A retrospective drug utilisation study of antimicrobials in a private primary health care group

N. L. Katende-Kyenda

A retrospective drug utilisation study of antimicrobials in a private primary health care group

Norah Lucky Katende-Kyenda

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Supervisor: Prof. Dr. M.S. Lubbe

Co-supervisor: Prof. Dr. J.H.P. Serfontein

Co-supervisor: Prof. Dr. I. Truter

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Dedication

"I dedicate this dissertation to my late grandmother and late father for their wish to be fulfilled, to my mother, brothers and sisters for their constant prayers. To my husband and three sons for their continuous support, encouragement and best wishes."

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Abstract

A retrospective drug utilisation study of antimicrobials in a private primary health care group

The commonest prescribed group of drugs is antimicrobials. Various studies have shown that they are overused globally. Since Primary health care represents the first tier of the health care system, evaluation of antimicrobial use in primary health care settings is a necessity to ensure rational and cost-effective use of these agents in the treatment of infectious diseases.

It has been reported by Hooton and Levy (2001: 1088) that 20% to 50% of antimicrobials are inappropriately used in developing countries. According to Rehana *et al.* (1998: 175) the increasing overuse of antimicrobials has resulted in an enormous escalation in the total costs of drugs contributing to 15% to 30 % of the total health budget. Hooton and Levy (2001:1087) reported in a study that inappropriate use and overuse of antimicrobials are risk factors for the emergence of antibiotic resistant bacteria. There is a high incidence of infectious diseases in developing countries that are due to the rapid spread of resistant strains through over-crowding, poor sanitation and unsafe sexual practices (Liu *et al.*, 1999: 540).

The general objective of the study was the analysis and interpretation of the usage and related costs of antimicrobial prescriptions in a private primary health care setting in South Africa.

The study is a non-experimental, quantitative, retrospective drug utilisation review of antimicrobial usage in a private primary health care setting. Data were obtained from the central database of a private primary health care service provider. Data of nine randomly selected clinics, situated in different geographical areas of South Africa, were extracted for the period 1st January to 31st December 2001. The study population was made of the total patient population of patients using antimicrobials during this one year period.

Antimicrobial usage was analysed according to: number of patients, age and gender distribution, diagnosis, pharmacological groups.

The total number of patients who visited the nine clinics during the year was 83 655 of which 59.50% were females and 40.22% males. In 0.28% of the cases gender was not indicated. Patients in age groups 6 (20-40 years) and 7 (40-60 years) accounted for the highest number of patients (66.31%, n = 54 964). A total of 515 976 medicine items costing R1 716 318.90 were prescribed, of these, 18.69%, (N=96 423) were antimicrobials costing 60.89%, (R1 045 108.00). Of the total number of patients that visited the nine clinics, 65.34% (N=54 663) were prescribed antimicrobials. The total number of diagnoses (140 723) where antimicrobials were prescribed accounted for 68.52% (N=96 421).

The highest number of antimicrobial prescriptions according to pharmacological and age groups were: penicillins followed by sulphonamides and tetracyclines. The diagnoses with the highest number of antimicrobial prescriptions were the respiratory tract infections (viral influenza, acute bronchitis and upper respiratory tract infection) and pelvic inflammatory disease

The prescribing of antimicrobials in respiratory tract infections could indicate overuse and inappropriate use of these drugs. Because most of these infections are caused by viruses or other non-bacterial agents, are self limiting. Therefore, the use of antibiotics courses is neither necessary nor appropriate in these conditions. The overuse and inappropriate use of such drugs have an effect on the health of the patients needing cure, and the general budget on health care service. It is recommended that further studies are conducted on antimicrobial prescribing and use.

KEY WORDS

Antimicrobials, primary health care, managed health care, disease management, pharmacoepidemiology, pharmacoeconomics, drug utilisation, recommended standard treatment guidelines.

Opsomming

'n Retrospektiewe studie van die gebruik van antimikrobiese geneesmiddels in 'n privaat primêregesondheidsorggroep

Antimikrobiese geneesmiddels is dié groep middels wat die meeste voorgeskryf word. Talle studies het aangetoon dat hulle wêreldwyd oormatig gebruik word. Omdat primêre gesondheidsorg die eerste skakel in die gesondheidsorgstelsel is, is dit noodsaaklik om die gebruik van antimikrobiese middels in hierdie omgewing te beoordeel om rasionele en koste-effektiewe gebruik daarvan vir die behandeling van infeksies te verseker.

Hooton en Levy (2001: 1088) het berig dat 20% tot 50% van antimikrobiese middels in ontwikkelende lande op ontoepaslike wyse gebruik word. Volgens Rehana *et al.* (1998: 175) het die toenemende oormatige gebruik van antimikrobiese middels, wat 15% tot 30% van die totale begroting van gesondheidsorg bedra, tot 'n geweldige styging in die totale koste van medisyne gelei. Hooton en Levy (2001: 1087) het in 'n studie gerapporteer dat ontoepaslike en oormatige gebruik van antimikrobiese middels risikofaktore vir die ontwikkeling van weerstandige bakterieë is. Daar is 'n hoë voorkoms van infeksiesiektes in ontwikkelende lande vanweë die vinnige verspreiding van weerstandige stamme deur oorbevolking, swak sanitasie en onveilige seksuele praktyke (Liu *et al.*, 1999: 540).

Die algemene doel van hierdie studie was die insameling en interpretasie van data oor die gebruik van voorgeskrewe antimikrobiese middels en die koste daaraan verbonde in 'n private primêregesondheidsorgomgewing in Suid-Afrika.

Die studie is 'n nie-eksperimentele, kwantitatiewe, retrospektiewe oorsig van die gebruik van antimikrobiese middels in 'n private primêregesondheidsorgomgewing. Data is van 'n sentrale databasis van 'n verskaffer van primêre gesondheidsorg verkry. Data vir die periode van 1 Januarie tot 31 Desember 2001 is van nege ewekansig geselekteerde klinieke van verskillende geografiese gebiede in Suid-Afrika bekom. Die studiepopulasie het bestaan uit die totale populasie van pasiënte wat antimikrobiese middels in hierdie periode van een jaar gebruik het.

Die gebruik van antimikrobiese middels is ontleed volgens die aantal pasiënte, ouderdom en geslag, diagnose, farmakologiese groepe en koste van behandeling.

Die totale aantal pasiënte wat die nege klinieke deur die jaar besoek het, was 83 655 waarvan 59.50% vroulik en 40.22% manlik was. In 0.28% van die gevalle was die geslag nie vermeld nie. Pasiënte in ouderdomsgroepe 6 (20-40 jaar) en 7 (40-60 jaar) het die grootste deel van die pasiënte uitgemaak (66.31%, n = 54 964). 'n Totaal van 515 976 items wat R1 716 318.90 gekos het, is voorgeskryf en hiervan was 18.69% (n = 96 423) antimikrobiese middels wat 60.89% (R1 045 108.00) van die koste bedra het. Antimikrobiese middels is voorgeskryf aan 65.34% (n = 54 663) van die totale aantal pasiënte wat die nege klinieke besoek het.

Die grootste aantal voorskrifte vir antimikrobiese middels volgens farmakologiese en ouderdomsgroepe was penisilliene gevolg deur sulfoonamiede en tetrasikliene. Die diagnoses waarvoor die grootste aantal voorskrifte gegee is, was lugweginfeksies (virale griep, akute brongitis en infeksies van die boonste lugweg) en pelvisinflammasie.

