THE INVESTIGATION OF ANTIMICROBIAL PRESCRIBING PATTERNS AT THEMBA HOSPITAL, KABOKWENI

by

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RESEARCH DISSERTATION

Submitted in fulfilment of the requirements for the degree of

MASTER OF SCIENCE
in
MEDICINE (PHARMACY)

in the

FACULTY OF HEALTH SCIENCES
(School of Health Care Sciences)

at the

UNIVERSITY OF LIMPOPO
(MEDUNSA CAMPUS)

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2010

DECLARATION

I, **Karolina Z Danysz**, hereby declare that this research report is my own work. It is being submitted for the degree of Master of Science (Medical) in Pharmacy at the University of Limpopo, Pretoria. It has not been submitted before for any degree or examination at this or any other University.

Signed _____ on the _____ day of _____

ACKNOWLEDGEMENTS

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ABSTRACT

Introduction:

Antibiotics are among the most commonly prescribed drugs in the hospital setting. Because of an overall rise in health care costs, lack of uniformity in drug prescribing and the emergence of antibiotic resistance, monitoring and control of antibiotic use are of growing concern and strict antibiotic policies and prescribing guidelines are warranted. The aim of the study was to monitor the antibiotic prescriptions in a general outpatient setting in a rural regional hospital in Mpumalanga and to determine the impact of an education intervention on the prescribing patterns and adherences to the EDL/STD

Method:

Randomly selected adult outpatients files, at Themba Hospital, Mpumalanga, were selected to review the antibiotic prescribing patterns. The antibiotic prescriptions, diagnosis or symptom complex, and category of prescriber were recorded. The antibiotic prescriptions were cost according to the 2007 Hospital price list. Prescriptions were recorded in two phases; Phase 1; September, October and November 2006 and again January, February and March 2007 for Phase 2. Lectures on antibiotic prescribing, the use of the EDL/STG and the risk of antibiotic resistance were provided to all medical doctors in the first two weeks of January 2007. The prescription patterns, compliance with EDL/STG and the cost of the pre and post lectures were compared.

Results:

During the six-month study, a total of 1021 (Phase 1 = 505; Phase 2 = 520) prescriptions were reviewed and of those, 368 [Phase 1 = 230(46%); Phase 2 = 138 (27%)] prescriptions contained one or more antibiotics. Although the total number of antibiotics prescribed decreased from 338 in Phase 1 to 172 in Phase 2 the non-adherent to the EDL/STD for each antibiotic for the different diagnoses increased from 90% to 98% in Phases 1 and 2 respectively. There was no improvement in non-adherent prescriptions from the Community Medical Officers (CMO) and the Medical Interns after the lecture. The total antibiotic cost for the study period was R4 235.29 the calculated cost as per STG for the different diagnoses was R1 485.02 a decrease of 285%

Conclusion:

The number of prescriptions with antibiotics and the number of antibiotics decreased after the lecture. The antibiotics were not prescribed according to the EDL/STD. The lectures

had no impact on the EDL/STG adherence. The EDL/STG should be included in the teaching and learning of medical students as the junior staff prescribed the most non-adherent antibiotic prescriptions and a once off in-service lecture had little impact. Prescribing according to the STG could have a significant impact in decreasing the cost of antibiotics.

CHAPTER 1

INTRODUCTION

Antibiotics are among the most commonly prescribed drugs in the hospital setting. Because of an overall rise in health care costs, lack of uniformity in drug prescribing and the emergence of antibiotic resistance, monitoring and control of antibiotic use are of growing concern and strict antibiotic policies and prescribing guidelines are warranted.

Detailed knowledge of antibiotic prescribing patterns and related costs are important in order to re-emphasize and strictly implement national standard prescribing guidelines.

Because of the above concerns this study was conducted with the aim to monitor antibiotic prescription patterns and the cost implications in a general outpatient setting in a rural regional hospital in Mpumalanga, South Africa. The objectives of the study were to evaluate current trends in antimicrobial prescribing, to compare antimicrobial prescriptions to STGS/EDL, to make prescribers aware of standard treatment guidelines and correct dosages of appropriate medicines through training session and information leaflets, to investigate prescribing patterns post-training session and to determine cost of actual prescriptions and compare to the cost of recommended STG prescriptions.

CHAPTER 2

LITERATURE REVIEW

2.1   ESSENTIAL MEDICINES

Essential medicines, as defined by the World Health Organization (WHO) are "those drugs that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford" (WHO, 2009a).

South Africa's policy on essential medicines is generally based on the WHO's definition. The objectives of South Africa's National Drug Policy of 1996 are defined as "to ensure an adequate and reliable supply of safe, cost-effective drugs of acceptable quality to all citizens of South Africa and the rational use of drugs by prescribers, dispensers and consumers" (Department of Health, 2006).

The WHO has published a model list of essential medicines. Each country is encouraged to prepare their own lists taking into consideration local priorities. Currently over 150 countries have published an official essential medicines list (WHO,2009b).

The WHO list contains a core list and a complementary list. The core list presents a list of minimum medicine needs for a basic health care system after of and the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment. The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities are needed. In case of doubt, medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings. The compilation of an essential medicines list enables health authorities worldwide, especially in developing countries, to optimize pharmaceutical resources (Zweygarth and Summers, 2005).

The government of South Africa clearly outlines its commitment to ensuring availability and accessibility of medicines for all people in the health objectives of the National Drug Policy. The criteria for the selection of essential drugs for Primary Health Care in South Africa is based on the WHO guidelines for a national Essential Drugs List (EDL), which includes the following points (Department of Health, 2006.):

- Sufficient proven scientific data regarding effectiveness must be available
- Any drug included in the EDL should have a substantial safety and risk/benefit ratio
- Combination products, as an exception, will be included where patient compliance becomes an important factor, or two pharmacologically active ingredients are synergistically active in a product

Where drugs are clinically equally effective, the drugs will be compared on the following factors:

- The best-cost advantage
- The best researched
- The best pharmacokinetic properties
- The best patient compliance likelihood
- The most reliable local manufacturer (Department of Health, 2006)

2.2   CLINICAL GUIDELINES

Clinical guidelines (standard treatment guidelines, prescribing policies) consist of systematically developed statements to help prescribers make decisions about appropriate treatments for specific clinical conditions. Evidence-based clinical guidelines are critical to promoting rational use of medicines. They provide a benchmark of satisfactory diagnosis and treatment against which comparison of actual treatments can be made (WHO,2002a).

Clinical guidelines are also a proven way to promote more rational use of medicines provided they are:

- developed in a participatory way involving end-users
- easy to read
- introduced with an official launch
- promoted through training and wide dissemination
- reinforced by prescription audit and feedback.

The principal aim of an antibiotic policy is to improve the quality of prescribing. This should lead to a reduction of resistance, decreased cost to patient and improved patient care (Nathwani D,1999). Before embarking upon the development, dissemination and subsequent implementation of an antibiotic policy, clinicians and key decision-makers need to be clear on how they plan to evaluate its impact. Quality indicators need to be

identified. The number and complexity of these indicators must be specific to the organisation.These indicators can depend on local resources and should be simple, measurable and meaningful (Binyon and Cooke, 2000).

Guidelines should be developed for each level of care (ranging from paramedical staff in primary health care clinics to specialist doctors in tertiary referral hospitals), based on prevalent clinical conditions and the skills of available prescribers. Evidence-based treatment recommendations and regular updating help to ensure credibility and acceptance of the guidelines by practitioners. Sufficient resources are needed to reimburse all those who contribute to the guidelines, and to cover the costs of printing, dissemination and training (WHO, 2002b).

South Africa has had public sector Standard Treatment Guidelines (STGs) for Primary Health Care since 1996 (WHO, 1998). In 1998 these guidelines were revised, guidelines for hospital level (adult and paediatric) were added and an Essential Drugs List (EDL) were derived from them.

The guidelines are now widely available and used in public sector health facilities throughout the country. The public sector STG and EDL approach can only reach its full potential if adequate information about the medicines is made available. Providing this information has never been the purpose of the guidelines; they need to be supported by a medicines formulary.

The South African Medicines Formulary (SAMF) is currently in its 9th edition. However, as it contains information on medicines used in both the public and private sectors as well as at all levels of care, there has been a need for a more limited reference applicable to primary health care, particularly in the public sector. The *Primary Health Care Formulary* (Department of Health, 2003) was intended for this purpose. Its third edition was published in 2003, and it continues to be in demand.

In June 2003, the South African National Department of Health posted draft revised *Standard Treatment Guidelines for Primary Health Care* on the Internet for comment. At the same time, new legislation related to medicines control came into force. In the light of these developments, the task team decided to adapt the *WHO Model Formulary* to produce an up-to-date *Formulary for Primary Health Care,* which provides information on the medicines on the Government's revised Essential Drugs List for Primary Health Care. The process of compiling was started in October 2003, and the printed book was available in January 2004 (Zweygarth and Summers, 2005).

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The South African National Department of Health implemented STGs and an EDL for common health problems (including all infections) encountered at primary care and hospital level. STGs and the EDL are critical aspects of the health policy devised in the process of health care transformation in post-apartheid South Africa; adrress major health problems, initiating equity in health care delivery (availability and accessibility of essential drugs to all citizens), and, make provision for rational prescribing and dispensing. Pharmacokinetic and pharmacodynamic data, drug interactions, effects, routes of administration, concentrations at anatomical sites and cost are considered in the development of STGs and the EDL (Essack, 2006).

2.3   IRRATIONAL PRESCRIBING

Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. The overuse, under use or misuse of medicines results in wastage of scarce resources and widespread health hazards. Examples of irrational use of medicines include: use of too many medicines per patient ("poly-pharmacy"), inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; over-use of injections when oral formulations would be more appropriate, failure to prescribe in accordance with clinical guidelines, inappropriate self-medication, often of prescription-only medicines; non-adherence to dosing regimens (WHO, 2009a).

Antibiotic misuse is a worldwide problem in developed as well as developing countries (Kunin, 1993). However, antibiotics are grossly abused in developing countries, especially in Africa, through their purchase without prescription in local pharmacies and drug stores, and through inappropriate prescribing habits and an over-zealous desire to treat every infection. The need to formulate and adopt stringent policies for appropriate antibiotic usage is more pressing in developing nations, where the greatest levels of misuse and abuse are encountered. Well-established antibiotic policies go a long way towards achieving a reduction in irrational prescribing. Moreover, the issue can be addressed with a reasonable degree of success when prescribing physicians have adequate relevant knowledge of both the properties of chemotherapeutic agents and the pathogens that are likely to cause infection in the locality and their susceptibility or resistance profiles to commonly available antibiotics. Patient compliance is also vitally important and must be addressed (Ibeawuchi and Mbata, 2002).

