The role of the critical care nurse in the implementation of an antimicrobial stewardship programme in a resource-limited country

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Declaration

By submitting this thesis electronically, I, Briëtte du Toit, declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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Abstract

Antimicrobial resistance has become a major public health threat and is particularly a problem in low- to middle-income countries (LMICs) where there is a high burden of infectious diseases. The implementation of an antimicrobial stewardship programme (AMS) is essential to reduce the development of resistance. However, adequate resources are often a problem, hence the necessity to investigate the availability of alternative, more cost-effective solutions. Including nurses in antimicrobial stewardship teams can add value due to the fact that nurses are in an ideal position to monitor the duration of antimicrobial treatment. Furthermore, nurses are responsible for the administration of medication and the collection of appropriate specimens and are primarily responsible for the care of the patient.

The objectives of this study were to examine the role of the critical care nurse in the implementation of an antimicrobial stewardship programme in LMICs and to identify interventions where the critical care nurse plays a significant role as part of the AMS team.

A pre- and post-intervention interventional study design was followed where various interventions were implemented to establish which of these interventions can be implemented successfully by nurses with a meaningful impact on an AMS programme.

The study found that nurses can play an important role in the implementation of an AMS programme and that they are a cost-efficient resource. Nurses should be an essential part of an AMS team. Additional training about AMS and infection prevention and control (IPC) is necessary and the training should be directed at the team; including nurses, doctors and pharmacists.

Key words:

antimicrobial stewardship programme

infection prevention and control

nurses

resource-limited countries

South Africa

interventions

training

prescribing

Opsomming

Antimikrobiese weerstandigheid is ’n wesentlike bedreiging vir publieke gesondheidsorg en dit is veral ’n probleem in lae- tot middel-inkomste lande waar daar ’n groot las is van aansteeklike siektes. Die implementering van ’n antimikrobiese bewusmakingsprogram is belangrik om die ontwikkeling van weerstandigheid te verminder. Voldoende hulpbronne is egter dikwels ’n probleem en gevolglik moet ander beskikbare en koste-effektiewe bronne ondersoek word. Die insluiting van verpleegkundiges in antimikrobiese bewusmakingspanne kan moontlik waarde toevoeg as gevolg van die feit dat verpleegkundiges in ’n gunstige posisie is om die duur van behandeling met ‘n antibiotikum te monitor. Verder is verpleegkundiges ook verantwoordelik vir die toediening van medikasie en die verkryging van toepaslike laboratorium-monsters en is hulle primêr verantwoordelik vir die versorging van die pasiënt.

Die doel van die studie was om die rol van die kritieke-sorg verpleegkundige te ondersoek in die implementering van ’n antimikrobiese moniteringsprogram in lae- tot middel-inkomste lande en om verder te bepaal watter intervensies geïmplementeer kan word sodat die kritieke-sorg verpleegkundige ’n betekenisvolle rol kan speel in die implementering van ’n antimikrobiese moniteringsprogram.

Die studie-ontwerp was ‘n voor- en na-intervensie studie. Verskeie intervensies is geïmplementeer om te bepaal watter intervensies suksesvol deur verpleegkundiges geïmplementeer kan word om ’n beduidende invloed op ’n antimikrobiese moniteringsprogram te hê.

Die bevindinge van die studie was dat verpleegkundiges ’n belangrike rol kan speel in die implementering van antimikrobiese moniteringsprogramme en dat hulle ’n koste-effektiewe hulpbron is. Verpleegkundiges behoort deel te wees van ’n antimikrobiese span. Opleiding in antimikrobiese moniteringsprogramme en infeksievoorkoming en -beheer is egter nodig en moet gerig wees op die hele span, insluitende geneeshere, verpleegkundiges en aptekers.

Sleutelwoorde:

antimikrobiese moniteringsprogram

infeksievoorkoming en -beheer

kritiese-sorg verpleegkundige

lande met beperkte hulpbronne

Suid-Afrika

intervensies

opleiding

voorskryf

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List of acronyms and abbreviations

ADT	Admission/Discharge/Transfers
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
APIC	Association for Professionals in Infection Prevention and Control Epidemiology
ARNSF	Antimicrobial Resistance National Strategy Framework
C.diff	*Clostridium difficile*
CAUTI	Catheter-associated urinary tract infection
CCU	Critical care unit
CDC	Centre for Disease Control and Prevention
CLABSI	Central line-associated bloodstream infection
CRM	Clinical Risk Manager
DDD	Defined daily dosage
DoH	Department of Health
DOT	Directly Observed short course Therapy
ESBL	Extended Spectrum β-lactamase Producer
GNI	Gross national income
HAI	Healthcare-associated infection
HIV	Human immunodeficiency virus
IDSA	Infectious Diseases Society of America
IHI	Institute of Healthcare Improvement
IMCI	Integrated Management of Childhood Illnesses
IPC	Infection prevention and control
LMICs	Low- to middle-income countries
LOS	Length of stay
MDROs	Multi-drug resistant organisms
MRSA	Methicillin Resistant *Staphylococcus aureus*
PPE	Personal Protective Equipment
SAASP	South African Antibiotic Stewardship Programme
SHEA	Society for Healthcare Epidemiology of America
SSI	Surgical site infection
TB	Tuberculosis
VAP	Ventilator-associated pneumonia
VRE	Vancomycin resistant *enterococci*
WHO	World Health Organisation

Glossary

Antibiotic

Any class of organic molecule that inhibits or kills microbes by specific interactions with bacterial targets, without any consideration of the source of the particular compound of class (Davies & Davies, 2010:417)

Antimicrobial

A general term referring to a group of drugs, that includes antibiotics, antifungals, antiprotozoal drugs and antivirals that inhibits the growth of pathogenic micro-organisms (MedicineNet, 2015a; Merriam-Webster, 2015).

Antimicrobial stewardship

This refers to “coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration. Antimicrobial stewardship seeks to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce the cost of healthcare for infections and limit the selection for antimicrobial resistant strains” (Infectious Diseases Society of America (IDSA), 2000).

Care bundle

A care bundle is a structured way of improving processed of care and patient outcomes through a set of evidence-based interventions. It has proof that these interventions improve patient outcomes if implemented collectively every time (Institute of Healthcare Improvement, 2012).

Clinical pharmacist

A clinical pharmacist is a licensed specialist pharmacist working in an area of pharmacy involved with the science, practice, activity and service to develop and promote the rational and appropriate use of medicines, in the best interest of patients and the community (South African Society of Clinical Pharmacy, 2015).

Critical care nurse

A critical care nurse is a registered nurse with specialist training and knowledge of the critically ill and unstable patient and the skill and competency to function within a complex technological environment (South African Nursing Council, 2014).

De-escalation

The provision of effective initial antimicrobial treatment, while avoiding unnecessary antimicrobial use that would promote the development of resistance (Masterton, 2011:150).

Empiric antibiotic

Empiric antibiotics are normally broad-spectrum and are used for the treatment of both Gram-positive and Gram-negative bacteria. When more information is known (as from a blood culture), treatment may be changed to a narrow-spectrum antibiotic which more specifically targets the bacterium known to be causing disease or infection (Wikipedia, 2015a).

Hang time

Hang time refers to the time interval between prescription of an antibiotic and administration to the patient (South African Antibiotic Stewardship Programme, 2012).

Infectious diseases specialist

A physician or paediatrician with an additional specialised qualification in the management and treatment of infectious diseases and specialised knowledge of antimicrobials. (College of Medicine of South Africa, 2009).

Resource-limited countries

Any country that has a limitation in resources, such as available land, labour and capital. (Wikipedia, 2015b).

Low-middle income country (LMIC)

As of 1 July 2014, low-income economies are defined as those with a gross national income (GNI) per capita of $1 045 or less in 2013; middle-income economies are those with a GNI per capita of more than $1 045 but less than $12 746.

Lower-middle-income and upper-middle-income economies are separated at a GNI per capita of $4 125. South African is classified by the World Bank as a low middle-income country (World Bank, 2015a; World Bank, 2015b).

The term ‘LMICs’ replaces the term ‘resource-limited countries’ in the rest of the document.

CHAPTER 1
FOUNDATION OF THE STUDY

1.1 INTRODUCTION

Antimicrobials are effective in the treatment of infections, but inappropriate and unregulated use thereof has led to the development of resistance against most available antimicrobials; furthermore, aggravated by the emergence of untreatable strains such as *carbapenem* resistant *enterobacteriaceae* (Hurford, Morris, Fisman & Wu, 2012:203; Paruk, Richards, Scribante, Bhagwanjee, Mer, Perrie, 2012:613; Laxminarayan, Duse, Wattal, Zaidi, Wertheim *et al.*, 2013:1057). Inappropriate use of antimicrobials is not the only reason for antimicrobial resistance. Antibiotic resistance is a natural phenomenon. The natural evolution of living organisms to develop tolerance and resistance to therapeutic agents in itself is a major contributing factor to antimicrobial resistance (Davies & Davies, 2010:417). Resistant strains, capable of inactivating a drug will appear as soon as an antibiotic is used widely. Over time, these micro-organisms will develop resistance to more and more therapeutic agents (Davies & Davies, 2010: 419).

Antimicrobial resistance has become a major public health threat and is particularly a problem in low- to middle-income countries (LMICs) where there is a high burden of infectious diseases (Okeke, Laxminarayan, Bhutta, Duse, Jenkins *et al.*, 2005a:481; Sahoo, Tamhankar, Johansson & Lundborg, 2010:1; Mendelson & Matsoso, 2015:325). A situational analysis of available information related to antimicrobial resistance and the rapid implementation of a national antimicrobials stewardship (AMS) programme has become necessary (Suleman & Meyer, 2012:14; Nathwani, Sneddon, Malcolm, Wiuff, Patton *et al.*, 2011:17).

The implementation of an antimicrobial stewardship (AMS) programme to monitor antimicrobial usage and the prescribing habits of healthcare providers is essential to reduce the development of resistance (Dellit, Owens, McGowan, Gerding & Weinstein *et al.*, 2007:159). Recommended strategies are complicated and problematic to implement in LMICs. Evidence related to the successful and sustained implementation of AMS programmes in these countries is limited (Okeke, Klugman, Bhutta, Duse, Jenkins *et al.*, 2005b:568; Dellit *et al.*, 2007: 159). Clinical teams, comprising of a clinical pharmacist and infectious diseases specialist, are uncommon. Rural hospitals do not have access to these teams and clinical microbiologists and laboratory support are often lacking or inadequate.

Where resources are lacking, Abbo, Smith, Pereyra, Wyckoff and Hooton (2012:376) found that the inclusion of nurse practitioners in AMS programmes may improve the effective use of antimicrobials. Nurses are in an ideal position to monitor and audit prescriptions due to the nature of their work; however, their role in the multidisciplinary team is not clear (Edwards, Drumright, Kiernan & Holmes, 2011:6).

1.2 BACKGROUND AND RATIONALE

Paruk *et al.* (2012:613) stated that "the emergence of pan-resistant pathogens and the inappropriate use of antimicrobials is a global catastrophe receiving increasing attention from healthcare authorities". In addition to the natural development of resistance of micro-organisms to antimicrobials over time, other factors that contribute to the development and spread of resistant pathogens are poor socio-economic status, high burden of infectious diseases, misuse of antimicrobials, the publics' lack of knowledge and poor quality of antimicrobials available (Sahoo *et al.*, 2010:1; Al-Tawfiq, Stephens & Memish, 2010:767; Okeke, Lamikanra & Edelman, 1999:24; Radyowijati & Haak, 2003:733-734, Davies & Davies, 2010:419). Human behaviour has a significant impact on antimicrobial misuse and contributes to the development of resistance; impacting on societies worldwide (Laxminarayan *et al.*, 2013: 1057).

The lack of an effective infection prevention and control (IPC) programme contributes to the spread of antimicrobial resistant pathogens as there is very little evidence available on successful and sustainable interventions that have been implemented in LMICs (Okeke *et al.*, 2005a:481; Okeke *et al.*, 2005b:568). Many interventions focus on education, but these programmes have not been evaluated to measure their sustainable effectiveness or determine whether the prescribing behaviour of healthcare workers has been positively affected (Okeke, Aboderin, Byarugaba, Ojo & Opintan, 2007:1644; Yam, Fales, Jemison, Gillum & Bernstein, 2012:1148). Studies in the United States of America confirmed that in rural communities, the appointment of clinical pharmacists, together with weekly consultations with infectious diseases specialists demonstrated a significant reduction in inappropriate antimicrobial usage (Yam *et al.*, 2012:1142; Storey, Pate, Nguyen & Chang, 2012:2). LMICs do not necessarily have clinical pharmacists and infectious disease physicians and need to explore alternative sustainable methods of monitoring antimicrobial usage and ways to change behaviour of healthcare workers.

A multi-interventional approach is required comprising of the implementation of an AMS programme, together with protocol-specific empiric and therapeutic antimicrobials for the treatment of healthcare-associated infections (HAIs) and surgical prophylaxis (Dortch, Dossett, Fleming, Kauffmann, May & Talbot, 2011:15; Dellit *et al.*, 2007:159-160). Toth, Chambers and Davis (2010:746) and Coll, Kinnear and Kinnear (2012: 845) found that implementing a care bundle for antimicrobial stewardship increased appropriate de-escalation and improved adherence to evidence-based quality indicators, improving antimicrobial utilisation (Toth *et al.*, 2010: 746; Coll *et al.*, 2012: 845).

The implementation of simple interventions leads to a substantive cost saving on the use of antimicrobials and is therefore feasible in LMICs (Goff, Bauer, Reed, Stevenson, Taylor & West, 2012:587). Interventions such as stringent infection prevention and control (IPC) practices, surveillance, hand hygiene, monitoring of isolation precautions and antimicrobial stewardship is

required (Mendelson, Whitelay, Nicol & Brink, 2012:607; Chalfine, Kitzis, Bezie, Benali, Perniceni *et al.*, 2012:1).

A multi-disciplinary approach is required, which includes a clinical pharmacist, physician, infectious diseases specialist, microbiologist and an IPC practitioner (Dellit *et al.*, 2007:165; Tamma & Cosgrove, 2011:245). The involvement of a registered nurse has often been limited in these programmes (Edwards, Drumright *et al.*, 2011:6). Abbo and colleagues (2012:373) found that the role of the critical care nurse in the antimicrobial stewardship team should not be underestimated and should be explored further. Nurses provide the most consistent patient care and have specialised knowledge about their patients. They conduct daily chart reviews, monitor patients and alert the treating physician should there be a change in a treatment protocol, based on certain infectious markers or laboratory results (Edwards, Drumright *et al.*, 2011:9). Furthermore, critical care nurses can play a significant role in ensuring that appropriate specimens are collected prior to administration of an antimicrobial, antimicrobials are administered on time, at the correct dose and for the correct duration. Finally, nurses can advocate on behalf of the patient by reminding the physician of the number of antimicrobials with which the patient is treated and can question the appropriateness of such treatment.

Weiss, DiBardino, Rho, Sung, Collander and Wunderink (2013:1) reported that face-to-face prompting of prescribing physicians, using a written checklist, led to an almost four-fold reduction in the prescribing of empiric antimicrobials. Checklists with evidence-based procedures have proven to be a successful intervention to improve quality of care and are valuable tools in reducing errors of omission; improving outcomes in critical ill patients (Weiss *et al.*, 2013:1; Pronovost, Needham, Berenholtz, Sinopoli, Chu *et al.*, 2006:2731). Nurses utilising checklists might be a simple, cost-effective intervention that can have a positive effect on the implementation of an antimicrobial stewardship programme.

In order for nurses to play a significant role in the implementation of an AMS programme, it is necessary to improve their knowledge about pharmacology, clinical evaluation, IPC and quality improvement methodology.

Nurses can potentially be a cost-efficient resource that plays an important role in the implementation of an AMS programme, but their role needs to be defined (Edwards, Drumright *et al.*, 2011:9). The role of critical care nurses has not been evaluated in the implementation of an AMS programme.

1.3 RESEARCH QUESTION

What is the role of the critical care nurse in the successful implementation of an antimicrobial stewardship programme in a low-middle income country?

1.4 PROBLEM STATEMENT

The complexities associated with the implementation of AMS programmes, together with inadequate resources and lack of trained healthcare workers, are major limitations for the implementation of an AMS programme in low- to middle-income countries (LMICs).

The role of the critical care nurse has not previously been defined in the implementation of an AMS programme and should be explored and evaluated further.

1.5 HYPOTHESIS

The null hypothesis states that the critical care nurse does not play a role in the implementation of an antimicrobial stewardship programme.

1.6 RESEARCH GOALS

The goal of the study is to examine the role of the critical care nurse in the implementation of an antimicrobial stewardship programme in a private hospital in a low-middle income country.

1.7 RESEARCH OBJECTIVES

The objectives of this study are to examine:

- The role of the critical care nurse in the implementation of an antimicrobial stewardship programme.
- What interventions can be implemented by the critical care nurse to play a significant role in the implementation of an antimicrobial stewardship programme.

1.8 RESEARCH METHODOLOGY

A pre-and post-interventional study design was utilised for the research.

1.9 SIGNIFICANCE OF THE STUDY

The study is important in LMICs that do not have the tools nor the resources that are described by the literature for the implementation of an AMS programme. The existing skills of nurses have to be evaluated to establish what is needed to empower them to play a significant role in the AMS team and what interventions can be implemented successfully by nurses as part of the AMS team.

Although nurses are not expected to replace clinical pharmacists or infectious diseases specialists, they can be educated and empowered to play a vital role in the clinical management team of a patient with infection. The role of the nurse needs to be recognised and acknowledged as a clinical practitioner.

1.10 SCOPE OR LIMITATIONS

The study has been conducted in the critical care unit (CCU) of an acute care private hospital, in a LMIC over a period of thirteen months. The hospital has 247 operational beds and twelve critical care beds admitting both surgical and medical cases.

All patients, fifteen years and older, admitted or transferred into the critical care unit from within the hospital or elsewhere and remained in the unit for more than 24 hours were included in the study.

Monitoring of the appropriate surgical prophylaxis was not included in the study as most critical care nurses do not administer surgical prophylaxis; patients primarily receive prophylaxis in the general unit and are usually admitted to CCUs post-operatively if complications developed during or post-surgery.

CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

The research question and objectives were used as the basis for the topics and subjects of the literature review. The objective of the literature review was:

- To establish what methodology and resources are currently used in low- to middle-income countries (LMICs) for the implementation of an antimicrobial stewardship (AMS) programme;
- To determing what interventions are required for the implementation of an AMS programme internationally and specifically in LMICs;
- To explore the role of nurses in the implementation of an AMS programme in LMICs.

The literature review consists of the following subheadings:

- The global extent of antimicrobial resistance;
- Antimicrobial stewardship: Evidence-based solutions to reduce the problem;
- The implementation of outcome and process measures to evaluate the impact of an AMS programme;
- The results of the implementation of an AMS programme;
- Training and education of healthcare workers;
- The role of Infection prevention and control (IPC) in the implementation of an AMS programme;
- The role of the nurse practitioner in the implementation of an AMS programme.

2.2 SELECTION AND REVIEW OF THE LITERATURE

The literature review was conducted over a period of 28 months. It commenced prior to submission of the research proposal and continued during the study period and data analysis. Various articles, position statements and guidelines were reviewed and analysed during this period. During the study period, the literature review expanded to explore different avenues that had not been previously included.

The literature review was based on South African and international resources, with a focus on the implementation of AMS programmes in LMICs.

Search engines such as Google Scholar and the electronic library of Stellenbosch University, SUNSearch (Stellenbosch University library and Information Service) and several data bases were utilised to obtain the material for the literature review, including, PubMed, ScienceDirect, Elsevier, ProQuest and EBSOhost (Elton B Stephens Company Research Database). The majority of the articles were obtained from scientific journals; books, guidelines and reports were also included. The websites of the National Department of Health (NDoH), the Centre for Disease Control and

Prevention (CDC) and the World Health Organisation (WHO) were accessed in addition to published articles. Searches included resources from reference lists and key authors of other articles.

Keywords that were employed included: antimicrobial stewardship programme, infection prevention and control, nurses, resource-limited countries, South Africa, interventions, training and prescribing. A combination of these words was used.

The inclusion and exclusion criteria were as follow:

i) Inclusion criteria

- Articles found with the key words that were published in accredited journals;
- Open-access articles published online;
- Editorials; and
- Guidelines.

ii) Exclusion criteria:

- Studies that did not meet the inclusion criteria above; and
- Abstracts of studies.

2.3 THE GLOBAL EXTENT OF ANTIMICROBIAL RESISTANCE

The use of antimicrobials has changed the world and the way in which medicine has been practiced since its development. It enabled other medical interventions such as chemotherapy, transplants and replacement surgery (CDC, 2014:3). Antimicribials are effective in treating infections, but the inapproporate use has lead to the development of resistance amongst the majority of available antimicrobials (Hurford *et al.*, 2012: 203; Laxminarayan *et al.*, 2013:1057). Inappropriate use of antimicoribials is not the only contributing factor to the development of resistance. It is part of the natural evolution of living organisms to develop resistance to therapeutic drugs (Davies & Davies, 2010:417). As soon as an antibiotic is used widely, resistant strains of micro-organisms will develop, with increasing resistance to more drugs over time (Davies & Davies, 2010:419). A decrease in effective treatment and resistance to antibiotics of certain recognised pathogens were already observed by clinicians as early as 1940 and 1950 (Owens, 2008:110). Other contributing factors to resistance are the use of antibiotics in food production and the transmission of resistant organisms in healthcare facilities (WHO, 2012:2).

Antimicrobial resistance is a major public health threat that has the ability to affect current and future generations (Sahoo *et al.*, 2010:629). Improvements in healthcare during recent years is threatened by antimicrobial resistance and the treatment of many common diseases is complicated by resistant organisms. Doctors regularly have to prescribe “last resort” antibiotics and these are often more expensive and difficult to obtain in LMICs. Resistance to all the treatment options for two common infections affecting millions of people , e.g. gonorrhaoe and tuberculosis (TB) have

been reported (WHO, 2015a:3). As LMICs have a high burden of infectious diseases, antibiotics are vital for the treatment of these infections (WHO, 2015a:3).

At the Commonwealth Wilton Park meeting it was stated that the increase in antimicrobial resistance is a worldwide risk with detrimental effects on medical, economic and social wellbeing of global communities (Foreign & Commonwealth Office, 2015:1). The World Economic Forum highlighted the rapid spread of antimicrobial resistant pathogens and the economic and social impact that it has on communities as a global risk for 2015 (World Economic Forum, 2015). A global action plan is required, with all countries aligning their own strategies with the global action plan (Foreign & Commonwealth Office, 2015:1).

A call was made for an urgent global and national multi-sectoral response (WHO, 2011; WHO, 2012:2). On March 27 2015, the World Health Organisation (WHO) released a draft global action plan on antimicrobial resistance, stating that antimicrobial resistance (AMR) is a significant threat to human health (WHO, 2015a:1). AMR impacts negatively on the global economy and increases the cost of healthcare delivery (WHO, 2015a:1). The extent and impact of AMR in sub-Saharan Africa is unknown due to ineffective surveillance programmes, insufficient data and a lack of research in the field (Okeke *et al.*, 2005a:481; Omulo, Thumbi, Njenga & Call, 2015:1; Mendelson & Matsoso, 2015:325). The high burden of endemic infectious diseases demands the use of more antimicrobials and has a negative impact on already limited healthcare resources. Inadequate laboratory support and healthcare workers that have limited training on antimicrobial prescribing and usage are aggravating the problem (Omulo *et al.*, 2015:1-2).

South Africa has a high burden of infectious diseases and the additional burden of Human immunodeficiency virus (HIV) and TB leads to an increase in the use of antimicrobials, contributing to the pressure on the healthcare system (Mendelson & Matsoso, 2015:54). The impact of bacterial and fungal infections remains unknown due to an inadequate surveillance system and high empiric usage of antimicrobials. The unavoidable result of such a high burden of infections and antimicrobial usage is the development of resistance (Mendelson & Matsoso, 2015:55). South Africa was recently mentioned as one of the countries contributing significantly to antimicrobial consumption, especially in the utilisation of two “last resort” drugs, namely carbapenems and polymixins (Van Boeckel, Gandra, Ashok, Caudron, Grenfell *et al.*, 2014:742). The implementation of the Antimicrobial Resistance National Strategy Framework (ARNSF) is an urgent matter and the interventions that are proposed in the strategy document (SA NDoH, 2014b) can be duplicated in healthcare systems of other middle-income countries (Mendelson & Matsoso, 2015: 54).

In a prospective study conducted by Paruk *et al.* (2012:613), the antimicrobial prescription practices in CCUs of public and private hospitals in South Africa were evaluated to determine the relationship with patient outcomes. It was found that in 73.4% of patients, antimicrobials were initiated during their stay in CCU and that 55% of patients initially received an inappropriate drug. In 23.9% of patients, therapy was de-escalated and the duration of treatment was inappropriate in

72% of the cases. Some patients received up to ten different types of antimicrobials simultaneously. The authors concluded that the finding of the study demonstrates the lack of knowledge and insight regarding the appropriate use of antimicrobials amongst doctors working in CCUs in the public and private sector in South Africa and that drastic measures are necessary to review current antimicrobial prescription practices to prevent further development of antimicrobial resistance (Paruk *et al.*, 2012:615).

Suleman and Meyer (2012:44) stated that an urgent situational analysis was required to consolidate all available information related to AMR to enable the identification of inefficiencies and areas for improvement (Suleman & Meyer, 2012:44). National and international interventions are required to establish a more accurate assessment of the problem and to implement interventions to reduce the development and spread of AMR organisms (Okeke *et al.* 2005a:481).