Die voorskryf van antimikrobiese middels vir lugweginfeksies kan moontlik op oormatige en ontoepaslike gebruik van die middels dui. Omdat die meeste van hierdie infeksies deur virusse veroorsaak word, is hulle selfbeperkend. Daarom is die gebruik van antibiotika in hierdie gevalle nie nodig of gepas nie. Die oormatige en ontoepaslike gebruik van sulke middels het 'n invloed op die gesondheid van pasiënte wat behandel word en op die algemene begroting van gesondheidsdienste. Dit word aanbeveel dat verdere studies oor die voorskryf en gebruik van antimikrobiese middels gedoen word.

SLEUTELWOORDE

antimikrobiese middels, primêre gesondheidsorg, bestuurde gesondheidsorg, siektebestuur farmakoëpidemiologie, farmakoëkonomie, geneesmiddelgebruik, riglyne vir aanbevole standaardbehandeling

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ABSTRACTS ACCEPTED FOR PRESENTATIONS

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CHAPTER 1 INTRODUCTION

1.1 INTRODUCTION

The focus of the dissertation is to analyze retrospectively antimicrobial usage in nine private primary health care clinics, situated in different geographical regions in South Africa, using the database of a private primary health care clinic group.

1.2 PROBLEM STATEMENT

1.2.1 Brief introduction

The problem statement will cover the use of antimicrobials, as a group of drugs that are the most commonly prescribed, and probably their consequent overuse globally (Rehana *et al.*, 1998: 175). This overuse has led to the antimicrobials being used inappropriately. Hooton and Levy, (2001: 1087) in a study reported that millions of times each year physicians, regardless of speciality, prescribe antibiotics inappropriately. Polypharmacy, inadequate dosages, usage of antimicrobials for non-bacterial infections, and failure to prescribe in accordance with clinical guidelines, are all examples that may be defined as irrational prescribing (WHO, 2002a). The overuse and inappropriate use are risk factors for the emergence of antibiotic resistant bacteria which has become a major public health problem worldwide.

Antimicrobial usage will be discussed initially in relation to health care concepts like primary health care, managed care and disease management. Thereafter, a discussion on the instruments that can be used to evaluate the usage patterns and cost of antimicrobials which are: pharmaco-epidemiology, drug utilisation reviews and pharmaco-economics, will follow.

Usage of antimicrobials

Antibiotics are the most commonly prescribed group of drugs, leading to their abuse globally. Gyssens and Kullberg (1995: 163) stated in a study that in developed countries, 30% of all patients receive one or more antimicrobial drugs during their hospital stay. As reported by Hooton and Levy (2001: 1088), from 20% to 50% of antibiotic prescriptions in community settings are believed to be unnecessary.

Overprescription of antimicrobial drugs is resulting in enormous hospital expenditures (Kern *et al.*, 2001: 127). As a group, antibiotics contribute significantly to the cost of drugs and are claimed worldwide to account for 15% to 30% of the total health budget (Rehana *et al.*, 1998: 175). Educational programmes and careful assessment of inappropriate prescribing and a search for more cost-effective treatment strategies are urgently required.

Irrational prescribing

Irrational or non-rational use is the usage of medicines in a way that is not compliant with rational use. Worldwide more than 50% of all medicines are prescribed, dispensed, or sold inappropriately, while 50% of patients fail to take them correctly (WHO, 2002a). Common types of irrational medicine use are: the use of too many medicines per patient (poly-pharmacy); inappropriate use of antimicrobials, often inadequate dosage, for non-bacterial infections; and failure to prescribe in accordance with clinical guidelines (Das *et al* 2000: 59). Inappropriate use and over-use of medicines waste resources and can stimulate inappropriate patient demand, and lead to reduced access and attendance rates due to medicine stock-outs and loss of patient compliance in the health care system.

Possible causes of irrational use of antimicrobials

The semi-rational or irrational use of antimicrobials could be attributed to the use of multiple antimicrobials, non-use of first choice antimicrobials on the basis of provisional diagnosis, and recourse to irrational and unnecessary antimicrobials. The polypharmacy of antimicrobials observed in prescriptions may be due to empirical uses of antimicrobials without corroborative culture and sensitivity tests (Das *et al.*, 2002: 59).

Antimicrobials are often selected inappropriately, given in inappropriate dosages, used without clear indications, given for extended times and selected without the proper consideration for their pharmacokinetic and pharmacodynamic properties (Record *et al.*, 1995: 534) and over-prescriptions, most of the time inappropriate and

unjustified (Trémoliéres, 2003: 73). As reported by Karras *et al.* (2003: 835) physicians commonly prescribe antibiotics to meet patient expectations, even when antimicrobials are unnecessary. Prescribers and institutional authorities need to review their prescribing practices and modify them, if necessary, to facilitate better health care delivery. There is also a need to establish treatment protocols comparable to antimicrobial treatment guidelines.

Patterns of antimicrobial prescribing in developing countries

In developing countries, antibiotics are the most common drugs sold and frequently misused. Calva (1996: 1121) described the pattern of antibiotic use in a peri urban community in Mexico City. Of the 8279 individuals that were interviewed, 5% (n = 425) said they had used at least one antimicrobial in two weeks for acute respiratory tract ailments and gastroenteritis. Antibiotic therapy was given in 27% of respiratory diseases and in 37% of all diarrhoeal episodes. The data suggests that antibiotics are frequently misused and support the need to assess the determinants of self-medication, health-seeking behaviour and physician prescribing practices. The need for effective educational programmes for physicians to improve prescribers' decisions is stressed in this study.

Paluck *et al.* (2001: 521) investigated whether overprescribing was common in treatment of paediatric upper respiratory infections and examined factors that influence prescribing antibiotics for children. Relative to treatment guidelines developed for the study, more than half the physicians (56.5%) reported that they would immediately prescribe antibiotics for tympanic membrane dysfunction, and 79.4% indicated they would prescribe antibiotics for pharyngitis without obtaining culture. Approximately 25% of physicians did not believe that prior antibiotic use increased personal risk for acquiring drug-resistant infection, and 23.1% did not believe that antibiotic factor use was an important factor in promoting antimicrobial drug resistance in their communities. This study also emphasised that education in current treatment of paediatric upper respiratory tract illnesses and antimicrobial drug resistance is a necessity.

Antimicrobial Resistance

Antimicrobials have been called the wonder drugs of the 20th - century because their development led to a dramatic drop in deaths from infectious diseases, but shortly after they went into widespread use, a worrisome pattern began to emerge. Many of the infections targeted were becoming resistant to treatment. More and more bacteria developed resistance, which is one of the reasons why some antibiotics prescribed a decade ago are no longer likely to be effective against micro-organisms they originally eradicated (Aventis Pharmaceuticals, 2002). According to Viksveen (2003: 99) antibiotic resistance is a global public health problem. Once confined primarily to hospitals it is now increasingly common in primary care

Overuse or "inappropriate" use of antimicrobials is often cited as a risk factor for the emergence of antibiotic resistant bacteria (Lesch *et al.*, 2001: 149; Hemming & Harvey, 1999: 1). While these drugs are only effective against bacteria, they are often prescribed for viral infections, such as flu or a common cold, which generally resolves on their own and against which antibiotics are not effective.

Unnecessary visits to medical practitioners with upper respiratory tract infections seeking inappropriate antibiotic therapy are a burden on already over-stretched general medical practitioner (GP) services and this increase the problem of antibiotic resistance (Rugg & Loader, 2000: 265). There is a need to encourage patients to seek advice and over-the-counter remedies from their pharmacists rather than seeking antibiotics from their GPs for upper respiratory tract infections (URTI) and the educating of patients about appropriateness of antibiotic prescribing.

Infectious Diseases

There is a high incidence of infectious diseases in developing countries that are caused by a multitude of micro-organisms, which can either be bacterial or viral and these are spread from one person to another through various ways. Liu *et al.* (1999: 539) stated in a study that a heavy burden of infectious diseases was due to excessive and irrational use of antimicrobials. According to Gezairy (2003: 86) no country is safe from infectious diseases and an outbreak in one country can easily and rapidly be transmitted across long distances to affect other countries through travel and trade.