Common patterns of irrational prescribing may therefore be manifested in the following

forms:

- The use of drugs when no drug therapy is indicated, e.g. antibiotics for viral upper respiratory infections
- The use of the incorrect drug for a specific condition requiring drug therapy, e.g. antibiotics in childhood diarrhoea requiring Oral Rehydration Solution
- The use of drugs with doubtful/unproven efficacy, e.g. the use of antimotility agents in acute diarrhoea
- Failure to provide available, safe, and effective drugs, e.g. failure to prescribe Oral Rehydration Solution for acute diarrhoea
- The use of correct drugs with incorrect route of administration, dosages, and duration, e.g. the use of IV metronidazole when suppositories or oral formulations would be appropriate
- The use of unnecessarily expensive drugs, e.g. the use of a third generation, broad spectrum antimicrobial when a first-line, narrow spectrum, agent is indicated (Vance and Millington, 1986)

Some examples of commonly encountered inappropriate prescribing practices in many health care settings include:

- Overuse of antibiotics and antidiarrhoeals for non-specific diarrhoea
- Indiscriminate use of injections, e.g. in bacterial infection treatment
- Multiple drug prescriptions (poly-pharmacy)
- Excessive use of antibiotics for treating minor ailments
- Minerals and tonics for malnutrition (Ross-Degnan *et al.*, 1992)

2.4   THE ROLE OF EDUCATION PROGRAMMES ON PRESCRIBING PATTERNS

Many studies have been done to document drug use patterns, and indicate that over prescribing, multi-drug prescribing, misuse of drugs, use of unnecessary expensive drugs and overuse of antibiotics and injections are the most common problems of irrational drug use by prescribers as well as consumers. Improving drug use would have important financial and public health benefits. Many efforts have been undertaken to improve drug use, but few evaluations have been done in this field. The majority of intervention studies are focused on prescribers in a public health setting, while irrational use of drugs is also widespread in the private sector. Furthermore, the magnitude of inappropriate drug use at community level is often overlooked and few interventions address drug use from a consumer's perspective (Le Grand *et al*, 1999).

Physician prescribing patterns can definitely be influenced. The first and most important step is to get the physician's attention by means of either personal contact or performance feedback that compares that physician to peers with the knowledge that the information is being shared with others. A combination of strategies is likely to be most effective including the provision of interactive opportunities for the physician to be involved in developing and experiencing the new therapeutic approach. Periodic reminders are also valuable. Undoubtedly, the most direct (and probably most effective) approach is the closed formulary adopted by many managed care organizations, where the patient is responsible for the full cost of a medication that does not meet formulary requirements. Risk sharing penalties and rewards are additional techniques by which to gain and maintain physician attention and cooperation (Sbarbaro, 2001).

A before-and-after intervention study was performed (Deuster *et al.*, 2010) in a 550-bed tertiary care teaching hospital in Switzerland, with an additional follow-up analysis one year later. The pre-intervention phase included chart analysis of current antibiotic use in 100 consecutive patients from the representative medical and surgical wards included in the study. Treatment guidelines were defined, taking into account published guidelines, the local antibacterial sensitivity of the pathogens, and the hospital antibiotic formulary defined by the drug and therapeutics committee. The guidelines were presented to the medical residents on a pocket card. They were informed and educated by the pharmacist (intervention). In the post-intervention phase immediately after the instruction, and in the follow-up phase one year later, a prospective analysis of antibiotic prescription was performed by chart review of 100 antibacterial treatments in consecutive patients to detect changes in antibiotic prescribing (treatment) and to determine whether these changes were sustained. Antibiotic treatment guidelines for the infections most commonly occurring in hospitalized patients resulted in a significant increase in appropriate antibiotic use. The programme was successful in changing prescription practice and achieved a sustained optimization of hospital-acquired-pneumonia therapy. Implementing, teaching and monitoring treatment guidelines can have a major impact on patient care.

2.5   ANTIMICROBIAL RESISTANCE

Since their discovery during the 20th Century, antimicrobial agents (antibiotics and related medicinal drugs) have reduced the threat posed by infectious diseases by helping to bring many serious infectious diseases under control. These drugs have also contributed to the major gains in life expectancy experienced during the latter part of the last century. These

gains are now seriously jeopardized by another recent development: the emergence and spread of microbes that are resistant to cheap and effective first-choice, or "first-line" drugs (WHO, 2002b).

Antimicrobial resistance (AMR) is one of the world's most serious public health problems. During the last decade, antimicrobial resistance has increased both worldwide (Jenkins, *et al.*, 2008). Many of the microbes (bacteria, viruses, protozoa) that cause infectious disease no longer respond to common antimicrobial drugs (antibacterial drugs including antibiotics, antiviral and antiprotozoal drugs). The problem is so serious that unless concerted action is taken worldwide, the risk exists of returning to the pre-antibiotic era.

WHO country data 2000-2003 show the following antimicrobial resistance global prevalence rates (WHO, 2005):

- malaria (chloroquine resistance in 81 out of 92 countries);
- tuberculosis (0-17% primary multi-drug resistance);
- HIV/AIDS (0-25% primary resistance to at least one antiretroviral drug);
- gonorrhoea (5-98% penicillin resistance);
- pneumonia and bacterial meningitis (0-70% penicillin resistance in streptococcus pneumonia);
- diarrhoea: shigellosis (10-90% ampicillin resistance, 5-95% cotrimoxazole resistance);
- hospital infections (0-70% resistance of staphylococcus aureus to all penicillins and cephalosporins).

The amount of antibiotics consumed in a community is directly related to the amount of antibiotic resistance found in the community (Austin *et al.*, 1999).

For instance, an ecologic study linked penicillin-nonsusceptibility in *Streptococcus pneumoniae* with β-lactam and macrolide use in 12 European countries. Penicillin-nonsusceptible *S. pneumoniae* and macrolide-resistant *S. pneumoniae* are markers of resistance to antibiotics commonly used as first-line drugs for respiratory tract infections. Although penicillin-resistant *S. pyogenes* has never been observed to date, the increasing rates of macrolide-resistant group A streptococci pose considerable clinical problems in many countries (Monnet and Harbath, 2004).

Inappropriate use of antibiotics, particularly for respiratory infections, has contributed to the major public health problem of antibiotic resistance (Mainous *et al.*, 2006). When a person is infected with an antibiotic-resistant bacterium, not only is treatment of that

patient more difficult, but the antibiotic-resistant bacterium may spread to other people (FDA Consumer Health Information, 2008).

In many ways, antibiotic resistance has developed along basic Darwinian evolutionary principles. As more and more antibiotics are used, organisms that possess genes that make them resistant to antibiotics are more likely to thrive and, therefore, are more likely to pass on those genes. Over many years, this pattern has had a significant effect on the evolution of infection-causing organisms.

With the evolution of multi-drug resistant strains of bacteria such as vancomycin-resistant *Staphylococcus aureus* (VRSA) and multi-drug resistant *Streptococcus pneumoniae*, it is no longer possible to treat infections that were commonly treated using antibiotics only a few years ago. For instance gonorrhea, a disease that was commonly treated with penicillin, has now become almost completely resistant to that drug.

Antibiotic resistance is usually an outcome of natural selection. Nature endows all bacteria with some low level of resistance. Thus a small fraction of the bacteria, in the order of one in a million, is naturally resistant to the antibiotic. Many studies have shown that the existence of these resistant strains predates the use of antibiotics as a treatment for infectious disease (Levy, 1992).

Natural selection is not the only mechanism by which resistance evolves. Bacteria possess the ability to directly transfer genetic material between each other using a mechanism known as plasmid transfer. Plasmids are packets of genetic material that serve as a vehicle for the transfer of resistance between different bacterial species. They are believed to be responsible for the geographical spread of bacterial resistance from one region of the world to another.

 A third mechanism through which resistance is induced in bacteria is by mutation. By this process, bacteria spontaneously change their genetic composition in response to an attack by antibiotics. Over time, the continued use of antibiotics encourages greater levels of mutation, leading to high levels of bacterial resistance (Laxminarayan and Brown, 2000).

To use fluroquinolones as an example, initial studies on the development of quinolone resistance demonstrated that there were two basic strategies that bacteria could adopt to circumvent the action of quinolones: (i) alterations in DNA gyrase (the target of the quinolones) and (ii) mutations that lead to reduced access of quinolones to DNA gyrase (either efflux systems, which are found in both Gram-positive and Gram-negative bacteria,

or alterations in the outer membranes of Gram-negative bacteria).Alterations in the structure of DNA gyrase have been the most commonly identified resistance mechanism in clinical isolates (Thomson, 1999).

Although antibiotic resistance has been an increasingly important concern in recent years, it is not a new challenge. Antibiotic resistance has been an issue as long as antibiotics have been in use. Even when penicillin was initially developed, researchers saw that some organisms were resistant to it. With each new antibiotic there has always been a percentage of organisms that was resistant.

Alexander Fleming, who discovered penicillin, recognized both the benefits and potential harms of antimicrobials right from the start. He was gravely concerned about their indiscriminate prescription by doctors and that people would be able to purchase them without a doctor's prescription. In 1947, he wrote: "*The greatest possibility of evil in self medication is the use of too-small doses, so that instead of clearing up the infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred-out which can be passed on to other individuals and perhaps from there to others until they reach someone who gets a septicaemia or a pneumonia which penicillin cannot save. In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted*".

His calls remained unheeded, for this was the beginning of the 'antibiotic age' (Van Bogaert and Ogunbanjo, 2004). The problem of antibiotic overuse is an international one and alarm has been expressed in the United States for several years (American Society for Microbiology [ASM], 1994). Although there is no absolute proof that antibiotics cause resistance, most authorities believe that a link is almost certain (Laxminarayan and Brown, 2000).

The existing link between the over- or improper use of antibiotics in different admission set-ups and the development of antibiotic resistance is well known (Filius and Liem, 2005; Lorian, 1995). About 30-50% of patients receive antibiotic therapy without any clinical indications. In some countries, antibiotics can be obtained as OTC medications (Shapiro *et al*., 1995). Antimicrobial resistance substantially raises already-rising health care costs and increases patient morbidity and mortality (Krivoy *et al*, 2007).

In recent years, many pharmaceutical companies have reduced investments in antibiotic research and development because the more profitable drugs are those intended to treat

chronic diseases over many years. A further concern is that if or when a new antibiotic is developed, there may be pressure to limit its use to treatment of only the most serious cases or when there is resistance to other antibiotics (Norrby *et al.*, 2005).

2.6   RATIONALISING MEDICINE USE

The need for promoting appropriate use of drugs in the health care system is not only because of the financial reasons with which policy makers and managers are usually most concerned. Appropriate use of drugs is also one essential element in achieving quality of health and medical care for patients and the community. Obviously, this should also become the concern of practitioners and prescribers. Actions or intervention programmes to promote the appropriate use of drugs should, therefore, be continuously implemented and systematically incorporated as an integral part of the health care system.

