</td>
</tr>
<tr>
<td>4</td>
<td>Patient exhibits brisk response to light glabellar tap or loud auditory stimulus</td>
</tr>
<tr>
<td>5</td>
<td>Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus</td>
</tr>
<tr>
<td>6</td>
<td>Patient exhibits no response</td>
</tr>
</tbody>
</table>

(Obtained from Ramsay, *et al.*:1974)

Although almost all the patients received midazolam and morphine therapy, this was only administered for an average of 2-3 days according to the Ramsay scale. In cases when patients needed continued pain therapy, morphine boluses were given when necessary.

Most patients (n=42; 92%) also received a daily multi-vitamin supplement, because of the increased nutritional need of the critical ill patient. According to Corcoran, O’Neill, Webb & However (2009) nutritional support in the critically ill is now considered standard care. The association between vitamin concentrations and disease risk may be confounded by inflammation, and during episodes of infection, serum concentrations of retinol and antioxidant vitamins decrease drastically. In the S-ICU of Steve Biko Hospital, only oral multivitamin syrup was used, which does not contain either Vitamin B12 or Vitamin A. The administration of the sucralfate suspension before the multivitamin syrup also
had an influence on the absorption of oral vitamins. An education session was given to the nursing staff on this aspect.

All patients that was not on therapy for bleeding gastric ulcers, received sucralfate 1g six-hourly, daily to prevent stress ulcer formation. In a study by Tryba in 1991, which compared the efficacy of sucralfate with H2-receptor antagonists, it was concluded that sucralfate is an effective drug for the prevention of stress bleeding that also minimizes the risk of nosocomial pneumonia in long-term ventilated ICU patients (Tryba:1991). PPI's can also be used for stress-ulcer prophylaxis, but not one of the three regimens (sucralfate, H2-RA or PPI) has been shown to be superior to the others. Enteral nutrition represents an alternative to medical therapy for the prophylaxis of stress ulcer (Quenot, Thiery & Barbar:2009).

The number of medications per patient is depicted in Figure 4.5.

![Number of medicine per patient (n = 51)](image)

*Figure 4.5: Number of medicines per patient*
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One patient received only four medications (the least) while one patient received 26 different medications (the most). This patient also had the longest ICU stay. The median number of medications prescribed to patients in the S-ICU were 12 (eight patients received 12 medications). The patient who stayed for one day (admitted and discharged from ward on the same day) was admitted post Aorta bifemoral Bypass. She was only stabilized in the ICU and could then be transferred to the general cardiac ward, as she was not intubated. According to Biswal, et al. (2006) this seems to be in line with international trends. Biswal, et al. stated that the longer the patient stayed in ICU, the more medications were prescribed.

4.1.5 Antibiotic usage in the SICU

The surgical ICU uses antibiotic data-collection forms for every patient admitted to the ward, where antibiotic use is indicated as prophylaxis, empiric use or whether cultures have been done. Figure 4.6 shows an example of the antibiotic forms used for collecting this data.

<table>
<thead>
<tr>
<th>Patient name</th>
<th>Mrs X</th>
<th>Patient number</th>
<th>Date</th>
<th>Antibiotic prescribed</th>
<th>Empiric treatment Y/N</th>
<th>Cultures obtained Y/N</th>
<th>Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>14/03/2011</td>
<td>Meropenem</td>
<td>Y</td>
<td>Y</td>
<td>Meropenem/Amikacin</td>
</tr>
</tbody>
</table>

*Figure 4.6: Antibiotic usage form*

Where positive cultures were obtained, a susceptibility test for different antibiotics was done. The antibiotic use for the S-ICU was evaluated for the period of January 2011 (before commencement of the study) and compared to the
antibiotic use during March of 2011, while the researcher was present in the ward. Figure 4.7 shows a comparison between the two periods.

![Figure 4.7: Comparison of antibiotic use before and during the study](image)

Fewer patients were admitted during the study period compared to before commencement of the study. There were also fewer patients that were not treated with antibiotics, fewer patients who received antibiotics and considerably fewer deaths. It is not conclusive whether this is a result of the researcher being present in the ward, as there are too many variables between the two periods. The data on the antibiotic forms were also not always complete.

The antibiotic forms and the pharmaceutical care forms were used to develop an antibiotic policy for the ward. The policy was not tested as part of the study, but was designed as an outcome of the study.
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Table 4.6 contains a list of the antibiotics that are available for use in the S-ICU.

Table 4.6: Antibiotics available for use in S-ICU

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Meropenem</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>Linezolid</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Piperacillin-Tazobactam</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Co-Amoxyclav</td>
<td>Gentamicin</td>
</tr>
</tbody>
</table>

The prescribing of antibiotics for VAP is done according to the patient’s CPIS (Clinical Pulmonary Infection Score) score. This is a tool used in the ward to assess the severity of the patient’s sepsis. The tool was developed specifically for use in the Intensive Care unit to effectively diagnose patients with ventilator associated pneumonia. If the patient score six or more, treatment for VAP is started on the latest microbiology results, or empirically. Table 4.7 is an example of the tool.

Table 4.7: CPIS score

<table>
<thead>
<tr>
<th>CPIS score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tracheal secretions</td>
<td>Rare</td>
<td>Abundant</td>
<td>Abundant/Purulent</td>
</tr>
<tr>
<td>Chest X-ray infiltrates</td>
<td>None</td>
<td>Diffused</td>
<td>Localized</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>≤36.5-38.4</td>
<td>38.5-38.9</td>
<td>≥39 or ≤36</td>
</tr>
<tr>
<td>Leucocyte count per mm2</td>
<td>≥4000 or ≤11000</td>
<td>&lt;4000 or &gt;11000</td>
<td>&lt;4000 or &gt;11000 Band forms &gt;500</td>
</tr>
<tr>
<td>PaO2/FIO2 mmHg</td>
<td>240 or ARDS</td>
<td></td>
<td>≤240 and no evidence of ARDS</td>
</tr>
<tr>
<td>Microbiology</td>
<td>Negative</td>
<td></td>
<td>Positive</td>
</tr>
</tbody>
</table>

(Obtained from S-ICU 4.9 ward protocol:2011)
4.1.6 Number of Antibiotics used

The different antibiotics used and the frequency of use in the unit is shown in figure 4.8. Piperacillin/tazobactam was the antibiotic most prescribed (n=22), but when the use of the carbapenems [imipenem (n=11) and meropenem (n=11)] are added, the carbapenems usage was equal to piperacillin/tazobactam. This is because the policy in the ward states that the carbapenems must be used alternatively on alternative patients, to achieve antibiotic heterogeneity. Antibiotic heterogeneity (Kollef:2005) is also known as antibiotic rotation. The concept has been suggested as a potential strategy for reducing the emergence of antimicrobial resistance. In theory, a class of antibiotics or a specific antibiotic drug is withdrawn from use for a defined period of time and reintroduced at a later point in time in an attempt to limit bacterial resistance to the cycled antimicrobial agents. The rotation of carbapenems as used in this ICU, cannot be defined as antibiotic rotation, and may result in increased resistance to the entire class.

Cefazolin was used on 13 patients, all post-op for surgical prophylaxis. The head and neck surgery patients received a prophylaxis course of five days cefazolin.
According to guidelines, the use of prophylactic antibiotics during head and neck surgery depends on the procedure type. Head and neck procedures involving an incision through a mucosal layer carry a higher risk for systemic infection. The normal flora of the mouth is polymicrobial, both anaerobe and Gram-positive aerobes. Typical 1g doses of cefazolin are ineffective for anaerobic infections, but a 2g dose produces concentrations high enough to inhibit these organisms. A single dose of clindamycin is however adequate for prophylaxis in maxillofacial surgery, unless the procedures lasts for more than four hours, in which event, a second dose should be administered. There is no additional benefit in extending therapy beyond 24 hours (Devlin, Kanji, Janning & Rybak:2002). The antibiotic policy designed for the ward (see Appendix15) gives guidelines for the use of prophylactic antibiotics.

Fluconazole was used on seven patients, of which five had positive cultures for *Candida albicans*. One of the two patients receiving fluconazole without positive cultures, was admitted to the unit from the medical ICU with multiple antimicrobials for more than two weeks, which were stopped on admission to the unit. The other patient was clinically very ill, but no positive culture results were obtained for him from the laboratory. The reason for this was that the original samples were handled incorrectly, and no growth was reported. He was also treated with other antibiotics without any laboratory results. Despite treating him with multiple antimicrobial agents, he deteriorated rapidly, and died.

### 4.2 Pharmaceutical Care Interventions

As was shown by the patient demographics in Section 4.1.1, there was a variety of medication used from short to more extensive periods of time. In the S-ICU ward setting, there were many opportunities for the pharmacist to provide pharmaceutical care. This section will describe and discuss the pharmaceutical care interventions performed.

A total of 181 interventions were performed and documented for the 51 study patients during the study period of 40 days. Of these interventions, 127 were
accepted, achieving a success rate of 70%. Interventions that were not achieved were mostly because the patient was transferred from the ward before laboratory results or levels could be obtained, and interventions could not be completed.

4.2.1 Frequency of drug therapy interventions

A total of 181 interventions were suggested for the 51 study patients during the research period of 40 days. The average number of interventions per patient ranged from 0 to 13 with a median of 3.5 interventions per patient.

4.2.2 Types of pharmaceutical care interventions

Figure 4.9 illustrates the most frequent types of interventions.

![Pie chart showing the most frequent types of interventions]

- Untreated medical conditions (15.5%)
- Investigations indicated/outstanding (12.2%)
- Prescribed doses and dosing frequency inappropriate (11%)
- Length or course of therapy inappropriate (13.8%)
- Due to system error or non-compliance (9.9%)
- Factors hindering achievement of therapeutic effect (5.5%)
- Other

*Figure 4.9: Most frequent types of interventions*
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Untreated medical conditions constituted the issue addressed most frequently (28; 15%), followed by length or course of therapy inappropriate (25; 13.8%) and investigations indicated or outstanding (22; 12.1%).

Interventions were also made regularly to address:

- Inappropriate dosing frequency (20; 11%);
- System errors or non-compliance (18; 9.9%);
- Factors hindering achievement of therapeutic effect (10; 5.5%).

Other interventions made, included:

- Medication prescribed without indication;
- Relative safety of chosen medication;
- Therapy tailored to individual patient.