These are the leading causes of patients' trips to the doctors' clinics and are responsible for several deaths each year, accounting for a quarter to a third of the estimated 54 million deaths worldwide (Aventis Pharmaceuticals, 2002).

These infectious diseases are due to rapid spread of resistant strains through overcrowding, poor sanitation, and unsafe sexual practices. The spread of infectious diseases results as much from changes in human behaviour, including lifestyles and land use patterns, increased trade and travel, and inappropriate use of antibiotic drugs as from mutations in pathogens. Developing and former communist countries will continue to experience the greatest impact from infectious diseases because of malnutrition, poor sanitation, poor water quality and inadequate health care (Aventis Pharmaceuticals, 2002).

An important issue being faced in infectious disease treatment is whether improvement in antibiotic usage can achieve better quality of care, reduce healthcare costs and optimize healthcare systems through greater cost effectiveness (Carbon, 1996: 78). In many countries, infectious disease specialists are assisting physicians to diagnose and treat serious infections. Especially in the case of nosocomial infections, the emergency of bacterial resistance has made treatment more difficult and sometimes even impossible (Lemmen *et al.*, 2001: 219).

Infectious diseases in South Africa

In South Africa, in spite of relatively high levels of health care expenditure, there is a higher infant mortality rate and shorter life expectancy than many other middle income countries Infectious diseases account for at least 14% of potential years of numbers of lives lost and perinatal conditions contribute 17% (Bloom & McIntyre, 1998: 1529). Both of these conditions tend to be related to poor living conditions and inadequate basic health services. The prevalence of infectious diseases should be determined and recommendations should focus on prevention and improved treatment without antimicrobial agents.

Infectious diseases in USA

In the USA, the estimates for community-acquired pneumonia, a common serious illness, account for 4 million cases annually, and a rate of 12/1000 adults cases per year. It is the sixth leading cause of death due to infectious diseases, and the twenty-fifth most common condition treated by primary health care providers (Najib *et al.*, 2000: 461).

Primary Health Care.

In South Africa, a mixture of public and private provider and institutions provides health care services. Basic preventive and curative services are provided by a hospital - and primary health care clinic - based public system (Naylor, 1988: 1153). Since primary health care represents the first tier of the health care system, it is required that evaluations like antimicrobial use are done to ensure rational use of drugs (Uppal *et al.*, 1993: 671). In India, a survey was carried out to assess the extent and pattern of use of antimicrobials at two primary health care centres (PHC). At both PHCs 20% to 40% of all drugs were antimicrobials and the pattern of infectious diseases was similar at both PHC's (Uppal *et al.*, 1993: 671).

Keith Klugman of the South African Institute of Medical Research (as referred to by Bell, 2004: 2), expressed his concerns on antibiotic use in communities and how to improve it.

For many infections, the optimal dose and duration of therapy are unknown. Antibiotics are often prescribed inappropriately because physicians are uncertain when antibiotics are indicated and patients demand them; educating both of these groups is a challenge. Better diagnostics to reduce empiric therapy would be helpful

In a Joint Report by The Director-General of World Health Organization and the United Nations Children's Fund (1978: 2) to the Alma-Ata conference in September, 1978, (as referred to by Mellish, 1984: 23) the following definition was given:

"Primary Health Care is essential health care made universally accessible to individuals and families in the community by means acceptable to them, through their full participation and at a cost that the community and country can afford. It forms an integral part, both of the country's health system of which it is the nucleus and of the overall social and economic development of the community".

Primary health care addresses the main health problems in the community, by addressing the socio-economic causes of poor health, and makes provision for basic health needs by providing promotive, preventive, curative and rehabilitative services accordingly. It encourages community empowerment, ensuring that people are fully able to manage resources that are available to them and prioritises the people who are most disadvantaged, ensuring that health care is accessible, equitable and affordable to all (Mellish, 1984: 23).

Managed Care

During the period of current political transition, concern for the future of South Africa's health services have led to increased interest in different models for the provision and financing of health care. These debates have included an examination of the concept of managed care and the idea of health care maintenance organisations to promote the private health care sector to provide care and meet health needs and seek an equitable health care system for a future democratic South Africa (London, 1993: 1521).

Managed care is no longer just a way to finance health care; it also represents a collection of responsibilities that includes patient education, self care, and promotion of wellness, early identification of disease, all aspects of utilization management, and provision of financial incentives to care providers (Fox, 1996: 3).

Managed care, within the South African context, is a term used to refer to a diverse range of healthcare organizational strategies aimed at controlling cost, improving access and assuring higher levels of quality of care provided to those covered by medical schemes (Council for Medical Schemes, 2004).

Disease Management

One of the ways of achieving managed care is through disease management which is a mechanism aimed at improving the cost effectiveness of care. It views patients as entities experiencing the clinical course of a disease, rather than viewing their care as a series of discrete episodes (Hunter & Fairfield, 1997: 50). One of the earliest attempts at risk sharing between a managed-care and a pharmaceutical company in the infectious disease management programme was initiated since 1993 in India and Arizona. Protocols were built around eight infectious disease states, and it was recognized that second-line antibiotics were often prescribed when more economic first-line antibiotics would be equally effective (Wert, 1996: 366).

Pharmaco-epidemiology

Pharmaco-epidemiology sums up two different areas: pharmacology (the study of interactions between drugs and living organisms and epidemiology (the study of the relationships between diseases and biological phenomena and other factors (e.g., lifestyle) that can influence the frequency distribution and evolution of these diseases). Thus, pharmaco-epidemiology can be defined as the study of the use of and effects of drugs in large numbers of people (Van Boxtel & Wang, 1997: 205). According to Solomon and Avorn (2003: 122) pharmacoepidemiology is the branch of epidemiology that focuses on medication and their outcomes, including both adverse events and intended consequences.

Antibiotic exposure is one of the determining factors in the evolution of bacterial resistance. Studies on antibiotic selective pressure have generally only focused on one aspect, e.g. genetic, cellular, clinical, or epidemiological problems, without taking into consideration a more interconnected scientific approach. According to Van den Bogaard and Stobberingh (2000: 327) monitoring the prevalence of resistance in indicator bacteria such as feacal *Escherichia coli* and enterecocci in different populations, animals, patients and healthy humans, would make it feasible to compare the prevalence of resistance. This would also detect transfer of resistant bacteria from animals to humans and vice versa. As reported by Henriet and Guillemot (2000:

160S) the time has come to consider antimicrobial resistance as an environmental issue and to develop a pharmaco-epidimiological multidisciplinary approach.

Pharmaco-economics

Pharmaco-economics is the science used to identify and compare the costs and consequences of drug therapy in terms of efficacy, safety, and overall health care (Paladino, 1999: S25).

The pharmaco-economics of antibacterial treatment is a decision tool, as in any other therapeutic field. The ecological implications of treatment for the individual and for society should be considered when assessing the cost and consequences of antibacterial treatment. The development of pharmaco-economics as a decision-making tool should enable practitioner to prescribe the right antibiotic therapy to the right patient, at the right time (Beresniak & Bouvenot, 2000: 133).

Drug Utilisation Studies

Drug utilisation studies can be defined as studies of the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences (Sacristan & Soto, 1994: 299).

Rehana *et al.* (1998: 175) did a study to find out the prescribing practices with special emphasis on the utilisation pattern of antimicrobials and to compare the drug prescribing practices of physicians in developing countries. The results revealed that the average number of drugs per prescription was 5.26. Eight-four percent of all prescriptions contained antimicrobial agents as the most commonly prescribed (42.8%) group of drugs. The duration of treatment was not mentioned in 45.6% of all the drugs prescribed. The results indicate that there is a scope for improving prescribing habits and minimizing the use of antimicrobial agents. This could be facilitated by periodic prescriber's education.