WHO advocates 12 key interventions to promote more rational use, namely:

- Establishment of a multidisciplinary national body to coordinate policies on medicine use
- Use of clinical guidelines
- Development and use of national essential medicines list
- Establishment of drug and therapeutics committees in districts and hospitals
- Inclusion of problem-based pharmacotherapy training in undergraduate curricula
- Continuing in-service medical education as a licensure requirement
- Use of independent information on medicines
- Public education about medicines
- Avoidance of perverse financial incentives
- Use of appropriate and enforced regulation
- Sufficient government expenditure to ensure availability of medicines and staff (WHO, 2009b)

With regards to antibiotics, policies are surveillance based and have an impact on the rational use of antibiotics. Rational use encompasses: restricting the use of particular agents, (especially those to which resistance emerges rapidly); and specifically defining indications for use (including the definition of optimum dosage to maximise cures and minimise selection of resistance genes, the optimum duration of antibiotic treatment for specific infections, the costs versus benefits of withholding antibiotics in cases of non-life threatening infections, and, the value of cycling a regimen in an effort to prevent the emergence of resistance in an institution). Choosing an antibiotic with a narrow spectrum

when a pathogen is known and the limiting of oral and topical therapy with drugs that may have to be used parenterally must be considered (Gould, 1999).

Reducing excessive and unnecessary use of antibiotics is essential to fighting antibiotic resistance. Appropriate and judicious use of antibiotics will go a long way to combat antibiotic resistance, but this area needs a lot of work. The situation can be difficult, especially for primary care physicians and paediatricians. Patients and parents often demand an antibiotic. The priority may be to provide optimal care to the patient in front of them, with less concern about the broader issue of antibiotic resistance (Lewis, 2009).

2.7   PHARMACOECONOMICS

Pharmacoeconomics refers to the scientific discipline that compares the value of one pharmaceutical drug or drug therapy to another (Wikipedia, 2009 a). Health economics is the science of assessing cost and benefits. The aim is to identify what is most efficient, so that the greatest amount of benefit can be bought for a given amount of money or resources. Pharmacoeconomics is a branch of health economics that particularly considers drug therapy. It is of particular interest to pharmaceutical companies who in developing a new drug and after the usual hurdles of efficacy, safety and tolerability must now jump over a fourth hurdle of cost effectiveness. A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or enhanced quality of life) of a pharmaceutical product. There are several types of pharmacoeconomic evaluation: cost, cost-benefit analysis (it is an analysis of the cost effectiveness of different alternatives in order to see whether the benefits outweigh the costs) cost-effectiveness analysis (is a form of economic analysis that compares the relative expenditure (costs) and outcomes (effects of two or more courses of actions) and cost-utility analysis (the purpose of CUA is to estimate the ratio between the cost of a health-related intervention and the benefit it produces in terms of the number of years lived in full health by the beneficiaries) (Bentkover and Corey, 2002).

An example of pharmacoeconomic studies is a study of the pharmaeconomics of antimicrobials for respiratory-tract infections. Having identified significant cost savings associated with regimens that are optimized for a particular patient on the basis of a drug's pharmacokinetic profile. Additional cost-effective measures for hospitals and health care institutions include the implementation of formalized IV-to-oral conversions and streamlining programmes. Pharmacoeconomic analysis of therapies for respiratory-tract and other infections demonstrates that reducing health care costs may, for example, best

be achieved by curing the infection in the shortest possible time through dosage optimization individualized to the patient (Paladino, 1999).

A pharmacoeconomic analysis is necessary for evaluating medicines in South Africa. Internationally, assessing new drug therapies for their cost effectiveness is becoming standard in an increasing number of countries.

In addition to Australia, Canada and several other countries, the Netherlands and Finland have also recently taken steps in the direction of introducing pharmacoeconomic guidelines within a formal evidence-based decision making mechanism.

A full cost-effectiveness analysis includes the following components:

- All relevant costs and clinical outcomes are included in the analysis and valued.
- The analysis is incremental in that it utilizes the difference in costs and difference in clinical outcomes between one specific pharmaceutical product as opposed to the alternate therapy.
- Cost and clinical outcomes may be discounted over time if the outcome is long-term (Rashid, 2004).

2.8   ANTIBIOTIC RESISTANCE ECONOMICS

The evolution of antibiotic resistance is strongly influenced by the economic behaviour of individuals and institutions. The more antibiotics are used (or misused), the greater the selective pressure placed on bacteria to evolve. The problem, therefore, arises from the lack of economic incentives for individuals to account for the negative impact of antibiotic use on social welfare. The economics literature on the topic of bacterial resistance is limited to a 1996 paper by Brown and Layton (1996) in which resistance is modelled as a dynamic externality. The reported rise in antimicrobial resistance has the potential to increase direct health-care resources and costs in patients with, for example, upper and lower respiratory tract infections. The reliance on empirical strategies in recent times may have reduced the costs associated with laboratory culture and susceptibility testing but unfortunately appears to have increased associated drug costs due to widespread use of broad-spectrum antimicrobials and increasing numbers of clinical failures (Nicolau, 2002).

2.9   CONCLUSION

There is general consensus that there is inappropriate and overuse of antibiotics internationally. Today, many experts believe that when it comes to the issue of antibiotic resistance, we may be on the brink of a worsening problem. Several major medical associations have warned that antibiotic resistance is the number one problem the medical community is now facing. One major contributor to resistance is inappropriate use of these drugs in animals and in humans.

CHAPTER 3

METHODS

3.1   INTRODUCTION

Due to a multitude of factors in the chosen setting and conditions, it is presumed that prescribers are, in general, not referencing and adhering to STGs either due to lack of awareness of STGs, inaccessible STG reference materials or a general non-conformance to STGs even though these issues can be resolved and should not be factors. Unnecessary antibiotic over-prescribing and incorrect prescribing is not only costing the South African healthcare system on both a local provincial level and a national level, but also potentially contribute to the emergence of antimicrobial resistance as well as draining pharmaceutical resources. The main factor contributing to bad prescribing practise is the lack of access to the STGs and possibly unintentional ignorance of the STGs resulting in non-STG compliant prescribing.

It is assumed that a single training session involving describing STGs and the distribution of the books to the various prescribers and departments would aid in promoting rational antimicrobial prescribing in accordance with the national STGs. It is assumed that with the 'new' knowledge, prescribers would adhere to STGs resulting in more rational prescribing practises, less antibiotic prescriptions and if required, correct antibiotics in correct doses would be prescribed ultimately based on sensitivity tests. A general drop in antibiotic prescriptions would be expected.

3.2   STUDY AIM AND OBJECTIVES

3.2.1   Aim
- To evalute current trends in antimicrobial prescribing and the costs implicated

3.2.2   Objectives
- To determine current trends in antimicrobial prescribing pre-training session
- To compare antimicrobial prescriptions to EDL and STGs

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- To make prescribers aware of standard treatment guidelines and correct dosages of appropriate medicines through training session and information leaflets
- To investigate prescribing patterns post-training session
- To determine and later compare the cost of prescriptions to cost of recommended STGs

3.3 HYPOTHESIS

Antibiotics are being prescribed unnecessarily over prescribed and not prescribed according to STGs at Themba Hospital. Overprescribing and non-adherence to STG result in overspending by hospitals and governments as well as increasing the likelihood of resistance and ultimately a super bug. Training of hospital personnel and distribution of STGs may reduce this.

3.4 METHODOLOGY

3.4.1 Setting

The study was conducted in the Casualty/Emergency and Outpatients Department of Themba Hospital, a public regional government hospital, in Kabokweni/White River, Mpumalanga, South Africa.

3.4.2 Study population and sample

Randomly selected, adult outpatients at Themba Hospital, Mpumalanga.

3.4.2.1. Inclusion criteria

- Out-patients (seen on daily basis during working week hours at the Outpatient Department)
- Casualty patients (seen on emergency basis, 24 hours a day, 7 days a week)
- Dental patients (seen on daily basis during the working week hours for consultation and medical treatment)

3.4.2.2. Exclusion criteria

- Chronic Clinic Patients (Diabetic and hypertension patients seen on Tuesdays and Wednesdays for prescription of chronic medication and consultations)

- Tuberculosis Clinic Patients (seen on Thursdays at TB Outpatient Clinic. Diagnosis of TB by clinical tests and prescription of TB treatment)

- Disclosed/known HIV Patients (seen daily at the Bambanani clinic. Diagnosis of HIV from clinical tests; counselling; assessment for ARV treatment; prescription of prophylactic treatment such a co-trimoxazole for prevention of pneumonia; prescription of ARVs)

- Eye clinic patients

- Hospital in-patients

- Children

3.4.2.3.   Study method

- On a daily basis, after normal working hours, approximately 20 files were picked at random from the pile of files taken in during the day before the administrative staff took them back for filing in the offices. This ensured that the randomly selected adult outpatient patient files were assessed on the day. The number of antimicrobial prescriptions was recorded. The prescription data were collected from the files with antimicrobial prescriptions.

- Appendices A and B were completed according to the relevant subheadings and parameters. Conditions and diagnoses were copied directly from prescriber's scripts in exact same wording. Patient's sex and medical history were not taken into consideration. Only prescriptions containing antibiotics were assessed. Other antimicrobials (antivirals, antifungals, etc) were omitted, as they were more frequently prescribed for patient's that were excluded from the study.

- The study was carried out without an intervention for three months over September, October and November 2006. Approximately 500 prescriptions that were appropriate were assessed over this period.

- In early January 2007, on arrival of new medical staff and return of old staff, an intervention was staged in the form of a training and discussion session for the prescribers. There were 35 medical staff members who attended the session.

- Training involved an informal lecture conducted by the chief researcher. Printed material in the form of new EDL books were handed out to prescribers for reference. The EDL books had been ordered by the pharmacy beforehand and were placed at every department that may have required them. During the training session the focus was on irrational, non-formulary and over-prescribing of antimicrobials. The training session was followed by questions and answers

between the chief researcher and the medical prescribing personnel. The training was only held in January and not repeated during the study. Due to the training session being held at one of the initial meetings of the year, attendance was high with 35 out of the 40 prescribing staff including management staff being present.

- A PowerPoint presentation was shown to the staff discussing over-prescribing antibiotics, irrational prescribing of antibiotics and limiting of 'by special request' prescribing of antibiotics.

- Following the intervention, the study continued for a further three months over January, February and March 2007 in the same fashion as during the pre-intervention stage. Appropriate patient files were examined. The data from approximately 520 patient files were assessed and collected.

Data capturing

Data capturing involved transcribing patient diagnosis, medications prescribed and dosing instructions onto data forms in columns provided (Appendices A and B) .The remaining columns were completed after assessing the originally transcribed data from the patient files.

Data analysis

Descriptive statistics was used to analyze the data. Once all data were captured and data forms completed, the numbers of antibiotics, types of antibiotics, types of conditions and adherence to STGs were tabulated in an Excel spreadsheet and the results extracted by the university's statistician in the form of tables.