Of a total of 181 interventions suggested, 127 (70%) were accepted and implemented by the medical and nursing staff. Details are shown in Table 4.8.
## Table 4.8: Details of interventions made

<table>
<thead>
<tr>
<th>Problem Type</th>
<th>Description</th>
<th>Number (%) of intervention (n=181)</th>
<th>Achieved</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Without indication</td>
<td>4(2.2)</td>
<td>3</td>
<td>75%</td>
</tr>
<tr>
<td>2</td>
<td>Unidentified medications</td>
<td>1(0.5)</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>Untreated medical conditions</td>
<td>28(15.4)</td>
<td>17</td>
<td>61%</td>
</tr>
<tr>
<td>4</td>
<td>Investigations indicated or outstanding</td>
<td>22(12.1)</td>
<td>7</td>
<td>32%</td>
</tr>
<tr>
<td>5</td>
<td>Comparative efficacy of chosen medication(s)</td>
<td>8(4.4)</td>
<td>4</td>
<td>50%</td>
</tr>
<tr>
<td>6</td>
<td>Relative safety of chosen medication(s)</td>
<td>5(2.7)</td>
<td>3</td>
<td>60%</td>
</tr>
<tr>
<td>7</td>
<td>Therapy tailored to individual patient</td>
<td>5(2.7)</td>
<td>5</td>
<td>100%</td>
</tr>
<tr>
<td>8</td>
<td>Prescribed doses and dosing frequency inappropriate</td>
<td>20(11.0)</td>
<td>16</td>
<td>80%</td>
</tr>
<tr>
<td>9</td>
<td>Route/dosage form/mode of administration inappropriate</td>
<td>6(3.3)</td>
<td>6</td>
<td>100%</td>
</tr>
<tr>
<td>10</td>
<td>Doses scheduled to maximize therapeutic effect</td>
<td>9(4.9)</td>
<td>6</td>
<td>67%</td>
</tr>
<tr>
<td>11</td>
<td>Length or course of therapy appropriate</td>
<td>25(13.8)</td>
<td>20</td>
<td>80%</td>
</tr>
<tr>
<td>12</td>
<td>Any therapeutic duplication</td>
<td>4(2.2)</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>15</td>
<td>Symptoms drug induced, problem drug related</td>
<td>2(1.1)</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>16</td>
<td>Drug-Drug interactions</td>
<td>2(1.1)</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>17</td>
<td>Drug-Disease interactions</td>
<td>1(0.5)</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>19</td>
<td>Drug-Laboratory test interactions</td>
<td>2(1.1)</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>20</td>
<td>Use of social drugs problematic</td>
<td>3(1.6)</td>
<td>3</td>
<td>100%</td>
</tr>
<tr>
<td>22</td>
<td>Due to system error or non-compliance</td>
<td>18(9.9)</td>
<td>15</td>
<td>83%</td>
</tr>
<tr>
<td>23</td>
<td>Factors hindering achievement of therapeutic effect</td>
<td>10(5.5)</td>
<td>7</td>
<td>70%</td>
</tr>
<tr>
<td>24</td>
<td>Medication not cost effective</td>
<td>2(1.1)</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>26</td>
<td>Patient understand purpose, how to take, side effects of medication</td>
<td>4(2.2)</td>
<td>4</td>
<td>100%</td>
</tr>
</tbody>
</table>
4.2.3 Narrative description of interventions

Untreated medical conditions

Untreated medical conditions constituted the largest group of interventions. Of 28 interventions suggested, 17 (60.7%) were accepted. The interventions made in this problem category included:

- Reminding prescribers to prescribe the patients’ chronic blood pressure medication;
- Continuing a patients ARV treatment in hospital;
- Suggest antidepressants for patients with long ICU stay;
- Manage the patient’s pain level;
- Suggest antibiotic treatment according to the patient’s culture results, or empiric treatment for e.g. a bowel spill.

Interventions that were not successful were 11 (39.2%). The reasons why interventions were not successful included:

- Patient did not want HIV status disclosed, thus treatment could not be initiated for her;
- Doctor waited for patient’s CRP to normalize before initiating ARV-treatment;
- Positive blood culture for A. baumannii, which was not treated because doctor suspected it to be a colonizer, and the CVP were replaced;
- Dressings were suggested to treat a diabetic ulcer. No dressings were available from the pharmacy.

Length or course of therapy inappropriate

Of the 25 interventions in this category, 20 were accepted (80%). Most interventions of this type were made for anti-infective medication. The interventions made were:
• Stopping antibiotics after a course of five days;
  Antibiotics were only discontinued after assessing the patients infection markers like C-Reactive Protein, white cell count and procalcitonin. The patient’s clinical signs were also evaluated.
• Stopping prophylactic antibiotics after 24 hours;
  Most guidelines state that only one or two doses of antibiotics are necessary for surgical prophylaxis of infection. (See Antimicrobial protocol, appendix 15). Prophylaxis is not required for clean operations, and in other procedures only one dose is needed, except if the procedure is longer than four hours (Antibiotic Policy, Gauteng Province:2010).
• Stopping pantoprazole continuous infusion after 72 hours and change to twice a day dose;
  PPI therapy for upper GI bleeds is indicated as 8mg per hour for 72 hours. Studies have shown that a loading dose of 80mg, then a continuous infusion for 72 hours showed a mortality benefit and reduced incidence of re-bleeding. No PPI was found to be superior to another, but no benefit has been shown for a continuous infusion for longer than 72 hours (Carpenter:2007).
• Stopping carbapenems after a course of 10 days;
  For infection with certain resistant organism, (e.g. Serratiamarcesence) the use of carbapenems for 10 days is indicated. In these instances, the researcher made sure that it was not continued for longer than 10 days.

Investigations indicated or outstanding

Of the 22 interventions made in this category, only seven(32%) were successful. The interventions made in this type included:

• Outstanding results for blood cultures;
  Some culture results were never received from the laboratory.
• Therapeutic drug levels for phenytoin, valproate and vancomycin;
  phenytoin drug levels were taken, but sometimes just a peak or just a trough level was obtained. Four patients were transferred from the ward before
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Phenytoin levels were received, and another three were awaiting valproate levels from the laboratory, and interventions could not be performed.

- Outstanding HIV and TB results;
  Results were not available before the patient left the ward, thus intervention could not be completed.

Unsuccessful interventions resulted mainly from laboratory results not being available in time. Interventions were not so much unsuccessful than incomplete. In seven cases the patient was transferred from the ward before the therapeutic drug levels could be obtained from the laboratory and pharmaceutical care to the patient was discontinued. In four cases, there was no growth reported on cultures taken, although the patients had clinical signs of infection (temperature spikes, elevated CRP and procalcitonin, elevated white cell count).

*Prescribed dosages and dosing frequency appropriate*

Prescribed doses and dosing frequency constituted 11% (20; n=181) of all the interventions. Of the 20 interventions, 16 were accepted. The interventions listed under this category involved interventions that ensured that the dosages administered to the patients were within the usual therapeutic ranges and that the various patient factors were taken into consideration.

Frequently made interventions included:

- High dose of meropenem (2g 8h) not needed if not for meningitis;
- Vancomycin dose adjusted according to creatinine clearance;
  A patient’s creatinine clearance was calculated from the available serum creatinine, and vancomycin dosages were adjusted according to guidelines (Antibiotic Policy, Gauteng Province: 2010). Vancomycin is nephrotoxic and can cause further damage to already injured kidneys.
- Ciprofloxacin route of administration changed
- IV dose of ranitidine changed from 150mg to 50mg
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The doctor prescribed ranitidine IV 150mg, which is the oral dose. After consultation it was changed to the appropriate 50mg.

*Due to system error or non-compliance; Factors hindering achievement of therapeutic efficacy*

These two categories of interventions are grouped together, as both of them resulted in the same outcome. A total of 28 (n=18 due to system error or non-compliance, and n=10 on factors hindering achievement of therapeutic efficacy) interventions were made in these categories, which comprises 15% of the 181 interventions made.

In 11 cases, the medication prescribed to the patient, were not received from the pharmacy. The researcher then intervened to obtain stock from the pharmacy, or to suggest an alternative where the pharmacy could not supply stock. (e.g. when pantoprazole IV was not available, cimetidine was used for a few days; enoxaparin 40mg was not available from the pharmacy, thus enoxaparin 80mg [half a dose] was used)

In three cases, the wrong dose was administered to the patient. This happened when imipenem 1g were prescribed, but only one 500mg vial was administered, or when fluconazole 400mg were prescribed, but only one 200mg vial was administered. In another three cases, doses were missed completely. One patient maintained a high blood pressure, because his amlodipine was not administered by the nursing staff.

Categories in which six (3.3%) or less interventions were made, included

- *Medication without indication*

In this category four (2.2%) interventions were made, with three being successful.

Mostly the problems encountered were antibiotic treatment prescribed without any indication, as the patients did not have clinical signs of infection.
The patient admitted from the medical ICU was treated with numerous antibiotics for longer than two weeks, without any positive blood cultures or infectious markers.

- **Relative safety of chosen medication**
  Successful interventions were three from five (2.7%) suggested interventions. Interventions included monitoring the kidney function (creatinine clearance) of patients treated with amikacin. Therapeutic drug monitoring of amikacin levels can be used to manage kidney damage, but requested levels were not taken regularly. Amikacin may cause renal impairment as the result of proximal tubular epithelial cell damage leading to obstruction of the tubular lumen and back leak of the glomerular filtrate across the damaged tubular epithelium. The toxicity of aminoglycosides is related to cationic charge, which facilitates binding of filtered aminoglycosides to renal tubular epithelial cell luminal membranes. Cellular dysfunction and death may result (Nolan, Abraham & Matzke:2002).

- **Comparative efficacy of chosen medication**
  In this category eight (4.4%) interventions were made, of which four were accepted.
  High potency broad spectrum antibiotics were changed to more appropriate first line treatment, according to standard treatment guidelines. When meropenem and metronidazole was prescribed to a patient empirically for a septic lesion on her face, piperacillin/tazobactam was suggested as an alternative, since metronidazole with meropenem is a duplication of spectrum. The use of carbapenems also needs to be reserved.
• **Therapy tailored to individual patient**
  All five (2.7%) of the interventions made in this category were accepted. Doses were tailored mostly on calculating the patients' creatinine clearance. Doses of vancomycin and fluconazole were adjusted accordingly. A female patient was admitted after a motorbike accident. Vancomycin was prescribed to treat a co-agulase negative *Staphylococcus* infection. Her renal function deteriorated to a point where she had a creatinine clearance of less than 50 (CrCl=45.35 ml/min). The vancomycin dose was adjusted to 1g per day (instead of 1g twice a day) until her renal function improved (CrCl=60.75 ml/min), then adjusted back to 1g twice a day.

• **Route/dosage form/mode of administration appropriate**
  A total of six (3.3%) of the 181 interventions were made in this category. Interventions made by the researcher included changing of continuous infusion of pantoprazole to 40mg twice a day after 72 hours. Paracetamol IV was also changed to the oral preparation after 24 hours, since the indication for paracetamol IV is only for short term use 24 hours post-operatively.

• **Therapeutic duplication**
  Therapeutic duplication appeared in only four (2.2%) instances. This usually happens when a patient has chronic hypertension treatment and the registrar prescribe hypertension treatment from the same therapeutic class in the ward, (e.g. enalapril and perindopril).

• **Symptoms drug induced, problem drug related; Use of social drugs problematic**
  These two categories can be combined, as all four (2.2%) interventions made were regarding patients’ use of Grand-Pa® and Compral® tablets. All patients concerned with this intervention were admitted to the S-ICU with bleeding gastric ulcers. Both the patients (when they were awake and not
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sedated anymore) and some of their family members were counseled on the dangers of patent pain medication.

- **Drug-Drug; Drug-Disease; Drug-Laboratory value interaction**
  When combined, this category constituted five (2.7%) of the 181 interventions. Drug-drug interactions included the interaction of cimetidine with metronidazole and ARV’s. An intervention was made on a drug-disease interaction with an asthma patient who smokes. He also received theophylline treatment, which was reduced after discussing it with the registrar. The drug-laboratory interaction was for a patient with very low albumin levels, treated with phenytoin. Phenytoin is highly protein bound and low albumin could result in a much higher fraction of free phenytoin.

- **Patient understand purpose, how to take, side effects**
  A total of four (2.2%) interventions were made in this category. This mostly includes education to the patient on what the purpose of their different medication is, and to keep on taking their chronic medication even though they are feeling better. One patient refused to take his hypertension medication, and after counselling him, he was more willing to co-operate.