Poverty is the major driving force for the use of leftover medicine, incomplete courses and self-medication with antibiotics (Sahoo *et al.*, 2010:636). Paruk *et al.* (2012:613) stated further that the inappropriate prescribing patterns of doctors and misuse of antimicrobials is the main contributor to the development of antimicrobial resistance. These findings are in line with published studies from other LMICs (Sahoo *et al.*, 2010:1; Al-Tawfiq, Stephens & Memish, 2010:767; Okeke, Lamikanra & Edelman, 1999:24; Radyowijati & Haak, 2003:733-734).

2.4 ANTIMICROBIAL STEWARDSHIP: EVIDENCE-BASED SOLUTIONS TO REDUCE THE PROBLEM

The growing increase in resistant pathogens requires a consolidated strategy to prevent the further spread of resistant pathogens (Okeke *et al.*, 2005b:568). Various international guidelines recommend the implementation of antimicrobial stewardship (AMS) programmes to monitor antimicrobial usage and the prescribing habits of healthcare providers, to improve patient outcomes (Dellit *et al.*, 2007:159; CDC, 2014:3-4; Institute for Healthcare Improvement, 2012; WHO, 2012:2-3; WHO, 2001:1-2; Society for Healthcare Epidemiology of America (SHEA), Infectious Diseases Society of America (IDSA) & Pediatric Infectious Diseases Society (PIDS), 2012:322).

Antimicrobials stewardship (AMS) refers to the implementation of specific interventions to improve clinical outcomes and to minimise the unintended consequences of inappropriate antimicrobial usage with the subsequent development and transmission of antimicrobial resistant pathogens (Dellit *et al.*, 2007:159). The implementation of simple interventions can lead to a substantial reduction in cost and the utilisation of antimicrobials and is therefore feasible in LMICs (Goff *et al.*, 2012:587).

The WHO Global Strategy for Containment of Antimicrobial Resistance (WHO, 2001:1-2) recommended the following actions:

- Implement a comprehensive national plan;
- Strengthen surveillance programmes and laboratory support;
- Ensure continuous availability of necessary medication of good quality;
- Regulate and encourage appropriate use of medication, including in agriculture;
- Enhance infection prevention and control (IPC); and
- Encourage and support research and development of new resources and support material.

In the Draft global action plan on antimicrobial resistance of the WHO (WHO, 2015a: 2) the following strategic objectives are highlighted:

- Improve awareness and understanding of antimicrobial resistance;
- Improve knowledge about the extent of the problem through surveillance and research;
- Reduce incidence of infections;
- Improve the use of antimicrobials; and
- Implement sustainable programmes to reduce antimicrobial resistance.

The draft global action plan should be used as a framework for countries to develop their own programmes to prevent antimicrobial resistance (WHO, 2015a:3).

The CDC (2014:4) further recommended that the following Core Elements should be implemented in an antimicrobial stewardship program:

- Leadership commitment and the provision of necessary resources such as human, financial and information technology;
- Accountability: A physician leader with a knowledge of infectious diseases and/or antimicrobial stewardship who is responsible for implementation of the programme and the outcome;
- Drug Expertise such as a pharmacist with knowledge of infectious diseases or antimicrobial stewardship who is responsible to improve antimicrobial usage;
- Action: Implement at least one of the recommended actions at a time;
- Tracking and monitoring of antimicrobial prescribing and pathogen resistance;
- Reporting: Doctors, nurses and all relevant personnel need to be informed about antibiotic use and resistance patterns; and
- Education programmes to increase knowledge regarding prescribing and antimicrobial resistance.

The Society for Healthcare Epidemiology of America (SHEA) recommended a multidisciplinary team led by a physician for the implementation of an AMS programme. It is important that at least one member of the team is trained in antimicrobial stewardship. The team should include a

physician, pharmacist, clinical microbiologist and infection prevention and control (IPC) practitioner (SHEA, IDSA & PIDS, 2012:324).

In the recent Wilton Park meeting report (2015), countries were requested to formulate and coordinate a response to the increased problem of antimicrobial resistance and the threat that it poses to human and animal life (Foreign & Commonwealth Office, 2015: 3-10).

Some of the key discussion points were (Foreign & Commonwealth Office, 2015: 3-10):

- Antimicrobial resistance in humans, animals and the environment;
- Political leader support and national and international awareness of the problem;
- Improvement of surveillance systems to ensure adequate knowledge about the extent of the problem to be able to formulate scientifically proven interventions;
- The importance of behavioural change to ensure sustainable improvement;
- Access for communities to effective antimicrobials that are used appropriately in both humans and animals;
- Effective IPC programmes to prevent the transmission of resistant pathogens;
- Research and funding for new antimicrobials and rapid diagnostic tests.

South Africa is facing a similar problem with resistance. The *Antimicrobial Resistance Background Document* of the National Department of Health (SA NDoH, 2014a: 1-2) stated that there is an increase in resistant pathogens that cause severe infections; treatment options are limited and no new antibiotics are available for the treatment of Gram-negative infections (SA NDoH, 2014a:8-9; Mendelson *et al.*, 2012: 607; Brink, Feldman, Richards, Moolman & Senekal, 2008:586). Although AMS activities are reported in South Africa, there are limitations due to inadequate resources, insufficient surveillance programmes, lack of clinical pharmacists, infectious diseases specialists and IPC practitioners (SA NDoH, 2014b:9-16).

Dr Aaron Motsoaledi, South African Minister of Health, requested that "implementation of antimicrobial stewardship programmes should be prioritised locally and internationally, due to the risk of antimicrobial resistance to public health" (SA NDoH, 2014b:3). He further agreed to invest in sustainable health systems and to collaborate to strengthen capacity and systems (Chioro, Soll-Seck, Hoie, Moeloek, Motsoaledi, Rajatanavin & Touraine, 2015:439).

The goals of the Antimicrobial Resistance National Strategy Framework (ARNSF) (SA NDoH, 2014b:8-9) are:

- "To define the principles of interventions needed to preserve the effectiveness of antimicrobials for future generations;
- To improve the appropriate use of antibiotics in human and animal health;
- To improve the effective management of antibiotic resistant pathogens and prevent their transmission;

- To create an enabling environment for the successful and sustainable implementation of the strategic objectives".

The ARNSF consists of four strategic objectives and four key enablers as demonstrated in Figure 2.1.

<table>
<tr><td rowspan="3">Strategic objectives</td><td colspan="3">Governance
National Intersectoral Committee
Health establishment and district AMS committees and teams</td></tr>
<tr><td>Surveillance
National surveillance system for:
• resistant bacteria
• Antimicrobial usage
• Medication error reporting structures
• Antimicrobial quality</td><td>Prevention & Control
IPC activities in the community and hospitals
Immunisation against preventable infections
IPC strengthening in public health (water & sanitation etc)</td><td>Antimicrobial Stewardship
Policies & Protocols
Formulary restrictions
Pre-authorisation
Antimicrobial prescription forms
National prescribing guidelines
Stewardship at point-of-care
Diagnosis of infection
Appropriate antibiotic choice
Dose optimization, de-escalation and discontinuation</td></tr>
<tr><td colspan="3"></td></tr>
<tr><td rowspan="4">Strategic enablers</td><td colspan="3">Legislative and policy reform for health systems strengthening
Control of use and prescribing of antimicrobials in animal health
Minimum standards and norms for health care quality systems and process (National Core Standards)</td></tr>
<tr><td colspan="3">Education
Incorporate AMR strategies into medical, nursing and allied health student curricula
AMR/AMS CPD programmes for healthcare professions
Sustained public health campaigns</td></tr>
<tr><td colspan="3">Communication
Patient advocacy as part of a patient-centered care approach
Partnership with media, industry and other relevant stakeholders</td></tr>
<tr><td colspan="3">Research – IPC, AMS interventions, diagnostics</td></tr>
</table>

Figure 2.1: National Strategy Framework 2014-2024

Source: SA NDoH, 2014b:9.

The key messages are that IPC programmes should be improved; antimicrobials should be used appropriately; that education of healthcare workers in AMR is of vital importance; and that expertise in AMS is required to assist with implementation of AMS programmes. Accredited training modules must be developed and more IPC practitioners, microbiologists and infectious diseases specialists must be trained and appointed in healthcare facilities (SA NDoH, 2014b:11-14).

Recommended strategies to prevent further development of resistance are complicated to implement in LMICs and require skilled personnel (Okeke *et al.*, 2005b:568). Okeke *et al.* (2005b:568) further stated that there is limited published evidence of successful and sustainable AMS programmes in these countries. Based on the literature, it is further not clear what tools and resources are required for the successful implementation of an AMS programme in LMICs as recommended by international organisations (Dellit *et al.*, 2007: 159-172). Clinical teams consisting of clinical pharmacists and infectious diseases specialists responsible for AMS programmes are uncommon in LMICs.

The majority of facilities in South Africa have access to a clinical microbiologist or pathologist, an IPC practitioner, pharmacist and registered nurses. Microbiology laboratories play an important role in AMS programmes (Goff, 2011:17; Lowman, 2015:359). Apart from the correct analysis of specimens, the clinical microbiologist can play a significant role in the compilation and interpretation of unit specific antibiograms, which is an important aspect in the implementation of an AMS programme. Organism- and resistance profiles differ substantially between critical care units and the rest of the hospital. This information will assist with the development of local treatment protocols and with the correct empiric treatment (Goff. 2011:17; Lowman, 2015: 360; Ramsamy, Muckart & Han, 2013:371). Kothari, Sagar, Panigrahi and Selot found that daily rounds by clinical microbiologists in the absence of infectious diseases specialists and clinical pharmacists in India, has led to an improvement in the appropriate use of antimicrobials, reduction in the cost of antimicrobials and no negative impact on the outcomes of patients with sepsis (Kothari *et al.*, 2008:1187).

Yam *et al.* (2012:1142) investigated the implementation of an AMS programme in rural community hospitals without an infectious diseases physician and a few clinical pharmacists in the United States of America. As part of the implementation of the programme, infectious diseases physicians located away from the site were consulted weekly and additional clinical pharmacists were appointed or trained. Relevant staff members, including medical practitioners, were trained on the use of antimicrobials (Yam *et al*., 2012: 1142).

Goff *et al.* (2012:587) recommended the implementation of simple interventions such as intravenous-to-oral-conversion, automatic therapeutic substitution and formulary restriction in LMICs. The money that is saved on antimicrobials can be utilised more efficiently in other areas of healthcare delivery in LMICs, such as immunisation and preventative care to reduce the burden of disease in these countries Goff *et al*., 2012:587). However, this study by Goff and colleagues focused only on the financial benefits of an AMS programme and not on the improvement in clinical outcomes.

An essential part of an AMS programme is to take cultures prior to the administration of an antimicrobial and enhance daily communication between infectious diseases physicians and prescribers to encourage a reduction in the use of antimicrobials (Allen, 2005:197; Rimawi, Mazer, Siraj, Gooch & Cook, 2013:2099). Allen (2005:197) further stated that the clinical response of the patient should be considered when a decision is made about empirical treatment and that an IPC programme must be included in the implementation of AMS. The use of guidelines, restrictive formularies and education alone are not sufficient; good communication between team members is of vital importance for the success of the programme (Rimawi *et al.*, 2013: 2099).

In a systematic review Kaki, Elligsen, Walker, Simor, Palmay and Daneman (2011:1223) concluded that the implementation of AMS in CCUs was associated with a reduction in antimicrobial utilisation and subsequent cost, shorter duration of therapy and less inappropriate

antimicrobial use. AMS interventions for more than six months were associated with a reduction in multidrug resistant organisms (Kaki *et al.*, 2011:1223). This indicates that the implementation of an AMS programme is a long-term intervention and that there is no easy solution to the problem.

Radyowijati and Haak (2003:733) analysed the evidence available to improve the usage of antimicrobials in LMICs. They found that research on the impact of an AMS programme is limited and that future research is necessary to investigate the rational use of antimicrobials and the socio-cultural aspect of antimicrobial usage (Radyowijati & Haak, 2003:733).

Storey and colleagues (2012:2) stated that antimicrobial stewardship is a key strategy for addressing the problem of antimicrobial resistance and *Clostridium difficile (C.diff)*. However, practical examples of successful stewardship programmes in community hospitals are limited in the reported literature (Storey *et al.*, 2012:2).

Although programmes such as the Integrated Management of Childhood Illnesses (IMCI) and Directly Observed short course Therapy (DOTs) for tuberculosis have been implemented successfully in LMICs, it is not possible to follow a "one size fits all" approach (Okeke *et al.,* 2005b:568). Okeke *et al.* (2005b:568) further stated that interventions do not always have an impact on the emergence of resistant pathogens or change behaviour. The majority of studies evaluating the effect of the implementation of AMS programmes have been conducted in well-functioning and well-resourced healthcare systems in high-income countries (Okeke *et al.,* 2005b:568). Okeke *et al.* (2007:1644) concluded that many of the interventions implemented in LMICs focus on education, but these programmes have not been evaluated to measure their sustainable effectiveness.

LMICs do not necessarily have clinical pharmacists and infectious disease physicians. There might be more effective and cost-efficient interventions that need to be explored further in these countries (Okeke *et al.*, 2007:1644).

It is important to establish what resources, skills and tools are available in LMICs that can be developed further to assist with the implementation of an AMS programme. A multi-disciplinary approach is required and scarce resources must be utilised more effectively (Allen, 2005:198).

Nurses might be one of the resources that should be explored further. Nurses are constantly monitoring patients and are responsible for the administration of antimicrobials. They can potentially play an important role in the implementation and sustainability of an AMS programme (Royal College of Nursing, 2014:4; Abbo *et al.*, 2012:370; Gillespie, Rodrigues, Wright, Williams & Stuart, 2013: 365).

Nurses utilising a checklist might be able to assist with the implementation of an AMS programme. Weiss and colleagues (2013:1) found that using a checklist to remind prescribing physician led to a reduction in inappropriate antimicrobial prescriptions. Checklists are valuable tools in reducing errors of omission and assist with improving outcomes in critical ill patients (Weiss *et al.* 2013:1).

In an 18-month cohort study by Pronovost *et al.* (2006:2731) catheter-related bloodstream infections were significantly reduced utilising a checklist with five recommended evidence-based procedures. Similar methodology can be used for AMS programmes and nurses can be responsible for completing the checklist on a daily basis.

The implementation of a care bundle or scientifically proven interventions for antimicrobial stewardship appears to have a positive impact on outcomes (Toth *et al.*, 2010:746; Coll *et al.*, 2012:845; Patel, Lawson & Guglielmo, 2008: 219). Toth and colleagues (2010:746) demonstrated an increased in appropriate de-escalation from 72% to 90% (p=0.01) in a quasi-experimental study. Monthly in-service training programmes were included in the intervention and process and outcome measures are essential to evaluate the impact of the interventions (Toth *et al.*, 2010:746; Coll *et al.*, 2012:845).

2.5 THE IMPLEMENTATION OF OUTCOME AND PROCESS MEASURES TO EVALUATE THE IMPACT OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

A key element of an AMS programme is to measure the impact of the programme on antimicrobial usage and resistant patterns of micro-organisms (WHO, 2012: 41). The purpose of measuring the impact of interventions is to establish whether it has any value and whether changes should be made to achieve the appropriate outcome. Quality improvement methodology using process and outcomes measures, with clear aims and objectives is the preferred method to measure the impact of interventions (Dellit *et al.* 2007:171; Patel, Lawson & Guglielmo, 2008:209; Nathwani *et al.*, 2011:24; Institute of Healthcare Improvement, 2015).

Dellit *et al.* (2007: 161) recommended that both process and outcome measures should be part of the implementation of an AMS programme to measure the success and the impact on antimicrobial use and resistance patterns. A baseline should be established prior to the implementation of an AMS programme to monitor the progress of the interventions implemented over time (Owens, 2008:125; SHEA, IDSA & PIDS, 2012:326). Examples of such measures might be the prevalence of *C.Diff* rates, hang time, multi-cover and excessive duration of therapy (SHEA, IDSA & PIDS, 2012:326; McGowan. 2012:332).

Process measures are used to measure the degree to which a specific intervention changes a certain aspect of a programme (Dellit *et al.* 2007:161). An example will be to what extent were healthcare workers compliant to the different bundle elements that were implemented (Institute of Healthcare Improvement, 2015). Rules of run charts can be utilised to measure the impact of these interventions (Perla, Provost & Murray, 2011:46).

Outcome measures on the other hand refer to the degree of success achieved with implementation, e.g. whether the processes implemented impact on the development of resistant organisms or on antimicrobial usage (Dellit *et al.* 2007: 161). An example of a successful outcome

measure will be whether the implementation of an AMS programme had a significant reduction in Methicillin Resistant *Staphylococcus aureus* (MRSA) rates.

McGowan (2012: 331) stated that historically AMS programmes mainly focused on process measures, such as the proportion of healthcare institutions that have implemented specific measures, the availability of a functional AMS team or the proportion of correct prescriptions according to guidelines or antibiograms. A reduction in cost of antimicrobials does not necessarily equate to an improvement in patient outcomes. It is recommended that stewardship programmes focus more on patient safety, improved clinical outcomes and a reduction in resistance (McGowan. 2012:332; Goff. 2011:19).

Pulcini, Defres, Aggarwal, Nathwani and Davey (2008:1384-1388) used a care bundle with four evidence-based elements to improve empiric antibiotic use. Improvement methodology was used to test and implement changes (Pulcini *et al.*, 2008:1384-1388). A care bundle is a structured way of improving processes of care and patient outcomes through a set of evidence-based interventions. It proved that interventions implemented consistently improved patient outcomes (Institute of Healthcare Improvement, 2012:2). The authors acknowledged that the complete bundle needs to be consistently implemented to have an effect (Pulcini *et al.*, 2008:1386). Selective application of the bundle will not result in the anticipated outcome. They further acknowledged that not all the elements in the bundle had adequate evidence to support its inclusion in the bundle (Pulcini *et al.*, 2008:1386).

The implementation of a bundle, together with training, improved IPC measures and a team approach; decreased antimicrobial therapy by 41%; and demonstrated a reduction in hyper-virulent *C. diff* from 51% to 13% (Patel, Lawson & Guglielmo, 2008:219).

Using certain targeted antimicrobials as a process measure is an effective way of measuring outcomes. It provides an indication of how many antimicrobials are used and the cost thereof (Owens, 2009:696). The use of defined daily dosage (DDD) is a reliable measure to standardise antimicrobial classification and consumption (WHO, 2012:11). With the use of defined daily dosages, grams of antibiotics are converted into DDDs per 1 000 patient days and this data allows for benchmarking and comparison between different healthcare facilities (Owens, 2009:696; Dellit *et al.*, 2007:171).

Other examples of outcome measures are the number of correct prescriptions for antimicrobials, duration of therapy, as well as the incidence of colonisation or infection due to resistant pathogens (Arnold & Strauss. 2009:5).

2.6 THE RESULTS OF THE IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

Studies have demonstrated that the implementation of an AMS programme has the ability to reduce antimicrobial consumption, resistance and the development of healthcare-associated infections (HAIs).

After an eight-year-old observational study, Dortch and colleagues demonstrated a reduction in HAIs due to multidrug resistant (MDR) Gram negative organisms from 37.4% (2001) to 8.5% (2008) and an overall reduction of 0.78 per 1 000 patient days (Dortch *et al.*, 2011:15).

Clinical pharmacists and weekly consultations with infectious diseases specialists in rural community hospitals demonstrated a significant reduction in antimicrobial usage (Yam *et al.* 2012:1142; Storey *et al.*, 2012:2). Healthcare-associated *C. diff* infections decreased from an average of 5.5 cases per 10 000 patient-days to 1.6 cases per 10 000 patient-days (Yam *et al.* 2012:1146). Training of staff, including medical practitioners, on appropriate antimicrobial usage is essential (Yam *et al.*, 2012:1148).

Several authors had similar findings and were able to show a reduction in antimicrobial use and associated cost (Nowak, Nelson, Breidenbach, Thompson & Carson, 2012:1500; Malani, Richards, Kapila, Otto, Czerwinski & Singal, 2013:145). An overall reduction in the rates of HAIs with *C. diff* (p=0.018) and Vancomycin Resistant *enterococci* (VRE) (p=0.0004) were reported (Nowak *et al.*, 2012:1504).

The implementation of an AMS programme in a 535-bed community hospital led to a reduction in the cost of antimicrobials and *Clostridium difficile* rates. Important to note is that the hospital had two permanently-employed infectious diseases specialist and three clinical pharmacists (Malani *et al.*, 2013:146 -148). This demonstrates the importance of adequate trained resources for the successful implementation of an AMS programme.

Three years after the implementation of an AMS programme in a community hospital, Yu-Shiuan, I-Fen, Yung-Fen, Pei-Ching, Yu-Chih *et al.* (2013:1072) reported a reduction in the cost of broad spectrum antimicrobials. Interventions implemented included training, multidisciplinary teamwork and feedback regarding outcomes measures. The clinical pharmacist and IPC practitioner played a major role in the multidisciplinary team (Yu-Shiuan *et al.*, 2013:1072).

Until recently, the majority of studies focused on the cost benefit of AMS programmes and not on the quality of studies and the improvement of clinical outcomes (McGowan, 2012:233-334). More evidence is needed to prove improved clinical outcomes and a reduction in AMR (McGowan, 2012:335).

The implementation of a national AMS programme in Scotland proved to reduce *C. diff* infections and a restrictive antimicrobial policy appears to not have negatively impacted on the mortality rate (Nathwani, Sneddon, Patton & Malcolm, 2012:2). Nathwani and colleagues further highlighted the importance of clinical leadership and organisational accountability.

In a systematic review done by Wagner, Filice, Drekonja, Greer, McDonald and colleagues (2014:1209), the authors concluded that various studies have been published demonstrating a decrease in antimicrobial usage, and associated reduction in the cost of antibiotics and reduction in resistant pathogens. However, there is less published data and limited strong evidence on improved clinic outcomes and sustainability of these programmes (Wagner *et al.*, 2014:1209).

2.7 TRAINING AND EDUCATION OF HEALTHCARE WORKERS

Inadequate knowledge of prescribers and other healthcare workers is a major contributing factor to inappropriate antimicrobial usage (Pulcini & Gyssens, 2013:192; WHO, 2015a:3). Training on antimicrobials is traditionally directed at medical practitioners after graduation (Pulcini & Gyssens, 2013:192).

Training is an important element of an AMS program, especially if the programme needs to change behaviour and influence practice (Dellit *et al.*, 2007:165; SHEA, IDSA & PIDS, 2012: 325). Training on antimicrobial prescribing should be part of the training curriculum of undergraduate medical students and other healthcare workers such as nurses and pharmacists (Pulcini & Gyssens (2013:192). Various methods such as e-learning modules, brochures, leaflets and lectures are available for training as passive training alone is not enough (Pulcini & Gyssens, 2013:192; CDC, 2014:13; SHEA, IDSA & PIDS, 2012:325; Dellit *et al.* 2007:165: Nathwani *et al.*, 2011:22). Interactive, participating training sessions provided by mentoring physicians have much more value and influence to change behaviour (Pulcini & Gyssens, 2013:199). In a Cochrane review Arnold and Strauss (2009:13-14) found that interactive learning sessions such as workshops, outreach programmes, reminders, audit and feedback might be more beneficial than learning sessions through conference attendance and lectures.

In a qualitative study conducted in India, Sahoo and colleagues concluded that it is important to improve physician and consumer knowledge and behaviour to use antimicrobials more appropriately and rationally (Sahoo *et al.*, 2010:636). Gillespie *et al.* (2013:356-366) demonstrated that by providing additional training for nurses on AMS and the indications for therapy, they were able to play a significant role in the implementation of an AMS programme that lead to a subsequent reduction in *Staphylococcus areus* bloodstream infections. (Gillespie *et al.*, 2013:356-366). Similarly, Moongtui, Picheansathian and Senaratana (2011:107) stated that after training on IPC and AMS, nurses can play a role in AMS programmes, particularly through timeous notification of infections, isolation of patients and the implementation of transmission-based precautions, hand

hygiene compliance and environmental cleaning. Improved knowledge has the ability to change behaviour (Moongtui *et al.*, 2011:107).

In an AMS training programme directed at rural hospitals, Kellie (2011:1181) found that using resources such as video conferences, electronic guidelines and articles, regular lectures with the opportunity to ask questions and share experiences, all participating rural hospitals increased their AMS activities with 38%. One of the limitations of the study was that the sustainability and the impact of the interventions were not measured. The positive aspect of the study was that onsite training was provided to staff of rural hospitals without having to travel (Kellie, 2011:1181-1183). These aspects make a programme like this very favourable for implementation in rural and LMICs.

Cisneros, Neth, Gil-Navarro, Lepe, Jimenez-Parrilla *et al.* (2014:83) demonstrated that there is value in using one-to-one counselling interviews with prescribers as part of a training programme to improve appropriate use of antimicrobials. Clinical data was reviewed during interviews and the treatment was compared to the clinical diagnosis, using a standardised questionnaire (Cisneros *et al.*, 2014:83). A limitation of the study for implementation in LMICs is that the consulting team consisted out of infectious diseases specialists, clinical pharmacists, intensive care and preventative medicine specialists, paediatricians and a microbiologist (Cisneros *et al.*, 2014:83). All of these resources are not readily available in the majority of hospitals in LMICs. Another limitation of this study was that the clinical outcomes were not measured, but only the usage of antimicrobials (Cisneros *et al.*, 2014: 84).

Budwall (2010:116) stated that pharmacists specialising in infectious diseases or antimicrobials are in an ideal position to train doctors and nurses on the appropriate use of antimicrobials. Other healthcare professionals should be included in the training programmes (Budwall, 2010:116).

An effective training programme can contribute to a reduction in HAIs and the transmission of communicable diseases, as mentioned by Mehtar, Marais and Aucamp (2011:1-7). It is important to conduct a baseline assessment prior to commencing with a training programme to establish the existing level of knowledge. Mehtar *et al.* (2011: 2-3) highlighted the fact that senior management support is vital for the successful implementation of a training programme, but that the rapid turnover of staff has a negative impact on training programmes (Mehtar *et al.*, 2011:1-7).