Ethics

Ethics approval had been obtained from the Mpumalanga Province Department of Health as well as Themba Hospital management prior to commencing data capturing. Ethics and study approval was obtained from MEDUNSA Research Ethics Committee prior to commencement of study (refer to Appendices C and D).

The findings of the study are presented in the next chapter.

CHAPTER 4

RESULTS

4.1   ANTIBIOTIC PRESCRIBING PATTERNS

4.1.1   The number of prescriptions reviewed and the number of prescriptions with antibiotic treatment

During the six-month study a total of 1021 prescriptions were reviewed. Of the reviewed prescriptions, 368 contained one or more antibiotics. As shown by Figure 4.1, 505 prescriptions were reviewed during the first three months (September to November 2006), of which 230 (45.5%) prescriptions contained antibiotics. The training session took place in early January 2007 on the arrival of new staff and the return of old staff from holiday. Approximately 30 staff prescribers attended the training session.
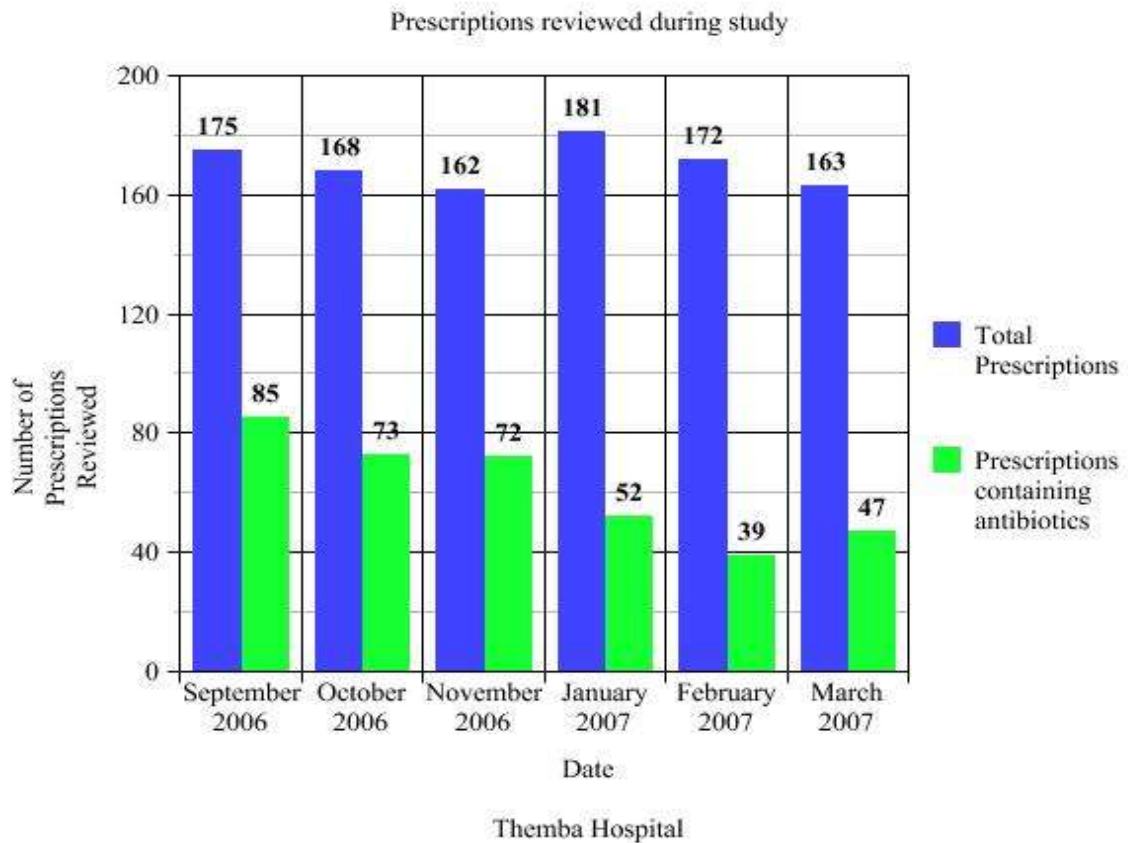
Figure 4.1 Vertical bar graph comparing prescriptions containing antibiotics to total prescriptions each month (Total prescriptions n=1021; Prescriptions containing antibiotics n=368)

After the intervention, the prescriptions were reviewed for a further three months (January to March 2007), where 516 prescriptions were reviewed of which 138 (26.7%) contained antibiotics. A decrease of 18.8% of prescriptions with antibiotics was noted.

Themba Hospital
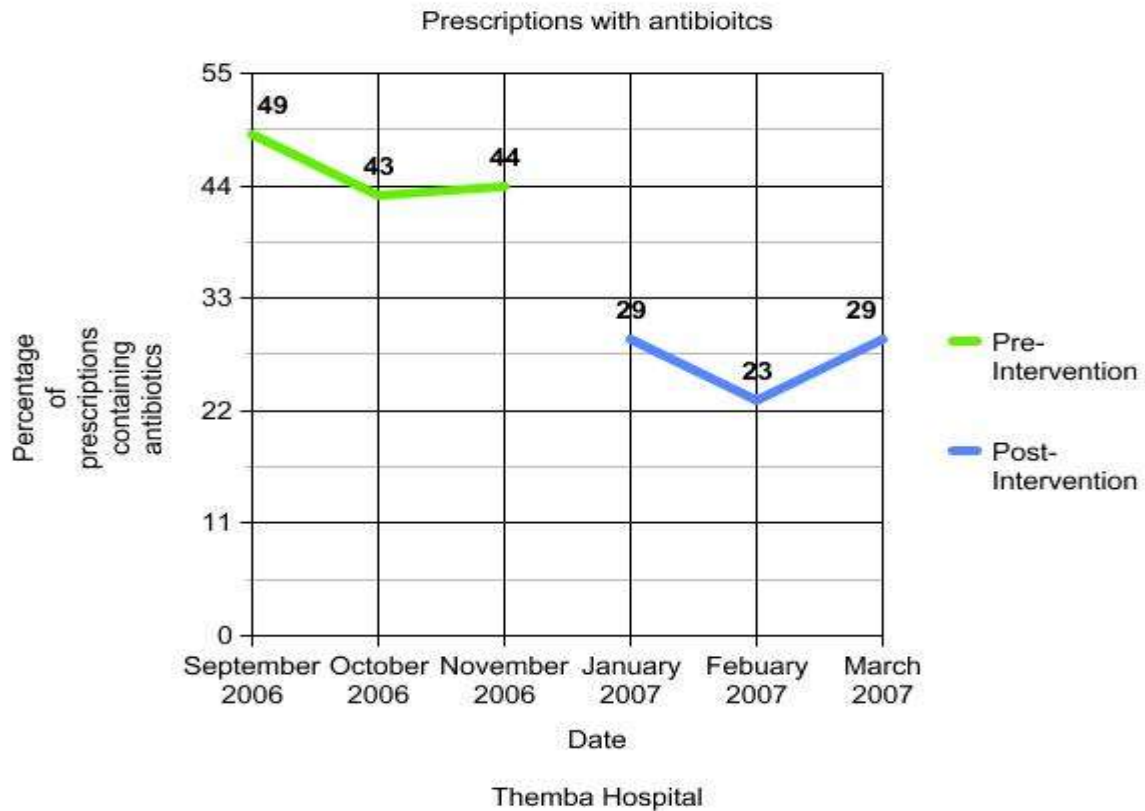
Figure 4.2 Line graph of the percentage of prescriptions containing antibiotic treatment (Average pre-intervention n=45%; Average post-intervention n=27%)

There was a decrease in prescribing of antibiotics as a percentage (Figure 4.2). The highest percentage of antibiotics prescribed was at the beginning of the study, September 2006, at 49% (85;n=175). The lowest percentage of antibiotics prescribed was after the training session in February 2007, at 23% (39;n=172).

4.1.2   Number of antibiotics per prescription

The number of antibiotics prescribed over each period, pre- and post-intervention, was taken into account and an average for both periods was derived at (Table 4.2). A reduction in the number of of antibiotics prescribed was noted from pre-to post-training phase. The pre-test phase showed that a total average of 1.47 (SD) antibiotics was

prescribed pre-intervention. The number of antibiotics per prescription decreased from an average of 1.49(SD) in October 2006 to 1.23(SD) in Jan and Feb 2007. The training session had an effect on reducing the number of antibiotics prescribed since a general decrease in antibiotic prescriptions was noticed. October 2006 showed the highest number of antibiotics prescribed at 1.49 per prescription, while January and February 2007 showed the least number of antibiotics prescribed at an average of 1.23 antibiotics per prescription.

Table 4.1 Average number of antibiotics per prescription per month

Phase	Month	Number of prescriptions with antibiotics	Number of antibiotics prescribed	Antibiotics per prescription
Pre-test	September 2006	85	124	1.46
	October 2006	73	109	1.49
	November 2006	72	105	1.46
	Total, pre-test	**230**	**338**	**1.47**
Post-test	January 2007	52	64	1.23
	February 2007	39	48	1.23
	March 2007	47	60	1.28
	Total, post-test	**138**	**172**	**1.25**
Grand total		**368**	**510**	**1.39**