4.2.4 **How were interventions achieved**

The interventions were made during ward rounds with the registrars or consultant. The researcher did a pharmaceutical care round first thing in the morning, (her work day started at 7:00) so that she could be up to date on the patients’ latest laboratory results and prescriptions. Thereafter the patient’s clinical status was known when a ward round was done with the registrars or consultant, and interventions could then be discussed during these rounds. The interventions were accepted or rejected immediately, and were then recorded on the *Pharmaceutical Care Worksheet*.
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Interventions made by the researcher concerning problems with the pharmacy, or counselling of patients or nursing staff, occurred after the ward round, and were then recorded on the *Pharmaceutical Care Worksheet*.

### 4.2.5 Factors which limited the achievement of pharmaceutical care

The study period was very short, and it took up a lot of time for the researcher to familiarize herself with the surroundings, ward routines and work procedures in the S-ICU. It also took a lot of time to build relationships with the doctors and nursing staff in the unit. Given more time, stronger relationships could have been established.

Rotating registrars were also a limitation, because at the beginning of each month new relationships had to be established, and the researcher had to again show the benefit of pharmaceutical care.

The slow turnaround time of results for various blood tests was a big limitation. Antimicrobial cultures need to be available more quickly to improve the use of antibiotics. Antibiotic therapy needs to be de-escalated more quickly than five or six days of treatment with potent broad spectrum antibiotics. Blood levels of anticonvulsants (phenytoin and valproate) were sometimes only available a day after the sample has been taken.

### 4.3 Perceived need for pharmaceutical care by healthcare professionals in S-ICU

At the beginning of the study and after completing the study, a needs assessment was performed with nursing staff and doctors (doctors only post-study), to determine the staff’s perception of the benefits of a pharmacist rendering pharmaceutical care in the ward setting. Separate questionnaires were used for nurses and doctors, and both nurses and doctors received an
information leaflet as well as a consent form to give permission to use their input in the study. (See Appendix 9, 10&11).

4.3.1 Doctors Questionnaires

Doctors questionnaires were only answered post-study, because they felt they were too busy in the ICU-setting to complete the questionnaires twice. There were three registrars per month rotating in the S-ICU, and one consultant who was responsible for the unit. He was supported by two temporary consultants doing rounds once a week and an international exchange physician. The questionnaires were completed by six registrars and one consultant. The registrars rotated only for one month in the ICU, thus in two and a half months, only six of the nine could be questioned. The registrars present during the first two weeks of the study period did not complete the questionnaires, since they did not spend enough time with the researcher.

The results of the questionnaires:

**Question 1:**

*Do you feel that there is a need for a pharmacist to routinely visit the ICU and High Care wards?*

All six registrars and the consultant felt that there was a need for a pharmacist to visit the ICU routinely.

Some verbatim comments:

“*Many decisions made during ICU ward rounds requires the input of a pharmacist*”

“*Polypharmacy is ubiquitous and drug interactions is under estimated.*”

“A pharmacist can detect interactions and inappropriate dosing”
**Question 2:**

*Do you benefit from having the pharmacist present in the wards while you are conducting ward rounds?*

All of the doctors completing the questionnaires felt that they have benefitted from having a pharmacist present in the ward.

A verbatim comment:

“The pharmacist provides very valuable and up-to-date information on drugs used in ICU”

**Question 3:**

*Is the pharmacist able to provide you with adequate information regarding your information requests?*

All seven doctors answered “Yes”, but did not give any comments.

**Question 4:**

*Do you feel that interventions made by a pharmacist would improve the rational use of antimicrobials in your department?*

All of the doctors completing the questionnaires felt that interventions made by the pharmacist improved the use of antimicrobials.

Some verbatim comments:

“Definitely – with the pharmacists’ input, much thought goes into prescribing antibiotics/antimicrobials.”

“Always – The use of antimicrobials need continuous improvement and assessment.”
Question 5:

*Do you feel that the provision of pharmaceutical care would decrease the expenditure of antimicrobials in your department?*

All seven doctors felt that pharmaceutical care would have a positive outcome on expenditure of antimicrobials in the ICU setting.

Some verbatim comments:

“Less interactions and less inappropriate medication use = less morbidity and less costs.”

“Antimicrobials are prescribed with great care in our department BUT the choice of antibiotic and interactions with other drugs will definitely be useful.”

### 4.3.2 Nurses Questionnaires

The questionnaires were administered to the nurses to determine the need for a pharmacist in the S-ICU ward setting, and also to determine the various functions they feel a pharmacist should perform at ward level. The nursing staff of the S-ICU consists of 38 registered nurses, working in two day-time and two night time shifts. (An average of nine registered nurses per shift) The permanent staff is supplemented by registered nurses from an agency. Questionnaires were distributed to 14 nursing sisters before commencement of the study and to nine nurses after the study were completed. At the end of the study, a lot of the nursing staff were on leave, since it was the Easter Holidays. The questionnaires were only distributed to the day staff, as the researcher was not working night duty.
The results of the questionnaires:

**Question 1:**

*Do you feel that there is a need for a pharmacist to routinely visit the ICU and High Care wards?*

One sister in the pre-study group felt that there is no need for a pharmacist to visit the ICU. The rest of the nursing staff (13) felt that they could benefit from a pharmacist visiting the ward, and of the post-study group all felt that there is a need for a pharmacist to visit the ward.

Some verbatim comments:

“The pharmacist needs to advice, correct and monitor correct usage of drugs and other pharmaceutical components.”

“She can give input during rounds on best option for the patient.”

“Desperately”

“She will be able to help staff with drug education, and checking of drug interactions.”

“She can advise doctors on the correct dosage of drugs and how to give them.”

“To advise the doctors about the doses and effectiveness of treatment.”

The comment from the nurse who answered that there is not a need for a pharmacist in the S-ICU:

“As long as there is always a pharmacist available, within the hospital, that can be contacted easily.”
Question 2:

*What activities do you feel the pharmacist could fulfil within your department?*

Activities listed were:

- Patient counselling/education
- Drug identification
- Prescription chart reviews
- Drug ordering for patients
- Checking for drug interactions
- Staff education
- Checking ward stock for expiries
- Dealing with pharmaceutical queries
- Schedule 5,6 ordering
- Checking for adverse drug reactions.

Figure 4.10 shows the activities which they feel a pharmacist should perform in the ward setting.
Figure 4.10: Pharmacist functions in the ward as perceived by nursing staff

The functions that the nursing staff felt a pharmacist should perform included mainly dealing with pharmaceutical queries (13.93%), checking for adverse drug reactions (13.93%) and prescription chart reviews (12.72%). The researcher performed these functions on a daily basis while rendering pharmaceutical care to all the patients in the study. They also felt a pharmacist should check ward stock expiry dates, which the researcher did twice during the study period. Drug identification and drug ordering for patients was only done when required, and assistance with ordering was only done in special circumstances, e.g. when authorization was needed to acquire a product. The researcher never ordered schedule 5 and 6 drugs as the counting and ordering of scheduled medication was done by the night staff. The researcher assisted once when receiving scheduled medication, and ensured that the registers balanced.
CHAPTER 4: RESULTS AND DISCUSSION

**Question 3:**

*Do you feel that a pharmacist round would facilitate improved drug distribution to your department?*

All of the nursing staff, pre- and post-study, felt that a pharmacist round would facilitate improved drug distribution to their department. They also felt that a pharmacist round will improve the service delivery to the department.

Some comments from nursing staff:

“To prevent over-stocking by personnel.”

“The pharmacist helped a lot with communication with pharmacy staff.”

“She is more educated on different drugs and would decrease activities of nursing staff.”

“Because she will be able to see if the medicines ordered has been issued and that patient get their medication at due time.”

“She will provide better communication when e.g. motivation for medication is needed and the treatment ordered for patient.”

“Correct amounts of drugs will be available for at least 24 hours until she comes on duty the following day.”

“She will intervene where there is a problem with prescribed medication.”

**Question 4:**

*Do you feel that there is a need for weekly education sessions with the pharmacist?*

Only two of the nursing staff felt that they don’t have a need for education sessions with the pharmacist. Both of these were pre-study, and they felt that
there is not enough time in the busy schedule of ICU for education sessions. These are the two comments quoted verbatim pre-study:

“ICU is a busy unit so if everyone does their work there is no need.”

“Nurses need only the basics of pharmacology. We are not pharmacists – in service training appreciated though.”

The rest of the staff (21; n=23) all felt that there is a need for education sessions, although there were some suggestions on doing it only once a month, and in short 10-15 minute sessions, since the unit is very busy. There were also some suggestions from them on training topics, e.g. types of antibiotics, drug interactions and administration methods.

Some comments on education:

“Trade names and brands change and nursing staff have to be kept updated.”

“To update nurses and doctors with recent information regarding drugs.”

“Even though she’s leaving, she will leave valuable information behind in the unit.”

“In order to familiarize personnel on drug interactions, prices and importance of giving certain drugs instead of others.”

“Takes time to teach and explain new drugs.”

Training given to the nursing staff by the researcher included a session on the legality of ICU prescriptions, a session on the interaction of sucralfate with oral multivitamin syrup and a session on the appropriate solvents used for mixing of certain intravenous medication. One-on-one impromptu training was also given to nursing staff at the patient’s bedside, on the correct dosing of antibiotics (the correct strength per dose of antibiotics like imipenem, ciprofloxacin and fluconazole). Short discussions were also initiated on the importance of administering ARV therapy on time and administering blood pressure medication.
regularly. In conclusion, there is a definite need for education on medications for nursing staff.

### 4.4 Time spent in ward

The time spend in the ward was recorded every day on the form titled “Pharmacist time spent in the Ward” (See Appendix 2) from the beginning of the study period which started on 14 February 2011 up to 25 April 2011. The time taken for different ward functions was recorded every day after pharmaceutical care was rendered to the ward.

It was challenging to keep track of the exact time spent on each intervention for each specific patient, as most of the interventions were done during ward rounds. Time spent on checking ward stock and handling stock queries from the pharmacy were listed separately, as the pharmaceutical care forms did not allow room for recording these interventions.

The time spent in the ward included the total duration of the study period (14 February to 26 April 2011) during working hours from Mondays to Fridays, excluding a total of 16 working days, i.e.:

- Six days study leave
- Ten days annual leave

The total time spent providing pharmaceutical care services within the Surgical ICU over the study period was 33 days (250 hours). The average time spent providing pharmaceutical services was 7.45 hours per day. The minimum hours spent in the ICU were 2.15 hours, and the maximum hours spent were 10.3 hours.
4.4.1 Functions performed by the pharmacist while rendering pharmaceutical care

Figure 4.11 shows the percentage of time the pharmacist spent on different functions in the ward, including pharmaceutical care interventions.

The researcher usually did a pharmaceutical care round first thing in the morning, where the patient evaluation was done, so she would be up to date on the patients’ status when attending the ward round with registrars and consultants.

Since Steve Biko hospital is a training hospital, ward rounds were done with registrars, dieticians, physiotherapists, microbiologists and even clinical technicians.

Ward functions that were performed included checking of ward stock expiry dates, checking of ward stock levels and giving information on different drugs. Two formal training sessions were done on the legality of prescriptions, and what is required from a ward prescription. A document was also compiled for the ward on the use of specific solvents for medications used in the ward (See Appendix 14).