The CDC (2014:13) and SHEA (2012:325) recommended that information about facility-specific antimicrobial usage should be shared with clinicians and other healthcare workers using presentations, newsletters and electronic communication to improve prescribing habits. Reviewing of cases should be used as an opportunity to educate personnel.

2.8 THE ROLE OF INFECTION PREVENTION AND CONTROL IN THE IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

Antimicrobial resistant bacteria are transmitted in healthcare facilities and have the potential to contribute to the increase in antimicrobial resistance worldwide (WHO, 2012:64; WHO, 2015a:3). Insufficient IPC programmes, including inadequate policies and procedures, challenges with design and infrastructure, inadequate staffing and skills mix and the behaviour of healthcare workers contribute to the problem. Patient and disease profiles further have an impact and contribute to the extent of the problem (WHO, 2012:65).

The Association for Professionals in Infection Control and Epidemiology (APIC) and the Society for Healthcare Epidemiology of America (SHEA) stated in their position paper that IPC programmes play a vital role in the implementation of an antimicrobial stewardship (AMS) programme and the prevention of the spread of multidrug resistant organisms (MDROs) (Moody, Cosgrove, Olmsted, Septimus, Aureden *et al.*, 2012:94). A renewed focus is necessary to highlight the importance of IPC programmes and to recognise the importance of collaboration with other healthcare services (Royal College of Nursing, 2014:5).

To implement and maintain a successful and sustainable IPC programme, a multimodal and multidisciplinary programme is needed to ensure a system- and behavioural change of healthcare workers (WHO, 2012:65: Chalfine *et al.,* 2012:1). This includes monitoring of isolation precautions, an AMS programme, availability of alcohol-based hand rubs and feedback to healthcare providers. These successful interventions reduced antimicrobial usage by 31% and healthcare-associated Methicillin Resistant *Staphylococcus aureus* (MRSA) bacteraemia by 93% (Chalfine *et al.*, 2012:1).

The Wilton Park report (Foreign & Commonwealth Office, 2015:6) recommended that IPC programmes are reviewed and that the spread of resistance pathogens through ecosystems and into the food chain should be explored. Sanitation in LMICs should improve and healthcare systems should be strengthened in order to prevent transmission of resistance. Hygiene practices and knowledge must be improved, with emphasis on the importance of hand hygiene, in both the community and healthcare facilities. Other important areas that need to be targeted are the new technology of rapid diagnostic tests and improved vaccination programmes (Foreign & Commonwealth Office, 2015:6).

Mendelson and colleagues (2012: 607) stated that IPC is a key element in an AMS programme to prevent the transmission of resistant pathogens in healthcare facilities (Mendelson *et al.*, 2012:607; WHO, 2012:68; Foreign & Commonwealth Office, 2015:6; Brink *et al.*, 2008:590). IPC is not only the responsibility of IPC practitioners, but of every healthcare worker and accountability of all in the healthcare industry is required (Mendelson *et al.*, 2012:607; Chalfine *et al.* 2012:1; WHO, 2012:68). Other important factors are screening and decolonisation, readmission alert systems that

notify healthcare workers if patients colonised or infected previous with MDROs are re-admitted, environmental cleaning and education of healthcare workers (WHO, 2012:68).

The WHO (2015a:5) recommended that a good IPC programme can be a cost-effective measure to prevent the transmission of AMR organisms and can be implemented in all healthcare settings, including LMICs.

2.9 THE ROLE OF THE NURSE PRACTITIONER IN THE IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

Nurses play a significant role in the prescribing and administration of antimicrobials in South Africa and other LMICs. The South African Nursing Council allows nurses to prescribe and dispense medication according to the Standard Treatment Guidelines and Essential Medicine list in primary healthcare settings after the successful completion of a suitable training programme (SA NDoH, 2015:1; Essack, Schellack, Pople, Van der Merwe, Suleman, Meyer, Gous & Benjamin, 2010:564). Nurses are widely used in LMICs to initiate treatment for tuberculosis as well as antiretroviral treatment for HIV and the syndromic treatment for sexually transmitted diseases (Colvin, Fairall, Lewin, Georgeu, Zwarenstein, Bachmann, Uebel, Bateman, 2010:212; Georgeu, Colvin, Lewin, Fairall, Bachmann, Uebel, Zwarenstein, Draper, Bateman, 2012:11). However, currently nurses are not used in acute care settings in South Africa to prescribe antimicrobials. At present, prescribing antimicrobials is the prerogative of the treating physician alone.

Although antimicrobial stewardship programmes follow a multi-disciplinary approach, it mostly includes a clinical pharmacist, physician, infectious diseases specialist, microbiologist and possibly an infection prevention and control (IPC) practitioner (Tamma & Cosgrove. 2011:245). The involvement of registered nurses has been limited (Edwards, Drumright *et al.*, 2011:6; Tamma & Cosgrove, 2011:245). A large proportion of healthcare workers consist out of nurses and their role and contribution in the implementation of AMS programmes should be recognised and acknowledged (Royal College of Nursing, 2014:4). In order to implement a successful AMS programme, all disciplines within a healthcare setting have to be included in the implementation of the programme (Royal College of Nursing, 2014:4). Senior nurses should be included as core members of an antimicrobial stewardship team (Ladenheim, Rosembert, Hallam & Micallef, 2013:47).

Curry and colleagues (2014:6-7; CDC, 2014:6) further stated that nurses can play a significant role in the implementation and adherence to IPC principles, education, vaccination programmes, quality improvement projects, by obtaining specimens prior to commencement of an antimicrobial and to ensure that the correct antimicrobial is administered on time and documented (Royal College of Nursing, 2014:6-7; CDC, 2014:6). Nurses can review prescription charts, monitor patients, interpret blood results and evaluate the duration of therapy. They can further confirm allergies and administer the correct drug at the correct time for the correct duration (Ladenheim *et al.*, 2013:48)

and discuss the results and indication of antibiotic treatment with medical practitioners, as well as the duration of treatment (CDC, 2014:6).

Edwards, Loveday, Drumright and Holmes (2011:4) stated that nurses provide the most consistent patient care and that they should play a bigger role in the multidisciplinary collaboration to implement antimicrobial stewardship. Nurses can potentially be a cost-efficient resource. Furthermore, Edwards, Drumright *et al.* (2011:9) noted that the role of the nurse in the implementation of an antimicrobial stewardship programme is not clear and it should be investigated further since reducing antimicrobial resistance extends beyond the responsibility of prescribing physicians and pharmacists.

As patient advocates, nurses have a responsibility to ensure that antimicrobials are prescribed appropriately and to educate patients on the correct use of antimicrobials (Edwards, Loveday *et al.*, 2011:4; Crombie, 2012:16). Although Crombie's study was based on experiences in primary healthcare settings, it can be applied in acute care settings. Crombie (2012:19) further stated that nurses can advise patients on the indications for an antibiotic, the advantage of flu vaccines for high-risk groups and the importance of following the instructions on when and how to take the prescribed medication.

A key responsibility of nurses is to administer medication (Gillespie *et al.*, 2013:356; Budwall, 2010:116; Moongtui *et al*., 2011:104). They are in an ideal position to monitor and audit prescriptions and Gillespie *et al.* (2013:365-367) found that nurses play an important role in questioning the appropriateness of treatment, but that additional training might be required. Barriers to their inclusion in the AMS team needs to be clarified and their role in the multidisciplinary team should be established (Edwards, Drumright *et al.*, 2011:9).

Gillespie *et al.* (2013:354) emphasised that nurses should not take the responsibility of prescribing the antimicrobial, but should ask questions about the appropriateness of the prescription. Their study highlighted the fact that additional training on antimicrobials is required (Gillespie *et al.* 2013:365-365). Influencing or confronting clinicians about prescribing practice might be challenging for nurses in the hierarchical environment of healthcare. Charani, Castro-Sanchez, Sevdalis, Kyratsis, Drumright, Shah and Holmes (2013:189-194) found that senior doctors will ignore policies if they feel it is undermining their authority and questioning their knowledge and decision-making ability. Policies will be followed if endorsed by senior colleagues. Nurses might therefore be hesitant to prompt and correct doctors. Healthcare workers in general are hesitant to question prescriptions of colleagues (Charani *et al.*, 2013:189-194).

Budwall (2010:116) stated that nurses can remind doctors to switch from intravenous to oral therapy, monitor therapeutic drug results and inform the physician about the results (Budwall, 2010: 116; Ladenheim *et al.*, 2013:47).

According to Charani, Cooke and Holmes (2010: 2276), nurses should be trained and educated regarding antimicrobial usage and be encouraged to participate in AMS programmes. Nurses, together with pharmacists, are the most consistent workforce. Healthcare workers need to be more actively involved in the decision-making process in order to make a sustainable change in prescribing practices (Charani *et al.*, 2010: 2276).

The question is whether the registered nurse working in the CCU can be empowered to play a significant role in the implementation of AMS programmes in facilities that do not have the resources as recommended in the literature (Dellit *et al.* 2007: 159-173).

In an anonymous electronic survey done by Abbo and colleagues (2012:373) the perceptions, attitudes and knowledge about antimicrobial use and resistance were tested amongst nurses in a university-affiliated hospital. Critical care nurses scored higher then nurses in other disciplines in the knowledge question (82% vs. 64%; $p<0.002$). The study concluded that AMS programmes require a team approach and that the role of nurse practitioners and more specifically critical care nurses, should not be underestimated and explored further (Abbo *et al.*, 2012:376).

Friedman (2013:400) stated that the implementation of an AMS programme is a long-term intervention that needs to be sustainable to be effective. He furthermore stated that LMICs might not have all the necessary resources for the implementation of an AMS programme as described in the literature (Friedman, 2013:410). Nurse practitioners are already responsible for the prescription of antibiotics in primary healthcare settings in many countries. The inclusion of nurse practitioners in AMS programmes might improve the effective use of antimicrobials and their role needs to be explored further (Abbo *et al.*, 2012:373; Edwards, Drumright *et al.*, 2011:9).

2.10 CONCLUSION

South-Africa has to identify resources to implement a national AMS programme as described in several guidelines (Dellit *et al.*, 2007; CDC, 2012; WHO, 2012; SA NDoH, 2014b:8-9). Private hospitals in South Africa have very few clinical pharmacists and even fewer infectious diseases specialists. Expertise for the implementation of an AMS programme is limited and the utilisation and training of alternative resources should therefore be explored to successfully implement an AMS programme. The CDC (2014:4) recommended that leadership commitment and the provision of necessary resources are essential for the implementation of an AMS programme. It is presently not clear which interventions can be successfully implemented in LMICs to reduce AMR. The majority of studies have been conducted in well-resourced and well-developed countries. Studies conducted in India and China indicated that training and improved IPC practices are important interventions to reduce the transmission of antimicrobial resistance (Yu-Shiuan *et al.*, 2013:1072, Moongtui *et al*., 2011:107, Sahoo *et al*., 2010: 629). It is uncertain which interventions related to AMS can be implemented by nurses.

In addition to current resources, critical care nurses should be included in the AMS team, considering the availability of other healthcare workers. Their role in the AMS team should be clarified and it should be established whether the utilisation of a checklist with evidence-based quality indicators can assist with the implementation of the programme.

Edwards, Drumright *et al.* (2011:6) suggested that nurses can play a role and can be responsible for specific activities such as the monitoring of duration of treatment, indication for antimicrobial treatment, prompts to de-escalate and switch from oral to intravenous treatment. Many of these interventions are performed by physicians and pharmacists in well-resourced countries, but can be executed by nurses. Nurses are involved in all levels of patient care and are in a position to continuously monitor the condition and treatment of the patient. The authors concluded that nurses can play a key role in AMS teams through the implementation of evidence-based measures and ensuring patient safety in healthcare facilities (Edwards, Drumright *et al.*, 2011:6).

The following chapter gives an overview of the research methodology employed in this study.

CHAPTER 3
RESEARCH DESIGN AND METHODOLOGY

3.1 INTRODUCTION

The previous chapters provided the background to the study including a review of the literature. The insufficiencies in the literature were highlighted. The aim of the study is to address some of the limitations identified in the research question.

Chapter 3 provides a detailed description of the study design and methodology that was followed to investigate the role of the critical care nurse in the implementation of an antimicrobial stewardship programme.

3.2 STUDY DESIGN

A quantitative method was used to prove the research question due to the measurable variables that can be used to objectively answer the research question and reach unbiased conclusions (De Vos, Strydom, Fouché & Delport, 2011:63).

A pre- and post-intervention study design was utilised for this research. The main reason for the selection of this specific study design was to establish whether any changes took place after the implementation of certain interventions. A control group was furthermore not included in the study to limit possible bias. It would have been problematic to find a hospital with a similar organism and disease profile. Nurses furthermore have different levels of knowledge and hospitals have different interpretations of policies and procedures. Although a control group would have been preferred and another unit in the hospital could have been used as a control, the researcher wanted to test the proposed interventions on a small scale to establish if there is merit in the interventions, before rolling it out to more departments in the hospital. A CCU is normally a more controlled environment and therefore provides a more favourable environment for interventions where daily checks are required.

3.3 STUDY SETTING

The study was conducted in the CCU of an acute care private hospital in the Limpopo province, South Africa from 1 May 2014 until 31 May 2015. The hospital has 247 operational beds, eight operating theatres and twelve critical care beds.

Both surgical and medical patients are admitted in the CCU with the majority being medical patients (60%). The bed occupancy in the unit is 84.81% with a median length of stay (LOS) of 5.78 days. Any specialist with admission rights are allowed to admit patients to the CCU.

The hospital has six physicians and five pharmacists. Medical practitioners are not employed by the hospital. They work as independent practitioners. There is no infectious diseases specialist or clinical pharmacist working at the hospital.

A clinical microbiologist has started visiting the hospital once a month from May 2014 and in addition to training, conducts a ward round with treating physicians and makes recommendations about treatment plans.

The staff component of the CCU consists of a unit manager, senior registered nurse, thirteen registered nurses, six enrolled nurses and two enrolled nurse assistants, as well as a ward administrative assistant. Three of the registered nurses have a critical care qualification.

A situational analysis preceded the study. No antimicrobial stewardship (AMS) programme had been implemented prior to commencement of the study. The main barrier was the unavailability of skilled personnel such as a clinical pharmacist, infectious diseases specialist or clinical microbiologist; all key resources in the implementation of an AMS programme.

3.4 PARTICIPANTS

The records of all patients fifteen years of age and older admitted or transferred into the CCU from other departments in the hospital or other healthcare facilities for longer than 24 hours were reviewed as part of the study. Patients admitted for post-operative monitoring were excluded from the study, except if the admission exceeded 24 hours due to post-surgery complications. The rationale behind excluding post-operative patients was based on the fact that antibiotics are not routinely administered, unless surgical prophylaxis is indicated. Prophylaxis is not generally administered for longer than 24 hours. The records of 407 patients were included in the pre- and post-intervention record review and a checklist was completed for all patients admitted to the CCU during the study period of 13 months.

Nurses working in the unit were included in the pre- and post-training knowledge assessment, training and data collection. Written consent was obtained from both the nurses taking part in the study as well as the hospital (Refer to Appendix A for the participants' information and consent form). Demographic information such as age, nursing qualifications and years of experience was collected. Date of birth was used to identify nurses who took part in both the pre- and post-assessment. All information was kept confidential.

The role of the nurses in the study was to implement a checklist and monitor on a daily basis whether there was adherence to the elements detailed on the checklist. They were furthermore responsible to ensure that the interventions stipulated on the checklist were executed and that it was not merely a checklist. The nurses were responsible for the following:

- Collect specimens prior to the commencement of an antimicrobial;
- Ensure that an antimicrobial was administered as soon as possible after a prescription was written;
- Remind the treating physician to de-escalate once an organism was cultured and the resistance pattern was known; and

- Remind the treating physician to review the necessity of treatment as well as the necessity of the invasive device.

The role of the researcher in the study was to coordinate the implementation of the programme, training of the nurses, auditing of adherence to IPC practices, collection and collating of data. The study hospital was visited three times during the study period and continued support and communication were provided via teleconferences and e-mail.

3.5 INTERVENTIONS

Several interventions were implemented as part of the study, namely:

- Infection prevention and control audits;
- Training of healthcare workers;
- Monthly ward rounds conducted by a clinical microbiologist; and
- Nurses utilising a checklist to monitor specific measures daily to measure compliance to evidence-based interventions as part of an antimicrobial stewardship programme.

Prior to the intervention, the study hospital was visited and the purpose of the study explained to all the stakeholders. During the visit, the critical care nurses, unit manager and IPC practitioner received training on basic IPC principles and antimicrobial stewardship. The checklist was discussed in detail as well as the importance of each measure on the checklist and the purpose of the daily completion and adherence to the different measures. The clinical microbiologist was introduced on the second visit and provided training on AMS to the medical practitioners and nurses in the form of presentations on a monthly basis. Ward rounds were conducted during his visits and the treatment of individual patients was discussed. The medical practitioners welcomed the discussions and continued to consult the clinical microbiologist telephonically.

The interventions that were implemented are discussed individually in detail in this chapter.

3.5.1 Record review

A retrospective record review was conducted by the researcher of patients admitted to the unit eight months prior to the interventions to establish a baseline and to ensure a large enough sample size (1 October 2013 to 31 May 2014) and repeated the same period at the end of the study.

The following information was collected:

- Demographic data such as age and gender;
- Length of stay in the critical care unit;
- Positive specimen prior to initiation of antimicrobial therapy;
- Duration of antimicrobial therapy; and
- Amount of antimicrobials prescribed.

3.5.2 Knowledge assessment

A baseline knowledge assessment utilising a paper-based questionnaire was done on registered and enrolled nurses working in the CCU to establish their knowledge about AMS and IPC prior to implementation of the different interventions (Refer to Appendix C). The knowledge assessment was repeated at the end of the study. The purpose of the knowledge assessment was to establish whether training assisted with an improvement in knowledge about IPC and AMS and improved adherence to IPC practices.

3.5.3 Infection Prevention and Control Audits

The researcher conducted an IPC audit pre-and post-intervention to establish compliance to IPC principles (Refer to Appendix E). The audit did not only evaluated environmental cleaning and hand hygiene, but included aspects related to training and surveillance.

3.5.4 Checklist with daily measures

A checklist measuring adherence to specific evidence-based interventions related to antimicrobial stewardship was completed daily by the critical care nurses (Refer to Appendix D). Completion of the checklist was however only part of the intervention. The nurses had to ensure that the necessary action had to be taken to ensure adherence. The completion of the checklist commenced on 1 June 2014 and concluded on 31 May 2015.

The following elements were included in the checklist:

i) Hang time

Hang time refers to the time from the generation of the prescription until the administration of the first dose of antimicrobials. Several studies and guidelines have demonstrated the importance of prompt administration of a broad-spectrum antimicrobial in critically ill patients with severe sepsis to reduce mortality

ii) Culture before treatment

Taking samples for microbiological culture before treatment was the second element on the checklist. The significance of this measure is to ensure that the most appropriate and narrow-spectrum antibiotic is prescribed for the organism that has been cultured and the clinical condition of the patient

iii) De-escalation of therapy

De-escalation of antimicrobial therapy was monitored and the significance of the measure was to ensure that patients receive targeted therapy as soon as the sensitivity of the organism had been established

iv) Duration of therapy

Duration of therapy was measured daily. In order to prevent resistance, treatment with an appropriate antibiotic needs to be as short as clinically possible. The nurse reminds the doctor at day seven to stop therapy.

v) Number of antimicrobials prescribed and administered simultaneously was another daily measure

vi) If device is *in situ*, remind the doctor to assess for removal

The last daily measure was the evaluation of the necessity of an indwelling device and the possibility of removal thereof. The purpose for including the measure is the additional risk of infection for patients with a device *in situ* and the increased risk of antimicrobial therapy for an extended period of time.

Other interventions included:

- Training sessions.
- Clinical microbiologist provided training on various aspects related to antimicrobial stewardship (AMS). The target audience was medical practitioners, pharmacists and registered nurses.
- A clinical pharmacist provided a three-hour session via video conference about antimicrobial stewardship to registered nurses.
- Quality improvement methodology was addressed during a three-hour session by a quality specialist
- IPC training was provided by an IPC specialist and by the IPC practitioner of the hospital.
- Training was conducted with Powerpoint presentations or via video conferencing.
- Clinical ward rounds conducted by a clinical microbiologist, treating physicians, IPC practitioner and nursing staff were introduced. Patients and their treatment were discussed and recommendations were made.
- The clinical microbiologist was a key role-player in the implementation of the programme. Apart from conducting ward rounds, he was also available for telephonic consultations and suggested treatment options for individual patients.
- Prescriptions were monitored for the duration of treatment and where multiple antimicrobials had been administered simultaneously for the same patient.
- Reviewing of the prescription and a stamp on day seven was given by a pharmacist to remind the treating medical practitioner to review the necessity of antimicrobial therapy.
- Daily ward rounds in the CCU were conducted by the IPC practitioner to monitor hand hygiene compliance, adherence to IPC principles, environmental cleaning and the implementation of appropriate transmission-based precautions.

- The use of antimicrobials (excluding antiretroviral therapy and antituberculosis drugs) during the pre-and post-intervention periods were evaluated and compared to establish whether there had been any change in prescribing practice.

Data on antimicrobial usage was obtained from the pharmacy data warehouse. Daily antimicrobial usage per patient was calculated (begin and end date). The number of antimicrobials that was used as well as the duration of treatment was calculated. Both antibacterial and antifungals were included. Antiviral therapy and antituberculosis drugs were excluded.

Antimicrobial usage was measured in defined daily dosages (DDDs). DDDs allows for comparison of usage of medication over a period of time and location. It also allows for international benchmarking. DDDs are the internationally recognised technical unit of measurement of medicine consumption recommended by the WHO (World Health Organisation, 2015b).

3.6 QUANTITATIVE VARIABLES

Data was collected using binary, categorical and discrete numerical variables as shown in Table 3.1.

Table 3.1: Type of variable

Type of variable	Data element		
Discrete numerical variable	Checklist with daily measures	One = Yes	Nil = No
Continuous numerical variable	Age	Number	
Binary variable	Knowledge assessment	Yes	No
Categorical variable	Resistance patterns of organisms	S=Sensitive	R=Resistant
Categorical variable	Gender	M=Male	F=Female

Percentages of either ‘yes’ or ‘no’ or ‘one’ and ‘nil’ were then calculated with the number of ‘yes’ divided by all the documented responses on the checklist to provide a percentage. The same methodology was followed for the knowledge assessment. The number of correct answers to open-ended questions was added and divided by the total of the particular answer to provide a percentage.

Appropriate specimen collected was presented as a percentage of the total study population and the change pre- and post-implementation was calculated.

Documentation of the antimicrobial included the name and duration of therapy.

Continuous numerical data was used to record the duration of therapy and the total number of antimicrobials. Duration of therapy was defined as a start and end date and the days on therapy calculated by adding the days. The number of antimicrobials administered simultaneously was added to provide a total. The type of antimicrobial (name) was documented as a categorical variable and the total amount of antimicrobial usage was measured in DDDs.

Data was imported onto Microsoft Excel©. Statistical significance of the data was calculated using STATA software and Microsoft Excel©.

3.7 DATA SOURCES/MEASUREMENT

Data collection was done in a structured way through the utilisation of measuring instruments such as questionnaires and checklists.

Paper-based tools were utilised for the collection of data related to:

- The knowledge assessment questionnaire;
- IPC audit; and
- Daily checklist.

Data was captured in Microsoft Excel©, analysed and presented in graphs and tables.

Electronic data sources, namely the patient administration system (AS400) and the IPC electronic surveillance programme (ICNet) were utilised to obtain information related to:

- Patient demographics such as age and gender;
- Antimicrobials prescribed and duration of treatment;
- Organisms cultured; and
- Resistance patterns of organisms.

Data was exported into Microsoft Excel©, presented in graphs and tables and analysed.

3.8 DATA COLLECTION INSTRUMENT

Questionnaires and checklists were utilised to collect data. The purpose of using these instruments was to ensure that the objectives are met and that there is correlation between the research objectives and problem statement and to furthermore ensure that the same data elements are collected continuously in a standardised method.

The researcher designed the knowledge assessment questionnaire. It was tested on a group of registered nurses at the 2013 Critical Care Congress prior to the study and adapted. The questionnaire included demographic detail such as age, qualifications, year of completion of study and prior IPC and AMS training (Refer to Appendix C for the final knowledge assessment questionnaire).

The majority of the questions were close-ended questions with either a ‘yes’ or ‘no’ answer; ‘true’ or ‘false’ or multiple choice. Although close-ended questions limited the participants to the options provided, the purpose of the questionnaire was to test knowledge and therefore no open-ended questions were asked.

The checklist utilised for the daily monitoring of the AMS interventions was based on the elements recommended by the Antibiotic Stewardship Driver Diagram and Change package of the Institute for Healthcare Improvement and the Centre for Disease Control and Prevention (2012). The researcher developed the checklist and included a section that explains the rationale behind the selection of the different elements for clarification.

This checklist was completed daily by the registered nurse caring for the patient. Compliance to the different elements was measured and monitored (Refer to Appendix D for the checklist).

The researcher originally used a template in Microsoft Excel© to collect data from patient records by reviewing each file individually. It was established that all the required data was available from electronic data bases and this data was used for the post-intervention assessment.

3.10 SAMPLE SIZE

The researcher selected one of the most remote hospitals within the private hospital group to conduct the study. The size of the CCU was an important factor to ensure a large enough sample size. The unit has twelve beds and in order to compensate for the size of the unit, the study was conducted over a longer period (13 months).

The patients admitted to the CCU represent a portion or sample of the population of the community, including the disease and organism profiles of the community. By including all patients admitted or transferred into the unit for longer than 24 hours, in the study, the researcher attempted to reduce selection bias and sampling error and to ensure a large enough sample size. The records of 407 patients were reviewed pre-and post-intervention and a checklist was completed for all patients qualified according to the inclusion criteria.