So far, no formal studies on usage of antimicrobial agents in private primary health care settings in South Africa have been conducted and published in scientific journals, despite the fact that these drugs account for the largest proportion of drug expenditures, particularly in developing countries. This study focuses on the prevalence of antimicrobials prescribed and their cost in nine private primary health care clinics in South Africa.

The results from the study will give an idea of antimicrobial usage in private primary health care settings in South Africa, and recommendations will be made, where possible, on how these agents can be used in a more rational and cost-effective manner.

1.3 Research Questions

- What does antimicrobial treatment entail?
- What is the prevalence of antimicrobial usage in both the private and public health care sector in South Africa?
- What do primary health care and managed care entail?
- Why is it necessary to carry on drug utilisation studies on antimicrobials?
- What roles do pharmaco-epidemiology and pharmaco-economics play in the treatment with antimicrobials?
- What is the number of patients, consultations, and age and gender distribution in each clinic?
- What is the frequency and number of medicine items prescribed according to pharmacological groups, age and gender per year cost in each clinic?
- What is the total and average cost of medicine items per consultation in each clinic?
- What is the frequency and type of diagnoses per patient visit in each clinic?
- What is the frequency of antimicrobials in comparison to other medicine items in each clinic?
- What is the average number of antimicrobials per consultation per year in each clinic?
- What is the influence of age and gender on the frequency and cost of antimicrobials for the different diagnoses, according to individual and pharmacological groups in each clinic?

- What is the total cost of antimicrobials in each clinic?
- Are antimicrobials prescribed according to the recommended antimicrobial standard treatment guidelines in South Africa?
- What are the recommendations as to the use of antimicrobials in the different diagnoses?

1.4 Research Objectives

The research objectives are divided into the general and specific objectives:

1.4.1 General Objective

The general research objective will be an analysis and interpretation of the usage and costs associated with the prescribing of antimicrobials in a private primary health care setting in South Africa.

1.4.2 Specific Research objectives are:

The specific research objectives of study are:

- To investigate from the available literature the usage and prescribing patterns of antimicrobials (irrational and causes of).
- To determine from the literature what antimicrobial resistance is and its causes are.
- Investigate infectious diseases and treatment thereof.
- To conceptualise primary health care, its aims and objectives.
- To conceptualise managed health care, disease management, pharmaco-epidemiology, pharmaco-economics and drug utilisation studies as applied to antimicrobials.
- To determine the prevalence of patients who received antimicrobials in a private primary health care setting.
- To determine the prevalence of prescriptions of antimicrobials as well as the total costs associated with it in a private primary health care setting.
- To investigate the influence of age on the prescribing of antimicrobials in a private primary health care setting.
- To investigate the influence of gender on the prescribing of antimicrobials in a private primary health care setting.

- To investigate the prescribing of antimicrobials and their costs for different diagnoses.
- To determine the use of antimicrobials according to diagnoses.
- To determine if antimicrobial usage in the private primary health care setting are and were according to the standard treatment guidelines and essential drugs list for South Africa.
- To formulate recommendations regarding the usage of antimicrobials in different diagnoses.

1.5 Research Methodology

The research methodology will entail two phases in conjunction with the specific objectives:

- Literature review.
- Empirical investigation.

1.5.1 Phase one: Literature review on specific objectives

The literature review were divided into two steps, the first being a discussion of antimicrobials, antimicrobial resistance and infectious diseases and treatments thereof, and the second will be a discussion on primary health care, managed health care, disease management, pharmacoepidemiolgy, pharmaocoeconomics and drug utilization studies as applied to antimicrobials.

1.5.2 Phase Two: Empirical Investigation

The empirical investigation consisted of the following steps, namely:

- **The selection of the research design**

A non-experimental, quantitative, retrospective drug utilization review was used in order to obtain the essential outcomes and achieve the specific objectives for this study.

- **The composition of the study population**

The data utilised in this research project were obtained from the central database of a private primary health care service provider. Data of nine randomly selected clinics were extracted for the period 1st January – 31st December 2001. The study population was composed from

the total patient population of patients using antimicrobials for the period of 1st January – 31st December 2001.

- **The selection and application of the criteria and measuring instruments for data analysis**

Measuring instruments and statistical calculations applicable to this study were implemented (see Chapter 4).

- **Data application and data analysis**

Data were analysed by using the Statistical Analysis System, SAS 8.1® (SAS Institute Inc., 1999-2000).

- **Reliability and validity of the research instruments**

The data was obtained directly from the central databases of private primary health care service provider and no direct manipulation of the data by the researcher was possible. The research was conducted with assumption that all data obtained from the database were correct and accurate.

- **The report and discussion of the results of the empirical investigation**

In Chapter five the results will be illustrated in tables and figures and will be explained in a detailed discussion.

- **The conclusion and recommendations based on the results of the empirical investigation as well as the limitations of the study.**

A conclusion based on the results of the study will be offered in Chapter six, as well as recommendation made in relation to the findings derived from the results.

The Research methodologies will be discussed in detail in Chapter four.

1.6 DIVISION OF CHAPTERS

The chapters will be presented as follows:

Chapter 2: Antimicrobials.

Chapter 3: Primary health care, managed health care, disease management, pharmaco-epidemiology, pharmaco-economics and drug utilisation studies.

Chapter 4: Research methodology.

Chapter 5: Results and discussion.

Chapter 6: Conclusions, recommendations and limitations.

1.7 CHAPTER SUMMARY

In this chapter the problem statement, research questions, research objectives, research method and division of chapters were discussed.

Antimicrobials will be discussed in Chapter 2.

CHAPTER 2 ANTIMICROBIALS

2.1 Introduction

Antimicrobial therapy is different from other forms of pharmacotherapy. Antimicrobial therapy is not only based on the characteristics of a patient and a drug, but also on the characteristics of an infection. There is a complex interrelationship between humans, microorganism and antimicrobial drugs with multiple interactions between the patients, the drug, the pathogen(s) and commensal flora (Gyssens, 2001: 9).

2.2 Principles of Antimicrobial Drug Therapy

There are several reasons to aim for appropriate antibiotic use. The most important being to cure or prevent infections using the best agent available in the shortest time and with the least side effects. Another reason is to minimize the emergence and spread of resistant micro-organisms. Prevention of the emergence of resistance and dissemination of resistant micro-organisms will also reduce costs. And finally, to provide appropriate healthcare services at a reasonable cost (Guven & Uzun, 2003: 91).

2.2.1 General principles in choosing an antimicrobial agent

According to Guven and Uzun (2003: 92), the following general principles should be considered in choosing an antimicrobial agent:

- Clinical efficacy of antimicrobial drugs.
- The known suspected pathogen and its susceptibility pattern.
- The efficacy of alternative.
- Drug side effects, interactions and individual conditions of the patient such as pregnancy, immunosuppression or renal impairment.
- Likelihood of patient compliance.
- After efficacy and toxicity issues and cost considerations are important.

2.2.2 Indications

Antimicrobial drugs are used for either prophylactic or therapeutic indications, and the wrong indication is a major determinant of irrational antibiotic use. Several studies have demonstrated that a substantial portion of the antibiotics prescribed in the outpatient setting are given for viral illness or bacterial diseases where the benefit of antibacterial therapy is marginal (Colgan & Powers, 2001: 999). Therefore, the physician should be familiar with the clinical situations in which they should provide antibiotics and those in which they may safely be withheld. They should understand the motivations of patients who are seeking antibiotics and provide education, empathy and alternative treatments. The history of the illness, including host factors such as age, presence of immunosuppression, and severity of disease and travel history should be properly evaluated to determine the objective of antimicrobial use.