The meetings that were attended included the two-weekly critical care meeting, the mortality and morbidity meeting of the department and the antibiotic stewardship meeting of the hospital.
CHAPTER 4: RESULTS AND DISCUSSION

Figure 4.1: Percentage of time spent in the ward

- Patient evaluation: 28.50%
- Ward rounds: 18.07%
- Ward functions: 7.83%
- Meetings: 6.33%
- Drug monitoring: 21.70%

n = 250 hours

Patient evaluation included reviewing the patients prescription chart, vital signs like temperature and blood pressure and laboratory results. This information was indicated on the pharmaceutical care form every day. On the grounds of these pharmaceutical care rounds, interventions could later be suggested on the ward rounds with the registrars or consultant.

On some instances more than one ward round was done per day, because of the different specialties doing rounds. These rounds were very interactive, and the researcher got a lot of information from them.

Drug monitoring was done by evaluating the patients’ prescription charts, and monitoring the medication orders from the pharmacy as well as the dosing of the different medications. The pharmacist checked that the correct medication was received from the pharmacy, and that it was administered correctly to the patient.

The researcher spent an average of 7.45 hours per day during the study period on the provision of pharmaceutical care. This included the functions performed in the ward and meetings attended. After the two month period, it can be established
that a pharmacist can definitely play a role in the ward-setting, and that there is enough tasks to perform to warrant a full time position for a clinical pharmacist in the ICU setting.

4.5 Cost of treatment used by patients before and after provision of pharmaceutical care

Table 4.8 shows the daily cost difference for the patients where interventions were successful. These are the costs of antibiotics and other medication used by patients the day before the provision of pharmaceutical care and the day after. The cost difference was R14 353.19. The study number of the patient on whom the intervention was made, is listed in column 1. The specific interventions made during the study period and the outcomes are also listed. The last column states the amount saved by the intervention. This amount is only a direct calculation and only the cost for one day after the intervention. No calculations were made for indirect cost implications of interventions.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Problem</th>
<th>Outcome of intervention</th>
<th>Cost saving</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meropenem &amp; metronidazole administered together</td>
<td>Stop both &amp; change to Piperacillin/tazobactam</td>
<td>R1692.36</td>
</tr>
<tr>
<td>1</td>
<td>Meropenem dose 2g 8h (only indicated for use in treatment of meningitis)</td>
<td>Change dose to 1g 8h</td>
<td>R856.53</td>
</tr>
<tr>
<td>2</td>
<td>Piperacillin/tazobactam treatment day 9</td>
<td>Stop treatment</td>
<td>R359.58</td>
</tr>
<tr>
<td>3</td>
<td>Pantoprazole continuous infusion &gt;72hrs; treatment only indicated for 72 hours.</td>
<td>Change dose to 40mg bd</td>
<td>R255.86</td>
</tr>
<tr>
<td>6</td>
<td>Cefazolin day 7; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R53.58</td>
</tr>
<tr>
<td>6</td>
<td>Adjust vancomycin dose according to CrCl (low)</td>
<td>Change dose to 500mg bd</td>
<td>R92.20</td>
</tr>
<tr>
<td>6</td>
<td>Vancomycin day 7; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R146.72</td>
</tr>
<tr>
<td></td>
<td>Treatment/Prescription</td>
<td>Change/Action</td>
<td>Cost</td>
</tr>
<tr>
<td>---</td>
<td>------------------------</td>
<td>---------------</td>
<td>-------</td>
</tr>
<tr>
<td>7</td>
<td>Pantoprazole continuous infusion &gt;72hrs; treatment only indicated for 72 hours</td>
<td>Change dose to 40mg bd</td>
<td>R336.96</td>
</tr>
<tr>
<td>8</td>
<td>Meropenem dose 2g 8h (only indicated for use in treatment of meningitis)</td>
<td>Change dose to 1g 8h</td>
<td>R818.85</td>
</tr>
<tr>
<td>10</td>
<td>Adjust Fluconazole dose according to CrCl (low)</td>
<td>Change dose to 200mg d</td>
<td>R1142.04</td>
</tr>
<tr>
<td>10</td>
<td>Meropenem day 7; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R33.10</td>
</tr>
<tr>
<td>13</td>
<td>Co-amoxiclav was prescribed for only 3 days</td>
<td>Stop treatment</td>
<td>R84.93</td>
</tr>
<tr>
<td>15</td>
<td>Piperacillin/tazobactam and cloxacillin administered together – duplication of spectrum</td>
<td>Stop cloxacillin</td>
<td>R107.92</td>
</tr>
<tr>
<td>17</td>
<td>Perindopril and enalapril prescribed together – therapeutic duplication</td>
<td>Stop perindopril</td>
<td>R14.36</td>
</tr>
<tr>
<td>17</td>
<td>Meropenem and ciprofloxacin day 10; patient’s infection markers improved</td>
<td>Stop treatment</td>
<td>R1841.43</td>
</tr>
<tr>
<td>26</td>
<td>Piperacillin/tazobactam day 9; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R359.58</td>
</tr>
<tr>
<td>26</td>
<td>Meropenem day 10; course completed for treatment of <em>S. marcescens</em></td>
<td>Stop treatment</td>
<td>R856.71</td>
</tr>
<tr>
<td>27</td>
<td>Cefazolin prophylaxis &gt;48hrs</td>
<td>Stop treatment</td>
<td>R53.58</td>
</tr>
<tr>
<td>30</td>
<td>Meropenem and metronidazole together- therapeutic duplication</td>
<td>Stop metronidazole</td>
<td>R16.98</td>
</tr>
<tr>
<td>30</td>
<td>Imipenem day 8; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R1067.52</td>
</tr>
<tr>
<td>29</td>
<td>Co-amoxyclov day 5; only prescribed for 5 days</td>
<td>Stop treatment</td>
<td>R84.93</td>
</tr>
<tr>
<td>31</td>
<td>Meropenem dose 2g 8h (only indicated for use in treatment of meningitis)</td>
<td>Change dose to 1g 8h</td>
<td>R818.85</td>
</tr>
<tr>
<td>31</td>
<td>Cefazolin day 5; only prescribed for 5 days</td>
<td>Stop treatment</td>
<td>R53.58</td>
</tr>
<tr>
<td>33</td>
<td>Meropenem, amikacin, vancomycin day 18; no indication for long antibiotic use</td>
<td>Stop treatment</td>
<td>R1030.42</td>
</tr>
<tr>
<td>33</td>
<td>Pantoprazole continuous infusion &gt;72 hours; treatment only indicated for 72 hours</td>
<td>Change dose to 40mg bd</td>
<td>R255.86</td>
</tr>
<tr>
<td>35</td>
<td>Pantoprazole continuous infusion &gt;72 hours; treatment only indicated for 72 hours</td>
<td>Change dose to 40mg bd</td>
<td>R255.86</td>
</tr>
<tr>
<td>39</td>
<td>Paracetamol IV only for 24 hours; only indicated for 24 hours post-operative</td>
<td>Change to oral paracetamol 1g 8h</td>
<td>R143.20</td>
</tr>
<tr>
<td>42</td>
<td>Paracetamol IV only for 24 hours; only indicated for 24 hours post-operative</td>
<td>Change to oral paracetamol 1g 8h</td>
<td>R143.20</td>
</tr>
<tr>
<td>42</td>
<td>Piperacillin/tazobactam day 11; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R479.44</td>
</tr>
<tr>
<td>43</td>
<td>Cefazolin day 9; patient’s infection markers normal</td>
<td>Stop treatment</td>
<td>R53.58</td>
</tr>
</tbody>
</table>
The additional cost due to pharmaceutical care interventions are depicted in Table 4.9. In these instances an additional medication was suggested by the researcher, or the prescriber was reminded of a medication that was left out on the patient’s prescription. The positive outcome resulted in a prescription and supply of medication. The cost was calculated for the difference of the cost the day before the intervention and the day after the intervention. The total additional cost for the study period was R92.68.

### Table 4.9: Medication cost increases

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Problem</th>
<th>Outcome</th>
<th>Additional cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>Patient need antibiotic for bowel spill; antibiotic indicated</td>
<td>Suggest co-amoxyclov since the soiling was not severe</td>
<td>R47.25</td>
</tr>
<tr>
<td>46</td>
<td>Pyridoxine not prescribed with TB medication</td>
<td>After discussion, registrar prescribed pyridoxine 25mg daily</td>
<td>R1.47</td>
</tr>
<tr>
<td>34</td>
<td>Patient phosphate levels low; needs to be supplemented</td>
<td>Supplement with phosphate syrup</td>
<td>R3.14</td>
</tr>
<tr>
<td>17</td>
<td>Chronic blood pressure medication not prescribed; patient is a known hypertensive, though not on treatment since admitted to the ward</td>
<td>Prescribed perindopril and amlodipine (chronic treatment)</td>
<td>R19.61</td>
</tr>
<tr>
<td>43</td>
<td>Patient phosphate levels low; needs to be supplemented</td>
<td>Supplement with phosphate syrup</td>
<td>R3.14</td>
</tr>
<tr>
<td>29</td>
<td>Patient has distended abdomen and vomiting – suggest prokinetic agent</td>
<td>Metoclopramide and Lactulose syrup prescribed</td>
<td>R18.07</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>R92.68</strong></td>
</tr>
</tbody>
</table>

The cost saved by the pharmacist in the ward during the study period was enough to appoint a part time pharmacist to the ward on a permanent basis. Only the direct cost saving was calculated, and only for one day after the intervention. Potentially, the cost saving can be more. Having a pharmacist as a permanent member of the multidisciplinary team may be a great cost saving benefit for the unit.
4.6 **Antibiotic protocol**

An antibiotic protocol was designed by the researcher for the surgical ICU, after the procedures done regularly in the ICU and the resistance patterns of the unit were studied. The protocol were designed according to international standards, and adapted for use in the specific unit (Ballot *et al*.:2007).

The protocol includes definitions for prophylactic antibiotic treatment, empiric antibiotic treatment and treatment of specific conditions. A septic screen needs to be done before the commencement of antibiotics. This includes a full blood count, blood cultures, inflammatory markers, urine microscopy, culture and sensitivity as well as chest X-rays. The optimum duration of treatment for prophylactic and empiric treatment is also discussed.

The protocol consists of two sections, one for the prophylactic treatment for different procedures, and one for the empiric treatment of different conditions. The protocol also offers alternatives for patients with penicillin allergies, and dose-adjustments for patients with renal impairment.

Figure 4.12 illustrates an excerpt of the protocol. The full protocol is also attached as Appendix 15.
## SURGICAL ANTIBIOTIC PROPHYLAXIS

<table>
<thead>
<tr>
<th>Orthopaedic surgery</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery</td>
<td>Likely pathogens</td>
</tr>
<tr>
<td>Joint replacement</td>
<td><em>S. aureus</em>, <em>S. epidermidis</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastro-intestinal surgery</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery</td>
<td>Likely pathogens</td>
</tr>
<tr>
<td>Colo-rectal and appendectomy</td>
<td>Enteric Gram negative bacilli, anaerobes</td>
</tr>
</tbody>
</table>

*Figure 4.12: Sample of the Antibiotic Protocol of S-ICU*

The first column states the type of surgery, and the second column the likely pathogens present at the site of incision. The third column is the recommendation for antibiotic prophylactic regimen, which also include alternatives for β-lactam allergies. The last column provides comments on high-risk patients or where complications are encountered or alternative therapy is needed.

The same format was used for empiric treatment of different infections, with likely pathogens and recommended empiric treatment. The protocol on empiric treatment also includes a column with necessary microbiologic specimens to be taken when treatment starts.