3.11 DATA ANALYSIS AND STATISTICAL METHODS

Data was summarised using tables, graphs and descriptive statistics as appropriate. Numerical data was described as means or medians when it was skewed. Population estimates have been provided by means of 95% confidence intervals.

Associations between the pre- and post-intervention periods of the study were evaluated. Categorical outcomes were compared by means of the Chi-squared test, Fisher exact and the unpaired and two-tailed t-test. Significance level of $p = < 0.05$ was used. Statistical tests were two-sided.

The z-test was used to establish the p-value for two independent proportions.

Quality improvement methodology and rules for run charts were used to establish whether there had been improvement in compliance with the daily measures.

Calculations were performed using Microsoft Excel©. Demographic and outcomes variables compared the pre- and post-implementation period using the t-test. Lengths of stay (LOS) between

the admission and discharge dates in the CCU were compared between the pre-and post-interventions periods using the unpaired t-test.

Only nurses who had completed both the pre- and post-intervention knowledge assessments were included in the data analysis. Only one checklist per patient was included in the data analysis.

3.12 ETHICAL CONSIDERATIONS

Ethical clearance for the study was obtained from Stellenbosch University and the ethical committee of the hospital group and hospital management in which the study was conducted. Informed consent was obtained from the nursing personnel taking part in the knowledge assessment.

Patient information was protected and confidential. Access to information was restricted. Information regarding prescription patterns has not been linked to specific patients. All data was anonymised.

3.12.1 Beneficence

The results of the study do not directly benefit the patients, but the findings of this study will benefit patients in future if antimicrobials are used more conservatively and with more consideration, thus resulting in lower resistance. The treatment options for severe infections are currently very limited and action needs to be taken to prevent the development of further resistance. It means that all studies that are investigating interventions to improve prescription habits and reduce resistance will benefit the patients.

3.12.2 Non-maleficence

Patients did not receive any treatment that was not indicated or that could harm them. No treatment was withheld as part of the study. The study did not focus on whether an antimicrobial should be given or not; it only monitored the duration of treatment and the amount of antimicrobials prescribed. The study merely prompted prescribing practitioners to carefully consider their prescriptions, rather than blindly prescribing out of habit.

3.12.3 Justice

Participants had been included in the study in line with the inclusion and exclusion criteria. Participants were not discriminated against based on age, race, gender, place of origin or income or any other factor not listed in the eligibility criteria.

3.12.4 Autonomy

Patients were not researched directly and were not harmed in any way. The data that was collected for the study is part of the nursing routine in the critical care unit. It was not “people” who were researched, but prescribing practices and the effect of the interventions on antimicrobial consumption and subsequently on antimicrobial resistance.

3.12.5 Informed consent

All data was anonymised. A request for waiver of informed consent by patients was approved by the Stellenbosch University Ethics committee. Participants working in the unit provided consent. (Refer to Appendix A for the consent form and Appendix B for the approval letters from Mediclinic and Stellenbosch University.)

3.12.6 Confidentiality

All information was regarded as confidential and patient information was anonymised. All Excel spreadsheets and data bases were password protected. Only the primary researcher had access to the data bases and the statistical analysts and study supervisors had access to the Excel spreadsheets.

3.12.7 Uncovering gross violations

No gross violations were uncovered during the study.

3.13 CONCLUSION

The checklist was completed as part of the critical care nurses' routine daily record keeping. In addition to the completion of the checklist she had to ensure that the required actions had been executed. The findings of the study will benefit the patients and the staff working in the unit. By having data that supports statements, practices can be changed to ensure improved outcomes for patients.

The following chapter explores the findings in detail.

CHAPTER 4
RESULTS, DATA ANALYSIS AND INTERPRETATION

4.1 INTRODUCTION

This section of the thesis provides an overview of the data that was collected and the analysis and interpretation thereof.

The different interventions and their outcomes are discussed in separate sections of the chapter.

4.2 DATA ANALYSIS AND STATISTICAL METHODS

Data was imported into Microsoft Excel© and graphs and tables were compiled. Statistical significance of the data was calculated using STATA software and Microsoft Excel©. Refer to Section 3.11 for full details of the data analysis and statistical methods of this study.

4.3 KNOWLEDGE ASSESSMENT

The same standardised questionnaire was used for the pre- and post-knowledge assessment. Questions about basic infection prevention and control (IPC) and antimicrobial stewardship (AMS) were asked, under the supervision of the IPC Practitioner of the hospital. The completed questionnaires were returned by mail.

Eighteen staff members (n=18) took part in the pre-intervention knowledge assessment. Seventy eight percent (n=14) of the staff were registered nurses and 17% (n=4) were enrolled nurses. One participant (6%) had a degree in Nursing. Three of the staff members (17%) had a critical care qualification. The median years of experience amongst the staff were 11 years. Three participants (17%) had previous IPC training ranging from an hour-long workshop to one day; only one (6%) had a previous one-hour information session on antimicrobial stewardship.

Twelve staff members took part in the post-training knowledge assessment. The other six were either transferred to other nursing units, resigned or were not available on the day of the test. Three of the staff with IPC training indicated that they completed the in-house course in Fundamentals in IPC. Only the results from participants who had completed both the pre- and post-knowledge assessment were included in the analysis (n=10).

4.3.1 Elements of standard precautions

During the pre-assessment, none of the respondents could name even five standard precautions. Only two were able to provide four correct answers to the question. Four participants (40%) had three correct answer and four (40%) had two correct answers (Figure 4.1).

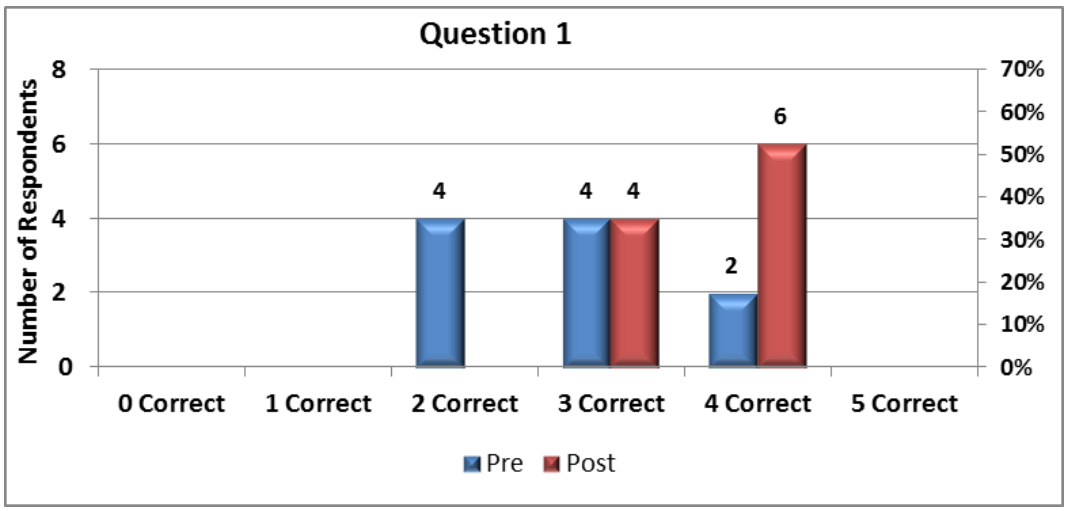


Figure 4.1: Question 1: Elements of standard precautions

Although nobody could name five standard precautions in the post-intervention assessment, six participants (60%) had four correct answers. Four participants (40%) had three correct answers.

4.3.2 Transmission-based precautions

The second question asked to state the three types of transmission-based precautions. Three participants (30%) were able to get full marks for the question. Three participants (30%) provided two correct answers and three (30%) had one correct answer. In the pre-intervention group three participants (30%) did not had one correct answer compared to one person (10%) in the post-intervention group (Refer to Figure 4.2).

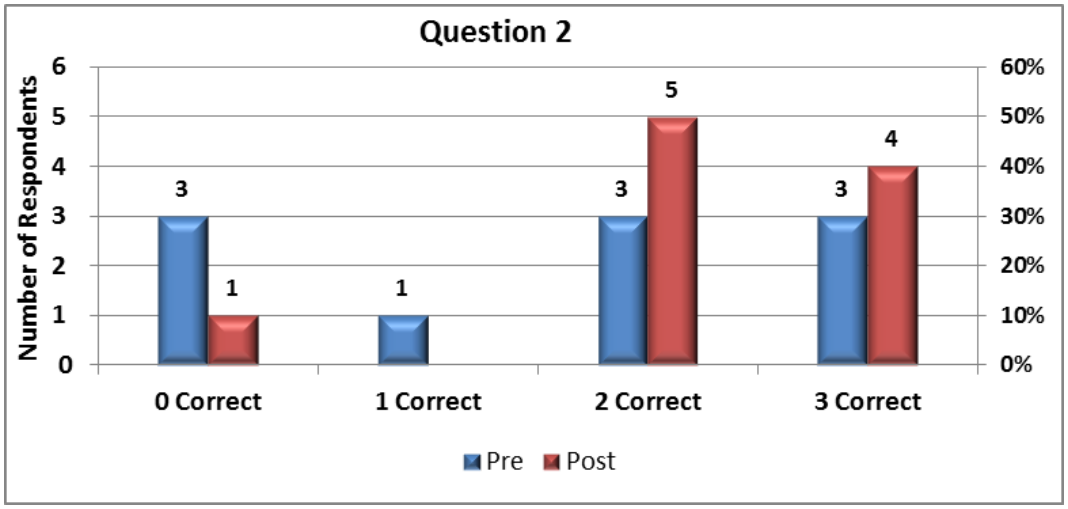


Figure 4.2: Question 2: Transmission-based precautions

There was an increase in the number of correct answer in the post-assessment group for question two.

4.3.3 Routes of transmission of organisms

The question on the routes of transmission of micro-organisms was poorly answered by the pre-intervention group and five participants (50%) were unable to name even one correct answer. One respondent (10%) could name one route of transmission, two (20%) had two correct answers. Two participants (20%) had three correct answers; none of the respondents could name four routes of transmission.

In the post-assessment six participants (60%) were able to have four correct answers to question three and one participant (10%) had all four answers correct (Figure 4.3).

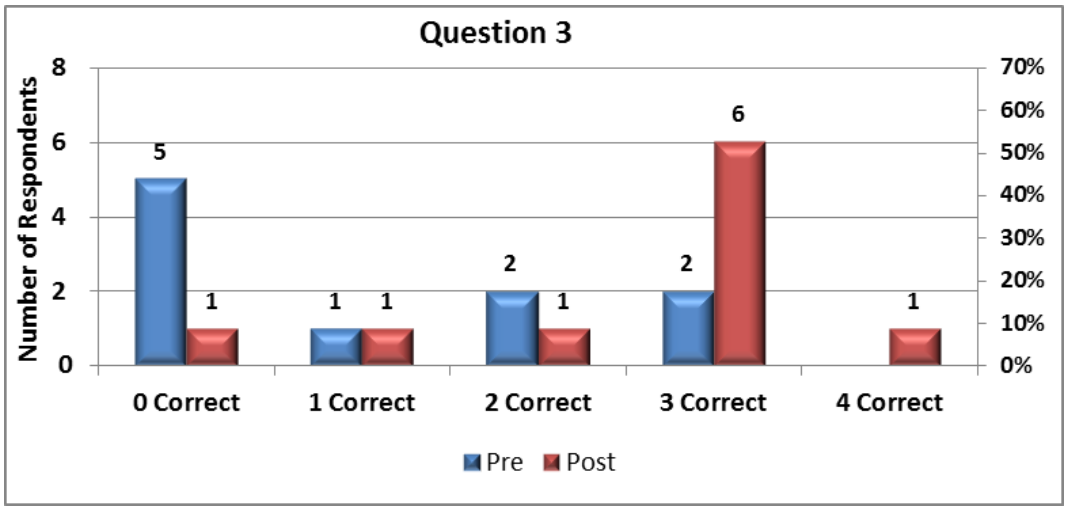


Figure 4.3: Question 3: Routes of transmission of organisms

4.3.4 Infection vs. Colonisation

Question 7 tested the understanding of participants of "colonisation" compared to "infection" (Figure 4.4). The question asked whether an antimicrobial should be prescribed whenever an organism was cultured. In the pre-assessment none of the participants could answer the question correctly.

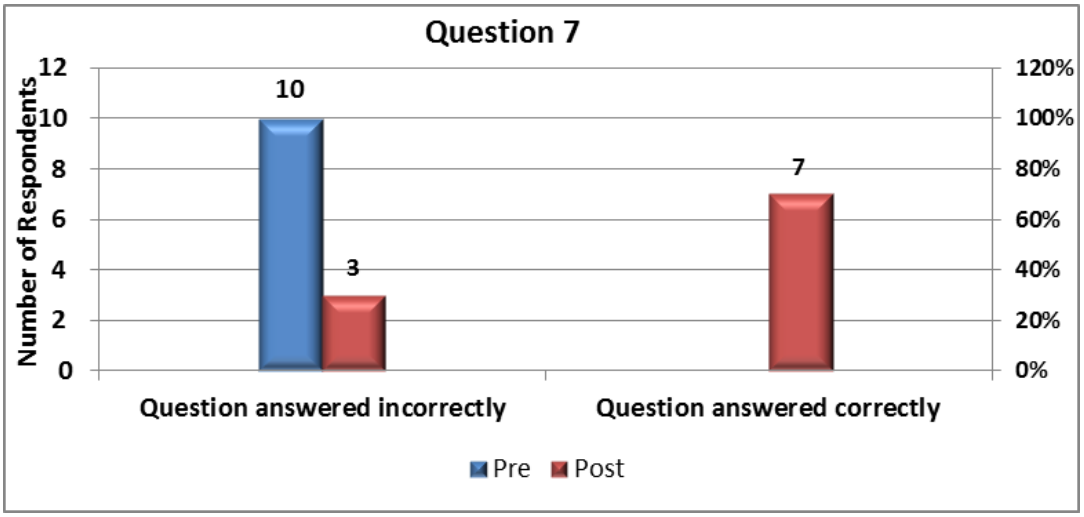


Figure 4.4: Question 7: Infection vs. Colonisation

4.3.5 Medication

Three participants (30%) knew which antibiotics are a third generation cephalosporin and all participants could name at least one carbapenem. All the participants, except one who answered “maybe” indicated that they need more training on IPC and AMS.

4.3.6 Summary

The Wilcoxon rank sum test was used to compare the pre- and post-intervention knowledge assessment. The analysis demonstrated that there was a statistically significant improvement in IPC knowledge after training (p=0.002). Baseline IPC knowledge was inadequate prior to the intervention.

4.4 PRE- AND POST-INTERVENTION RECORD REVIEW

Administrative data from 407 records were reviewed and compared. This included the records of 190 patients admitted for more than 24 hours in the CCU from 1 October 2013 to 31 May 2014 prior to the intervention and 217 patients from 1 October 2014 to 1 May 2015.

4.4.1 Gender and Age distribution

More males than females were admitted in the CCU during the study. During the pre-intervention period 47.4% (n=90) females vs. 52.6% (n=100) males were admitted compared to 43.4% (n=93) females and 56.6% (n=124) males during the post-intervention period (Refer to Figure 4.5 and Figure 4.6).

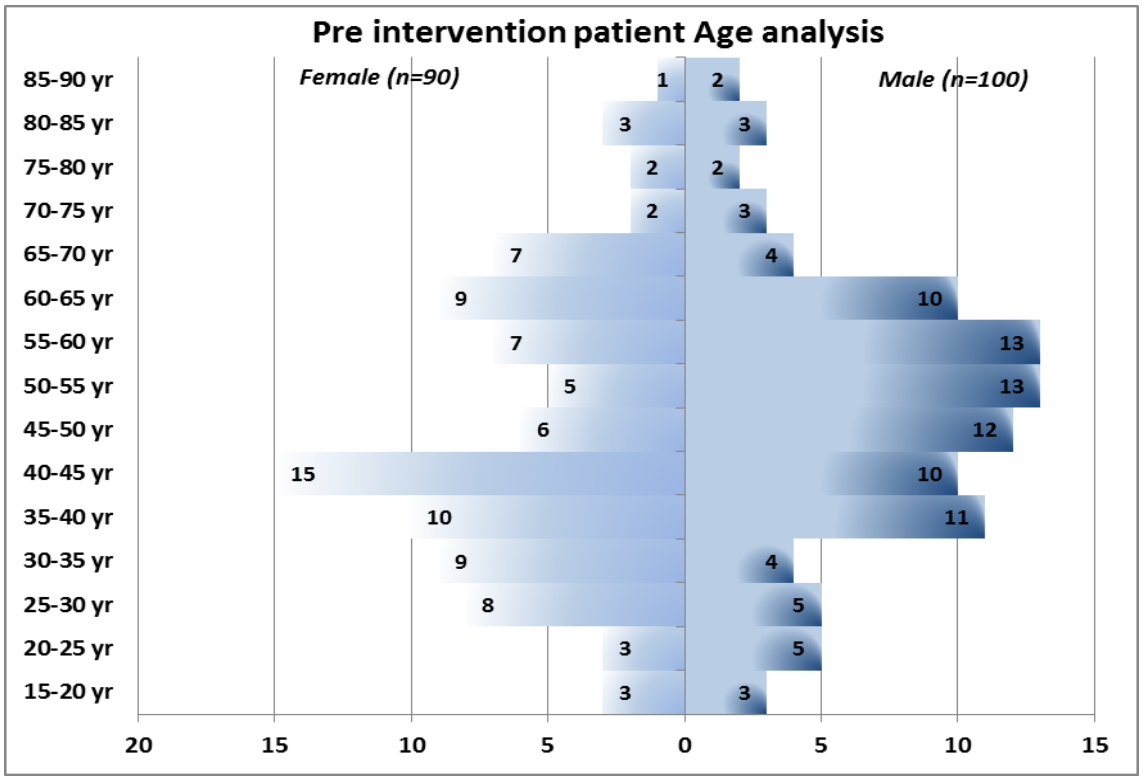


Figure 4.5: Gender and Age distribution pre-intervention

The ages of the patients remained similar; ranging from 15 to 88 with a mean age of 48 years pre-intervention and 15 to 86 post-intervention (mean age 50 years). Having similar age groups in both the pre- and post-intervention groups limits confounding factors associated with the different risk factors in specific age groups.

Figure 4.6 demonstrates that the age distribution in both the pre-and post-intervention groups remains more or less similar, except for an increase in the age group 45 to 60 years in the post-intervention group.

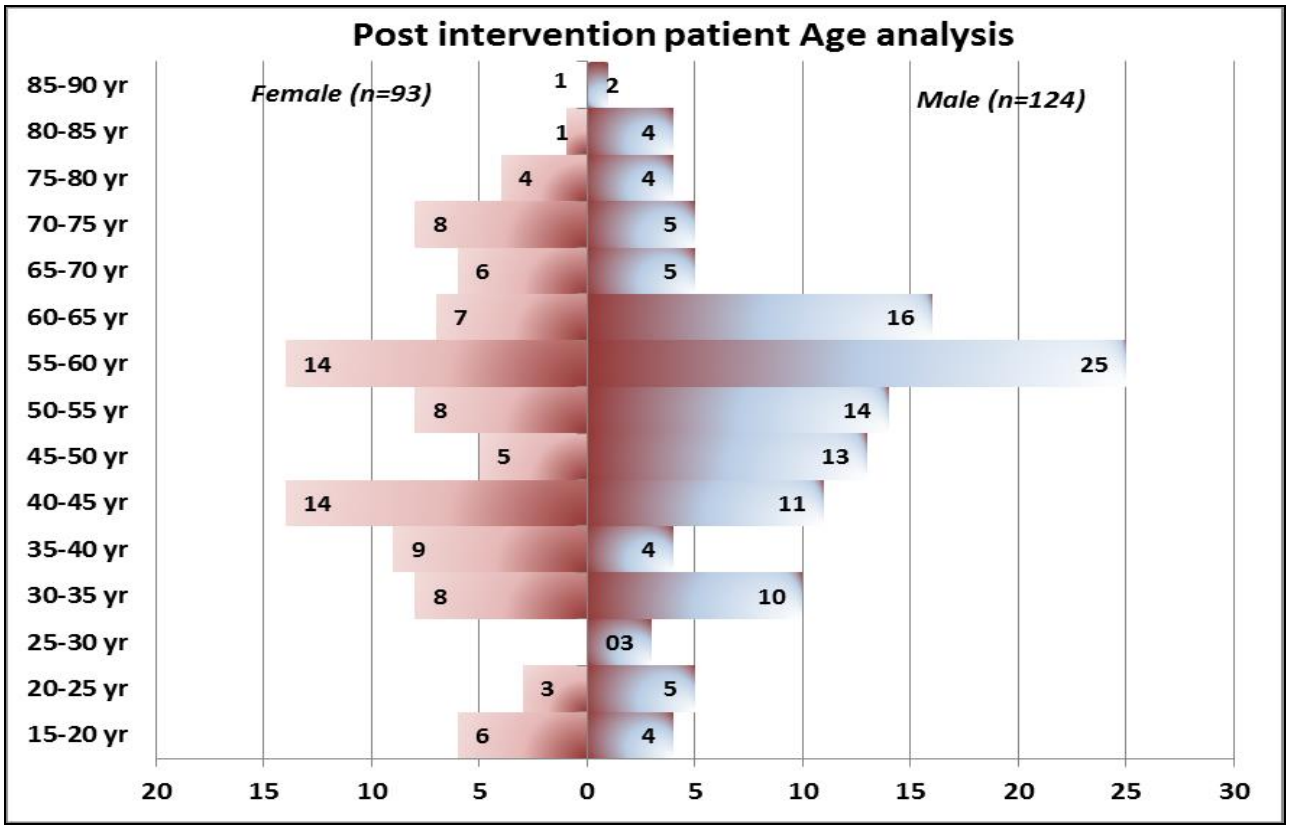


Figure 4.6: Gender and Age distribution post-intervention

The t-test was used to compare the two datasets and no statistically significant difference between the two groups was observed.

4.4.2 Length of stay

The length of stay (LOS) in CCU varied between two to 81 days with a median LOS of four days for the pre-intervention group. The post-intervention group had a LOS of two to 90 days, with a median of four days. There were several patients in the post-intervention group with an increase in LOS (Refer Figure 4.7).

Non parametric tests were used to compare the stay in CCU.

There was no statistically significant difference between the LOS of the two groups.

LOS in the post-intervention group was longer for individual patients, but the median LOS stayed at four days.

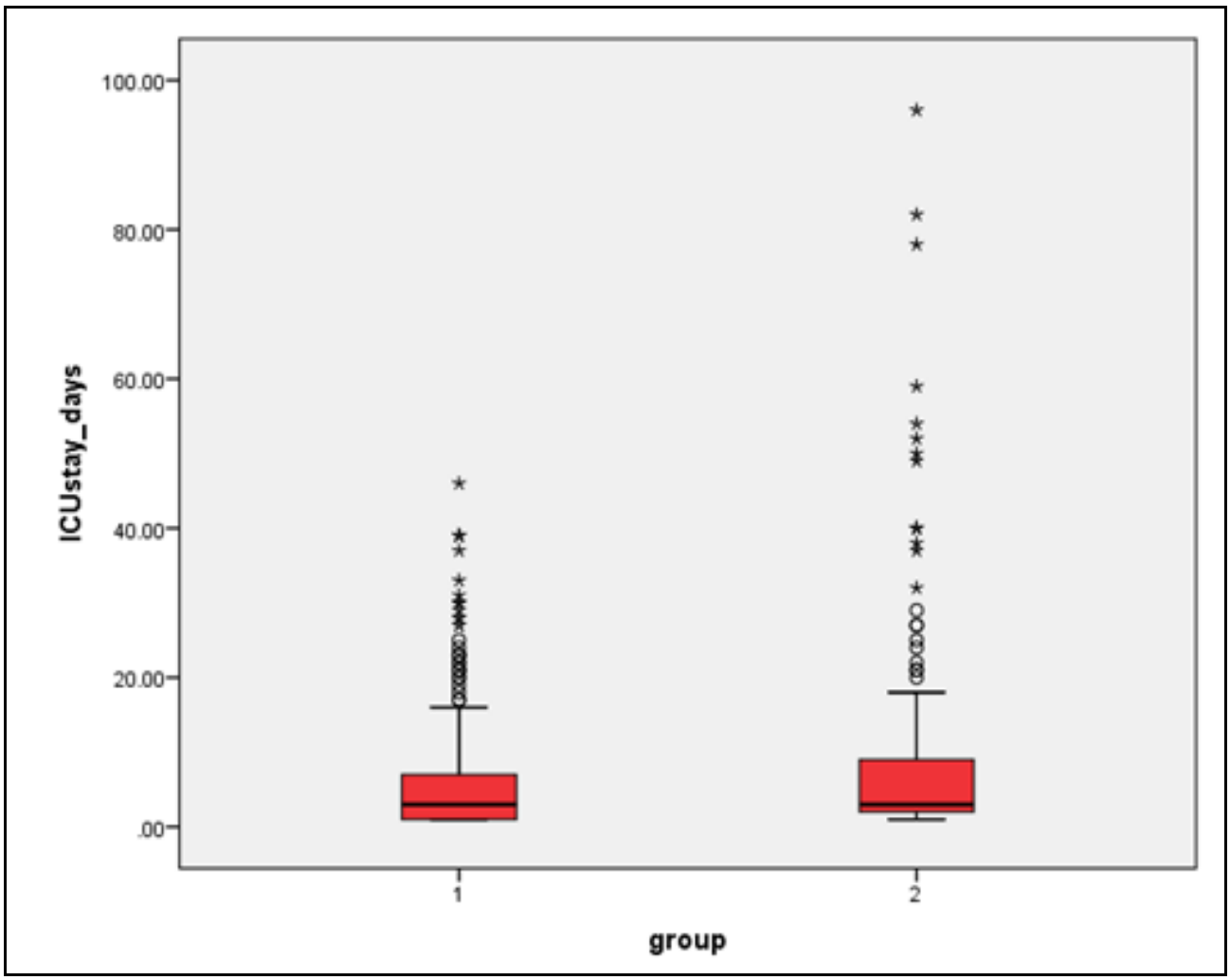


Figure 4.7: Length of stay in critical care unit

4.4.3 Antimicrobial therapy

Three hundred and fifty six (87.5%) of all patients admitted to CCU received an antimicrobial during the study period. Ninety percent (n=171) during the pre-intervention period and 85% (n= 185) during the post-intervention period (Refer to Figure 4.8). This is a reduction of 5,3% and is not statistical signifiant.