2.2.3 Dose

The goal of antimicrobial therapy is to deliver the drug to the site of infection in concentrations sufficient to inhibit or kill the organism. The elimination of the drug is effectively complete after four hour half-lives. Therefore, in clinical practice, the dosing interval is usually calculated as three to four times the serum half-life of the drug. The dose of an antimicrobial has to be calculated to attain optimal serum concentrations according to minimum inhibitory concentrations (MICs) of suspected pathogens. Optimal therapy requires concentrations well above the MIC. In immunocompromised patients and for difficult to reach infection sites (meningitis, abscesses), it is agreed that multiples of MICs are needed. For drugs with concentration-dependent effect, such as amino-glycosides, the most effective strategy is to give an initial large dose (6 or 7 mg/kg) to all patients and to adjust subsequent doses (or intervals) with individual pharmacokinetic monitoring as soon as possible (Kashuba *et al.*, 1999: 623).

2.2.4 Dosing interval

Optimal frequency is dependent on half-life and the mechanism of action of the drug. For example by using amino-glycosides in a once-daily dosing schedule, optimal pharmacodynamic principles are combined with minimal toxicity. These agents exhibit a pronounced post antibacterial effect (Hoppe, 1996b: 581).

Based on time-dependent mechanism of action of β-lactams, continuous infusion has been used for administration. In parental therapy, reduced frequencies of administration are associated with cost savings. For drugs with concentration dependent bactericidal action, the rate of bactericidal activity is maximal at the peak serum concentrations and parenteral drugs like ceftriaxone, that can be administered once-daily, permit home therapy for serious infections (Gyssens, 2001: 13).

2.2.5 Duration of therapy

There is no ready means of determining optimal duration of therapy. The site of infection, the pathogen involved, pharmacodynamics of the selected antimicrobial therapy, response to treatment and toxicity of the regimen should be evaluated. For surgical prophylaxis, the use of antimicrobials beyond 24 hours is not indicated (Guven & Uzun, 2003: 93).

2.2.6 Route of administration

It is a common practice to treat serious infections with parenteral antimicrobial agents. Since the rate of absorption from the muscle depends on local perfusion and may be erratic following intramuscular injection, intravenous administration is preferred for treating life-threatening infections. In certain clinical settings, sequential or 'switch' therapy is preferred (Guven & Uzun, 2003: 93). According to Gyssens (2001: 14) parenteral route administration is used for empirical therapy in patients with gastrointestinal dysfunction and for drugs with poor oral bioavailability. Attaining sufficiently high serum and tissue concentrations is the main criterion for oral therapy. As infrequent dosing increases compliance, the oral drugs should have a half-life of at least one hour to permit twice-daily dosing interval (Gyssens, 2001: 14).

2.3 Antibiotic Resistance

2.3.1 Introduction

Since the introduction of antimicrobial agents, there has been an association between antibiotic use and the development of antimicrobial resistance. Antibiotic therapy eradicates not only pathogenic organisms but also the protective normal flora. This so-called "selective pressure" results in colonization with bacteria that are resistant to the original therapy.

The result has been an increase over the past two decades in antibiotic resistance among common bacterial causes of outpatient infections (Colgan & Powers 2001: 999).

Antibiotic resistance is one of the most challenging problems facing modern medicine (Hellinger, 2000: 842). According to the WHO (2002b) antimicrobial resistance is becoming a major concern for public health worldwide. Resistant strains of common human pathogens are emerging and spreading more rapidly than ever before. The reasons for this are complex and are associated with the overuse and misuse of antimicrobials in humans and animals.

2.3.2 Causes

The appearance of resistance to antibiotics is a direct consequence of antibiotic use as stated by Boccia *et al.* (2004: 115), and the rising prevalence of antibiotic resistance, in turn, is due to the selective pressure exerted by these drugs (Henriet & Guillemot, 2000: 160s). According to Van den Bogaard and Stobberingh (2000: 327) an inevitable side effect of the use of antibiotics is the emergence and dissemination of resistant bacteria.

Lesch *et al.* (2001: 149) in their study stated that overuse or "inappropriate" use of antimicrobials is often cited as a risk factor for the emergence of antibiotic resistant bacteria. In developing tropical countries, Okeke *et al.* (1999: 1) acquired bacterial resistance to antimicrobial agents is common in isolates from healthy persons and from persons with community-acquired infections. Complex socioeconomic and behavioural factors associated with antibiotic resistance include: misuse of antibiotics by health professionals, unskilled practitioners, and laypersons; poor drug quality; unhygienic conditions; and inadequate surveillance.

Garau and Dagan (2003: 1936) reported that antimicrobial resistance in respiratory pathogens had become a common clinical problem that has serious public health implications. Inappropriate use of antibiotics for the treatment of viral upper respiratory tract infections (URTIs) has contributed to the development of resistant microorganisms. Antibiotic resistance results in increased morbidity, mortality, and costs of health care (Gross & Pujat, 2001: 1155).

The following well-documented observations have been reported by Shlaes *et al.* (1997: 589) about antibiotic resistance:

- Changes in antimicrobial use are paralleled by changes in prevalence of resistance.
- Increasing duration of antibiotic treatment of patients is associated with increasing rates of colonization with resistant organisms.
- Antimicrobial resistance is more prevalent in nosocomial than community-acquired strains.
- Areas of highest antibiotic use in hospitals have the highest rates of resistance.
- During nosocomial outbreaks, patients with resistant strains have received antibiotics more often than have controls.

2.3.3 How resistance works

Antibiotics are effective against bacteria because they interfere with a pathogen's basic life functions. They interrupt protein synthesis, prevent cell-wall synthesis, and inhibit DNA replication (Brown, 2000: 93). Unfortunately bacteria have developed the ability to overcome these effects. The current patterns of antibacterial resistance can be explained by 4 general mechanisms as stated by Brown, (2000: 95).

- Production of enzymes that destroy or inactivate antibiotics.
- Development of substitute proteins within the bacteria that are not targeted by drugs.
- Alterations in the permeability of bacteria to antibiotics.
- Presence of pumps that remove the antibiotics from the cell.

2.3.4 Mechanisms of antibiotic resistance

Brown (2000: 101-102) described the following mechanism of antibiotic resistance:

2.3.4.1 Enzymes

The best known example of an enzyme that inactivates antibiotics is beta-lactamase. The beta-lactam ring found in penicillins and cephalosporins is opened in the presence of the enzyme. This prevents the compound from binding to its target and makes the antibiotic ineffective.

2.3.4.2 Substitute proteins

In this mechanism there is development of substitute proteins within the bacteria to which the antibiotic cannot bind. The proteins may be found within the bacterial cell wall, cell membrane, or cytoplasm and carry out the same biological functions as the original proteins. The antibiotic can not exert its damaging effect on the bacteria when it does not bind to its target. Alteration of penicillin-binding proteins is one of the most important examples of bacteria using substitute proteins to confer antibiotic resistance

2.3.4.3 Alterations of porin proteins

This is the alteration in the permeability of bacteria to antimicrobials. Alteration of porin proteins may prevent or slow the entry of antibiotics into the cell, thus decreasing their chances of binding to their targets.

2.3.4.4 Efflux pumps

Efflux pumps actively remove antibiotics from the cytoplasm of cells before they can bind to their target. These pumps take on increased importance when antibiotic permeability is decreased because fewer antibiotics within the cell cytoplasm are available to bind to the target.