Figure 4.3 shows the number of prescriptions written containing antibiotics as well as the actual number of antibiotics prescribed each month. It shows a marked decrease in both figures from the pre-intervention phase (September, October and November 2006) to the post-intervention phase (January, February, March 2007). The highest number of antibiotics prescribed was 124 in September 2006 while the lowest number of antibiotics prescribed was 48 in February 2007. There was an increase in antibiotics prescribed in March 2007 increased again.
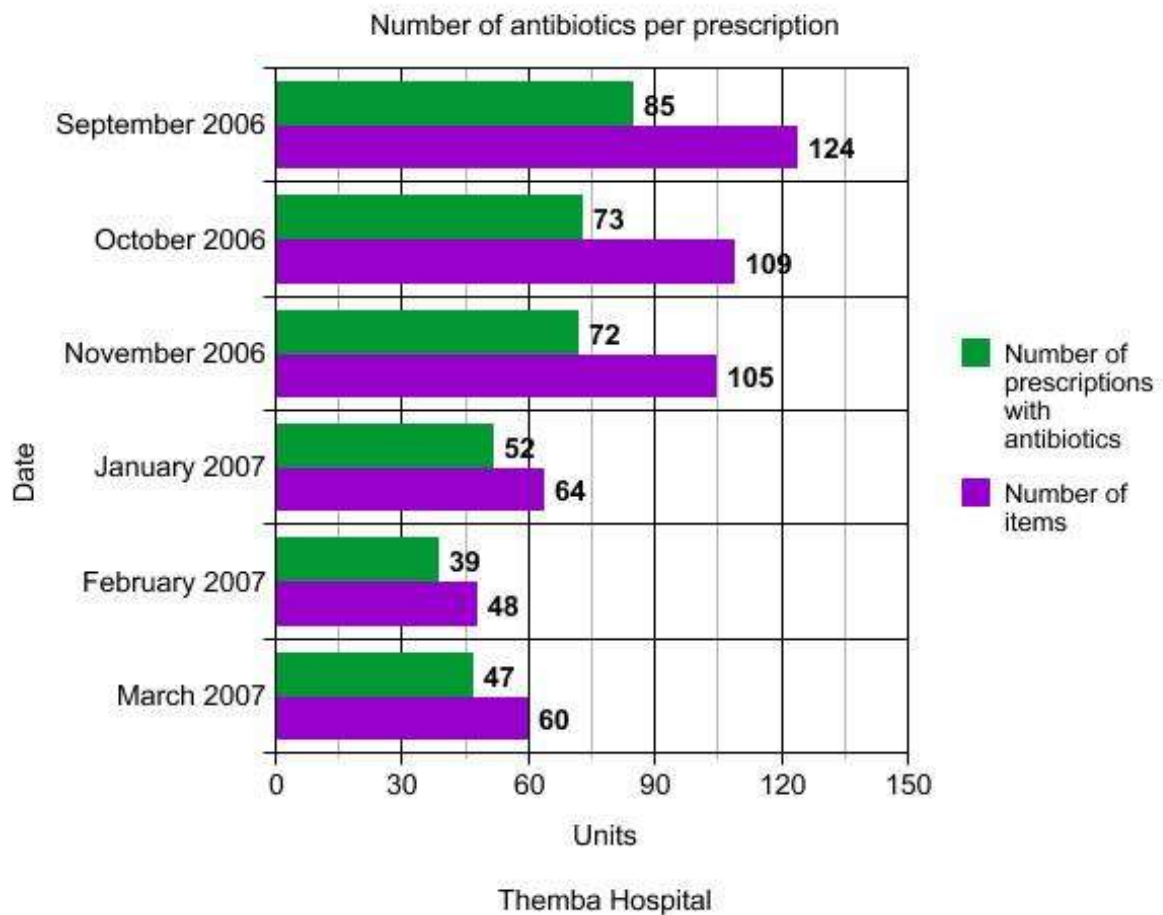
Figure 4.3 Horizontal bar graph of cumulative amount of prescriptions and total number of antibiotics prescribed per month (Number of prescriptions containing antibiotics n= 368; Total number of antibiotics n= 510)

4.1.3   The type and number of antibiotics prescribed

During the pre-intervention phase of the study, a total of 338 antibiotics were prescribed. Amoxicillin was the most prescribed antibiotic constituting 21.3% of all antibiotic prescriptions (72 n= 338). It was followed by metronidazole (17.8%;60;n=338) and cloxacillin (15.7%;53; n=338) (see Figure 4.4).

Figure 4.4 shows the antibiotics prescribed during study at Themba Hospital, with a vertical bar graph comparing Pre-Intervention (Sept, Oct, Nov 2006) and Post-Intervention (Jan, Feb, Mar 2007) prescriptions.
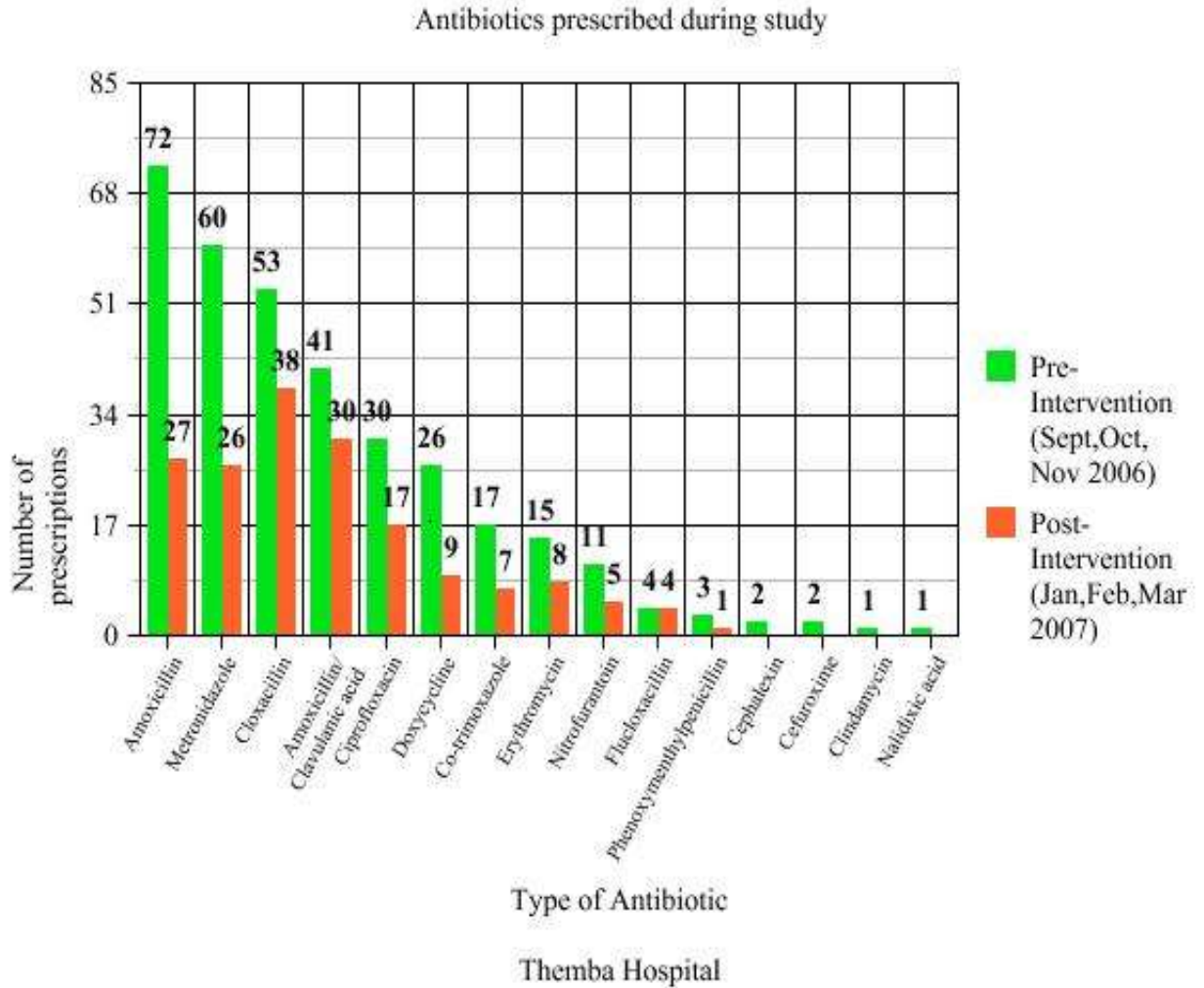
Figure 4.4 Vertical bar graph of type and number of each antibiotic prescribed (Number of antibiotic prescriptions pre-intervention n=338; Number of antibiotic prescriptions post-intervention n= 172)

There was a marked decrease in the total number of antibiotics prescribed after the intervention. Only 172 antibiotics were prescribed during January, February and March 2007 compared to 338 antibiotic prescriptions during the pre-intervention. Cloxacillin (n = 38; 22.1%) was the most commonly prescribed antibiotic during the post-intervention study followed by amoxicillin/clavulanic acid (n = 30; 17.4%) and amoxicillin (n = 27; 15.6%).

Table 4.2 Most prescribed antibiotic pre- and post-intervention

Prescriptions for:	Pre-intervention			Post-intervention		
	Number	Percent	Rank	Number	Percent	Rank
Amoxicillin	72	21%	1	27	16%	3
Metronidazole	60	16%	2	26	22%	4
Cloxacillin	53	18%	3	38	15%	1
Amoxicillin/clavulanic acid	41	12%	4	30	17%	2
Ciprofloxacin	30	9%	5	17	10%	5
Doxycycline	26	8%	6	9	5%	6
Co-trimoxazole	17	5%	7	7	4%	8
Erythromycin	15	4%	8	8	5%	7
Nitrofurantoin	11	3%	9	5	3%	9
Flucloxacillin	4	1%	10	4	2%	10
Phenoxymethylpenicillin	3	1%	11	1	1%	11
Cephalexin	2	0%	12		0%	
Cefuroxime	2	1%	13		0%	
Clindamycin	1	1%	14		0%	
Nalidixic acid	1	0%	15		0%	
Total	**338**	**100%**		**172**	**100%**	

4.2 THE NON-COMPLIANCE WITH STGS

4.2.1 Diagnosis or symptom complex and prescribing in adherence with STGs

All conditions (diagnosis and/or symptom complex) classified with corresponding ICD-10 codes that were accessed during the study are listed in Table 4.4. The conditions are listed according to the number of items prescribed, STG compliant and STG non-compliant , pre- and post-test.472 STG non-compliant items were prescribed during both pre- and post-test periods. 45 condtions were treated with antibiotics. Injuries (14%), acute bronchitis (12%), urinary tract infections (9%), boils and abscess (8%) and sexually transmitted infections (7%) were the five most frequently diagnoses or symptom complexes treated with antibiotics.

Most of the prescriptions for antibiotics were not prescribed according to the STGs. Antibiotics for only 34 (11%) and 4 (2%) diagnoses or symptom complexes were according the STGs for the pre- and post-tests, respectively.