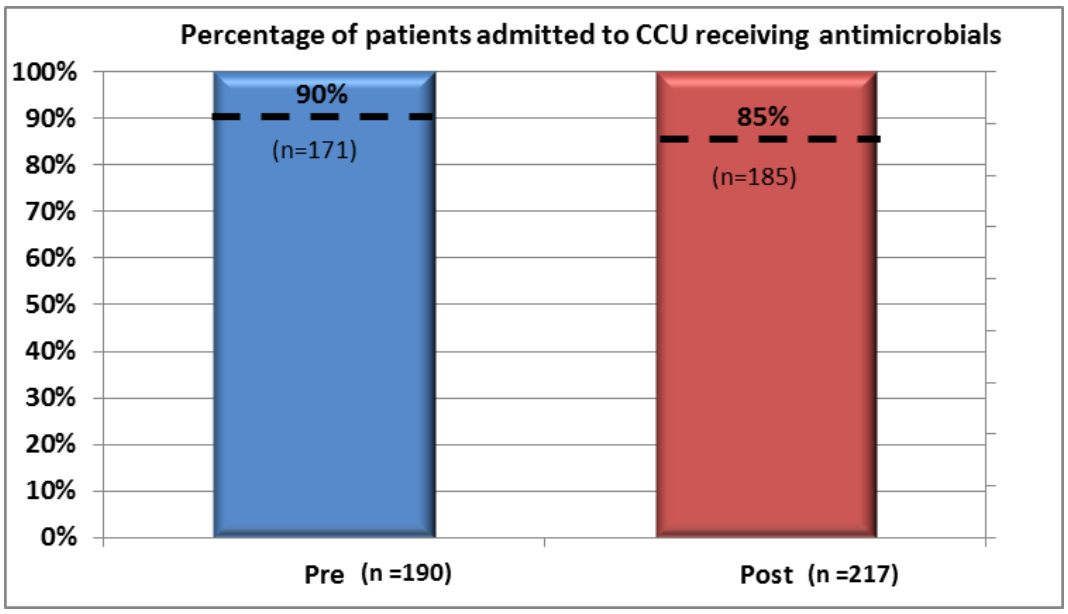


Figure 4.8: Percentage of patients admitted to CCU on antimicrobial therapy

During the pre-intervention period, 36% (n=68) of patients admitted to the CCU were treated with more than three antimicrobials and 35% (n=77) during the post-intervention period (Figure 4.9). This was not a statistically significant improvement (p=0.515).

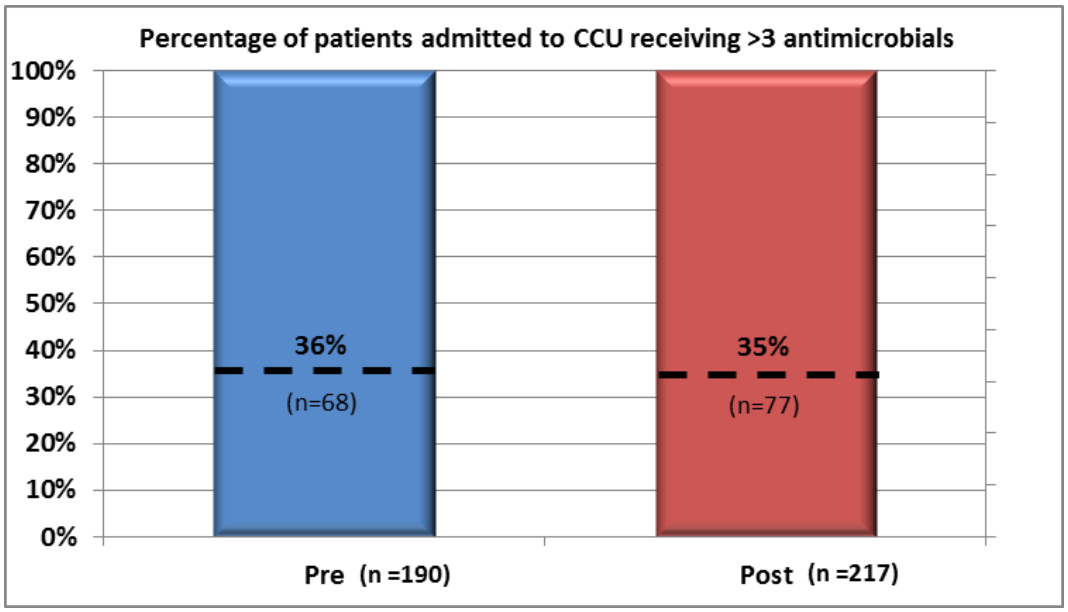


Figure 4.9: Percentage of patients on more than three antimicrobials

Due to limitations in the data collection and data warehouse, it is not possible to know whether the antimicrobials were given simultaneously; it merely states that more than three different antimicrobials were administered during the stay in CCU.

Duration of treatment with an antimicrobial ranged from a minimum of one day to a maximum of thirty-three days in the pre-intervention group; median six days. The maximum duration of therapy with one antimicrobial in the post intervention group was fifty-two days, with a median of six days (Refer Figure 4.10).

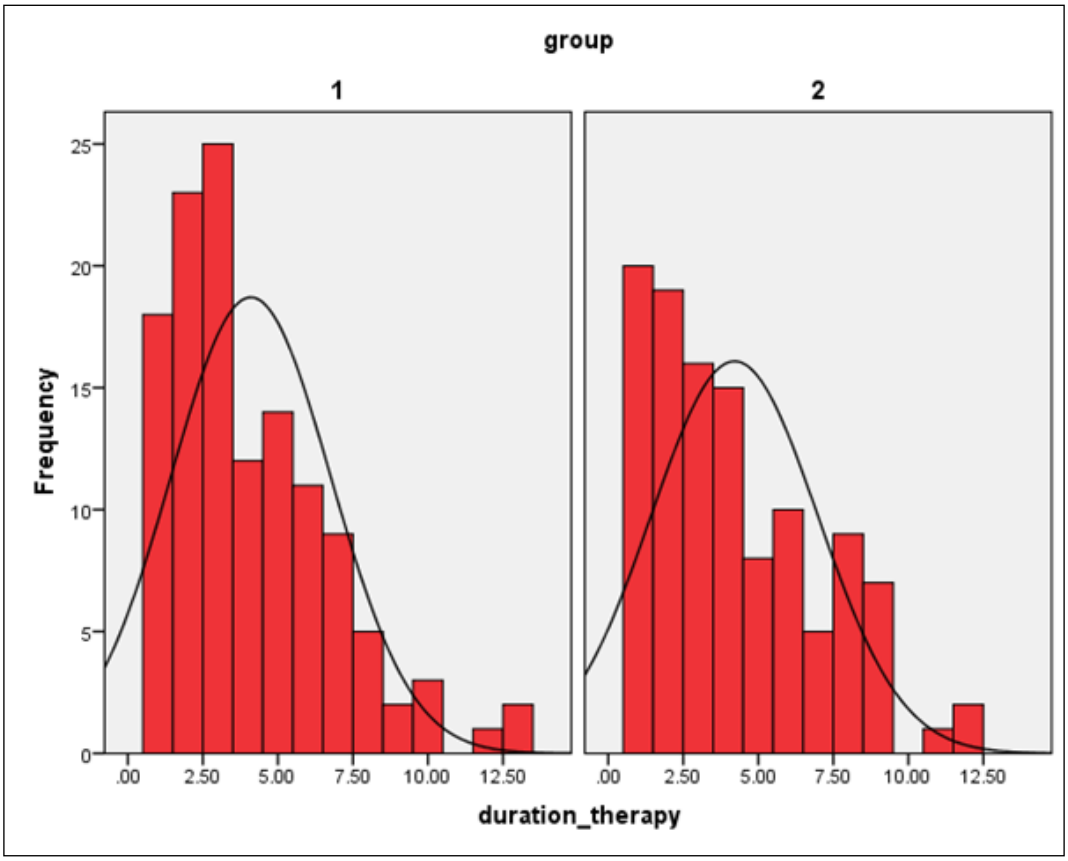


Figure 4.10: Duration of therapy

The number of patients on antimicrobial therapy for more than 14 days were 12% (n=20) in the pre-intervention group and sixteen (9%) in the post-intervention group. The redution in duration of therapy of 26% is not statistically significant (p=0.381). The majority of patients on antimicrobial therapy for more than 14 days, were treated with an antifungal agent.

Sixty-five percent (n=13) in the pre-intervention group and 63% (n=10) in the post-intervention group received an antifungal for more than 14 days. This represents a decrease of four percent in the duration of treatment in the post-intervention group without a statistically significant recuction.

The classes of antimicrobials that were most frequently used, were β-lactams, followed by carbapenems, quinolones and antifungals (Figure 4.11). No statistically significant difference in the use of different classes of antimcirobials was observed between the pre- and post-intervention groups., altought there was a slight increase in the user of β-lactams and carbapenems in the post-intervention group. β-lactams and carbapenems remained to be used most frequently.

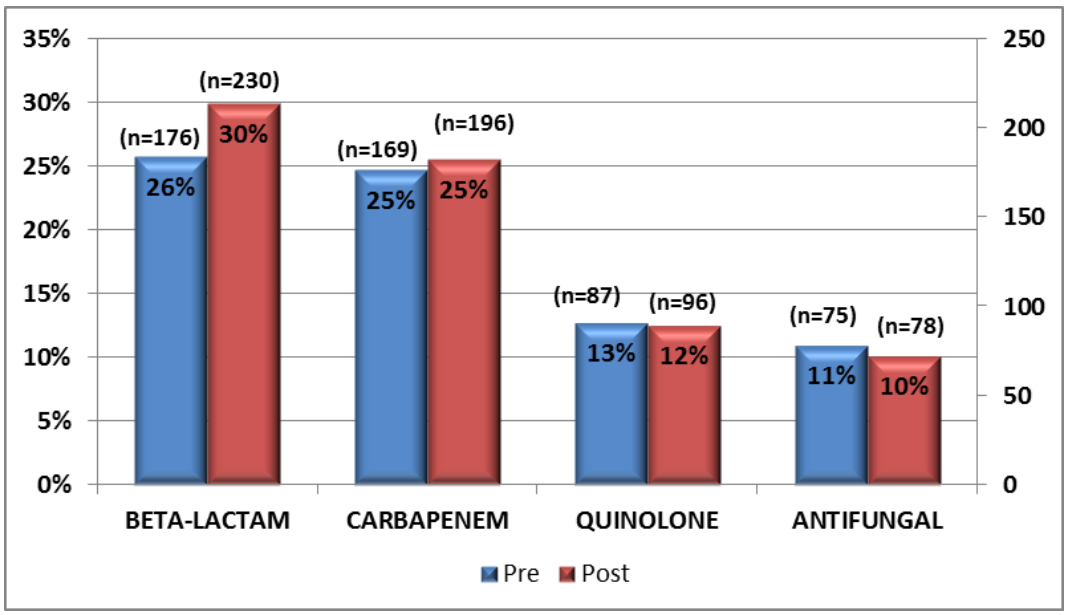


Figure 4.11: Classes of most frequently-used antimicrobials

The most frequently-used antimicrobial was cefuroxime followed by ertapenem and piperacillin in both groups and no statistical difference was observed between the pre- and post-intervention groups.

4.4.4 Positive culture before treatment

Taking an appropriate specimen prior to commencement of therapy is important to ensure that de-escalation can be practiced and to ensure that the correct antimicrobial is prescribed.

There was an 8% increase in the number of positive specimens cultured prior or on the day of commencement of therapy between the pre- and post-intervention groups (n=38 vs. n=42). However, this increase was not statistically significant.

Although there was a decrease of 44% in the number of patients who commenced an antimicrobial before a specimen was taken (Figure 4.12), it was not yet statistically significant (p=0.317).

Only positive specimens were used in the analysis. Due to ineffeciencies of the IPC surveillance system, the number of specimens sent for analysis is not known. Although there is an improvement in the number of positive specimens before antimicrobial treatment post-intervention, it is not yet a statistically significant improvement in the number of positive specimens prior to the commencement of an antimicrobial.

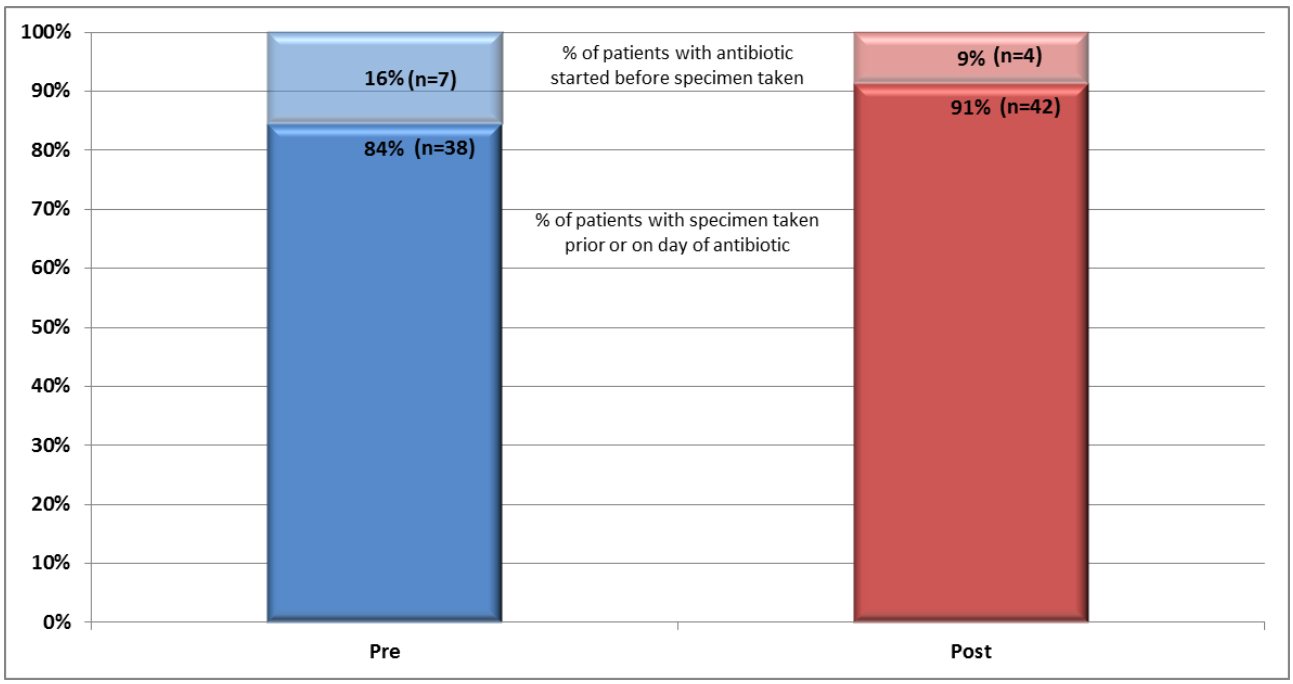


Figure 4.12: Specimens taken prior to treatment

4.5 INTERVENTION

4.5.1 Checklist with daily measures

The checklist with specific evidence-based interventions was completed daily. Improvement methodology was followed as well as rules for run charts to interpret the results. At least ten consecutive data points are required to establish a median and six consecutive data points above the median is an indication of a statistically significant improvement.

4.5.2 Culture before treatment

A “shift” is clearly observed where six data points are visible above the median (Figure 4.13). This indicates a statistically significant improvement in compliance to measuring whether a culture was taken prior to commencement of antimicrobial therapy. There was a 25% improvement in compliance since the beginning of the intervention. This improvement is reflected in the previous section where the record review also indicated an improvement in positive specimens prior to commencement of an antimicrobial.

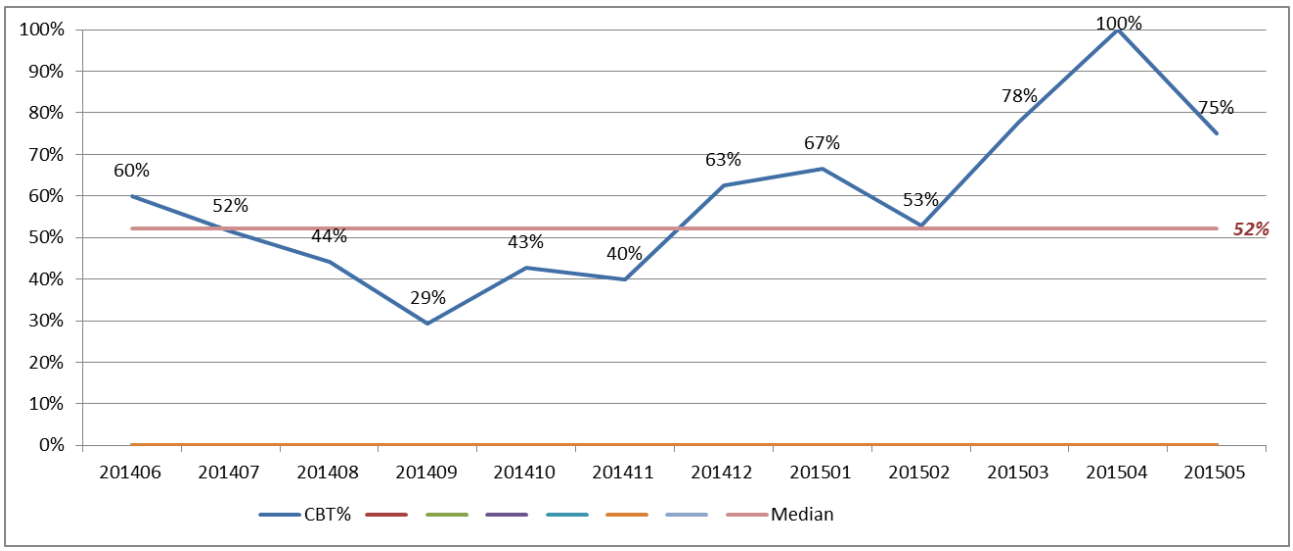


Figure 4.13: Culture before treatment

4.5.3 De-escalation

If a culture was not obtained prior to treatment or if there was a negative culture, de-escalation cannot be implemented. Medical practitioners are often hesitant to de-escalate due to a number of reasons.

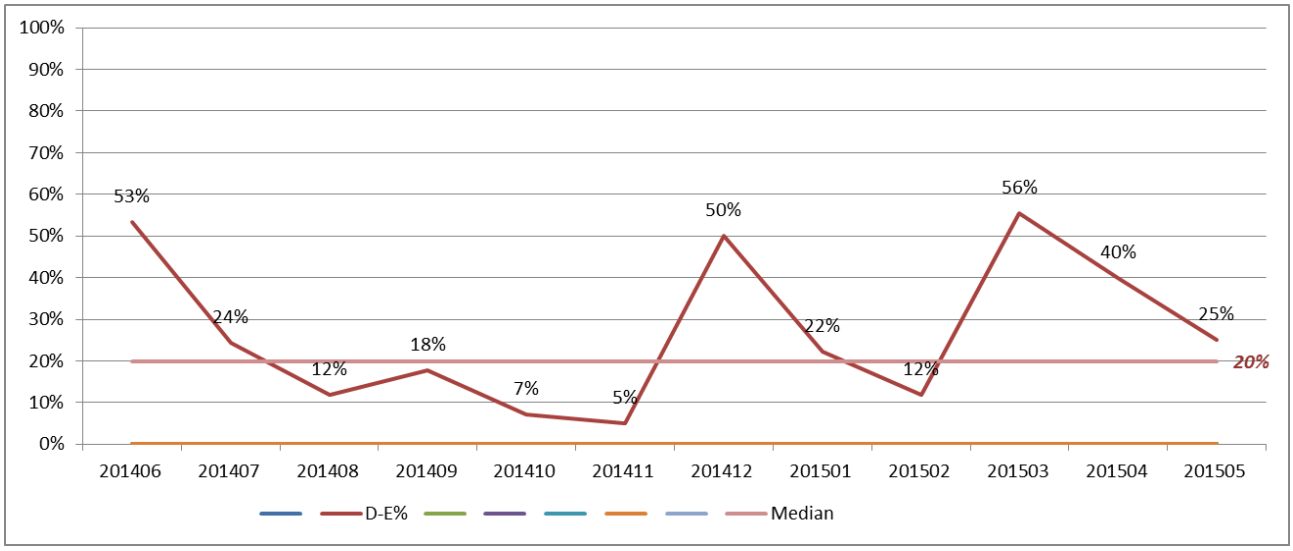


Figure 4.14: De-escalation of therapy

There was a 53% decrease in compliance to de-escalation as seen in Figure 4.14. .

4.5.4 Days on therapy

Although there are four data points above the median and an increase of 275% in compliance to the measuring of “days on therapy”, the improvement was not yet statistically significant. (Figure 4.15).

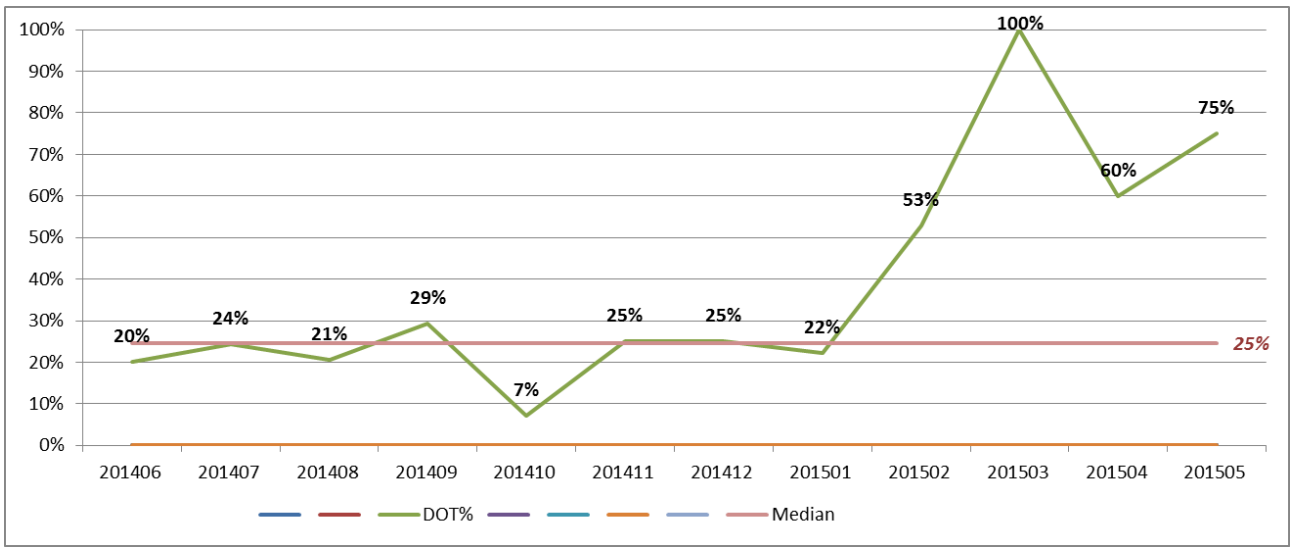


Figure 4.15: Duration of therapy

4.5.5 Number of antimicrobials

Compliance to monitoring the number of antimicrobials with which a patient had been treated, was recorded consistently throughout the study. Figure 4.16 demonstrates the percentage compliance to the daily measure that recorded the number of antimicrobials with which a patient was treated. Throughout the study this measure was 100% and the number of antimicrobials was recorded daily.

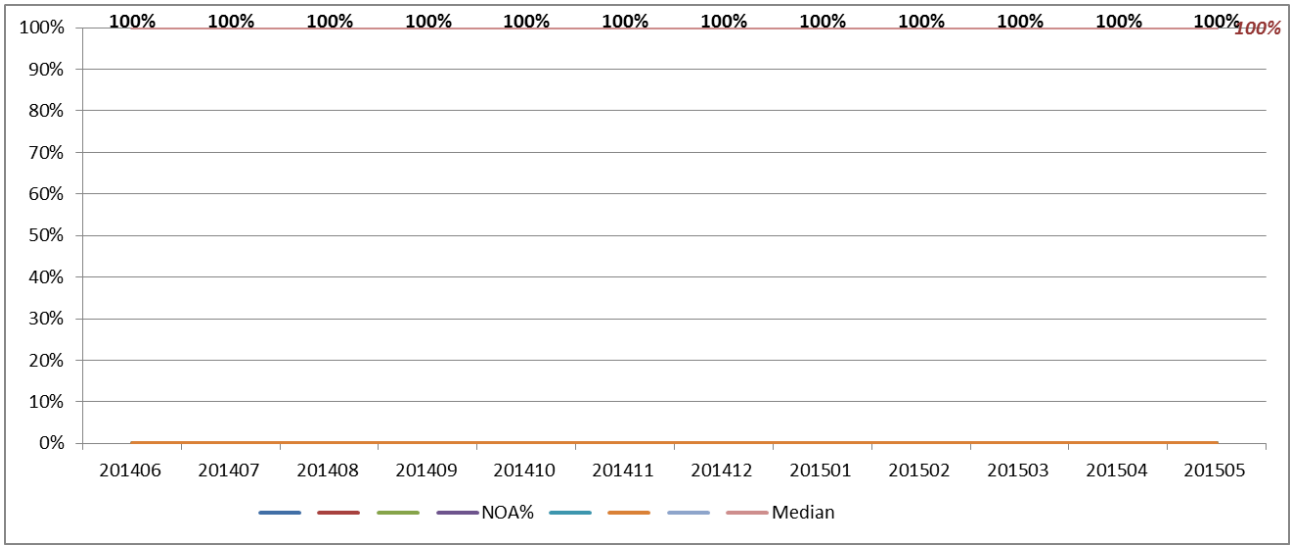


Figure 4.16: Number of antimicrobials

4.5.6 Assessment of device removal

The removal of devices was carried out with a median compliance of 66% (Figure 4.17) and a 25% increase in compliance since the implementation of the intervention. It was done fairly well since commencement of the study. Although there are currently three data points above the median, there is not yet a statistically significant improvement in compliance to the measure.