2.3.5 Interventions

The following practical recommendations have been made regarding the control of emerging antibiotic resistance (Shlaes *et al.*, 1997: 584):

- establishing a system of monitoring and reporting bacterial resistance and antibiotic usage;
- establishing practice guidelines and other institutional policies to control the use of antibiotics and respond to data from the monitoring system;
- adopting the recommendations of the Centers for Disease Control and Prevention (CDC) "*Guidelines for Isolation Precautions in Hospitals*," as concerns the isolation of patients colonized or infected with resistant microorganisms;

- utilizing hospitals committees to develop local policies and to evaluate and adopt, as appropriate, guidelines from state advisory boards and national societies;
- recognize that the financial well-being of the institution and the health of its patients are at stake and therefore that the hospital administration should be accountable for the implementation and enforcement of policies adopted by hospital committees;
- measuring outcomes and evaluating the effectiveness of the policies that are put in place; and
- clinicians to alter antibiotic prescribing for the treatment of infectious diseases, patients to change their perception of the need for these drugs and pharmacists to play a major role through clinician education and focused clinical services (Dickerson *et al.* 2000: 711).

2.3.6 Recommendations to hospitals

In the summary of a document presented to WHO (2002b) the following recommendations were written "*Although most antimicrobial use occurs in the community, the intensity of use in hospitals is far higher, hospitals are therefore particularly important in the containment of antimicrobial resistance. In hospitals it is crucial to develop integrated approaches to improve the use of antimicrobials, reducing the incidence and spread of hospital-acquired (nosocomial) infections, and linking therapeutic and drug supply decision-making. This will require training of key individuals and the allocation of resources to effective surveillance, infection control and therapeutic support, factors that may strongly influence their prescribing habits, such as economic incentives, promotional activities and inducements by the pharmaceutical industry*".

2.4 MIMS™ and ATC classification of drugs

2.4.1 MIMS™ (Monthly Index of Medical Specialties) classification.

This is a list that is compiled on a cumulative basis for the current year and month and arranged in alphabetical sequence giving product trade name together with the month of addition. In the case of additions the pharmacological classification is given after the product trade name (Snyman, 2004: 5a). This classification was used to classify antimicrobials according to pharmacological groups for the empirical studies (refer to Chapters 4, 5 and 6).

2.4.1.1 Structure

The classification contains the followings : Proprietary name of the drug, name of applicant/division of applicant in abbreviated form, the active ingredient, approved main indications, scheduling status, presentation of the product, usual dosage regimen of relevant presentation for adults only, nappi codes , strength of single active ingredient, contraindications, side effects, special precautions, drug interactions, warnings and cross-references (Snyman, 2004: 5a).

2.4.2 The ATC classification

ATC (Anatomical Therapeutic Chemical) classification is an internationally accepted classification system used for international drug utilization studies. According to Ronning (2002: 233) the purpose of the ATC system is to serve as a tool for drug utilization research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at international and other levels (WHO, 2002c). This classification was also used to classify antimicrobials for the empirical studies (refer to Chapters 4, 5 and 6).

2.4.2.1 Structure

The drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Drugs are classified in groups at five different levels. The drugs are divided into fourteen main groups (1st level), with one pharmacological/therapeutic subgroup (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroup and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups when that is not considered more appropriate than therapeutic or chemical subgroups (WHO, 2003). Refer to Table 5.26 for a short summary of the ATC classification system.

2.4.2.2 Principles

Medicinal products are classified according to the main therapeutic use of the main active ingredient, on the basic principle of only one ATC code for each pharmaceutical formulation (i.e. similar ingredients, strength and pharmaceutical form). A medicinal product can be given more than one ATC code if it is available in two or more strengths or formulations with clearly different therapeutic uses (WHO Collaborating Centre for drug statistics methodology, 2003).

2.5 Pharmacological groups

Antimicrobials are classified into different pharmacological groups as described in MIMS™. These groups include: Beta-lactams, macrolides, aminoglycosides, tetracyclines, chloramphenicols, sulphonamides and trimethoprin, quinolones, antimycobacterials, antifungals, anti-protozoals and anti-virals.

2.5.1 Beta-lactams

The beta-lactams are grouped into two classes: Penicillins and Cephalosporins (Antimicrobial Therapy, 2001).

2.5.1.1 Penicillins

2.5.1.1.1 Structure

The basic structure of penicillin consists of a 5-membered sulfur-containing thiozolidone ring fused to a beta-lactam ring. The beta-lactam bond within the beta-lactam ring is the portion of the molecule susceptible to beta-lactamase. The R-group attached to the beta-lactam ring determines the antibacterial spectrum and other properties of the agent (Brown, 2000: 94).

2.5.1.1.2 Classification

Penicillins consist of the following:

- Narrow spectrum penicillins (mainly active against Gram-positive) for example benzyl penicillin (Bennet and Brown, 2003: 217).

- Narrow spectrum penicillins that are penicillase-resistant, e.g. methicillin.
- Broad spectrum penicillins whose activity extends beyond the Gram-positive and Gram-negative cocci which are susceptible to benzyl penicillin, and include many Gram-negative bacilli. e.g. amoxycillin, ampicillin, and augmaxcil (Bennet & Brown, 2003: 219).
- Penicillins with delayed absorption e.g. benzathine penicillin G.
- Penicillins combined with beta-lactamase inhibitors e.g. amoxycillin with clavulanic acid (Bennet & Brown, 2003: 217).

2.5.1.1.3 Antimicrobial Activity:

Penicillin derivatives exert their principal antibacterial activity by binding to protein-bound polysaccharides and inhibiting cell-wall synthesis (Brown, 2000: 94).

2.5.1.1.4 Resistance

Resistance to penicillins occurs through the destruction of drug to beta-lactamase enzyme. There are two approaches to the beta-lactamase problem (Verhoef & Gillissen, 2003: 501). New antibiotics have been developed that are inherently resistant to beta-lactamase (for example cefixime, a third-generation cephalosporin). The second approach is to combine a beta-lactam antibiotic with a beta-lactamase inhibitor, amoxycillin/clavulanate, ampicillin/sulbactam, tcarcillin/clavulanate, and piperacillin/tazobactam (Brown, 2000: 94). Methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to all penicillins, cephalosporins, and many other drugs such as erythromycin, tetracycline (WHO, 2002b: 18; Lesch *et al.*, 2001: 149; Hellinger, 2000: 842 and Monroe & Polk, 2000: 496).

2.5.1.1.5 Therapeutic uses

Penicillin G and penicillin V are effective against Streptococcus pyogenes, Streptococcus *viridans*, anaerobic gram-positive cocci, *Neisseria meningitis*, and many strains of *S pneumonia*. Therefore penicillin G is used most often intravenously for the treatment of serious infections such as meningitis and endocarditis once susceptibility patterns are established. In its oral form, the medication is used to treat streptococcal infections of the skin and throat as well as dental infections of mild to moderate severity (Brown, 2000: 94).

In the treatment of bacterial meningitis, in the very young and the elderly populations in which *Listeria monocytogenes* is fairly common, ampicillin 100mg/kg given intravenously every eight hours is recommended as an empiric therapy (Bartfield, 2000: 49). According to Hoppe (1996a: 570), long acting penicillin, benzathine penicillin, is suitable for preventing the occurrence of acute rheumatic fever.

2.5.1.1.6 Adverse Effects of Penicillins

The following adverse effects can be experienced with penicillins:

- The main hazard with the penicillins is allergic reactions. These manifest themselves as rash, either urticarial or maculopapular fever and angiodema (Pilzer, 1996: 2970).
- Penicillins are also associated with a rather high rate (10 % to 15%) of gastrointestinal adverse effects (Hoppe, 1996b: 579). Diarrhea due to alteration in normal intestinal flora which may progress to *Clostridium difficile*-associated diarrhea.
- Large doses of penicillins can cause adverse central nervous system (CNS) effects.
- Augmaxcil and flucloxacillin given in high doses for prolonged periods in the elderly may cause hepatic toxicity (Bennet & Brown 2003: 217).