Table 4.3: Conditions accessed with number of STG compliant and non-compliant items prescribed pre and post test

ICD10	Diagnosis	Pre-test		Post-test		Total
		STG com-pliant items	Non-STG-com-pliant items	STG com-pliant items	Non-STG-com-pliant items	
A03.0	Shigellosis		1			1
A04.1	Enterotoxigenic E. coli infection				2	2
A09	**Enteritis NOS haemorrhagic septic**		**11**		**2**	**13**
A54	*Gonococal infection*				*3*	*3*
A59	Trichomoniasis		4			4
A64	Unspecified sexually transmitted disease. (Venereal disease NOS)	14	12		9	35
A69.1	*Necrotizing ulcerative (acute) gingivitis*	*3*	*9*	*1*	*11*	*24*
B11.1	Viral influenza		2			2
B18.9	Chronic viral hepatitis, unspecified		2			2
B20.9	**HIV disease**		**12**		**1**	**13**
B44.9	Aspergillosis, unspecified		3			3
B54	Malaria.	1				1
D64.9	*Anaemia, unspecified*				*2*	*2*
H60.9	Otitis externa		2			2
H66.3	Otitis media, chronic suppurative		3			3
H66.9	**Otitis media, acute**		**6**		**1**	**7**
J01.9	Acute sinusitis, unspecified		1			1
J03.9	Acute tonsillitis, unspecified		5		6	11
J11.1	Common cold and influenza (virus not identified)		4			4
J18.9	Pneumonia, unspecified	2	11		7	20
J20.9	**Acute bronchitis, unspecified**	**1**	**42**		**18**	**61**
J44.9	COPD, unspecified.		11		8	19
J46	Status asthmaticus				1	1
K04.7	Dental abscess NOS	2	11	3	4	20
K05.1	Chronic gingivitis		6		6	12
K12.0	Recurrent oral aphthae		2			2
K30	Dyspepsia. Indigestion.		1		5	6
K52.9	Noninfective gastroenteritis and colitis, unspecified		14		5	19
K60.2	Anal fissures, unspecified		2			2
K81	Cholecystitis				2	2
L01.0	Impetigo		1			1
L02.9	Boil, abscess		18		21	39
L03.9	Cellulitis		3		1	4
L08	*Septic wound*				*7*	*7*
L08/L97	Sepsis		2			2

ICD10	Diagnosis	Pre-test		Post-test		Total
		STG compliant items	Non-STG-compliant items	STG compliant items	Non-STG-compliant items	
N11.9	Pyelonephritis, acute		3			3
N39.0	**Urinary tract infection, uncomplicated**	**5**	**27**		**13**	**45**
N73.9	Pelvic inflammatory disease	6	8		5	19
R05	Cough		3		1	4
R11	Nausea and vomiting, non-specific		2			2
R50.9	Fever		1			1
R52.9	Pain control in terminal cancer		2			2
T14	**Injuries**		**50**		**20**	**70**
T14.1	Bites, animal and human		6		6	12
T30.0	Burns		1		1	2
Total number of conditions treated: 45	**TOTAL**	**34**	**304**	**4**	**168**	**510**

4.2.2 Prescribers compliance with Standard Treatment Guidelines

Figure 4.5 shows which prescribing group prescribed the most STG non-compliant antibiotics during pre and post interventions. Community Medical Officers (CMO) prescribed the most STG non-adherent antibiotics pre and post intervention. During September, October and November 2006, 106 out of a total of 304 (35%) STG non-compliant antibiotics prescribed were prescribed by CMO's.

The STG non-compliant prescriptions for the conditions in **bold** decreased in the post-test. The conditions in *italics* show an increase in STG non-compliant items being prescribed during the post-test phase.

Figure 4.5 Group of prescribers vs. Number of STG non-compliant antibiotics prescribed (pre-intervention: n= 304; post-intervention: n= 168)

During January, February and March 2007, 54 out of 168 STG non-compliant antibiotics were prescribed by Community Medical Officers (32%). CMOs and Medical Interns (MI) were the majority of prescribers as they were usually the first prescriber contact that an outpatient would have in the hospital. In general, except for two occasions, there was a decrease in the number of STG non-complaint antibiotics being prescribed after the training session in early January 2007.

In Figure 4.6 the results are erratic and there was no clear trend to see which prescriber group adhered to STGs.The total number of STG compliant antibiotics prescribed was 38. Most prescribers when prescribing antibiotics. There is a clear difference in prescribing patterns before or after the intervention (training session). In this case the results were inconclusive. Although it could be guessed that there was a general decrease in antibiotic prescribing altogether due to the data assessed in other sections.
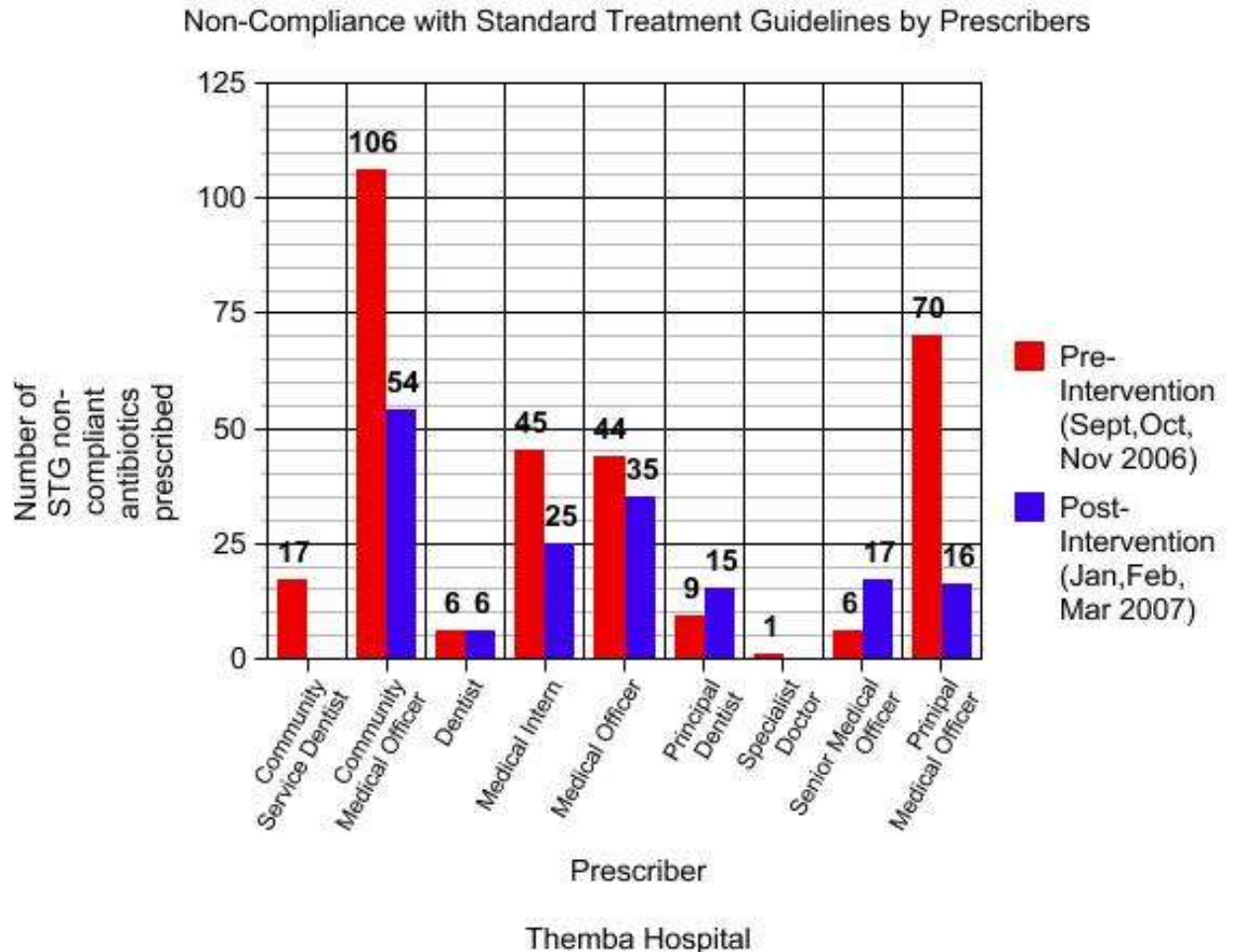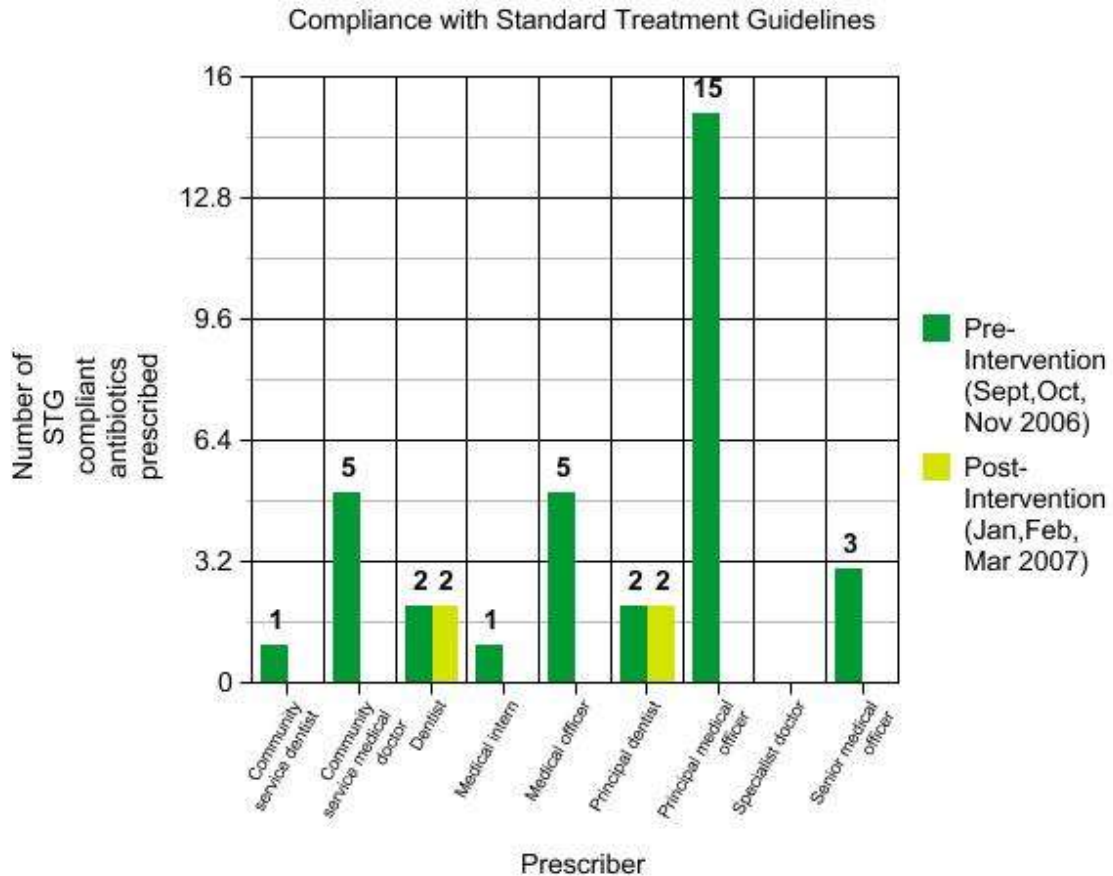
Figure 4.6 Group of prescribers vs. Number of STG compliant antibiotics prescribed (pre-intervention: n=34; post-intervention: n= 4)

The percentage of STG-compliant items prescribed by each different rank is shown for the pre-intervention period and the post-intervention period. Compared to post intervention phase there were more STG-compliant items prescribed during the pre-intervention period. One would have expected a rise in STG-compliant items being prescribed post-intervention but the graph shows the opposite. The difference between pre- and post-intervention may be attributed to the general decrease of antibiotic prescribing as concluded from other results.