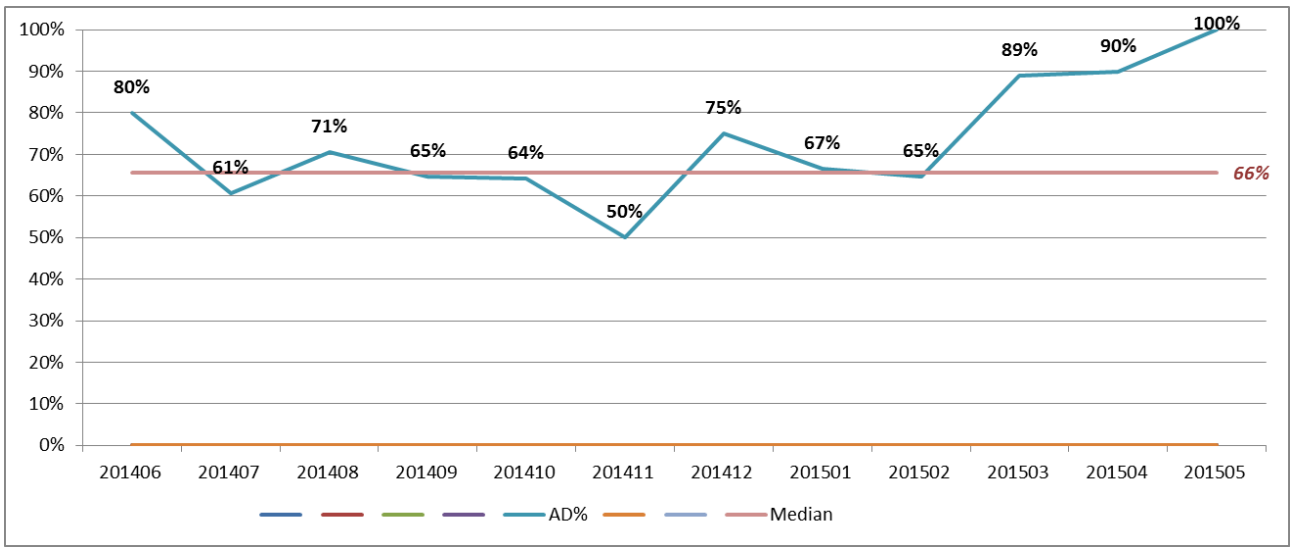


Figure 4.17: Assessment of device removal

4.5.7 Hang time

Hang time was the final measure that was monitored daily for compliance. Although there was a 41% increase in compliance since the beginning of the intervention, no statistically significant improvement was observed (Figure 4.18).

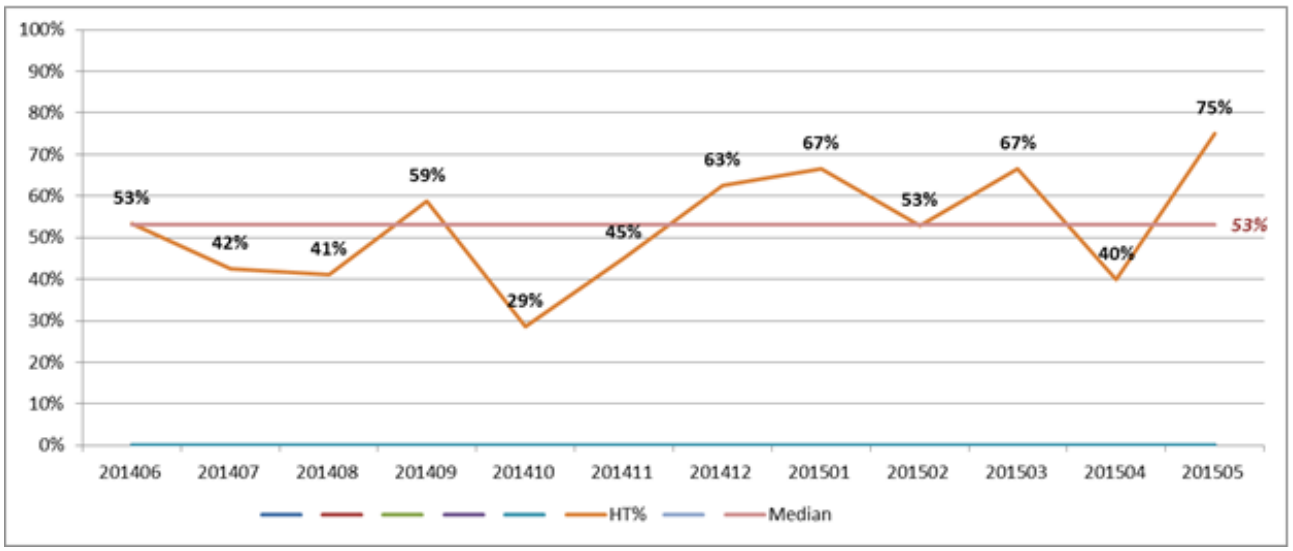
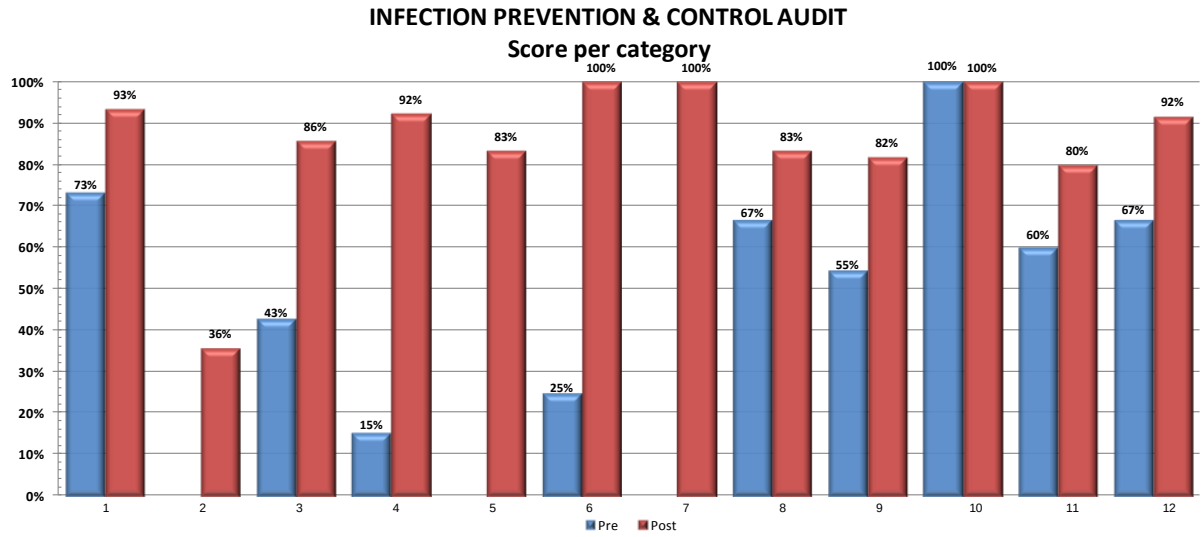


Figure 4.18: Hang time

Although the checklist for compliance was monitored daily, a statistically significant improvement to compliance was observed only with the first measure, “culture before treatment”. This is also reflected in the data from the record review where an increase in the number of positive specimens that were collected prior to commencement of antimicrobial therapy was observed.

4.6 INFECTION PREVENTION AND CONTROL AUDIT

The pre-intervention infection prevention and control (IPC) audit identified some deficiencies that needed correction. The inadequacies were highlighted and after training and information sessions, a significant improvement were noticed (Figure 4.19).



	1 RISK MANAGEMENT	2 INFECTION PREVENTION AND CONTROL: SURVEILLANCE	3 NOTIFICATION OF NOTIFIABLE CONDITIONS	4 ISOLATION AND TRANSMISSION-BASED PRECAUTIONS	5 IPC WARD HYGIENE AUDITS	6 PERSONNEL DEVELOPMENT AND EDUCATION	7 TRAINING	8 POLICIES AND PROCEDURES	9 HAND HYGIENE	10 WASTE MANAGEMENT - HEALTHCARE RISK WASTE	11 SLUICE	12 HOUSEKEEPING
Pre	11 / 15	0 / 14	3 / 7	2 / 13	0 / 6	1 / 4	0 / 6	4 / 6	6 / 11	6 / 6	6 / 10	8 / 12
Post	14 / 15	5 / 14	6 / 7	12 / 13	5 / 6	4 / 4	6 / 6	5 / 6	9 / 11	6 / 6	8 / 10	11 / 12

Figure 4.19: Infection Prevention and Control audit (pre- and post-intervention)

The Fisher exact test was used to compare the pre- and post-intervention IPC audit. A statistically significant improvement in the outcome of the audit was observed (p=0.000).

4.7 CALCULATION OF ANTIMICROBIAL USE

Data about antimicrobial usage was obtained from the pharmacy warehouse and was measured in defined daily dosages (DDDs). A decrease in the total use of antimicrobials in the hospital was observed, although there was an increase in the use of antifungals (Figure 4.20). Due to limitations in the data warehouse, it was not possible to isolate the data from only the CCU and Figure 4.20 demonstrates the antimicrobial use of the hospital, measured in DDDs.

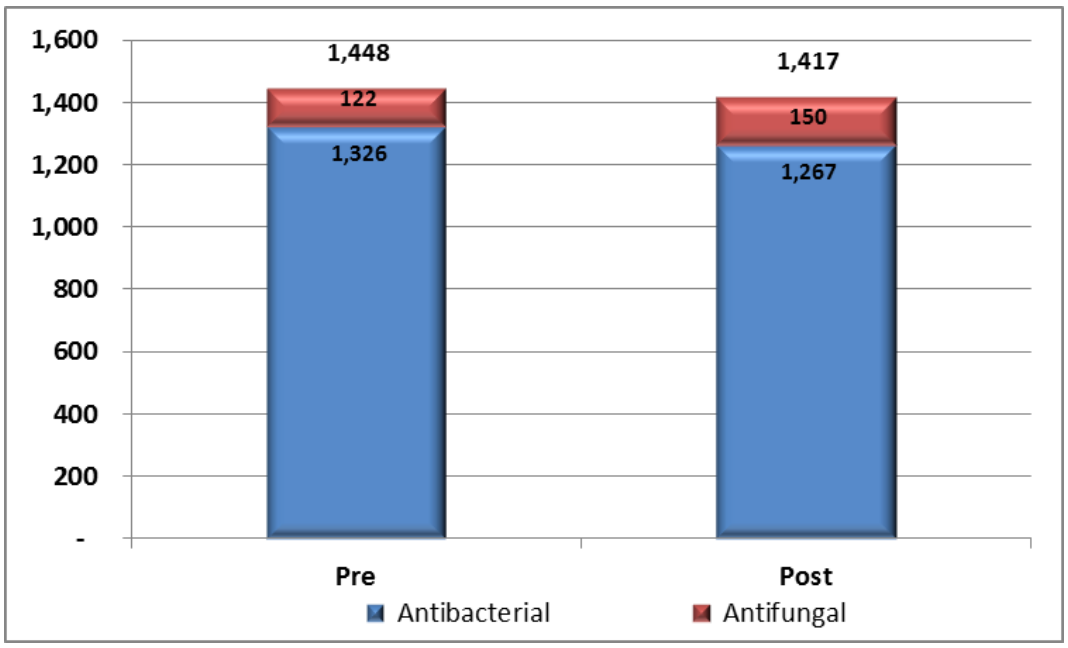


Figure 4.20: Defined daily dosages of antimicrobials

Although there was a decrease in the number of antimicrobials used in the pre- and post-intervention groups, it was not yet significant.

4.8 ORGANISM PROFILES

During the pre-intervention period (1 October 2013 to 31 May 2014) a total of 154 positive specimens were cultured. The majority of the positive cultures were Gram negative organisms of which 19% were *Klebsiella pneumoniae,* followed by *Pseudomonas aeruginosa, Stenotrophomonas maltophilia* and *E.coli* (Figure 4.21). During the post-intervention period (1 October 2014 to 31 May 2015) there was an increase of 32% in the number of positive specimens (n=227) cultured compared to the pre-intervention period (n=154). *Klebsiella pneumoniae* was cultured in 14% of positive specimens collected during the post-intervention group vs. 19% in the pre-intervention group. This is a statistically significant reduction of *Klebsiella pneumoniae* (p=0.05).

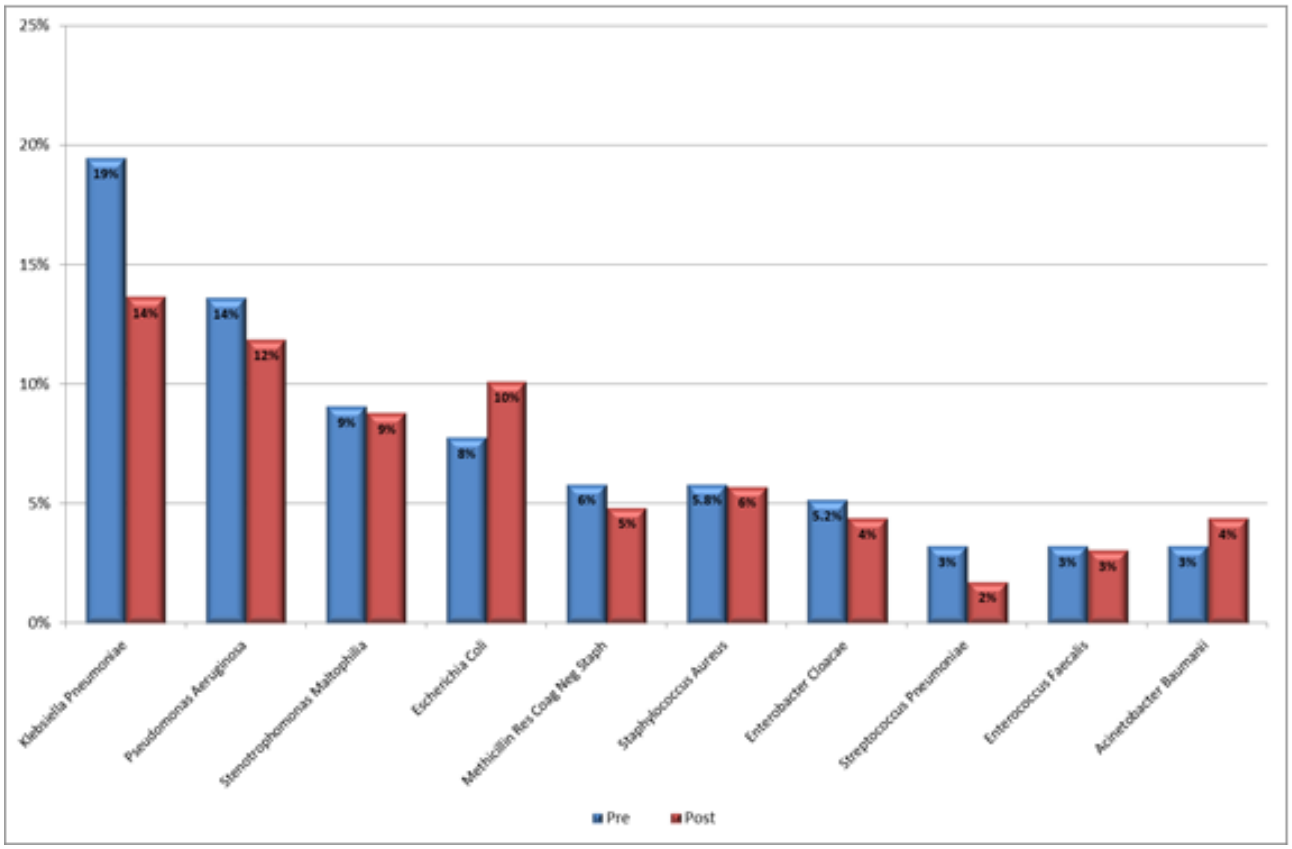


Figure 4.21: Pre-and post-intervention isolates

The organism profiles in the unit remained more or less similar pre- and post-intervention as demonstrated in Table. 4.1.

Other organisms that were cultured were low in numbers and included the following:

- *Haemophilus influenzae*;
- *Proteus mirabilis;*
- *Mycobacterium complex* and *tuberculosis;*
- *Enterobacter aerogenes;*
- *Candida parapsilosis;*
- *Candida dubliniensis;*
- *Bacteroides fragilis;*
- *Citrobacter freundii;*
- *Citrobacter koseri;*
- *Klebsiella oxytoca;*
- Methicillin resistant *Staphylococcus haemolyticus;*
- *Streptococcus viridans;*
- *Streptococcus spp.*

Table 4.1: Organism profiles in the CCU pre- and post-intervention

Pre-intervention			**Post-intervention**		
Name of organism	**Number**	**Percentage positive**	**Name of organism**	**Number**	**Percentage positive**
Klebsiella pneumoniae	30	19%	*Klebsiella pneumoniae*	31	14%
Pseudomonas aeruginosa	21	14%	*Pseudomonas aeruginosa*	27	12%
Stenotrophomonas maltophilia	14	9%	*Stenotrophomonas maltophilia*	20	9%
Escherichia coli	12	8%	*Escherichia coli*	23	10%
Staphylococcus aureus	9	6%	*Staphylococcus aureus*	13	6%
Enterobacter cloacae	8	5.2%	*Enterobacter cloacae*	10	4%
Candida albicans	7	4.5%	*Candida albicans*	10	4%
Streptococcus pneumoniae	5	3%	*Streptococcus pneumoniae*	4	2%
Enterococcus faecalis	5	3%	*Enterococcus faecalis*	7	3%
Acinetobacter baumannii	5	3%	*Acinetobacter baumannii*	10	4%

Figure 4.22 demonstrates that the organism profiles in the critical care unit remained similar, apart from a statistically significant reduction (p=0.05) in *Klebsiella pneumoniae*.

The susceptibilities of the most prevalent organisms to frequently-used antimicrobials were compared pre- and post-intervention.

A decrease in susceptibility of *Klebsiella pneumoniae* is observed against Amoxycillin-Clavulanate, Cefuroxime and Piperacillin-Tazobactam. Susceptibility to Ertapenem and Meropenem remained similar pre- and post-intervention (Figure 4.22). A decrease in Extended Spectrum β-lactamase Producing (ESBL) *Klebsiella pneumoniae* was however observed. Fourteen out of 29 isolates were ESBL producers in the pre-intervention group compared to ten out of 31 in the post-intervention group. This reduction was not yet statistically significant (p=0.292).

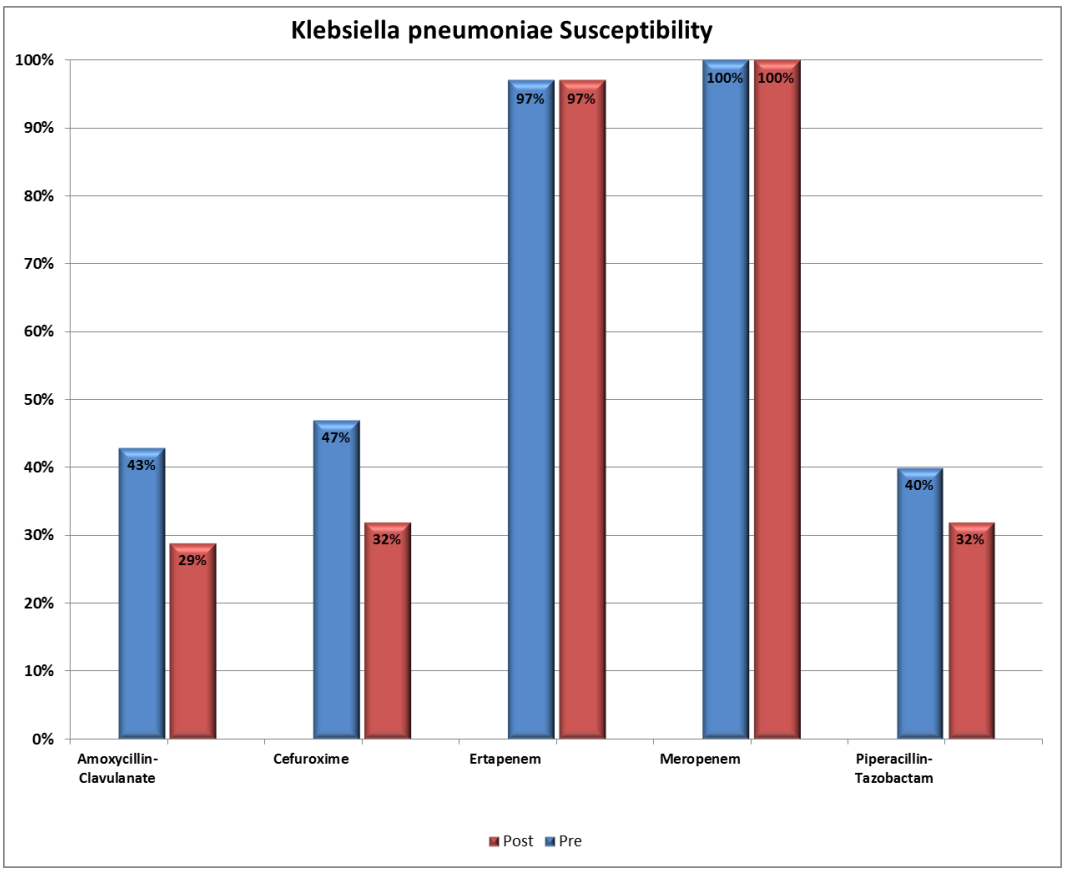


Figure 4.22: Susceptibility of *Klebsiella pneumoniae*

There was a decrease in susceptibility of *Pseudomonas aeruginosa* against both Meropenem and Piperacillin-Tazobactam (Figure 4.23), and concerning is the statistically significant decrease in sensitivity to Meropenem (p = 0.037).

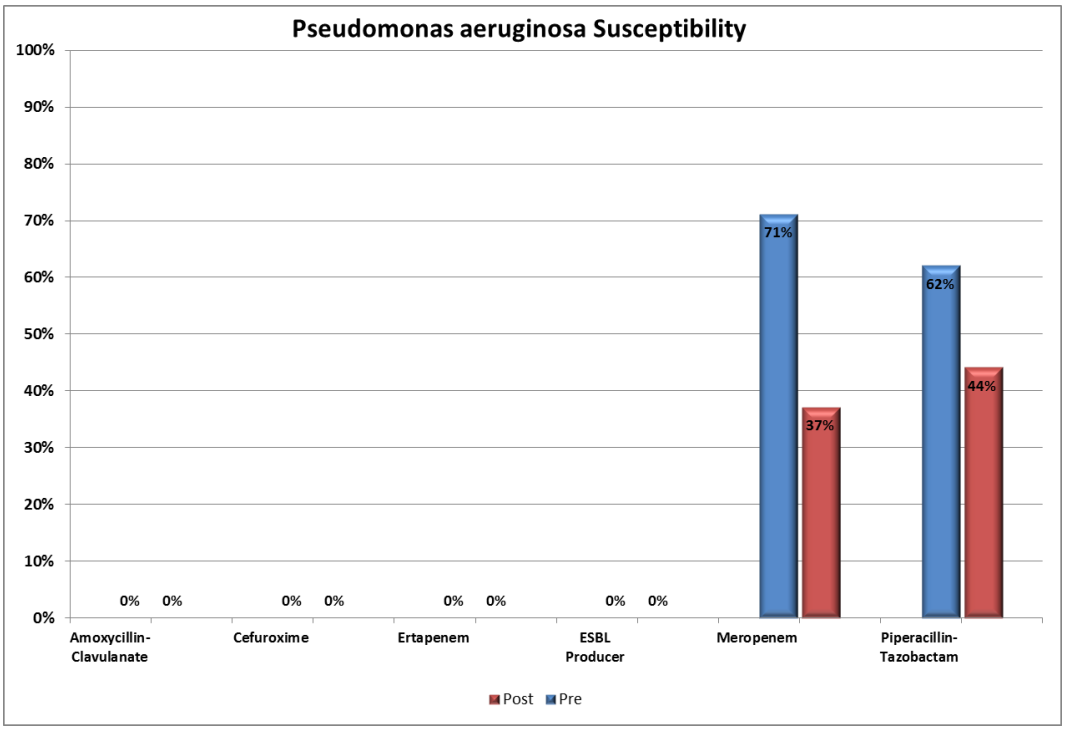


Figure 4.23: Susceptibility of *Pseudomonas aeruginosa*

Figure 4.24 demonstrates an increase in the susceptibility of *E.coli* against Amoxycillin-Clavulanate. It is however not statistically significant.