2.5.1.2 Cephalosporins

2.5.1.2.1 Structure

The cephalosporin antibiotics consist of a four-membered β-lactam ring bounded to a six-membered dihydrothiazine ring. Modifications at position 7 of the β-lactam ring alter antimicrobial activity. Substitutions at position 3 of the dihydrothiazine ring alter pharmacokinetics and toxicity of the drug (Christian & Christian, 1997: 168).

2.5.1.2.2 Classification

Although the cephalosporin antibiotics are often categorized by generation (first, second, and third), it may be more appropriate to discuss these agents in terms of their spectrum of activity, e.g. limited-, intermediate-, and broad-spectrum cephalosporin. (Examples of limited-spectrum of activity are ceftriaxone, cefonicid, and cefaclor. Most of the newer drugs with extended spectrums, including cefoteten, cefoxitin, and cefipime injectables, and new oral agents, such as cefixime (Christian & Christian, 1997: 168).

2.5.1.2.3 Antimicrobial Activity

The cephalosporins, like other beta-lactam antibiotics, are bactericidal. By binding to penicillin-binding proteins, cephalosporins inhibit various bacterial functions leading to cell lysis. Cefditoren, a third generation orally administered aminothiazolyl cephalosporin, has demonstrated bactericidal activity against many gram-positive and gram-negative bacterial pathogens and stability against clinically important beta-lactamases (Johnson *et al.*, 2000: 99).

2.5.1.2.4 Resistance

Bacteria possess at least three mechanisms for resisting the bacterial effect of cephalosporins. First, the bacteria can alter cell wall permeability. Second, certain gram-positive and gram-negative bacteria achieve resistance to cephalosporins via mutations in penicillin-binding proteins. The third and most important is the production of beta-lactamase, enzymes that hydrolyze the lactam ring (Christian & Christian, 1997: 169).

2.5.1.2.5 Pharmacokinetics

Most of the cephalosporins achieve peak serum levels of 30-100mg/mL after a single 1 g intravenous dose (Christian & Christian, 1997: 169). The mean peak serum level of cefepime following a 2 g intravenous dose is 130 – 140 mg/mL. The serum half-lives of most of these agents are 1 to 2 hours. Cefditoren pharmacokinetics demonstrate a T $_{½}$ of 1.5 to 2 hours and Cmax values of 2.8 and 4.6 mg/ml for 4 to 6 h ours (33-50% of dosing interval) (Johnson *et al.*, 2000: 99). Cefotaxime is cleared both by renal route and biotransformation, which produces a desacetyl metabolite (Urien *et al.* 2004: 11). However, because peak serum levels are high relative to minimal inhibitory concentration, most cephalosporins are administered at intervals equal to several half-lives, generally every 6, 8, 12, or 24 hours. Plasma protein binding is variable among cephalosporins.

2.5.1.2.6 Clinical Uses

The cephalosporin antibiotics are often used for prophylaxis against post-operative infection in obstetric/gynecologic surgical procedures such as unscheduled cesarean delivery and vaginal hysterectomy. Because most *N gonorrhoerae* is resistant to penicillin, cephalosporin antibiotics are used in the management of cervical, rectal, and pharyngeal gonorrhea.

Cephalosporins are also used in urinary tract infections, respiratory infections, sinusitis, otitis media, endomyometritis, pelvic inflammatory disease and cuff cellulites (Christian & Christian, 1997: 171). Among the antimicrobial agents tested, third-generation cephalosporins have been shown to possess excellent in vitro activity against ⇆-lactamase-positive and – negative isolates, corresponding with proven clinical efficacy in a wide range of respiratory tract infections (Verhoef & Gillissen, 2003: 501). Cefdinir has been shown to be more active in vitro against typical urinary pathogens such as *Escherichia coli* and *Klebsiella pneumoniae* than other cephalosporins. Therefore it is a more appropriate agent for empiric therapy of urinary tract infections (UTI) than older cephalosporins (Leigh *et al.*, 2000: 824). According to Bartlett *et al.* (1998: 832) the recommendation for hospitalized patients is a β-lactam antibiotic (e.g. cefotaxime, ceftriaxone) for atypical pneumonia (pneumonia due to *Legionella* species, C. *pneumonia*, or M. *pneumonia).* Johnson *et al.* (2000: 99) stated from the results of the study that cefditoren clearly possesses the most potent activity among the studied oral cephalosporins against commonly isolated bacterial pathogens causing bronchitis, pneumonia, sinusitis, or pharyngitis.

2.5.1.2.7 Adverse Effects

The following adverse effects cephalosporins were described by Christian and Christian (1997: 172).

- Allergic reactions to cephalosporins antibiotics are rare. Rashes and other cutaneous manifestations are the most common findings.
- Other adverse effects include gastro-intestinal (GI) and hematologic symptoms.
- Ceftriaxone can be associated with the formation of biliary sludge, which can lead to a clinical scenario similar to acute cholecystitis.
- Cefoperazone and moxalactam have been associated with disulfiram-like reactions and abnormal bleeding due to hypoprothrombinemia.
- Pain at the injection site can be severe, and with the exception of ceftriaxone, intramuscular administration is not used.
- Phlebitis and intravenous site irritation can be observed if extravasation of the drug occurs.

2.5.2 Macrolides

The macrolide antibiotics include the following drugs: erythromycin, clarithromycin and azithromycin (McConnell & Amsden, 1999: 404).

2.5.2.1 Antimicrobial activity

All macrolides block protein synthesis by binding to the 23S-component of the 50S-subunit of prokaryotic ribosomes. Specifically, they act by stimulating dissociation of peptidyl-tRNA from the ribosomes during the elongation phase of bacterial growth, leading to inhibition of mRNA-dependent protein synthesis and inhibition of bacterial growth (McConnell & Amsden 1999: 405). According to Kremer (2002: 174) azithromycin exerts its effect by reversibly binding to the 50S subunit of the bacterial ribosome. This action interferes with microbial protein synthesis by preventing transpeptidation and translocation reactions. Although it is bacteriostatic in general, it is bactericidal against *Streptococcus pyrogens*, *Streptococcus pneumoniae*, and *Hemophilus influenza.* Azithromycin has been shown, both in vitro and in vivo, to be active against the following microorganisms:

- Gram-positive aerobes: *Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae* and *Strephylococcus aureus.*
- Gram-negative aerobes: *Moraxella catarrhalis*, and *Neisseria gonorrhoeae.*
- Other pathogens: *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae* (Kremer, 2002: 174).

2.5.2.2 Resistance

In general, resistance occurs through ribosomal alteration so that the macrolides no longer binds. The clinical relevance of macrolide resistant S *pneumoniae* might be dependent on the type of resistance expressed by a particular strain. The most common mechanism of resistance includes methylation of a ribosomal target that is encoded by the gene and efflux of the macrolides by cell membrane protein transporter (File, 2003: 1995).

Resistance to clarithromycin occurs as a result of point mutations in 23S RNA, and interferes with normal protein synthesis (Ferrero *et al.*, 2000: 245).

2.5.2.3 Pharmacokinetics

Macrolides differ in absorption, half-life, and gastro-intestinal effects (Nightingale, 1997: 438). Azithromycin for example has improved oral bioavailability, higher tissue concentration, and fewer side effects over erythromycin. It has enhanced antimicrobial activity and a longer half-life, which allows for once daily dosing. After oral administration, azithromycin is rapidly absorbed and widely distributed through the body. Tissue concentrations peak approximately 48 hours after administration and persist for several days afterward. Its average half-life is 68 hours, an important feature that allows once-daily dosing. The serum protein binding is variable, ranging from 12% to 50%, depending on concentration. It is eliminated through the faeces, as unchanged drug is excreted in bile.