In general, the number of antibiotic prescriptions decreased post-intervention and so was STG compliance (Figure 4.7), antibiotic prescriptions were reduced post-intervention but STG compliance did not increase. Compliance with STGs reduced post-intervention but that may be due to a general decrease in antibiotic prescriptions.
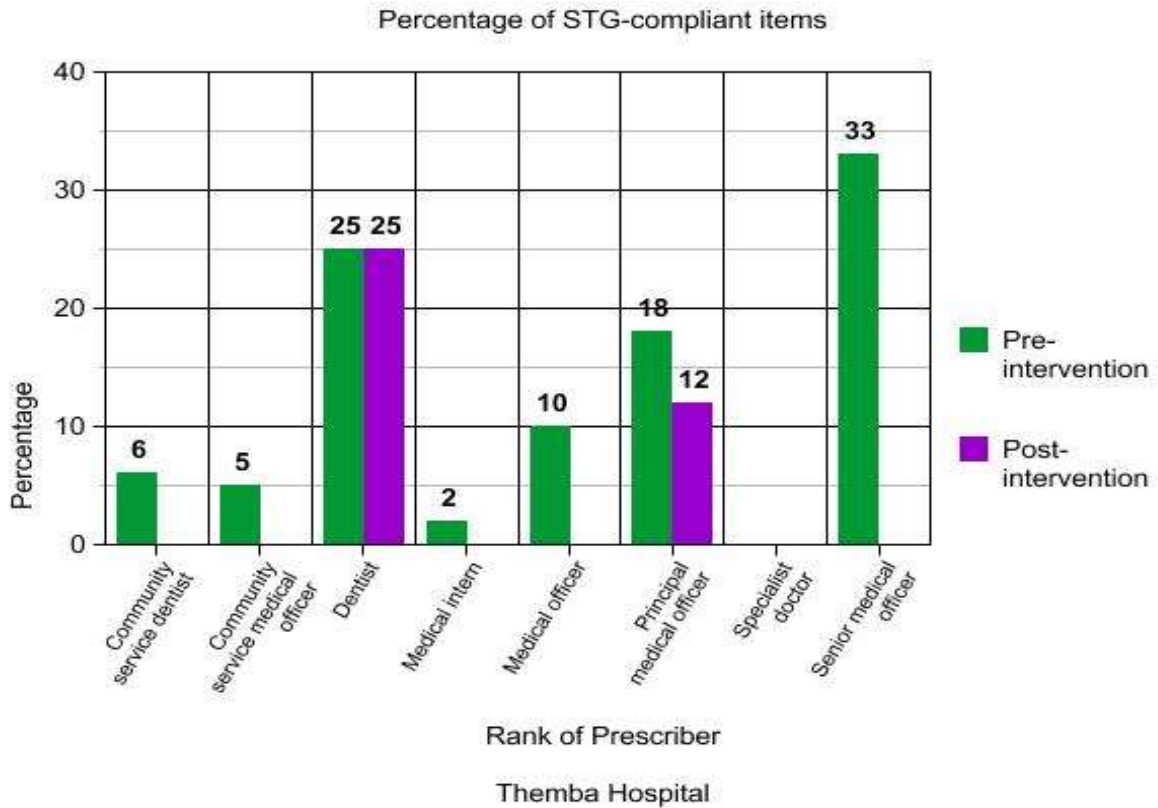
Figure 4.7 STG-compliant items vs. Group of prescribers

Prescribing not according to STGs may be attributed to the unavailability of STGs books, which were distributed during the training session to the healthcare professionals, and extra copies were left at the departments. Prescribers were not aware of the STGs before the training session as they were not previously introduced or trained formally on the STGs.

4.2.3   Antibiotic prescribed according to Standard Treatment Guidelines

In general, the number of antibiotic prescriptions decreased post-intervention and so was STG compliance (Figure 4.7), antibiotic prescriptions were reduced post-intervention but STG compliance did not increase. Compliance with STGs reduced post-intervention but that may be due to a general decrease in antibiotic prescriptions.

Of the 72 Amoxycillin prescriptions prescribed during the pre-phase, about 10%(7;n=72) prescriptions were according to STG. Nine percent (5;n=55) of the Metronidazole prescriptions were STG compliant. None of the Cloxacillin (n=53) and Clavulanic acid (n=41) prescriptions were STG compliant. However, it was observed from the less

frequently prescribed antibiotics that 40% (12;n=30) of Ciprofloxacin and 38.5% (10;n=26) of Doxycycline prescription was observed to be STG complaint (Table 4.5).

Table 4.5 Prescribing in adherence to standard treatment guidelines (STGs): antibiotics

Antibiotic	Number of items prescribed				
	As per STG	**Not as per STG**	**As per STG**	**Not as per STG**	**Total**
Amoxicillin	7	65	2	25	99
Cloxacillin		53		38	91
Metronidazole	5	55	2	24	86
Amoxicillin/clavulanic acid		41		30	71
Ciprofloxacin	12	18		17	47
Doxycycline	10	16		9	35
Co-trimoxazole		17		7	24
Erythromycin		15		8	23
Nitrofurantoin		11		5	16
Flucloxacillin		4		4	8
Phenoxymethylpenicillin		3		1	4
Cephalexin		2			2
Cefuroxime		2			2
Clindamycin		1			1
Nalidixic acid		1			1
Total	**34**	**304**	**4**	**168**	**510**

Of the 27 Amoxycillin prescriptions prescribed during the post-phase, about 7%(2;n=27) prescriptions were according to STG. Eight percent (2;n=26) of the Metronidazole prescriptions were STG compliant. None of the Cloxacillin (n=38) and Clavulanic acid (n=30) prescriptions were STG compliant (Table 4.5).

Although the number of non-STG adherent prescriptions decreased the percentage did not improve, in fact it worsened.

4.2.4   Prescriptions based on pathogens identified (susceptibility testing)

Table 4.6 Antibiotics prescribed based on sensitivity testing

Diagnosis	Antibiotic	STG-compliant	Total
Chronic viral hepatitis, unspecified	Cefuroxime Erythromycin	N N	1 1
Otitis media, chronic suppurative	Augmentin Ciprofloxacin Metronidazole	N N N	1 1 1
Urinary tract infection, uncomplicated	Co-trimoxazole Nitrofurantoin	N N	1 3
Total			**9**

Only three antibiotic prescriptions out of the entire study sample were based on microbial sensitivity tests. Out of the three, none were compliant with STGs.

4.3   COST OF TREATMENT AS PER STGS

4.3.1   Cost of actual treatment more than STGs treatment

Table 4.7 shows a few examples of the difference in cost of prescribing according to STGs and actual prescriptions. Only antibiotic prescriptions were taken into account for the calculations. The results are a total of the pre- and post-intervention prescriptions assessed. The two study periods were not divided in this case. The most outstanding example is ICD-10 code J20.9 (acute bronchitis, unspecified) where, according to STGs, the cost of antibiotics prescribed should be zero, but actual antibiotic prescriptions cost a total of R1000.56. Sixty-one antibiotics were prescribed. The other most outstanding difference in cost is for ICD-10 code N 39 (urinary tract infection, uncomplicated) where the difference in cost between prescribing according to STGs and actual antibiotic prescription is R603.58. As per pharmacy price list in the public sector at Themba Hospital of September 2007, by adding the difference in cost of STGs prescriptions and actual antibiotic prescriptions in Table 3.7, the hospital overspent R3058.73. This amount is calculated on the basis of the sample study done.

Table 4.7 Cost of STG compliant treatment vs. Cost of actual treatment prescribed (more expenditure)

ICD-10 code	Condition	Number of items	Total cost of treatment as per STG (R)	Total cost of prescribed treatment (R)	Diffe-rence (R)
B11.1	Viral influenza	2	0.00	37.38	37.38
H60.9	Otitis externa	2	0.00	37.87	37.87
H66.3	Otitis media, chronic suppurative	2	0.00	66.12	66.12
H66.9	Otitis media, acute	7	21.00	101.50	80.50
J03.9	Acute tonsillitis, unspecified	11	43.86	144.69	100.83
J11.1	Common cold and influenza	4	0.00	47.34	47.34
J18.9	Pneumonia, unspecified	20	75.16	344.84	269.68
J20.9	Acute bronchitis, unspecified	61	0.00	1,000.56	1,000.56
J44.9	COPD, unspecified.	19	64.40	319.01	254.61
J46	Status asthmaticus	1	0.00	48.67	48.67
K04.7	Dental abscess	20	45.24	61.72	16.48
K52.9	Noninfective gastroenteritis and colitis, unspecified	19	0.00	76.96	76.96
N39.0	Urinary tract infection, uncomplicated	45	14.56	618.14	603.58
N73.9	Pelvic inflammatory disease	19	18.40	57.15	38.75
R05	Cough	4	0.00	64.15	64.15
T14	Injuries	70	168.33	467.02	298.69
T14.1	Bites, animal and human	12	43.44	67.24	23.80
T30.0	Burns	2	0.00	14.80	14.80
TOTAL		**320**	**494.39**	**3575.20**	**3080.77**

4.3.2   Cost of actual treatment less than STG treatment

Table 4.8 Cost of STG compliant treatment vs. Cost of actual treatment prescribed (less expenditure)

ICD-10 code	Condition	Number of items	Total cost of treatment as per STG (R)	Total cost of prescribed treatment (R)	Diffe-rence (R)
A59	Trichomoniasis	4	8.13	6.15	-1.98
A64	Unspecified sexually transmitted disease	17	160.13	84.73	-75.40
A69.1	Necrotizing ulcerative (acute) gingivitis	24	61.44	57.12	-4.32
L02.9	Boil, abscess	39	492.73	449.83	-42.90
L08	Septic wound	7	178.80	69.84	-108.96
L08/L97	Sepsis	2	89.40	14.50	-74.90
TOTAL		**93**	**990.63**	**682.17**	**-308.46**

Table 4.8 shows some examples that were extracted from the study sample where the cost of actual antibiotics prescribed was less than the cost of antibiotics prescribed according to STGs prescribing, i.e. fewer were prescribed or incorrect type of antibiotic was prescribed. The most notable examples were ICD-10 code L08 (septic wound) and A64 (unspecified sexually transmitted disease) where the treatment was R108.96 and R75.40 respectively, which was lower than the cost according to the STGs/EDL in the negative.

CHAPTER 5

DISCUSSION

5.1 THE NUMBER OF PRESCRIPTIONS REVIEWED AND THE NUMBER OF PRESCRIPTIONS WITH ANTIMICROBIAL TREATMENT

During the pre-intervention study, September, October and November 2006, an average of 46% (n = 505) prescriptions had one of more antibiotic as part of the prescription. During the post-intervention phase the average was 27% (n = 516). The percentage for the pre-intervention phase compared well with the results of the Essential Drug Programme survey in 2003. During the survey in Mpumalanga Province 48% (n = 585) of the prescriptions contained one or more antimicrobial (Mashego and Minnie, 2003).

Of the 7813 prescriptions recorded In the Madibeng District in the North West Province, 1991 (25.5%) contained one or more antimicrobial (Gous *et al.*, 2005).