Implementation of the protocol in the ward took place after feedback from the microbiologist was incorporated and the protocol was approved by Professor Jan Pretorius, the head of the Critical Care Department. Unfortunately, implementation took place right at the end of the study period, and no measure of
CHAPTER 4: RESULTS AND DISCUSSION

the influence on antibiotic prescribing patterns could be established. This will be a recommendation for a future study.
5.1 Limitations

The limitations and challenges encountered whilst conducting the research will be discussed under three headings:

- **Time**
  The study period was very short and it took considerable time for the researcher to familiarize herself with the surroundings and routines in the unit. More time is also needed to establish good relationships with the doctors and medical staff in the ward.

- **TDM and other Laboratory Results**
  The performing of therapeutic drug monitoring was compromised because often the procedure for collecting blood samples or TDM was not followed, or the results of the levels taken were not available in time. The antimicrobial culture results also need to be available more readily to ensure effective de-escalation of antimicrobial treatment.

- **Academic Setting**
  The rotation of registrars limited the building of a relationship with prescribing doctors, since they worked in the unit for only four weeks at a time.

5.2 Conclusions

**Pharmaceutical care**

The aim of this study was to assess the need for the provision of pharmaceutical care in the Surgical ICU of Steve Biko Academic Hospital. The nurses and the
doctors also identified that the pharmacist is an integral part of the multidisciplinary team. The provision of PC focused on the role of the pharmacist in assessing prescribing patterns, recognizing and recording drug-related interventions and the time needed to provide pharmaceutical care by a pharmacist to a ward.

Before the study, the staff in the Surgical ICU only had contact with a pharmacist, when the pharmacist or pharmacist-intern came to the ward to order the ward-stock. They also knew the pharmacist as someone who presented them with problems if they needed certain medications for their patient. No clinical or pharmaceutical care was available in the ward. The researcher extended the role of the pharmacist in the ward by establishing a ward-based system including patient care, educational activities and direct communication with the hospital pharmacy.

Interventions

Interventions were required regarding a wide variety of drug-related problems; from therapy that was not tailored to the individual patient’s needs, to problems with dosages and duration of use, and laboratory results that were outstanding. Interventions suggested at ward rounds supplied a good platform for discussions regarding the correct use of antimicrobials, or specific doses of medications.

Comments from doctors and nursing staff

Both the doctors and nursing staff indicated that they can benefit from having a pharmacist present in the ward as part of the multidisciplinary team. As the relationship with the pharmacist developed, they relied more on the input of the pharmacist during ward rounds and on decision-making regarding especially antimicrobial prescribing. Nursing staff came to rely on the researcher for assistance with ward stock and communication with pharmacy personnel.
CHAPTER 5: LIMITATIONS, RECOMMENDATIONS

Time spent in the Ward

Although the study period was short, the researcher has shown that clinical services can be an integral part of patient care provided. The more time the researcher spent on clinical functions and interventions in the ward, the more she became part of the clinical health care team in the ward. Registrars and nursing staff felt more at ease asking drug-related questions as the study period progressed.

Antibiotic prescribing patterns

The general antibiotic prescribing patterns in the ward were not according to any antibiotic protocol. However, a close watch was kept on antibiotic prescribing, and generally antibiotics were not grossly misused. Although the unit had a policy of antibiotic cycling regarding the use of the carbapenems, they misinterpreted the term cycling, and alternate the use of meropenem and imipenem between patients in the ward, and not over time.

The pharmacist also intervened at patient level to optimize the dosing and duration of antibiotics, e.g. vancomycin. Having the pharmacist present at the ward round also forced registrars to put some thought into antibiotic prescribing, and a few discussions happened on the ward round regarding appropriate antibiotic use.

The amount of medication prescribed to the patients admitted to the unit during the study period provided opportunities for the researcher to perform numerous interventions, and the conclusion can be made that the continued presence of a pharmacist in the ward will be beneficial to the patients’ outcomes. The provision of pharmaceutical care has the potential to improve the quality of care.

5.3 Recommendations

Based on the findings of this study, the researcher proposes recommendations aimed at promoting pharmaceutical care in an Intensive Care Unit.
• The pharmacist needs a longer period of induction to the routines and surroundings of the intensive care unit. Alternatively a permanent pharmacist needs to be appointed to the unit to be able to provide a consistent level of care to patients in the ward.

• The pharmacist needs to build a good relationship with the department of microbiology, so that drug serum-level results and results of microbial cultures could be obtained faster.

• The use of the antibiotic protocol for the ward needs to be enforced. A permanent clinical pharmacist can assist with this function.

Further studies may be conducted to establish the current microbial resistance patterns in the ward, and to further develop the antimicrobial guidelines for the ward.

The antimicrobial protocol and the influence on prescribing patterns and resistance in the unit need to be tested in a further study.

A more intensive study of the direct and indirect cost implications of having a pharmacist present in the ward is also recommended.
REFERENCES


REFERENCES


REFERENCES


Kollef MH. 2006. Is antibiotic cycling the answer to preventing the emergence of bacterial resistance in the intensive care unit? *Clinical Infectious Diseases*, 43:S82-8.


REFERENCES


REFERENCES


REFERENCES


WHO Collaborating Centre for Drug Statistics Methodology. Available at http://whocc.no/atc_ddd_index (Assessed 15 September 2011)


## Appendix 1: Pharmacists’ patient database forms

### PHARMACEUTICAL CARE FORMS

### PHARMACIST PATIENT DATABASE FORM

<table>
<thead>
<tr>
<th>STUDENT NAME:</th>
<th>DATE:</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDENT NO:</td>
<td>(COMMENCEMENT OF PHARMACEUTICAL CARE)</td>
</tr>
</tbody>
</table>

### DEMOGRAPHIC AND ADMINISTRATIVE INFORMATION

<table>
<thead>
<tr>
<th>Name:</th>
<th>Patient No:</th>
<th>Ward No:</th>
<th>Bed No:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td>Dr:</td>
<td>Date of birth/age:</td>
<td>Gender: M / F</td>
</tr>
<tr>
<td>Height:</td>
<td>Weight:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission date:</td>
<td>Discharge date:</td>
<td>Occupation:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HISTORY OF PRESENT ILLNESS</th>
<th>VITAL SIGNS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O/A</td>
</tr>
<tr>
<td></td>
<td>WEIGHT</td>
</tr>
<tr>
<td></td>
<td>TEMP</td>
</tr>
<tr>
<td></td>
<td>BP</td>
</tr>
<tr>
<td></td>
<td>PULSE</td>
</tr>
<tr>
<td></td>
<td>RESPIRATION</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PAST MEDICAL HISTORY/SURGERY</th>
<th>MEDICATION PRIOR TO REVIEW DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chronic:</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute:</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FAMILY AND SOCIAL HISTORY</th>
<th>SOCIAL DRUG USE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ALCOHOL: Y / N</td>
</tr>
<tr>
<td></td>
<td>CAFFEINE: Y / N</td>
</tr>
<tr>
<td></td>
<td>TABACCO: Y / N</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LIFESTYLE</th>
<th>ALLERGIES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO KNOWN DRUG ALLERGIES</td>
</tr>
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### PHARMACIST’S PATIENT DATABASE FORMS

**CURRENT DRUG THERAPY**

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<td><strong>Problem list, Clinical Response, Changes</strong></td>
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Patient name: ____________________________
Patient number: ____________________________
Weight: ____________________________
Ward number: ____________________________
Pharmacist: ____________________________
PHARMACIST’S PATIENT DATABASE FORMS

LABORATORY DATA

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OTHER MONITORING PARAMETERS
PHARMACIST’S PATIENT DATABASE FORMS

MICROBIOLOGY

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<th>Date</th>
<th>Sample</th>
<th>Organism</th>
<th>Day Cultured</th>
<th>Sensitivity</th>
<th>Diagnosis</th>
<th>Antimicrobial Rx</th>
<th>Cost Implication</th>
<th>Intervention made</th>
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<td>Category of Problem</td>
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<tr>
<td><strong>Correlation between drug therapy and medical problem</strong></td>
<td>1. Are there drugs without medical indication?</td>
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<td>2. Are there medication unidentified (not labelled or unknown)?</td>
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<td>3. Are there untreated medical conditions? If “Yes”, do they require drug therapy?</td>
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<td>4. Are investigations indicated or outstanding</td>
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<td><strong>Appropriate drug selection</strong></td>
<td>5. What is the comparative efficacy of the chosen medication?</td>
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<td>6. What is the relative safety of the chosen medication(s)? Are there contraindications, precautions or warnings to consider?</td>
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<td>7. Has the therapy been tailored to this individual patient?</td>
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<td><strong>Drug regimen</strong></td>
<td>8. Are the prescribed doses and dosing frequency appropriate (within the usual therapeutic range and/or modified for patient factors)?</td>
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<td>9. Is the route/dosage form/mode of administration appropriate, considering efficacy, safety, convenience, patient limitations and cost?</td>
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<td>10. Are doses scheduled to maximize therapeutic effect and compliance and to minimize adverse effects, drug interaction and regimen complexity?</td>
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<td>11. Is the length or course of therapy appropriate?</td>
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<td><strong>Therapeutic duplication</strong></td>
<td>12. Is there any therapeutic duplication?</td>
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<td><strong>Drug allergy or intolerance</strong></td>
<td>13. Is the patient allergic to or intolerant of any medicine (or chemically related medications currently being taken)?</td>
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<td>14. Is the patient using any method to alert health care providers of the allergy/intolerance (or serious medical problem)?</td>
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<td><strong>Adverse drug events</strong></td>
<td>15. Are there symptoms or medical problems that may be drug induced? What is the likelihood that the problem is drug related?</td>
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<td><strong>Interactions</strong></td>
<td>16. Are there drug-drug interactions? Are they clinically significant?</td>
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<td>17. Are any medications contraindicated given patient characteristics and current/past disease states?</td>
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<td>18. Are there drug-nutrient interactions? Are the clinically significant?</td>
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<td>19. Are there drug-laboratory test interactions? Are they clinically significant?</td>
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<td><strong>Social or recreational drug use</strong></td>
<td>20. Is the patient’s current use of social drugs problematic?</td>
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<td>21. Could sudden decrease or discontinuation of social drugs be related to patients symptoms?</td>
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<td><strong>Failure to receive therapy</strong></td>
<td>22. Has the patient failed to receive a medication due to system error or non-compliance?</td>
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<td>23. Are there factors hindering the achievement of therapeutic efficacy?</td>
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<td><strong>Financial impact</strong></td>
<td>24. Is the chosen medication(s) cost effective?</td>
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<td>25. Does the cost of the drug therapy represent a financial hardship for the patient?</td>
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<td><strong>Patient knowledge of drug therapy</strong></td>
<td>26. Does the patient (or carer) understand the purpose of his/her medication(s), how to take it, and the potential side effects of therapy?</td>
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<td>27. Would the patient (or carer) benefit from education tools (written patient education sheets, wallet cards or reminder packaging)?</td>
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1. A problem exists
2. More information is needed for a determination
3. No problem exists or an intervention is not needed
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<th>Problem No.</th>
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<th>Description of problem</th>
<th>Proposed Action / Intervention</th>
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## PHARMACIST’S CARE PLAN MONITORING WORKSHEET (MW)

Patient name: __________________________

Patient number: __________________________

Ward number: __________________________

Pharmacist: __________________________

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<th>Description of problem</th>
<th>Proposed action / Intervention / Monitoring Parameter(s)</th>
<th>Pharmacotherapeutic Goals and Desired Endpoints</th>
<th>Outcome(s) Achieved? Y / N</th>
<th>Explain How / Why Outcome was Achieved / Not Achieved</th>
<th>Consultant with whom Intervention was Discussed</th>
<th>Cost Implication of Implementation of Intervention</th>
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Appendix 2: Pharmacist’s Time Spent in the Ward