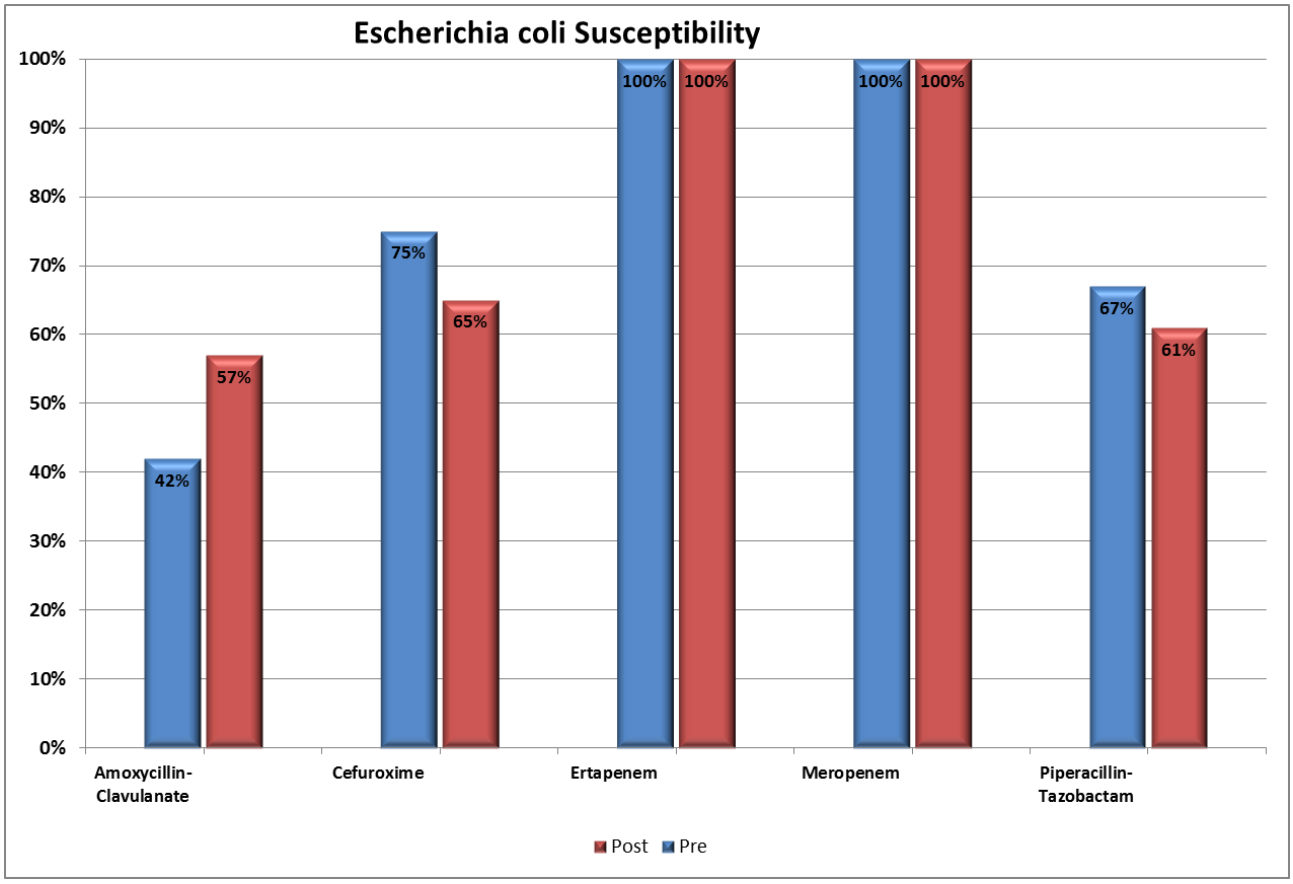


Figure 4.24: Susceptibility of *Escherichia coli*

Although not statistically significant, a decrease in ESBL producing *Klebsiella pneumoniae* (p=0.292) and *E.coli* (p=0.464) was observed in the post-intervention group (Figure 4.25).

The organism profiles in the unit remained more or less similar during the pre- and post-intervention periods. However, the decrease in the susceptibility of *Pseudomonas aeruginosa* to carbapenems is a major concern, especially in the light of the increase in carbapenem resistance worldwide. Nevertheless, the decrease in the ESBL producing *Klebsiella pneumonaie* and *E.coli* is encouraging.

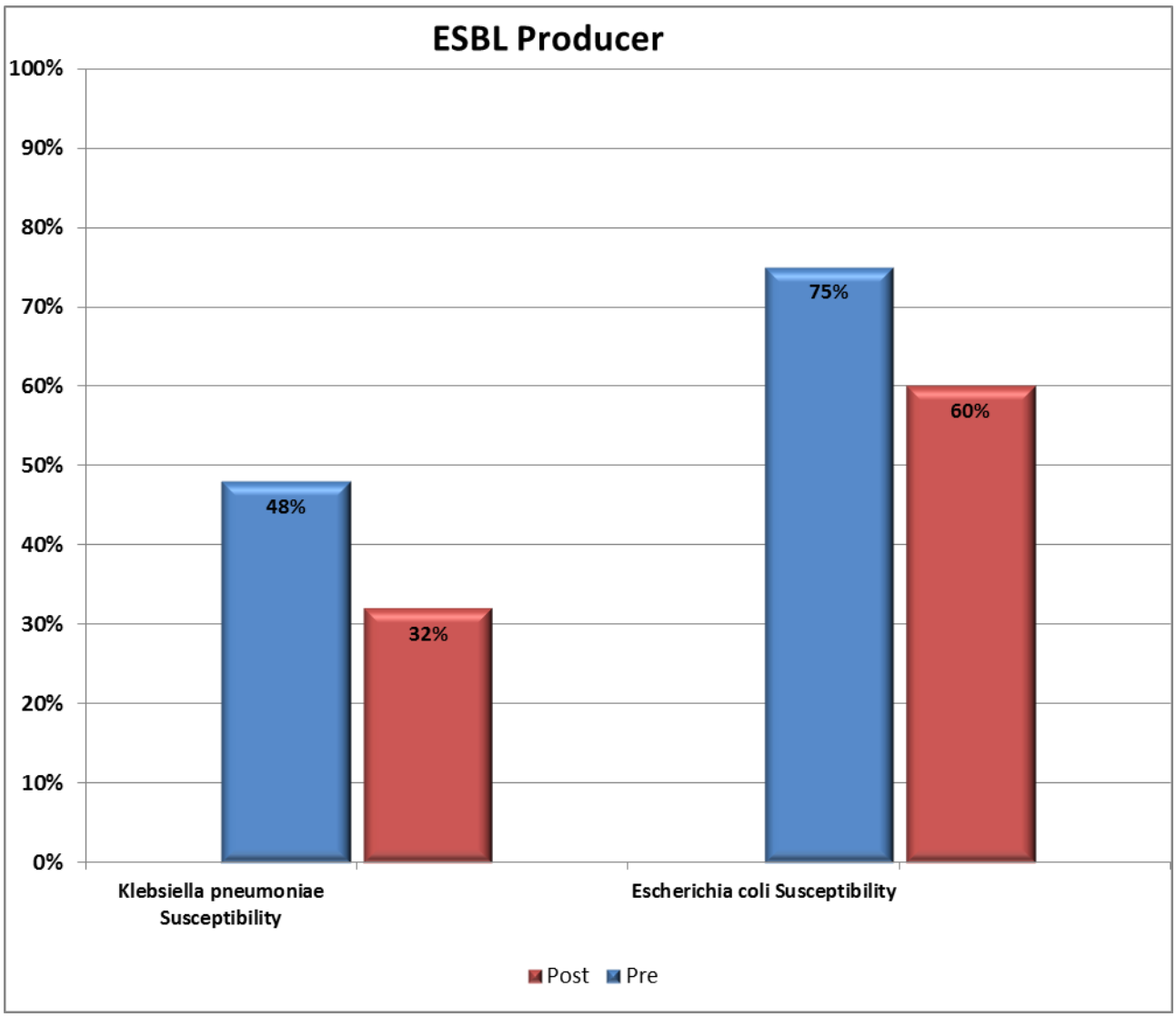


Figure 4.25: ESBL Producers

4.9 CONCLUSION

The research methodology and data collection were discussed in detail. Information from various data sources was analysed and interpreted. Statistically significant improvements were observed in the knowledge of nurses after training, as well as in adherence to infection prevention and control (IPC) practices as demonstrated in the IPC audit. These improvements had a positive impact on the prevalence of ESBL producing pathogens in the CCU. More positive specimens were noted prior to commencement of antimicrobial therapy and there was a decrease in the duration of therapy. Nurses played a key role in driving the majority of these improvements.

The following chapter discusses the findings and offers some recommendations.

CHAPTER 5
DISCUSSION, RECOMMENDATIONS, LIMITATIONS AND CONCLUSION

5.1 INTRODUCTION

This chapter is a discussion of the study results; outcomes, recommendations and the shortcomings identified.

5.2 ADDRESSING THE STUDY OBJECTIVES

The goal of the study was to examine the role of the critical care nurse in the implementation of an AMS programme in hospitals in LMICs. The discussion that follows addresses the findings of the study in relation to the objectives.

5.3 DISCUSSION

5.3.1 Study design and setting

A pre- and post-interventional study design was the most suitable for the purpose of this research. One hospital was utilised for the study to limit possible confounding factors, despite the fact that a control group to measure the difference between a group with interventions and one without would have been preferred,

Several interventions were implemented and the impact of these had to be measured and tested. The researcher was concerned about the impact of confounding factors such as different disease, patient and organism profiles, as well as differences in staff and their interpretation and implementation of the proposed interventions on the outcome of the study. An increase in the duration of a study of this nature might possibly have more meaningful results if it is performed over a longer period as described in the literature (Dortch *et al*., 2011:15; Yu-Shiuan *et al.,* 2013:1072).

5.3.2 Knowledge assessment

Basic IPC knowledge was inadequate prior to training of the nurses. Knowledge about the routes of transmission of organisms and standard precautions was limited. In the pre-assessment a limited number of nurses knew the difference between colonisation and infection. This inadequate knowledge in itself poses a risk of unnecessary treatment with antimicrobials that contributes to the development of AMR.

However, there was a statistically significant improvement (p=0.0002) in knowledge about IPC and AMS of the nurses who took part in the study after training. Improved knowledge could have been a contributing factor to the improvement in adherence to IPC principles and the IPC audit results. The results demonstrate that IPC training is important and that it positively influences adherence to IPC practices (Mehtar *et al*., 2011:1; Desai, Philpott-Howard, Wade & Casewell, 2000:197-198).

5.3.3 Record review pre- and post-intervention

The patient population remained more or less similar in terms of age and gender pre- and post-intervention. There was no remarkable difference in the LOS of patients between the two groups. Although not statistically significant, a decrease in the number of patients admitted in the CCU receiving an antimicrobial in the post-intervention group was observed. Due to limitations in the pharmacy billing system, the decrease in the amount of antimicroibals used in the specific unit could not be established.

A 26% reduction in the duration of antimicrobial therapy for more than 14 days was observed in the post-intervention group. Although not yet statistically signifiant, nurses played an important role to remind the doctor to evaluate the necessity of treatment. There was a significant increase in compliance in the daily measure “days on therapy” performed by nurses, utilising a checklist. The awareness about the significance of extended therapy created by the visiting clinical microbiologist could also have influenced the decrease in duration of treatment.

Alhough the decrease in the use of antimicrobials might have been causal, the fact that specimens were taken prior to the administration of an antimicrobial might have had an influence on the decision of the physicians about the necessity for treatment.

Prescribing habits of treating physicians remained the same and there was no difference in the use of different classes of antimicrobials after the implementanion of an AMS programme. Again the duration of the study was not long enough to observe a meaningful difference. Of concern was the increase in carbapenem resistant *Pseudomonas aeruginosa.*

The study did not investigate the indication or appropriateness for antimicrobial therapy, because nurses have an insignificant role to play in the decision regarding the necessity of treatment and the type of antimicrobial that is prescribed in acute care settings.

There was a reduction in the amount of patients commencing with treatment before a specimen was taken in the post-intervention group. Nurses are responsible for the collection of specimens as well as for the administration of antimicrobials and are in a position to ensure that it is being done prior to commencement of antimicrobial therapy. It appears that after training, nurses had a better understanding of the relevance and importance of collecting an appropriate specimen before commencement of treatment.

Altough nurses might have adequate knowledge about antimicroibals, they are not currently in a posititon to significantly influence the selection of therapy or duration thereof. They are however in a position to remind the physician to evaluate the appropriateness of treatment and question its indication. Despite the fact that nurses are already prescribing antimcrobials in the primary healthcare setting in South Africa for minor ailments and in the treatment of TB, HIV and the syndromic treatment of sexually transmitted diseases, their training and current scope of practice does not allow prescribing medication in the complex environment of critically ill patients.

Gillespie *et al.* (2013: 356-366) demonstrated that by providing additional training to nurses, they were able to play an important role in the implementation of an AMS programme and a subsequent reduction in *Staphylococcus areus* bloodstream infections. The role of the nurse is not being undermined or diminished, but in the current environment physicians remain the primary precribers of medication in acute care settings. Abbo *et al.* (2012:373) demonstrated that critical care nurses had more knowledge about antimicrobials than nurses in other departments and can play a more significant role in AMS programmes and the selection of appropriate treatment once they have received additional training.

5.3.4 Intervention with a checklist

The checklist with specific evidence-based interventions was completed daily, but not always with the necessary insight. Additional training was required to ensure that nurses understood the significance and importance of completing the checklist and that it was not merely a checklist, but that they had to ensure that the measures are executed consistently. Similar methodology had been implemented successfully to reduce catheter-associated bloodstream infections (Institute of Healthcare Improvement, 2012:2; Pronovost *et al*., 2006:2725). The researcher believes that similar methodology can be utilised to improve other clinical outcomes. Walker, Reshamwalla and Wilson (2012:51-52) proved that a checklist can be utilised to ensure safety in surgery, but that additional training and a culture change were required. Similarly, additional training for both nurses and medical practitioners, as well as a culture change will be necessary in order to implement AMS programmes successfully.

Knowledge about the causative organism is important to prevent the unnecessary treatment with an inappropriate antimicrobial with an increased risk of the development of resistance (Dellit *et al.*, 2007:168; CDC, 2014:6; IHI & CDC, 2012:6). There was a statistically significant improvement in the measure “Culture before treatment” which correlated with an increase in the number of positive specimens that were collected prior to commencement of an antimicrobial. A limitation is that it is not known how many specimens were collected in total; only the number of positive specimens is known. Important to note is the fact that the collection of specimens and the administration of an antimicrobial is a nurse-driven intervention. It is evident that if nurses are requested to implement an intervention and they understand the rationale behind it, they will ensure that it is being done.

There was no improvement in the de-escalation measure. De-escalation is an important intervention to reduce the development of resistance by adapting treatment to a more targeted antimicrobial as soon as the result of the microbiological culture is available. (Dellit *et al*., 2007:168; Derenski, 2007:179-180; IHI & CDC, 2012:7; Brink *et al*., 2008: 590). Medical practitioners are often hesitant to de-escalate due to a number of reasons. Paruk *et al*., (2010:614) found that only for 23.9% of patients in South African private and public critical care units antibiotic treatment had been de-escalated.

It is important to note that nurses currently have very little influence on the treatment of patients in acute care settings. They can inform the treating physician of the culture result and remind him to de-escalate, but it remains the choice of the physician to prescribe another antimicrobial.

Despite the increase in compliance with the “days on therapy” measure, the improvement was not yet statistically significant. Nurses play an important role in informing physicians about the improvement in the condition of the patient and to remind the doctor to evaluate the necessity to continue with treatment. Chastre, Wolff, Fagon, Chevret, Thomas, Wemert, Clementi, Gonzalez, Jusserand, Asfar, Perrin, Fieux and Aubas (2003:2588) found that there was no significant difference in outcome between patients treated for eight versus fifteen days, but that there was an increase in resistant pathogens, especially Gram negative pathogens and more infective episodes with a longer treatment period.

The number of antimicrobials administered simultaneously should be limited. Nurses should question the necessity of the addition of a new antimicrobial if a previous prescription had not been stopped. Although pharmacists are primarily responsible to monitor the number of antimicrobials prescribed, nurses administer medication and they play a significant role in monitoring the number of antimicrobials that a patient receives during administration of medication, especially if more than one prescription chart is utilised.

Another important aspect that needs monitoring by nurses is the reviewing of the necessity of invasive devices. The significance of the measure is to minimise the risk for the patient of acquiring a healthcare-associated infection and subsequent treatment with additional antimicrobials or an increase in the duration of treatment if devices are *in situ* for too long periods of time. Devices need to be removed as soon as possible and due to the nature of their work, nurses have to suggest removal to physicians based on an improvement in the condition of the patient.

Hang time was the final measure that was monitored daily for compliance. No statistically significant improvement was observed, despite a 41% increase in compliance since the beginning of the intervention. However, the unit implemented various strategies to improve compliance to the measure, such as increasing the ward stock on antimicrobials that are most frequently used to reduce the time needed to collect prescriptions at the pharmacy.

Nurses are primarily responsible for the administration of medication and they need to ensure that it is administered as soon as possible after being prescribed by the physician and that the correct dose is furthermore administered at the correct time.

5.3.5 Infection prevention and control

An effective infection prevention and control (IPC) programme is one of the most important interventions to prevent the spread of resistant pathogens and reduce the impact of antimicrobial resistant (AMR) organisms (Royal College of Nursing, 2014:5; Moody *et al*., 2012:94).

Nurses are responsible for the implementation and adherence to IPC programmes; including surveillance, hand hygiene, environmental cleaning and the implementation and adherence to standard and transmission-based precautions (Mendelson *et al.*, 2012:607; Chalfine *et al.*, 2012:1; WHO, 2012:68). An important aspect of adherence to IPC principles is the prevention of the transmission of resistant pathogens. The IPC audit pre- and post-intervention demonstrated a statistically significant improvement in adherence to the IPC programme and IPC principles. A statistically significant reduction in the incidence of *Klebsiella pneumoniae* in the CCU was demonstrated. Improved adherence to IPC principles can be a contributing factor to the reduction in transmission of pathogens. Although not statistically significant, a reduction in the incidence of ESBL producing *Klebsiella pneumoniae* and *E.coli* was noted. The improvement in compliance to IPC practices is possibly one of the contributing factors for the reduction in ESBL producing pathogens.

Ghafur, Nagvekar, Thilakavathy, Chandra, Gopalakrishnan and Vidyalakshmi (2012:1-2) demonstrated similar results with the implementation of a stringent IPC programme; including strict adherence to transmission-based precautions, isolation, hand hygiene compliance and monitoring, together with an AMS programme. IPC is essential in all aspects of clinical service delivery and nurses have to be recognised as the drivers of the IPC programme and significant members of the multidisciplinary team (Royal College of Nursing, 2014:4).

5.3.6 Training

In order for AMS programmes to be successful, intensive training programmes for all stakeholders are required (Dellit *et al.*, 2007:165; SHEA, IDSA & PIDS, 2012:325).

Nurses have the potential to play a significant role in the implementation of AMS programmes, but need additional training (Gillespie *et al.*, 2013:356-366, National Healthcare System, 2014a:2). A one- or two-day training session is not adequate (Gillespie *et al.*, 2013:356-366). Basic microbiology and IPC must be part of an AMS training programme (Pulcini & Gyssens, 2013:199; National Healthcare system, 2014b).

There was a statistically significant improvement in knowledge about IPC and AMS of the nurses who took part in the study after training. Improved knowledge could have been a contributing factor to the improvement in adherence to IPC principles and the IPC audit results. This demonstrates that IPC training is important and that it has a positive impact on outcomes. Different methods should be used for training. The result of the knowledge assessment post intervention indicated that nurses require more training on AMS.

E-learning modules are valuable, due to the interactive nature thereof (Nathwani *et al.*, 2011:22). However, availability and access to computers can potentially be a limitation in an e-learning approach. Not all healthcare workers have access to computers after hours and there is not necessarily adequate time to spend on studies during working hours. Video conferencing and applications used for communication, such as Webex and Lync communicator, are valuable tools in providing interactive learning sessions at remote locations without the need to travel (Kellie, 2011:1181-1183).

Educating nurses without educating pharmacists and doctors will not have the desired impact. The complete multi-disciplinary team needs training in order to have successful antimicrobial stewardship programmes (Sahoo *et al.*, 2010:636). Clinical pharmacists and microbiologists can assist with training in areas where infectious diseases specialists are not available (Budwall, 2010:116).

It is however important to note that improved knowledge alone is not enough for the implementation of any programme; a change in behaviour of all stakeholders is necessary in order to achieve sustainable improvement. Training programmes should incorporate quality improvement, change management and behavioural change (Dellit *et al.*, 2007: 165, Moongtui *et al.*, 2011:107, National Healthcare System, 2014b).

5.3.7 The role of the clinical microbiologist

The role of the clinical microbiologist in LMICs is indispensable, especially in the absence of infectious diseases specialists. The clinical microbiologist plays a significant role in communicating results to the treating physicians and recommending treatment plans. Clinical microbiologists can conduct ward rounds and provide training on antimicrobial usage and AMS to both doctors and nurses. Goff (2011:17) and Lowman (2015:359-360) stated that clinical microbiologists have an important role to play in compilation of unit-specific antibiograms with organism and resistant profiles. In this study, a clinical microbiologist played a key role in the implementation of the AMS programme in the hospital. He provided training, support and recommended treatment options and advised the critical care nurses on practices related to IPC.

5.3.8 The role of the critical care nurse

Nurses played a prominent role in the study. Although other role-players were involved, the study focused on the role of the nurse as a member of the multidisciplinary AMS team. As reported by various authors, nurses are the primary caregivers and the advocates of the patient (Edwards, Drumright *et al.*, 2011:4; Crombie, 2012:16; Royal College of Nursing, 2014:6). They are furthermore responsible for the collection of specimens, administration of medication and monitoring of side effects (Gillespie *et al.*, 2013:356; Budwall, 2010:116; Moongtui *et al*., 2011:2014). Despite the fact that nurses are not responsible for making decisions regarding the

type of antimicrobial that is prescribed, duration of therapy and de-escalating treatment, they can implement certain aspects of an AMS programme and adhere to the principles of the programme.

Nurses completing a checklist with specific evidence-based measures on a daily basis can assist with the implementation of and compliance to an AMS programme (Perla *et al.*, 2011:46; Pulcini *et al*., 2008:1384-1388). It has been demonstrated in this study that the use of a checklist can lead to an improvement in compliance to certain evidence-based measures. It is however important that the measures can be influenced and driven by nurses.

Nurses were responsible for the implementation of the intervention, more specifically the utilisation of a checklist to ensure that different evidence-based measures were implemented and adhered to.

In the study, nurses ensured that specimens were collected on admission of patients to the CCU where indicated and prior to commencement of therapy. This is demonstrated in the increase in the number of positive specimens that were cultured prior to treatment as well as in the "culture before treatment" measure with a statistically significant improvement in compliance (Perla *et al*., 2011:47; CDC, 2014:6).

Traditionally, nurses will wait for the instruction from the treating physician to obtain a specimen. Valuable time will be lost and treatment might commence without an appropriate specimen. Through training, nurses working in the CCU understood the importance of appropriate and timeous specimen collection. Nurses can play a key role to ensure that specimens are only taken when clinically indicated, that they are taken correctly and of good quality, that the specimens reach the laboratory within the shortest possible time and that they are stored and transported correctly to ensure accurate analysis (Royal College of Nursing, 2014:6). Furthermore, if nurses have the mandate to collect specimens when required, they will ensure that it is done.

Additional training ensured that nurses involved in the study understood the importance of hang time and implemented several measures to ensure that antimicrobials are administered promptly to critically ill patients to reduce mortality (Gaieski, Pines, Band, Mikkelen & Massone *et al*., 2010:1; Dellinger, Levy, Rhodes, Annane, Gerlach, et al., 2013:171; Dellit *et al*., 2007: 168; Surviving Sepsis Campaign, 2012:591). One of the most important interventions was to have frequently-used antimicrobials available in the unit to reduce the time of collecting prescriptions at the pharmacy.

Nurses can play a significant role in monitoring the duration of antimicrobial therapy by monitoring the clinical condition of the patient and reminding the treating physician on a daily basis to review the necessity of treatment (Ladenheim *et al.*, 2013:48; CDC, 2014:6). In this study, nurses played an important role to remind the treating physician to evaluate the duration of treatment. Although a statistically significant decrease in the duration of therapy was not recorded in the study, a decrease in the number of patients treated with an antimicrobial for more than 14 days was observed. Because nurses are responsible for the administration of antimicrobials, are familiar with the clinical condition of the patient and conducting ward rounds with the treating physician, they are

in an ideal position to remind the doctor of the duration of therapy and suggest that the treatment should be re-evaluated (Gillespie *et al.*, 2013:356; Budwall, 2010:116; Moongtui *et al*., 2011:2014). Nurses furthermore need to ensure that the prescription charts are completed correctly with the dose and duration of therapy and ensure that allergies are recorded. Nurses are also responsible for the education of the patient and family (Royal College of Nursing, 2014:7). It is important to note that it is not the responsibility of nurses to prescribe antimicrobials in acute care settings, but merely to remind the physician to evaluate the necessity of treatment (Gillespie *et al*., 2013:365).

Nurses can also utilise their knowledge about improvement methodology to ensure compliance to these measures and to test changes prior to implementation to ensure improvement and sustainability (Perla *et al*., 2011:46; Institute of Healthcare Improvement, 2015).

Nurses might not be in a position to directly influence the physician to change treatment (Charani *et al.*, 2013: 189-194), but they are significant role-players in the implementation of an AMS programme. Their key responsibilities must be to ensure that appropriate cultures are taken prior to treatment; that results are communicated to the treating physician; that antimicrobials are administered in the correct dose at the correct time and for the correct duration; and that it is documented (Edwards, Drumright *et al*., 2011:6; Abbo *et al*., 2012:376; Royal College of Nursing, 2014:6-7; Ladenheim *et al*., 2013:48; CDC, 2014:6).

Nurses play a key role in the implementation and adherence to an IPC programme with a subsequent reduction in the transmission of pathogens. This study demonstrated that improvement in adherence to IPC principles can have an impact on the prevalence of pathogens in a nursing unit. Key aspects of an IPC programme that nurses are responsible for, are improved surveillance, compliance to hand hygiene, standard and transmission-based precautions, and environmental cleaning (Royal College of Nursing, 2014:6-7; CDC, 2014:6; Chalfine *et al*., 2012:1; Mendelson *et al*., 2012:607; WHO, 2015a:5).