Overuse of antibiotics is jeopardizing the effectiveness of these essential drugs. The impact of the training session can be seen in the results of the post-intervention study were there is a noticeable difference in the amount of antibiotics prescribed. February 2007 showed the lowest amount of antibiotics prescribed with only 23 % of prescriptions in the study sample containing antibiotics. This shows that the training session held for the staff made a significant impact by decreasing the amount of antibiotics prescribed.

Current evidence for the effectiveness of interventions to change health professionals' behaviour in developing countries is either scanty or flawed due to poorly designed research. Given the recent drive to improve quality of care, this should be a priority area for researchers and international agencies supporting health systems development in developing countries (Siddiqi *et al*, 2005).

5.2 NUMBER OF ANTIBIOTICS PER PRESCRIPTION

During the course of the study it was noted that on occasion, more than one type of antibiotic was prescribed per prescription. The pre-intervention phase showed an average of 1.47 antibiotics prescribed per prescription, while the post-intervention phase showed the average number of antibiotics prescribed to be 1.25 per prescription (SD=510). There

are only a couple of conditions in the STG that require poly pharmacy with antibiotics with most relating to treatment of sexually transmitted infections or in some cases if a patient is allergic to penicillin.(Department of Health, 2006) Therefore according to STGs there is seldom reason to prescribe more than one type of antibiotic and yet results show that prescribers have been selecting more than one type of antibiotic for a treatment plan.In this study the average number of antibiotic per prescription does decline after the intervention and that does indicate that the training had an impact in reducing the number of antibiotics prescribed.

5.3   HEALTH CONDITIONS AND PRESCRIBING IN ADHERENCE WITH STGs

In this study, only 4% of antimicrobials prescribed for lower respiratory tract infections (pneumonia and acute bronchitis) adhered to the STGs, compared to 87% in the Madibeng District (Gous *et al.*, 2005). For STIs and UTIs the adherence at Madibeng District was 92% and 73% respectively (Gous *et al.*, 2005), which is much better than the 40% and 11% respectively in the current study. These differences further illustrate the very poor adherence to the STGs at Temba Hospital.

5.4   NON-COMPLIANCE WITH STGs

According to the study, only a small proportion of the prescriptions were in compliance with the STGs.   Of the 338 antibiotics prescribed, only 34 (10%) antibiotics were prescribed according to the STGs. In Madibeng District in North West Province 2414 (68%) antimicrobial prescriptions were compliant with the STGs (Gous *et al.*, 2005). According to John (2003) the compliance for the whole North West Province was 62%. The adherence in this study compared poorly with the studies in the North West Province.

5.5   COMPLIANCE WITH STGs BY DIFFERENT PRESCRIBER GROUPS CASE STUDIES

The study showed low STGs compliance across all prescribing groups in general. Community Medical Officers and Principal Medical Officers were the two prescribing groups most non-compliant with STGs during the pre-intervention phase. However, they were also the two prescribing groups most affected by the training session as the results showed the greatest decrease in STG non-compliance. STG non-compliance was only noted in respect to prescribing of antibiotics.

The results for this section of the study seemed to be a bit erratic and difficult to draw any deductions from. The training session seemed to impact on prescribing patterns by partially reducing antibiotic prescribing and partially increasing adherence to EDLs. The reduction of antibiotic prescriptions did not necessarily reduce the adherence to EDLs, but rather reduced prescriptions as a whole, hence less occasions to adhere to EDLs were presented.

5.6   THE TYPES AND AMOUNTS OF ANTIBIOTICS PRESCRIBED

In the first half of the study, 21% of the antibiotics prescribed were amoxicillin. A relatively high amount of amoxicillin was prescribed. It is a commonly prescribed antibiotic as it has a broad spectrum, generally safe to use, cheap and widely available in the hospital pharmacy. Amoxicillin was prescribed in 51% of the 500 prescriptions surveyed in the Vhembe District in Limpopo Province (Makhado, 2010).

Metronidazole was the second most popularly prescribed antibiotic during the pre-intervention phase as well as the most popularly prescribed antibiotic post-intervention. Both antibiotics feature on the EDLs and are regularly part of antibiotic treatment in the STGs. Therefore it is within reason that they are prescribed in the highest amounts in comparison to other antibiotics.

Sensitivity tests ought to be carried out before prescribing the next antibiotic. In an ideal setting, where there are no financial, time and human resource constraints, a sensitivity test would be done before each antibiotic was prescribed. Unfortunately, due to the problems mentioned previously, the prescriber takes the symptomatic approach and prescribes the most suited antibiotic. Out of a study sample of 1025 prescriptions during the entire study, only three prescriptions were based on susceptibility tests.

5.7   DIFFERENCE IN COST AS PER STGs AND ACTUAL PRESCRIBED TREATMENT

5.7.1   Cost of actual treatment more than STGs treatment

There were relatively high numbers of conditions during the study where the cost of prescribed antibiotics was higher than the cost of STG antibiotics medication. The most noteworthy condition was acute bronchitis, where R1000.56 was overspent on the condition in the study sample during both pre- and post-intervention phases. Acute

bronchitis does not require treatment with antibiotics hence it should not cost anything with regard to antibiotics. Antibiotics are clearly over-prescribed for acute bronchitis.

5.7.2   Cost of actual treatment less than STGs treatment

Six conditions were found to 'cost' less based on the study sample when compared to the antibiotic STGs treatment. This would indicate that STGs were not followed. Data from both pre- and post- intervention were combined. It is therefore impossible to deduce whether the training session made any impact on over- or under-spending due to changes in prescribing habits. Only approximately R308-00 was under-spent on antibiotic treatment during the study. Under-spending on treatment indicates that not only were STGs not followed, but treatment was not given at an optimal level.

There are a few examples that may attribute to this. The wrong type of antibiotic may be prescribed or the right antibiotic is prescribed in a sub-therapeutic dose. It is difficult to tell whether or not the alternative 'cheaper' prescription was better as patient outcomes were not recorded as part of this study.

The limitations of the study, recommendations from the findings and the conclusion are presented in Chapter 6.

CHAPTER 6

LIMITATIONS, RECOMMENDATIONS AND CONCLUSION

6.1   LIMITATIONS

- Patient outcomes were not recorded as part of the study
- Emergence of bacterial resistance was not investigated
- Gender of patient was not recorded
- Underlying health conditions and other risk factors were not assessed
- It was unknown whether a patient was returning for treatment of the same condition, as the outcomes were not monitored
- No comparison in numbers of different prescribing groups (MI's, PMO's, etc)
- Patient compliance unknown
- Only antibiotics taken into account for cost of treatment

6.2   RECOMMENDATIONS

- Annual training session on current and up-to-date national STGs and EDLs
- Distribution of STGs to all prescribers and departments
- Pharmacists cross-checking prescriptions for compliance with STGs and EDLs
- Enforcement of compliance with STGs and EDL with healthcare authorities or Ministry of Health
- Antibiotic prescriptions based on sensitivity test results instead of 'symptomatic' approach
- Tighter control on antibiotic dispensing through documenting the details of each antibiotic prescription dispensed
- Hospital specific prescribing policies and guidelines based on national prescribing policies

6.3   CONCLUSION

For the most part, the results of this study of a small cross section of the South African hospital public healthcare system indicate that prescribers are indeed over-prescribing antimicrobials to patients.

The number of prescriptions with antibiotics and the number of antibiotics prescribed per prescription decreased after the lecture. Antibiotics were not prescribed according to the STGs/EDL. The STGs/EDL should be included in the teaching and learning of medical students, as the junior staff prescribed the most non-adherent antibiotic prescriptions. A short series of lectures during tea breaks had no impact on the STGs/EDL adherence. Prescribing according to the STGS could have a significant impact in decreasing the cost of antibiotics.

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APPENDIX A: DATA COLLECTION FORM A

PATIENT NO:	DIAGNOSIS /SYMPTOM COMPLEX	PATHOGEN IDENTIFIED	ICD10	RANK OF PRESCRIBER	ANTIMICROBIAL/S PRESCRIBED	DOSAGE/ DURATION OF TREATMENT	STANDARD TREATMENT GUIDELINE ACCORDANCE?YES OR NO
1.							
2.							
3.							
4.							
5.							

APPENDIX B: DATA COLLECTION FORM B

PATIENT NO.	DIAGNOSIS	PRESCRIPTION OR NAME OF ANTIBIOTIC	DEFINED DAILY DOSE	TOTAL COST OF TREATMENT	STG TREATMENT COST	DIFFERENCE IN COST OF TREATMENT
1.						
2.						
3.						
4.						
5.						

APPENDIX C: POST-GRAUDATE COMMITTEE RESEARCH PROTOCOL APPROVAL

FROM PHARMACY 2   MON/OCT 9 2008 14:48/ST. 14:45/NO. 0412304164 P 2

UNIVERSITY OF LIMPOPO
Medunsa Campus

RESEARCH, ETHICS & PUBLICATIONS COMMITTEE

FACULTY OF MEDICINE

CLEARANCE CERTIFICATE

P O Medunsa
Medunsa
0204
SOUTH AFRICA

Tel: 012 - 521 4009
Fax: 012 - 560 0086

MEETING: 07/2006   PROJECT NUMBER: MP 97/2006

PROJECT: Title: The investigation of antimicrobial prescribing
                        patterns at Thamba Hospital, Kabokweni
          Researcher: Miss K Darysz
          Supervisor: Prof AGS Gous
          Department: School of Pharmacy
          Degree: MSc (Med) (Pharmacy)

DATE CONSIDERED: September 20, 2006

DECISION OF COMMITTEE:

REPC approved the project.

DATE: September 21, 2006

PROF GA OGUNBANJO
CHAIRMAN (RESEARCH) REPC OF FBM

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

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APPENDIX D: MPUMALANGA PROVINCIAL RESEARCH ETHICS APPROVAL

MPUMALANGA PROVINCIAL GOVERNMENT

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Department of Health and Social Services

Litiko Letemphilo Nemisebenti
Yenhlalakahle Yesive.

Umnyango WezePilo
neZenhlalakahle

Departement van Gesondheid
en Maatskaplike Dienste

Enquiries: Martha Mokoena x 3297

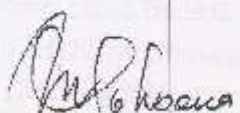TO : Ms Karolina Danysz
P. O Box 1664
Cramerwiew 2060

02 March 2007

APPLICATION FOR RESEARCH ETHICS APPROVAL FOR PROPOSED RESEARCH PROJECT: INVESTIGATION OF ANTI-MICROBIAL PRESCRIBING PATTERNS AT THEMBA HOSPITAL

Your research proposal has been approved. No ethical concerns have been detected.

Kindly ensure that you provide us with your report once your research is complete.

**M G MOKOENA
HEALTH INFORMATION & RESEARCH UNIT
DEPARTMENT OF HEALTH & SOCIAL SERVICES**