Date: ______________________

Start time: ____________________

Number of patients present in ward: ______________________

Time spent per patient: ____________________________ min

Time spent per pharmaceutical care intervention: ______________________ min

List other ward functions time spent on:

• ___________________________________

• ___________________________________

• ___________________________________

• ___________________________________

• ___________________________________

• ___________________________________

• ___________________________________

• ___________________________________

End time: ______________________
Appendix 3: Pharmaceutical care doctor’s questionnaire

Doctor’s Details

Rank: __________________________

Questions

1. Do you feel there is a need for a pharmacist to routinely visit the ICU and High Care wards?
   Yes: ☐
   No: ☐
   Comment: ___________________________________________________________________

2. Do you benefit from having the pharmacist present in the wards while you are conducting your ward rounds?
   Yes: ☐
   No: ☐
   Comment: ___________________________________________________________________

3. Is the pharmacist able to provide you with adequate information to your information requests?
   Yes: ☐
   No: ☐
   Comment: ___________________________________________________________________

4. Do you feel that interventions made by a pharmacist would improve the rational use of antimicrobials in your department?
   Yes: ☐
   No: ☐
   Comment: ___________________________________________________________________

5. Do you feel that the provision of pharmaceutical care would decrease the expenditure of antimicrobials in your department?
   Yes: ☐
   No: ☐
   Comment: ___________________________________________________________________
Appendix 4: Pharmaceutical care nurses’ questionnaire

Sister’s Details
Rank: __________________________

Questions:

1. Do you feel that there is a need for a pharmacist to routinely visit the ICU and High Care wards?
   Yes: 
   No: 
   Comment: 
   ________________________________________________________________

2. What activities do you feel the pharmacist could fulfill within your department?

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<th>Patient counselling/education</th>
<th>Staff education</th>
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<tbody>
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<td>Drug identification</td>
<td>Checking ward stock for expiries</td>
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<td>Prescription chart reviews</td>
<td>Dealing with pharmaceutical queries</td>
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<tr>
<td>Drug ordering for patients</td>
<td>Schedule 5, 6 ordering</td>
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<tr>
<td>Checking for drug interactions</td>
<td>Checking for adverse drug reactions</td>
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<td>Other:</td>
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</table>

3. Do you feel that a pharmacist round would facilitate improved drug distribution to your department?
   Yes: 
   No: 
   Comment: 
   ________________________________________________________________

4. Do you feel that there is a need for weekly education sessions with the pharmacist?
   Yes: 
   No: 
   Comment: 
   ________________________________________________________________
Appendix 5: Letter of intent

Dr BJ Ribeiro
Steve Biko Academic Hospital

Dear Dr Ribeiro

Letter of intent to conduct an operational study

We hereby requesting for Elmen Bronkhorst to conduct a study in the general surgical ward at Steve Biko Academic Hospital. Mrs Bronkhorst is enrolled for an MSc (Med) in Pharmacy at the University of Limpopo. Attached please find the proposal for the study entitled: “An assessment of the need for pharmaceutical care in the Intensive Care Unit (ICU) and High Care Unit of Steve Biko Academic Hospital in Gauteng Province”

The study has been approved by Prof J Pretorius who will also co-supervise the study. The proposal will be submitted to the School of Health Care Sciences and the Medunsa Research and Ethics Committee at the University of Limpopo (Medunsa Campus). The proposal will also be submitted to the University of Pretoria’s Ethics Committee for approval.

The aim of the study is:
To determine the need for provision of pharmaceutical care from the pharmacist to the ICU and High Care Unit of Steve Biko Academic Hospital.
The objectives are:
- To determine the need for the pharmacist at the ICU and High Care Unit
Appendix 6: Consent to given to access files/data base

PERMISSION TO ACCESS RECORDS / FILES / DATA BASE AT:
THE DEPARTMENT OF CRITICAL CARE – STEVE BIKO ACADEMIC HOSPITAL

13 October 2010

I, Prof JP Pretorius Head of Department of Critical Care hereby give Ms ElmienBronkhorst permission to do the following research study: “An assessment of the need for pharmaceutical services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province “at Steve Biko Academic Hospital in this Department and to access the information as requested.

Yours sincerely

Prof. J.P. Pretorius
MBChB (UP) MMed (Chir)(UP)
FCS (SA)
Head: Department Critical Care
Principal Specialist

Note: A signed copy of this letter will follow on Monday, 18 October 2010, as Prof Pretorius is currently not available for signature.

Faculty of Health Sciences
Department of Critical Care
Appendix 7: Ethical Clearance Certificate: Medunsa

UNIVERSITY OF LIMPOPO
Medunsa Campus

MEDUNSA RESEARCH & ETHICS COMMITTEE

CLEARANCE CERTIFICATE

MEETING: 02/09/11

PROJECT NUMBER: MREC/10/2011. P3

PROJECT:
Title: An assessment of the need for Pharmaceutical services in the intensive care unit and adult high care unit of Steve Biko Academic Hospital in Gaaieng

Researchers:
Mrs H Boehmick
Supervisor:
Dr N Boehmick
Co-supervisor:
Prof J Pretorius (University of Pretoria)
Prof ACG Gona

Hospital Superintendent:
Dr BL Roberts (Steve Biko Academic Hospitals)

Department:
Pharmacy

School:
Health Care Sciences

Degree:
MSc (Med) Pharmacy

DECISION OF THE COMMITTEE:

MREC approved the project.

DATE: 10 March 2011

[Signature]

PROF CA OGUNSANJO
CHAIRPERSON MREC

Notes:
1) Should any deviation be contemplated from the research procedure as approved, the researcher(s) must resubmit the proposal to the Committee.
2) The budget for the research will be considered separately from the protocol. PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.
The Research Ethics Committee, Faculty of Health Sciences, University of Pretoria, complies with ICH-GCP guidelines and has US Federal wide assurance.

* FWA 00002567, Approved dd 22 May 2002 and Expires 13 Jan 2012.

Appendix 8: Ethical Clearance certificate:
University of Pretoria

Faculty of Health Sciences Research Ethics Committee
Fakulteit Geneeskundewetenskappe Navoringsetiekskomitee

<table>
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<td>An assessment of the need for pharmaceutical service is the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province</td>
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<tr>
<td>INVESTIGATOR</td>
<td>Principal Investigator: Elmiem Bronkhorst</td>
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<tr>
<td>SURVEY INVESTIGATOR</td>
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</tr>
<tr>
<td>SUPERVISOR</td>
<td>Dr N Schellack  E-Mail: <a href="mailto:nscshellack@gmail.com">nscshellack@gmail.com</a></td>
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<tr>
<td>DEPARTMENT</td>
<td>Dept: Pharmacy  Phno: 082 747 1906  Fax: 012 387 0376</td>
</tr>
<tr>
<td>E-Mail: <a href="mailto:elmiem.bronkhorst@gmail.com">elmiem.bronkhorst@gmail.com</a></td>
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<tr>
<td>STUDY DEGREE</td>
<td>MSc(Med) Pharmacy</td>
</tr>
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<td>MEETING DATE</td>
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The Protocol and Informed Consent Document were approved on 26/01/2011 by a properly constituted meeting of the Ethics Committee subject to the following conditions:
1. The approval is valid for 1 year period [till the end of December 2011], and
2. The approval is conditional on the receipt of 6 monthly written Progress Reports, and
3. The approval is conditional on the research being conducted as stipulated by the details of the documents submitted to and approved by the Committee. In the event that a need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

Members of the Research Ethics Committee:

Prof M J Bester  [female] BSc (Chemistry and Biochemistry), BSc (Hons)(Biology), MSc(Biochemistry), PhD (Medical Biochemistry)
Prof R Deport  [female] BA at Sci., BComp (Hons) (Research Methodology), M Sc. (Physiology), PhD (Medicine), M Ed (Computer Studies in Education)

Prof TA Ker  [female] MSc(Pharm), MD – Vice-Dean (ex officio)
Dr NK Lakibi  [female] MSc in Pharmacy – Representing Gauteng Department of Health
Prof TS Marcus  [female] BSc(LBIE), PhD (University of Lodzi, Poland) – Social scientist
Dr MP Mathebula  [female] Deby CEO: Steve Biko Academic Hospital
Prof A Nienaber  [female] BA(Hons)(Wit), LLB, LLM(UP), PhD, Dipl. Biostatistics, UNISA – Legal advisor
Mrt MC Nzukwa  [female] BA(Hons), MSc(Biochemistry), MSc, (UCL, UK) – Community representative

Prof L M Ntsheni  [female] MSc(Hons): FCS(SA)
Snr Sr J Plaatje  [female] BSc(Bio), BE(Eng), BEng(Mnt), BSc(Hons), BEng, MEng, MSc(Hons), PhD, CEng, NEA, NSA – Engineering representative

Dr R Reynolds  [female] MSc (Pharmacology) – Interdisciplinary representative
Dr T Rossouw  [female] M.A. (Ch.B. (cum laude); M.Phil (Applied Ethics) (cum laude); MSc (Biostatistics and Epidemiology) (cum laude), D.Phil
Dr L Schoeman  [female] B.Pharm, B(Arts)(Psych), PhD – Chairperson: Subcommittee for students' research
Appendix 9: Consent form for nurses and doctors

Statement concerning participation in the Research Project*.

Name of Project:

An assessment of the need for pharmaceutical services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province

I have read the information on the proposed study and was provided the opportunity to ask questions and given adequate time to rethink the issue. The aim and objectives of the study are sufficiently clear to me. I have not been pressurized to participate in any way.

I understand that participation in this study is completely voluntary and that I may withdraw from it at any time and without supplying reasons. This will have no influence on the regular treatment that holds for my condition neither will it influence the care that I receive from my regular doctor.

I know that this Project has been approved by the Medunsa Campus Research and Ethics (MCREC), University of Limpopo (Medunsa Campus) / Dr George Mukhari Hospital. I am fully aware that the results of this study will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in this study

............................................................  ........................................................
Name of patient/volunteer  Signature of patient or guardian.

..............................................  ..............................................  ..............................................
Place.  Date.  Witness
Statement by the Researcher

I provided written information regarding this study

I agree to answer any future questions concerning the study as best as I am able.

I will adhere to the approved protocol.

....................................  ....................................  ..............

Name of Researcher Elmien Bronkhorst    Signature    Date    Place
Appendix 10: Information leaflet for Doctors

Dear Doctor

Re: An assessment of the need for pharmaceutical services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province.

The following study is going to be conducted in the surgical ward of Steve Biko Hospital.

The aim of the study is to determine the need for provision of pharmaceutical care from the pharmacist in the ICU and HCU of Steve Biko Hospital

Aspects that will be covered in your questionnaire include:

- A need for the pharmacist in the unit
- The benefit of the pharmacist during ward rounds
- Information provided by the pharmacist to you as the doctor
- Interventions performed by the pharmacist on rational drug use and antimicrobials
- The role of the pharmacist in expenditure in your unit

The questionnaire you have been requested to complete is to assess the need for a pharmacist in the surgical ward. Please could you complete the questionnaire it should take only ten minutes of your time. You are under no obligation to complete the questionnaire and you can withdraw from the study at any time, without providing a reason.

Should you have any questions please do not hesitate to contact the researcher.