Nurses are playing a significant role in the implementation of an AMS programme, but their role is not recognised and acknowledged. Without the contribution and cooperation of nurses, it will not be possible to implement an AMS programme.

5.4 FUTURE RESEARCH

Recommendations for future research are to evaluate the impact of an antimicrobial stewardship programme where nurses play a key role. Such research will have to be conducted over a longer period to evaluate the impact thereof.

Evaluating the impact of adding an infectious diseases specialist to an antimicrobial stewardship team where nurses play a more prominent role should also be considered as well as whether the utilisation of a dedicated antimicrobial prescription chart can change prescribing patterns sustainably. Comparing outcomes with a control group might have more significant findings.

5.5 LIMITATIONS

The distance to the hospital where the study was conducted was a limiting factor which made follow-up challenging. The duration of the study (thirteen months) and absence of a control group were additional limitations. Studies evaluating the effect of the implemenatation of an AMS programme need to be evaulated over a longer period.

5.6 BIAS

Due to the fact that exposure was not measured between two different groups, the possibility of bias is limited.

Confounding factors in the study might be an inadequate infection prevention and control programme. Measuring healthcare-associated infections (HAI) is not an outcome measure in the study. The acquisition of a HAI will therefore not have a direct influence on the results, but it might have an influence on the duration of treatment and the amount of antimicrobials prescribed if patients acquire a HAI during their stay in hospital. The length of stay in CCU is a contributing factor to the acquisition of HAIs.

Outbreaks of specific pathogens might have an influence, due to the fact that patients might require more antimicrobials for a longer duration. No outbreak was however notified during the study period.

The same time of the year was used for the pre-and post-data analysis to reduce confounding factors related to seasonal variations such as influenza.

Many interventions focusing on the role of the nurse in the implementation of an AMS programme had been implemented simultaneously. It is therefore problematic to say which one of the interventions was the most successful. It is important to note that with the implementation of an AMS programme several interventions need to be implemented together to have the desired outcome.

5.7 HYPOTHESIS

The null hypothesis had been rejected and the study demonstrated that critical care nurses can play an important role in the implementation of an antimicrobial stewardship programme. Although the statistical significance was limited, changes in practices were observed.

5.8 CONCLUSION

In many countries, nurses are responsible for the implementation of IPC programmes and for strategies to reduce healthcare-associated infections; including quality improvement projects (Royal College of Nursing, 2014:5).

Nurses have to be included in AMS programmes to successfully implement these programmes. They play a significant role in the implementation and execution of interventions and can ensure that these programmes are sustainable. The role of the nurse should be directed at nursing tasks related to the administration of medication, monitoring of the clinical condition of the patient, communication with the physician and implementation and adherence to IPC programmes. The role of the nurse in the AMS team should not be underestimated. With the necessary training on the use of antimicrobials, IPC and quality improvement, nurses will be able to play an important role in the implementation of an AMS programme.

The role of critical care nurses in the implementation of an AMS programme should be recognised and acknowledged by the multidisciplinary team.

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APPENDIX A:
PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

The role of the critical care nurse in the successful implementation of an antimicrobial stewardship program in a resource-limited country.

REFERENCE NUMBER:

S13/10/226

PRINCIPAL INVESTIGATOR:

Briëtte du Toit

ADDRESS:

Mediclinic Pty Ltd

Tijgerpark 1

Willie van Schoor Avenue

Bellville

7530

CONTACT NUMBER:

Mobile: 072 463 4444

Office: 021- 9436016

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the principal investigator any questions about any part of this project that you do not fully understand. Your participation is voluntary. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved.

This study has been approved by the Health Research Ethics Committee at Stellenbosch University **and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.**

WHAT IS THIS RESEARCH STUDY ALL ABOUT?

- *The study will only be conducted at Mediclinic Limpopo.*
- *The aim of the study is to examine the role of critical care nurses as significant role players in the implementation of an antimicrobial stewardship program in a hospital of a resource-limited country. Antimicrobial resistance is a problem worldwide and also in South Africa. We do not have the necessary resources such as clinical pharmacists and infectious disease specialists for the implementation of an antimicrobial stewardship program as described in various studies conducted in countries with adequate resources. Resource-limited countries therefore have to look for alternative resources to assist with the implementation of the program.*
- *An audit of the prescription charts will be conducted retrospectively to establish a baseline of prescribing practices.*
    - *Critical care nurses will then be trained on infection prevention and control, as well as on antimicrobial stewardship.*
    - *CPD lectures will be presented to the medical practitioners.*
    - *Daily audits of prescriptions charts will be conducted of patients in ICU utilising a checklist.*
    - *After the implementation period a post intervention audit will be conducted again to establish whether the intervention had the desired effect.*
- *There will not be any randomised process. All patients in ICU will be included, except for patients that is in the unit for post-operative monitoring.*

WHY HAVE YOU BEEN INVITED TO PARTICIPATE?

- *The researcher needs to include all medical practitioners admitting patients in the critical care unit and critical care nurses in the study to establish whether the implementation of certain interventions changes prescribing habits.*

WHAT WILL YOUR RESPONSIBILITIES BE?

- *The critical care nurses will have to do the daily audits in the critical care units, utilising a checklist.*
- *It will also be required of the critical care nurse to remind the doctor to review the prescription after 5 days.*
- *The study wants to proof that critical care nurses can be a significant role player in the implementation of an antimicrobial stewardship program.*
- *CPD lectures on antimicrobial utilisation will be presented to the medical practitioners.*
- *The study wants to proof that an increase in knowledge of antimicrobial stewardship will change prescribing habits. (It is currently an assumption that the prescribing habits of medical practitioners need to change.)*

WILL YOU BENEFIT FROM TAKING PART IN THIS RESEARCH?

- *The benefit of taking part in the study will be that the knowledge of the individual might improve.*
- *Patient outcomes might improve*
- *Antimicrobial resistance will reduce. The reduction of antimicrobial resistance is however a long term goal.*
- *The consumption of antimicrobials will be reduced.*

ARE THERE ANY RISKS INVOLVED IN YOUR TAKING PART IN THIS RESEARCH?

- *There are no risks in taking part in the study.*

WHO WILL HAVE ACCESS TO THE MEDICAL RECORDS?

- The information collected will be treated as confidential and protected. The identity of the *participants* will remain anonymous. It will only by the researcher and the statistical analyst who will have access to the information and the data will be anonymized.

WILL YOU BE PAID TO TAKE PART IN THIS STUDY AND ARE THERE ANY COSTS INVOLVED?

- No you will not be paid to take part in the study. It will be part of your daily tasks. There will be no costs involved for you, if you do take part.

IS THERE ANY THING ELSE THAT YOU SHOULD KNOW OR DO?

- You can contact Ms Briëtte du Toit at tel. 072 463 44444 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

DECLARATION BY PARTICIPANT

By signing below, I ……..……. agree to take part in a research study entitled: *The role of the critical care nurse in the successful implementation of an antimicrobial stewardship program in a resource-limited country.*

I declare that:

- I have read this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2014.

....

Signature of participant **Signature of witness**

DECLARATION BY INVESTIGATOR

I *(name)* ……..…… declare that:

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2014.

....

Signature of investigator **Signature of witness**

APPENDIX B:

LETTERS OF CONSENT FROM MEDICLINIC AND STELLENBOSCH UNIVERSITY

MEDICLINIC

MEDICLINIC OFFICES
STRAND ROAD
STELLENBOSCH
7600

PO BOX 456
STELLENBOSCH
7599

T +27 21 809 6500
F +27 21 809 6756
ETHICS LINE 0800 005 316

www.mediclinic.co.za

Ms B du Toit
Mediclinic
PO Box 456
STELLENBOSCH
7599

21 October 2013

Dear Ms Du Toit

RE: The role of the critical care nurse in the successful implementation of an antimicrobial stewardship programme in a limited resourced country

Your correspondence dated 18 October 2013 is acknowledged with thanks.

We will support your research at Mediclinic Nelspruit, subject to ethical approval from the university, and will load your project onto our research register once we are in possession of that approval.

Kind regards

Estelle Jordaan
NURSING EXECUTIVE

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Approved with Stipulations
New Application

02-Dec-2013
Du Toit, Briëtte B

Ethics Reference #: S13/10/226

Title: **The role of the critical care nurse in the successful implementation of an antimicrobial stewardship programme in a resource limited country.**

Dear Ms Briëtte Du Toit,

The **New Application** received on **30-Oct-2013**, was reviewed
Please note the following information about your approved research protocol:

Protocol Approval Period: **02-Dec-2013 -02-Dec-2014**

The Stipulations of your ethics approval are as follows:
1. Please explain why the specific hospital (Nelspruit Mediclinic) was used for this study. Also motivate how this hospital can fall under the classification of "resource limited" hospitals.

2. General checklist – incomplete, kindly complete and submit.

3. Please explain what is meant by "gross violations" and expand on the actions that will be taken.

4. Please discuss the role of the applicant in the study and also indicate which research assistants will be part of the study.

5. A waiver of consent for using patient data is granted, however, an Informed consent form needs to be compiled for both the nurses and medical practitioners that will participate in the study.

Please remember to use your **protocol number** (**S13/10/226**) on any documents or correspondence with the HREC concerning your research protocol.

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

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

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western

Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 483 9907) and Dr Helene Visser at City Health (Helene.Visser@capetown.gov.za Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.
For standard HREC forms and documents please visit: www.sun.ac.za/rds

If you have any questions or need further assistance, please contact the HREC office at 0219389207.

Included Documents:
Declarations_du Toit & Mehtar
Protocol
(informed consent)
S Mehtar CV
Synopsis
Application Form
CV Briette
General Checklist
Application signature

Sincerely,

Mertrude Davids
HREC Coordinator
Health Research Ethics Committee 2

Investigator Responsibilities

Protection of Human Research Participants

Some of the responsibilities investigators have when conducting research involving human participants are listed below:

1. Conducting the Research. You are responsible for making sure that the research is conducted according to the HREC approved research protocol. You are also responsible for the actions of all your co-investigators and research staff involved with this research.

2. Participant Enrolment. You may not recruit or enrol participants prior to the HREC approval date or after the expiration date of HREC approval. All recruitment materials for any form of media must be approved by the HREC prior to their use. If you need to recruit more participants than was noted in your HREC approval letter, you must submit an amendment requesting an increase in the number of participants.

3. Informed Consent. You are responsible for obtaining and documenting effective informed consent using **only** the HREC-approved consent documents, and for ensuring that no human participants are involved in research prior to obtaining their informed consent. Please give all participants copies of the signed informed consent documents. Keep the originals in your secured research files for at least fifteen (15) years.

4. Continuing Review. The HREC must review and approve all HREC-approved research protocols at intervals appropriate to the degree of risk but not less than once per year. There is **no grace period.** Prior to the date on which the HREC approval of the research expires, **it is your responsibility to submit the continuing review report in a timely fashion to ensure a lapse in HREC approval does not occur.** If HREC approval of your research lapses, you must stop new participant enrolment, and contact the HREC office immediately.

5. Amendments and Changes. If you wish to amend or change any aspect of your research (such as research design, interventions or procedures, number of participants, participant population, informed consent document, instruments, surveys or recruiting material), you must submit the amendment to the HREC for review using the current Amendment Form. You **may not initiate** any amendments or changes to your research without first obtaining written HREC review and approval. The **only exception** is when it is necessary to eliminate apparent immediate hazards to participants and the HREC should be immediately informed of this necessity.

6. Adverse or Unanticipated Events. Any serious adverse events, participant complaints, and all unanticipated problems that involve risks to participants or others, as well as any research related injuries, occurring at this institution or at other performance sites must be reported to the HREC within **five (5) days** of discovery of the incident. You must also report any instances of serious or continuing problems, or non-compliance with the HREC's requirements for protecting human research participants. The only exception to this policy is that the death of a research participant must be reported in accordance with the Stellenbosch University Health Research Ethics Committee Standard Operating Procedures www.sun025.sun.ac.za/portal /page/portal/Health_Sciences/English/Centres%20and%20Institutions/Research_Development_Support/Ethics/Application_package All reportable events should be submitted to the HREC using the Serious Adverse Event Report Form.

7. Research Record Keeping. You must keep the following research related records, at a minimum, in a secure location for a minimum of fifteen years: the HREC approved research protocol and all amendments; all informed consent documents; recruiting materials; continuing review reports; adverse or unanticipated events; and all correspondence from the HREC

8. Reports to the MCC and Sponsor. When you submit the required annual report to the MCC or you submit required reports to your sponsor, you must provide a copy of that report to the HREC. You may submit the report at the time of continuing HREC review.

9. Provision of Emergency Medical Care. When a physician provides emergency medical care to a participant without prior HREC review and approval, to the extent permitted by law, such activities will not be recognised as research nor will the data obtained from such activities should it be used in support of research.

10. Final reports. When you have completed (no further participant enrolment, interactions, interventions or data analysis) or stopped work on your research, you must submit a Final Report to the HREC.

11. On-Site Evaluations, MCC Inspections, or Audits. If you are notified that your research will be reviewed or audited by the MCC, the sponsor, any other external agency or any internal group, you must inform the HREC immediately of the impending audit/evaluation.

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Ethics Letter

03-Mar-2014

Ethics Reference #: S13/10/226
Title: The role of the critical care nurse in the successful implementation of an antimicrobial stewardship programme in a resource limited country.

Dear Ms Briëtte Du Toit,

Your letter dated 12 February 2014 refers.

The Health Research Ethics Committee approved the amended documentation.

The following amendments were approved:
Site change to Mediclinic Limpopo.

If you have any queries or need further help, please contact the REC Office 0219389207.

Sincerely,

REC Coordinator
Mertrude Davids
Health Research Ethics Committee 2

APPENDIX C:

KNOWLEDGE ASSESSMENT QUESTIONNAIRE

Hospital:	
Nursing unit:	
Date of completion:	
Permanent or Agency staff: (Please circle)	
Knowledge Assessment Critical Care Nurse	
1	Age in years
	Date of birth
	Age
2	Qualification
	Registered nurse
	Enrolled nurse/Staff nurse
	Bachelors in Nursing
	Nursing Diploma
	Post-graduate Diploma: Specify
	Critical Care Nursing Qualification
	Other: Specify
3	In which year did you qualify?
	Year:
4	Do you have any Infection Prevention and Control (IPC) Training?
	Yes
	No
	Unsure
5	**What was the duration of the training** (Please specify number of days, weeks, months, years)
6	Where did you receive the IPC training?
	Mediclinic
	University of Stellenbosch
	University of Witwatersrand
	Other (Please specify):
7	Did you have any training on antimicrobial stewardship?
	Yes
	No
	Unsure
8	**If yes, when?** (Specify the date (year) of the training)
9	**Duration of the training** (Please specify number of days, weeks, months, years)

	QUESTIONS
10	List 5 elements of Standard Precautions. (5)
10.1	
10.2	
10.3	
10.4	
10.5	
11	List the 3 types of Transmission-based Precautions. (3)
11.1	
11.2	
11.3	
12	Name 4 ways in which micro-organisms can be transmitted. (4)
12.1	
12.2	
12.3	
12.4	
13	Alcohol is a good disinfectant for surfaces and hands. (1)
	TRUE
	FALSE
14	Surfaces must be cleaned before it can be disinfected. (1)
	TRUE
	FALSE
15	Is it important to take a culture before an antimicrobial is prescribed? (1)
	Yes
	No
	Not always indicated
	Please motivate your answer.
16	A patient should always be treated with an antimicrobial when an organism is cultured? (1)
	Yes
	No
	It depends on clinical signs and symptoms of infection.
17	Name two carbapenems (1)
18	Which of the following antimicrobials is a third generation cephalosporin?(1)
	Cefepime
	Meropenem
	Gentamycin
	Ceftriaxone (Rocephin)
	Kefzol

	QUESTIONS
19	Is the statement true or false: The inappropriate use and over-use of antimicrobials contribute to the development of resistance amongst micro-organisms. (1)
	TRUE
	FALSE
20	The treatment of an infection depends on the sensitivity of the organism that was cultured. (1)
	Yes
	No
	The sensitivity is not an important aspect to consider. The type of organism that was cultured is more important than the sensitivity.
21	I would like to have more knowledge about IPC
	Yes
	No
	Unsure
22	I would like to have more knowledge about antimicrobial usage
	Yes
	No
	Unsure
	Total: 20

APPENDIX D:

CHECKLIST WITH DAILY MEASURES

Mediclinic Limpopo

Implementation of Antimicrobial Stewardship (AMS) in ICU

Stewardship measures Checklist

Activity Date																															
Day		**Day 1**			**Day 2**			**Day 3**			**Day 4**			**Day 5**			**Day 6**			**Day 7**			**Day 8**			**Day 9**			**Day 10**		
		Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A	Yes	No	N/A
1	Culture before antimicrobial therapy (**Only mark once on initiation of treatment**)																														
2	Hang Time (**Only mark once on initiation of treatment)**																														
3	De-escalation																														
4	Duration of therapy (**Mark daily: day 1/2/3/4)**																														
	Duration of therapy (**Mark daily: day 1/2/3/4)**																														
5	Number of antimicrobials (**on any given day**)																														
6	If device is in situ, assess for removal																														
7	Comments:																														

Definitions

Empiric antibiotic:

The initiation of treatment prior to the determination of a confirmed diagnosis and before an organism was cultured.

De-escalation:

To administer a targeted antibioticthat the organism is sensitive to once an organism was cultured.

Hang Time

The time interval between presribing of an antimicrobial and administration to the patient. **(Duration in minutes or hours) (MARK ONLY ONCE)**

Culture before treatment

It is important to know what organism was cultured and to what antibiotics it is sensitive. (MARK ONLY ONCE)

One dose of antibiotic can influence the susceptibility report.

Duration of therapy

Prolonged treatment with an antibiotic drive restance and increase collaterial damage (e.g. The risk to develop C.diff etc.)

Seven (7) days is appropriate to treat most infections in immuno competent patients. [MARK THE DAYS (1,2,3,4, etc)]

Number of antibiotics

APPENDIX E:

INFECTION PREVENTION AND CONTROL AUDIT

	MEDICLINIC INFECTION PREVENTION & CONTROL AUDIT			
	Infection Prevention and Control (IPC)			
	Hospital:			
	Date:			
	Surveyor:			
	Criteria	**Compliant**	**Non-Compliant**	**Comments / Recommendations**
1	**RISK MANAGEMENT**	**1**	**0**	
1.1	Clinical Risk Manager (CRM) trained in IPC			
1.2	Training was at least 6 months (provide details of IPC course)			
1.3	Dedicated assistant or successor			
1.4	Successor is trained in IPC (provide details)			
1.5	Work profile available for the CRM and assistant			
1.6	Competency Model available for the CRM and assistant			
1.7	5 Biggest IPC risks are identified (provide details)			
1.8	Quality improvement processes in place to improve outcomes (provide details)			
1.9	Best care always (BCA) implemented			
1.10	Catheter-associated urinary tract infection (CAUTI) Bundle			
1.11	Central line-associated bloodstream infection (CLABSI) Bundle			
1.12	Ventilator-associated pneumonia (VAP) Bundle			
1.13	Surgical site infection (SSI) Bundle			
1.14	Reduction in healthcare-associated infection (HAI) rates (provide details)			
1.15	Proof that action plans are implemented to improve rates			
				Total score: 15
2	**INFECTION PREVENTION AND CONTROL: SURVEILLANCE**	**1**	**0**	
2.1	ICNet accessed daily			
2.2	Number of open cases			
2.3	Admission/Discharge/Transfers (ADT) are complete			

2.4	Cases discharged and not only closed			
2.5	Isolation periods recorded			
2.6	HAI classification done for all organisms			
2.7	HAI classification done correctly			
2.8	Conditions recorded			
2.9	Notes imported			
2.10	CRM (and assistant) knows healthcare-associated infection (HAI) rates			
2.11	Evidence that HAIs are investigated			
2.12	CRM (and assistant) knows organism profiles of the hospital			
2.13	CRM knows which patients are in isolation and for what reason (organism cultured)			
2.14	Proof of daily visits to high-risk units and to follow patients up			
				Total score: 14
3	**NOTIFICATION OF NOTIFIABLE MEDICAL CONDITIONS**	**1**	**0**	
3.1	GW17/5 notification book is available			
3.2	The name and contact details of the CDC at the Department of Health (DoH) is available			
3.3	Proof of the weekly reports to the DoH			
3.4	Proof that Notifiable Medical Conditions are notified to the DoH			
3.5	There is a list of notifiable conditions in all departments			
3.6	Staff is familiar with the Corporate Policy (Notifications of Notifiable Medical Conditions)			
3.7	Staff knows the procedure related to priority A Notifiable Medical Conditions			
				Total score: 7
4	**ISOLATION AND TRANSMISSION-BASED PRECAUTIONS**	**1**	**0**	
4.1	The corporate policy "Isolation" is available and staff is familiar with its content			
4.2	Patients with multi-drug resistant organisms (MDROs) are isolated as far as possible			
4.3	Patients with diseases transmitted via the airborne route (measles, TB, chickenpox) can be isolated in a negative pressure ventilation room or alternatively can be isolated to prevent transmission to other patients			
4.4	N95 respirators are available and a fit test has been done on all staff members (Proof of training)			
4.5	Correct transmission-based precautions are implemented (Observed)			

4.6	There is proof that compliance to transmission-based precautions are monitored			
4.7	Appropriate Personal Protective Equipment (PPE) is worn			
4.8	Isolation poster is displayed and it is a reflection of the type of precautions that are implemented			
4.9	PPE is stored correctly			
4.10	Documentation is stored outside the room			
4.11	An area has been dedicated to accommodate a patient with a Viral Haemorrhagic fever			
4.12	There is documented evidence that staff members were trained on the donning and doffing of PPE			
				Total score: 12
5	**IPC WARD HYGIENE AUDITS**			
5.1	Proof that monthly hygiene audits are conducted			
5.2	Proof that non-compliance is addressed and action plan is available for corrective actions			
5.3	Environmental cleaning is monitored (Proof: Checklist)			
5.4	Temperature of fridges are monitored daily and recorded			
5.5	Only approved multidose vials are used (e.g. Insulin)			
5.6	All multidose vials have a date when it was first opened			
				Total score: 6
6	**PERSONNEL DEVELOPMENT AND EDUCATION**			
6.1	A succession strategy is available for Clinical Risk Manager (CRM)			
6.2	There is a person trained in IPC who can stand in for the CRM			
6.3	There is proof that the CRM/IPC assistant attended training sessions to further their knowledge			
6.4	CRM/IPS assistant belongs to IPC societies and regularly receive updates on new studies (e.g. IPC today, CDC updates, etc.)			
				Total score: 4
7	**TRAINING**			
7.1	IPC is presented as part of the induction of new personnel (on-boarding)			
7.2	IPC training is included is the annual training programme			
7.3	Proof of training sessions are available in the nursing units and for the hospital			
7.4	Proof on situational (on the spot) training (training records available)			

7.5	There are staff members who have completed the IPC course (number per year)			
7.6	The CRM/IPC assistant is involved in the IPC training of personnel			
				Total score: 6
8	**POLICIES AND PROCEDURES**			
8.1	CRM knows the content of the IPC policies			
8.2	Infection prevention and control policies are available to all personnel			
8.3	Personnel knows the content of the IPC policies			
8.4	Personnel knows where to access the IPC policies			
8.5	Personnel knows where to find policies that are only available electronically, and can access the Intranet/shared folder			
8.6	There is documented proof that personnel reads the policies			
				Total score: 6
9	**HAND HYGIENE**			
9.1	Alcohol hand rub is available and accessible at the point of care			
9.2	Alcohol hand dispensers are working and provide an efficient amount of solution (2-3 ml, i.e. enough to rub hands for at least 15-30 seconds)			
9.3	Paper towels and liquid soap are available at the basins			
9.4	Elbow-operated taps are available			
9.5	Pedal bins are available for discarding of used paper towels			
9.6	Hand hygiene compliance is measured on an ongoing basis			
9.7	Hand hygiene compliance rates are available			
9.8	There is evidence that hand hygiene is regularly addressed			
9.9	Hand hygiene posters are available and visible			
9.10	Staff is familiar with the 5 moments of hand hygiene (Ask staff)			
9.11	Gloves are used appropriately			
				Total score: 11
10	**WASTE MANAGEMENT - HEALTHCARE RISK WASTE**			
10.1	Correct packaging/labelling of waste			
10.2	Waste containers in nursing units are marked			
10.3	Method to dispose of empty glass vials (Name of recycler)			
10.4	Sharp containers are secured and available at the point of generation			

10.5	Filling line is marked (3/4) on the sharp containers			
10.6	Dedicated area for the storage of full sharp containers			
				Total score: 6
11	**SLUICE**			
11.1	Bedpan washer available that washes on a hot cycle			
11.2	If bedpan washer is not available, are bedpans disinfected: Explain			
11.3	No laundry are sluiced			
11.4	No instruments are cleaned in sluice			
11.5	Bedpans are stored inverted			
11.6	No objects are stored on the shelf underneath bedpans			
11.7	Patient wash basins are stored dry and inverted			
11.8	Patient wash basins are cleaned and disinfected after use			
11.9	Hand wash basin is available in sluice			
				Total score: 9
12	**HOUSEKEEPING**			
12.1	There is a contract and service level agreement with the cleaning company			
12.2	Evidence of pre-employment examinations available			
12.3	Evidence that housekeeping staff received Hep B vaccinations			
12.4	Evidence that housekeeping staff received IPC training			
12.5	IPC training programme available			
12.6	Cleaning policies and procedures available			
12.7	Staff knows the content of the policies and procedures			
12.8	Staff is familiar with the different disinfectants and its uses			
12.9	Staff is familiar with the colour coding system of cleaning			
12.10	There is dedicated trolleys for the cleaning of isolation rooms			
12.11	Cleaning staff members wear protective clothing during the cleaning procedure			
12.12	Cleaning staff members are familiar with the Isolation policy			
				Total score: 12
				Total score: 108