We value your participation

Sincerely

EimienBronkhorst

Researcher/Pharmacist

Telephone Number: 082 747 1906
Appendix 11: Information leaflet for Nurses

Dear Nursing Sister

Re: An assessment of the need for pharmaceutical services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province.

The following study is going to be conducted in the surgical ward of Steve Biko Hospital. The aim of the study is to determine the need for provision of pharmaceutical care from the pharmacist in the ICU and HCU of Steve Biko Hospital.

Aspects that will be covered in your questionnaire include:

- The need for a pharmacist in the ICU and HCU
- Ward activities that the pharmacist can participate in.
- The pharmacist role in improved drug distribution in the ICU and HCU
- The pharmacist role in educational sessions provided to the nurses

The questionnaire you have been requested to complete is to assess the need for a pharmacist in the surgical ward. Please could you complete the questionnaire it should take only ten minutes of your time. You are under no obligation to complete the questionnaire and you can withdraw from the study at any time, without providing a reason.

Should you have any questions please do not hesitate to contact the researcher.

We value your participation

Sincerely

Elmien Bronkhorst
Researcher/Pharmacist

Telephone Number: 082 747 1906
Appendix 12: Patient Information Leaflet and Informed Consent

INFORMATION LEAFLET AND INFORMED CONSENT FOR NON-CLINICAL RESEARCH

TITLE OF STUDY: “An assessment of the need for pharmaceutical services in the Intensive Care Unit and High Care Unit of Steve Biko Academic Hospital in Gauteng Province”

Dear Patient / Guardian/Surrogate

1) INTRODUCTION

We invite you to participate in a research study. This information leaflet will help you to decide if you want to participate. Before you agree to take part you should fully understand what is involved. If you have any questions that this leaflet does not fully explain, please do not hesitate to ask the investigator, Elmien Bronkhorst.

2) THE NATURE AND PURPOSE OF THIS STUDY

The study will be conducted to determine if a pharmacist working as part of the multidisciplinary team in the ward, can make a difference in patient care, including optimizing medication therapy, saving costs and providing information regarding medication. The aim of this study is to determine the need for pharmacy related services at ward level.

You as a patient are a very important source of information on whether there is a need for monitoring the use of medication at ward level.

3) EXPLANATION OF PROCEDURES TO BE FOLLOWED

This study involves a pharmacist working in the ward and checking your prescriptions and other records on a daily basis. We will ask you some questions about your previous or chronic medication use and history of illnesses. The pharmacist will monitor your prescription and administration of medication while you are admitted to the ward.

4) RISK AND DISCOMFORT INVOLVED

There are no risks in participating in the study. You are under no obligation to answer any questions if you don’t want to.

5) POSSIBLE BENEFITS OF THIS STUDY

Although you will not benefit directly from the study, the results of the study will enable us to optimize therapeutic treatment of patients in future.

6) WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

Your participation in this study is entirely voluntary. You can refuse to participate or stop at any time during the study without giving any reason. Your withdrawal will not affect you or your treatment in any way.

7) HAS THE STUDY RECEIVED ETHICAL APPROVAL?

This study has received written approval from the Research Ethics Committee.
of the Faculty of Health Sciences at the University of Pretoria. Ethical approval will be obtained from the University of Limpopo (Medunsa Campus). A copy of the approval letter is available if you wish to have one.

8) INFORMATION AND CONTACT PERSON

The contact person for the study is Elmien Bronkhorst. If you have any questions about the study please contact her at cell 082 747 1906. Alternatively you may contact my supervisor at 084 580 5205.

9) COMPENSATION

Your participation is voluntary. No compensation will be given for your participation.

10) CONFIDENTIALITY

All information that you give will be kept strictly confidential. Once we have analysed the information no one will be able to identify you. Research reports and articles in scientific journals will not include any information that may identify you or your hospital.

CONSENT TO PARTICIPATE IN THIS STUDY

I confirm that the person asking my consent to take part in this study has told me about nature, process, risks, discomforts and benefits of the study. I have also received, read and understood the above written information (Information Leaflet and Informed Consent) regarding the study. I am aware that the results of the study, including personal details, will be anonymously processed into research reports. I am participating willingly. I have had time to ask questions and have no objection to participate in the study. I understand that there is no penalty should I wish to discontinue with the study and my withdrawal will not affect any treatment in any way.

I have received a signed copy of this informed consent agreement.
Participant's name ..........................................................(Please print)
Participant's signature: ......................Date..................

Legal Guardian/Surrogate Name (1) .............................................(Please print)
Legal Guardian/Surrogate signature: ...................... Date................

Investigator's name Elmien Bronkhorst.............................................(Please print)
Investigator's signature ................................... Date..................

Witness's Name ..............................................................................(Please print)
Witness's Signature .................................. Date..................
VERBAL INFORMED CONSENT
I, the undersigned, have read and have fully explained the participant information leaflet, which explains the nature, process, risks, discomforts and benefits of the study to the participant whom I have asked to participate in the study.

The participant indicates that s/he understands that the results of the study, including personal details regarding the interview will be anonymously processed into a research report. The participant indicates that s/he has had time to ask questions and has no objection to participate in the interview. S/he understands that there is no penalty should s/he wish to discontinue with the study and his/her withdrawal will not affect any treatment in any way. I hereby certify that the client has agreed to participate in this study.

Participant's Name ..................................................................(Please print)
Signature .........................................Date................................

Legal Guardian/Surrogate Name (1) ........................................(Please print)
Signature .............................................Date..............................

Person seeking consent .Elmien Bronkhorst...........................(Please print)
Signature .............................................Date..............................

Witness's name (2) .................................................................(Please print)
Signature .............................................Date..............................

1  In cases where the patient is not able to sign consent
2  The witness sign that the process of verbal informed consent was followed
### Appendix 13: Medication used according to ATC classification

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<th>Medication</th>
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<td>Dose</td>
<td>Units</td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>------------------------------</td>
<td>------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>J02AC01</td>
<td>Fluconazole</td>
<td>7</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>J04AB02</td>
<td>Rifampicin/INH/pyrazinamide</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>J04AD03</td>
<td>Ethionamide</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>J04AK01</td>
<td>PZA</td>
<td>1</td>
<td>21</td>
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</tr>
<tr>
<td>J04AK02</td>
<td>Ethambutol</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>J05AF05</td>
<td>Lamivudine (3TC)</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>J05AF07</td>
<td>Tenofovir</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>J05AG03</td>
<td>Efavirenz</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>J07AL01</td>
<td>Pneumococcal vaccine</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>M01AB05</td>
<td>Diclofenac</td>
<td>1</td>
<td>21</td>
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</tr>
<tr>
<td>M03AC03</td>
<td>Vecuronium bromide</td>
<td>1</td>
<td>21</td>
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</tr>
<tr>
<td>N02AG01</td>
<td>Morphine</td>
<td>38</td>
<td>4</td>
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</tr>
<tr>
<td>N02BA01</td>
<td>Aspirin</td>
<td>4</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>N02BE01</td>
<td>Paracetamol oral</td>
<td>28</td>
<td>6</td>
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</tr>
<tr>
<td>N03AB02</td>
<td>Phenytoin</td>
<td>5</td>
<td>17</td>
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</tr>
<tr>
<td>N03AG01</td>
<td>Valproic acid</td>
<td>6</td>
<td>16</td>
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</tr>
<tr>
<td>N03AX12</td>
<td>Gabapentin</td>
<td>1</td>
<td>21</td>
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<tr>
<td>N05AA01</td>
<td>Chlorpromazine</td>
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<td>21</td>
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</tr>
<tr>
<td>N05AD01</td>
<td>Haloperidol</td>
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<td>15</td>
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</tr>
<tr>
<td>N05BA01</td>
<td>Diazepam</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>N05BA04</td>
<td>Oxasepam</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>N05BA06</td>
<td>Lorasepam</td>
<td>4</td>
<td>18</td>
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<tr>
<td>N05BB01</td>
<td>Hydroxyzine</td>
<td>4</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>N05CD08</td>
<td>Midazolam</td>
<td>32</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>N06AA09</td>
<td>Amitriptyline</td>
<td>3</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>N06AB03</td>
<td>Fluoxetine</td>
<td>4</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>N06AB04</td>
<td>Citalopram</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>P01AB01</td>
<td>Metronidazole</td>
<td>3</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>R03AA01</td>
<td>Adrenaline</td>
<td>9</td>
<td>13</td>
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</tr>
<tr>
<td>R03AC02</td>
<td>Salbutamol</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>R03BB01</td>
<td>Ipratropium bromide/Fenoterol</td>
<td>11</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>V03AF01</td>
<td>Mesna</td>
<td>1</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>V06B</td>
<td>Dipeptivan</td>
<td>5</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>
# Appendix 14: Drug Reconstitution

## Recommended Drug Reconstitution

### Antibiotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Active Ingredient</th>
<th>Diluent</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augmentin</td>
<td>Amoxycillin/clavulanate</td>
<td>NaCl only</td>
<td>20min. Use in 2 hours</td>
</tr>
<tr>
<td>Zovirax</td>
<td>Acyclovir</td>
<td>NaCl only</td>
<td>60min. Use in 12 hours. Don’t refrigerate</td>
</tr>
<tr>
<td>Fungizone</td>
<td>Amphotericin B</td>
<td>Dextrose 5% only</td>
<td>4-6 hours. Use in 24hrs at room temperature</td>
</tr>
<tr>
<td>Invanz</td>
<td>Ertapenem</td>
<td>NaCl only</td>
<td>30min. Use mixed bag within 6 hours</td>
</tr>
<tr>
<td>Rimactane</td>
<td>Rifampicin</td>
<td>Recons. and dilute with Dextrose 5%</td>
<td>Infusion over 3 hours</td>
</tr>
<tr>
<td>Erythrocin</td>
<td>Erythromycin</td>
<td>NaCl only</td>
<td>20-60 min per 300mg</td>
</tr>
<tr>
<td>Ampicillin/Petercillin</td>
<td>Ampicillin</td>
<td>NaCl only</td>
<td>30min/1g. Use in 4-8 hours</td>
</tr>
<tr>
<td>Benzylpenicillin</td>
<td>Benzylpenicillin</td>
<td>NaCl only</td>
<td>30min</td>
</tr>
</tbody>
</table>

- All other antibiotics can be reconstituted with water for injection and diluted with NaCl 0.9%, NaCl 0.45% or Dextrose 5%.
- Please note the storage instructions for antibiotics after reconstitution

### Other Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Active Ingredient</th>
<th>Diluent</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ativan</td>
<td>Lorasepam</td>
<td>NaCl or Water for injection</td>
<td>Refrigerate</td>
</tr>
<tr>
<td>Cordarone X</td>
<td>Amiodarone</td>
<td>Dextrose 5% only</td>
<td>150-300mg over 3 minutes</td>
</tr>
<tr>
<td>Epanutin</td>
<td>Phenytoin</td>
<td>NaCl only</td>
<td>Not greater than 50mg/min</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>Lignocaine</td>
<td>Dextrose 5% only</td>
<td>1-4mg/min</td>
</tr>
<tr>
<td>Nexiam</td>
<td>Esomeprazole</td>
<td>NaCl only</td>
<td>10-30min, or 8mg/hour</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>Phenylephrine</td>
<td>NaCl or undiluted</td>
<td>According to blood pressure</td>
</tr>
<tr>
<td>Sodium Bicarbonate</td>
<td>Sodium Bicarbonate</td>
<td>Avoid Calcium containing solutions</td>
<td>0.5-1ml/kg</td>
</tr>
<tr>
<td>Venofer</td>
<td>Iron(III)-sucrose</td>
<td>NaCl only</td>
<td>25ml over 15min, rest over 15 min</td>
</tr>
</tbody>
</table>
Appendix 15: Antibiotics policy for surgical ICU

Surgical/Trauma Critical Care Unit
Steve Biko Academic Hospital
Antibiotic Policy
Introduction

The Guidelines are in the main intended for the treatment of adults in the ICU setting. They are intended as a source of assistance to the clinician who should where possible, define the site of sepsis and then use these guidelines to formulate a rational therapeutic strategy.

Additionally, important to highlight a number of basic antibiotic prescribing principles:

- Identify the organisms whenever possible
- Consider the pharmacological and toxicological aspects of any agent before prescribing the drug.
- The host response is variable at the extremes of life, infancy and old age. Pharmacokinetic parameters in infants and in the elderly may not reflect function, e.g., serum creatinine measurements may not reflect true renal function.
- Recognize that diffusion into the site of infection may be achieved more readily with one agent than another, e.g., aminoglycosides penetrate pulmonary secretions less well than the β-lactams. The clinical relevance of this finding has not been proven.
- Environment may affect antimicrobial activity; e.g., decreased pH found in abscesses may decrease aminoglycoside activity.
- Antibiotic therapy should always be stepped down to a narrower spectrum and/or a safer antimicrobial that is active against the pathogen that has been isolated. This also involves removing gram-positive cover if the organism is gram negative and vice versa. Duration of therapy should be reduced wherever possible. > 8 days of therapy except in specific circumstances e.g. infective endocarditis, merely increases the likelihood of super-infection with resistant organisms and does not improve outcome. Additionally parenteral therapy should be switched to oral as soon as possible particularly if the bioavailability is similar for parenteral and oral formulations e.g. quinolones. This is usually done once the patient can take orally and/or the temperature has settled.

SEPTIC SCREEN

- Full Blood Count
- Blood Culture
- Inflammatory Markers (CRP and Procalcitonin)
- Urine microscopy, culture and sensitivity
- X-rays

DURATION OF EMPIRIC ANTIBIOTIC THERAPY

- Treat for 5 days (De-escalate antibiotics beforehand if cultures are reported or negative)
### Orthopaedic Surgery

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Likely pathogens</th>
<th>Recommended prophylaxis regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint Replacement</td>
<td><em>S. aureus</em>, <em>S. epidermidis</em></td>
<td>Cefazolin 1 g X preoperatively, then every 8 h for 48 hours</td>
<td>Vancomycin reserve for penicillin-allergic patients</td>
</tr>
<tr>
<td>Hip Fracture Repair</td>
<td><em>S. aureus</em>, <em>S. epidermidis</em></td>
<td>Cefazolin 1 g X preoperatively, then every 8 h for 48 hours</td>
<td>Compound fractures are treated as if infection is presumed</td>
</tr>
<tr>
<td>Open/compound fractures</td>
<td><em>S. aureus</em>, <em>S. epidermidis</em>, gram-negative bacilli, polymicrobial</td>
<td>Cefazolin 1 g X preoperatively, then every 8 h for the course of the infection</td>
<td>Gram negative coverage (i.e. aminoglycoside) may be indicated for severe open fractures</td>
</tr>
</tbody>
</table>

### Skin Infection

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Likely Pathogens</th>
<th>Recommended empiric Treatment</th>
<th>Microbiology Specimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis in non-diabetic patients</td>
<td><em>S. pyogenes</em>, <em>S. aureus</em> (less common)</td>
<td>Cloxacillin 2g 6g or Clindamycin 600mg 8h or amoxicillin/clavulanate 1.2g 8h iv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulitis in diabetic patients</td>
<td><em>S. aureus</em>, <em>S pyogenes</em>, sometimes <em>E. Coli</em>, <em>Pseudomonas</em> and <em>anaerobes</em></td>
<td>Amoxicillin/clavulanate 1.2g 8h or Piperacillin/tazobactam 4.5g 8h iv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic foot (life threatening)</td>
<td>Anaerobes, <em>S.aureus</em>, <em>Streptococci</em>, Gram negative bacilli</td>
<td>Piperacillin/tazobactam 4.5g 8h iv or Ciprofloxacin 400mg 12h + Clindamycin 600mg 8h iv or Carbapenem 8h iv + Vancomycin 1g 12h</td>
<td></td>
<td>Deep wound aspirate</td>
</tr>
<tr>
<td>Head and Neck surgery</td>
<td>Likely pathogens</td>
<td>Recommended prophylaxis regimens</td>
<td>Comments</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------</td>
<td>----------------------------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Maxillofacial surgery</td>
<td><em>Staphylococcus aureus</em>, <em>streptococci oral anaerobes</em></td>
<td>Cefazolin 2g or clindamycin 600 mg</td>
<td>Repeat intraoperative dose for operations longer than 4 hours</td>
<td></td>
</tr>
<tr>
<td>Head and neck cancer resection</td>
<td><em>S. aureus</em>, <em>streptococci oral anaerobes</em></td>
<td>Clindamycin 600 mg at induction and every 8 h x 2 more doses</td>
<td>Add an aminoglycoside (i.e. gentamicin) for clean-contaminated procedures</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nosocomial Infections</th>
<th>Type of infection</th>
<th>Likely Pathogens</th>
<th>Recommended Empiric treatment</th>
<th>Microbiologic Specimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck cancer resection</td>
<td>Hospital acquired pneumonia</td>
<td><em>S. aureus</em>, <em>streptococci oral anaerobes</em></td>
<td><em>Coagulate negative Staphylococci or S. aureus</em>, <em>Candida</em></td>
<td><em>Cloxacillin</em> 2g 6h iv or in case of penicillin allergy <em>Vancomycin</em> 1g 12h <em>Amphotericin</em> B or <em>Flucnazole</em> Four weeks of treatment, of which <em>Flucloxacillin</em> oral can be commenced after two weeks</td>
<td>Blood culture Catheter tip</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastro-intestinal surgery</th>
<th>Likely pathogens</th>
<th>Recommended Prophylaxis regimens</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-duodenal surgery</td>
<td>Enteric gram negative bacilli, gram-</td>
<td>Cefazolin 1g x1</td>
<td>High-risk patients only (obstruction)</td>
</tr>
<tr>
<td>Hospital acquired pneumonia</td>
<td><em>S. Pneumonia or Gram negative Klebsiella pneumonia, Pseudomonas aeruginosa, Acinetobacterbaumann iMRSA</em></td>
<td><em>Piperacillin/Tazobactam</em> 4.5g 8h or <em>Cefepime</em> 2g 8h or <em>Ciproflaxacin</em> 400mg 8h or <em>Ertapenem</em> 1g 24h</td>
<td>Blood culture and sputum or endotracheal aspirate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastro-duodenal surgery</th>
<th>Likely pathogens</th>
<th>Recommended Prophylaxis regimens</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-duodenal surgery</td>
<td>Enteric gram negative bacilli, gram-</td>
<td>Cefazolin 1g x1</td>
<td>High-risk patients only (obstruction)</td>
</tr>
<tr>
<td>Anatomical Site</td>
<td>Likely Pathogens</td>
<td>Suggested Regimens</td>
<td>Comments</td>
</tr>
<tr>
<td>----------------</td>
<td>------------------</td>
<td>--------------------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>positive cocc, oral anaerobe</strong></td>
<td>haemorrhage, malignancy, acid suppression therapy, morbid obesity</td>
<td>negatives Klebsiella pneumonia, Pseudomonas aeruginosa, Acinetobacter baumannii</td>
<td>aspirate resistant Acinetobacter</td>
</tr>
<tr>
<td><strong>Colo-rectal and Appendix</strong></td>
<td>Enteric gram negative bacilli, anaerobes</td>
<td>Cefazolin 1g + Metronidazole 500mg x1 If patient present with β-lactam allergy: Clindamycin 600mg x1 If perforation occurs, treat for infection with suitable course of antibiotics</td>
<td>Infective Endocarditis S. aureus (methicillin-susceptible) MRSA/MRSE Cloxacillin 2g 4h iv + Rifampicin 600mg 12h po for 6 weeks + Gentamycin 1mg/kg iv for 2 weeks Vancomycin 15mg/kg 12h iv + Rifampicin 300mg 8h po for 6 weeks, plus Gentamycin for 2 weeks</td>
</tr>
<tr>
<td><strong>Sepsis/Septic Shock</strong></td>
<td>Anatomic sites</td>
<td>Diagnosis</td>
<td>Likely Pathogens</td>
</tr>
<tr>
<td><strong>Intra-abdominal sources (secondary peritonitis)</strong></td>
<td>Streptococci, E. coli, Klebsiella, Enterobacter, S. aureus and anaerobes</td>
<td>Amoxycillin/clavulanic acid 1.2g 8h or Cefuroxime 1.5g 8h or Ceftriaxone 2g 24h or Cefotaxime 2g 8h + Metronidazole 500 8h or Ertapenem 1g 24h</td>
<td>Traumatic perforation with early operation &lt;6hr-24 hours, otherwise therapy for 5-7 days</td>
</tr>
<tr>
<td><strong>Primary spontaneous Bacterial Peritonitis</strong></td>
<td>Enterobacter, S. Pneumonia,</td>
<td>Cefotaxime 2g 8h iv or</td>
<td>Duration of treatment</td>
</tr>
<tr>
<td>Source</td>
<td>Pathogens</td>
<td>Antibiotics</td>
<td>Notes</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------------------------------------------</td>
<td>-------------------------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Biliary source</td>
<td>Enterobacteriaceae, Bacteriodes</td>
<td>Piperacillin/Tazobactam 4.5g 8h or Ceftriaxone 1g 12h + Metronidazole 500mg 8h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Biliary source</td>
<td></td>
<td>Depend on clinical response</td>
</tr>
<tr>
<td>Hepatic abscess</td>
<td>Enterobacteriaceae, Bacteriodes, Entamoebahystolitica</td>
<td>Metronidazole 500mg 8h + Ceftriazone 1g 12h or Piperacillin/Tazobactam 4.5g 8h</td>
<td></td>
</tr>
<tr>
<td>Splenic abscess</td>
<td>S. aureus, Streptococci</td>
<td>Cloxacillin 2g 4h iv or Vancomycin 1g 12h iv</td>
<td>Patients with splenectomy needs vaccination with Pneumovax</td>
</tr>
</tbody>
</table>
MEDICATION ADJUSTMENTS

Vancomycin in Renal Failure:

<table>
<thead>
<tr>
<th>Half-life (normal/ESRD)h</th>
<th>Dose in normal renal function</th>
<th>Adjustment for renal failure (according to CrCL)</th>
<th>Supplement for Haemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>6/200-250</td>
<td>&gt;50-90</td>
<td>10-50</td>
</tr>
<tr>
<td></td>
<td>1g 12h</td>
<td>1g 24-96h</td>
<td>1g every 4-7 days</td>
</tr>
</tbody>
</table>

Antibiotic serum level

<table>
<thead>
<tr>
<th>Name of antibiotic</th>
<th>Trough reference range</th>
<th>Peak reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>5-10mg/l</td>
<td>30-40mg/l</td>
</tr>
<tr>
<td>Amikacin</td>
<td>1-5mg/l</td>
<td>15-25mg/l (&gt;35mg/L toxic)</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>1-2mg/l</td>
<td>1-8mg/l</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1-2mg/l</td>
<td>5-10mg/l</td>
</tr>
</tbody>
</table>