2.5.2.4 Therapeutic uses

The three macrolides (erythromycin, azithromycin and clarithromycin) appear to be effective in the treatment of pulmonary infections caused by M. *pneumoniae*, C. *pneumoniae* and *Legionella* species (Bartlett *et al.*, 1998: 811). According to Woodhead *et al.* (1996: 1596) macrolides were the most frequently prescribed second-line antibiotics in the treatment of lower respiratory tract infections. Intravenous macrolides (azithromycin and erythromycin) are often used as first-line therapy in hospitalized patients for empirical treatment of community–acquired pneumonia either alone or in combination with other broad-spectrum antimicrobial agents (McConnell & Amsden, 1999: 404; Howard, 1999: 1521 and File, 2003: 1995). Because azithromycin is active against atypical bacteria, and has broader haemophilus influenzae coverage than erythromycin, and presents with less adverse effects, it is mostly used in the following clinical indications:

- Respiratory infections: pharyngitis, otitis media, sinusitis, community- acquired pneumonia, acute bronchitis, acute exacerbations of chronic bronchitis, and acute bacterial exacerbations of chronic-obstructive pulmonary disease (COPD).
- Skin and soft-tissue infections.
- Sexually transmitted diseases: chlamydia, chancroid, and gonorrhea.
- Clarithromycin in combination with other antibiotics (amoxycillin and metronidazole) is used in the treatment of peptic ulcers due to *Helicobacter pylori* (Ferrero *et al.*, 2000: 245).

- Koletar (1997: 16) reported in the study on the biggest impact macrolides had clearly had on the management of disseminated Mycobacterium avium complex (MAC) in HIV infected individuals.

2.5.2.5 Adverse Effects

McConnell & Amsden (1999: 408) reported in his study that the most frequent adverse effects associated with macrolide antibiotics are gastrointestinal (dyspepsia, diarrhea, abdominal cramping). Intravenous erythromycin as stated by Howard *et al.* (1999: 1521) is associated with a higher frequency of thrombophlebitis. Azithromycin is associated with the following commonest side effects:

- Gastrointestinal system: diarrhea (5%), nausea (3%), and abdominal pain (3%) (Kremer, 2002:175).
- Other side effects which occur in <1% of patients, include palpitations, chest pain, vomiting and headache.
- Laboratory abnormalities occur with a frequency of 1% to 2% and include elevated serum creatine phosphokinase, potassium, alanine aminotrasferase, gamma glutamyl-transpeptidase, and aspartate aminotransferase.
- Drug allergy.
- Cholestatic hepatitis associated with erythromycin estolate.

The macrolide antibiotics interact with some drugs like: terfenadine, carbamazepine, warfarin, etc. For azithromycin, aluminium- and magnesium-containing antacids reduce the peak serum levels. Unlike other macrolides (erythromycin, clarithromycin), azithromycin does not interact with cytochrome P450 system (McConnell & Amsden, 1999: 408).

2.5.3 Aminoglycosides

The aminoglycoside antibiotics include: gentamycin, amikacin, tobramycin and streptomycin.

2.5.3.1 Antimicrobial Activity

Aminoglycosides act inside the cell by binding to the ribosomes in such a way that incorrect amino acid sequences are entered into peptide chains. The abnormal proteins which result are fatal to the microbe, i.e. aminoglycosides show a concentration-dependent bactericidal effect

(Bartlett *et al.*, 1998: 832; Bennet & Brown, 2003: 224). These agents are active in vitro against the aerobic and facultative gram-negative bacilli, including *P.aeruginosa* and also exhibit activity against methicillin-susceptible *S. aureus.*

2.5.3.2 Resistance

Bacterial resistance to aminoglycosides is an increasing but patchily-distributed problem, notably by acquisition of plasmids, which carry genes coding for the formation of drug-destroying enzymes. Gentamycin resistance is rare in community-acquired pathogens in many hospitals in the United Kingdom (Bennet & Brown, 2003: 224).

2.5.3.3 Pharmacokinetics

Although many factors have been evaluated, controversy about which aminoglycoside pharmacokinetic and pharmacodynamic variables are linked to outcome persists (Kashuba *et al.*, 1999: 623). Data from in vitro studies and studies with animal models suggest the peak concentration in serum (Cmax) and total aminoglycoside exposure predict efficacy. Cmax and Cmax/MIC for the organism (Cmax/MIC are thought to be the best predictors of efficacy. Aminoglycosides are antibiotics with concentration-dependent killing activity. Antibiotic "therapeutic ranges" are usually inadequate for drugs with concentration-dependent killing activity, because the range of minimum inhibitory concentrations (MICs) for the bacteria will generally be larger than the therapeutic range (Kashuba *et al.*, 1999: 623). Aminoglycosides cannot be absorbed orally. They require IV/IM administration. They also have a poor cerebral spinal fluid (CSF) penetration (unless inflamed meningues). They are filtered unchanged by the kidney hence accumulate in renal impairment (Antimicrobial therapy, 2001).

2.5.3.4 Therapeutic Uses

Aminoglycosides have been used for over 30 years for the treatment of nosocomial pneumonia caused by gram-negative bacteria. Aminoglycosides in combination with beta-lactam antibiotics are effective in treating bacillary pneumonia caused by gram-negative bacteria (Kashuba *et al.*, 1999: 627; Bartlett *et al,* 1998: 832).

For some microorganisms, the combination of an aminoglycoside and a (penicillin or cephalosporin) results in synergic antibacterial activity in the treatment of bacterial endocarditis (Bennet & Brown, 2003: 225).

2.5.3.5 Adverse Effects

Aminoglycosides are associated with the following adverse effects (Kashuba *et al.*, 1999: 626):

- Ototoxicity. Both vestibular and auditory damage may occur, causing hearing loss, vertigo and tinnitus, which may be permanent.
- Nephrotoxicity. Dose-related changes, which are usually reversible, occur in renal tubular cells, where aminoglycosides accumulate.
- Neuromuscular blockade. Aminoglycoside may impair neuromuscular transmission and aggravate myasthenia gravis.
- Other reactions include: rashes, hematological abnormalities, hemolytic anemia and bleeding.

2.5.4 Tetracyclines

According to Bartlett *et al.* (1998: 832) there are multiple members of this class, but the one most frequently used in clinical practice is doxycycline because of its tolerability, good bioavailability and low price and because of the convenience of twice-daily dosing.

2.5.4.1 Antimicrobial Activity:

Tetracyclines inhibit bacterial protein synthesis by binding to 30S ribosomal subunit. According to Lynn (1996: 225) the tetracyclines are primarily bacteriostatic, preventing the organism from reproducing but not killing it outright. From the point of view of respiratory tract pathogens, the tetracyclines are active in vitro against the atypical organisms including *M. pneumoniae, C. pneumoniae*, and *Legionella* species.

2.5.4.2 Resistance

Tetracycline resistance occurs through drug inactivation by microbial enzymes. Tetracycline-resistant bacteria were first isolated in 1953 from *Shigella dysenteriae*, a bacterium that causes bacterial dysentery. Since then tetracycline –resistant bacteria have been found in increasing numbers of species and genera (Roberts, 1996: 1). This has resulted in reduced effectiveness of tetracycline therapy over time. Tetracycline resistance is normally due to the acquisition of new genes often associated with either a mobile plasmid or transposon.

Resistance is primarily due to either energy-dependent efflux of tetracycline or protection of the ribosomes from the action of tetracycline. As stated by Bartlett *et al.* (1998: 832) in the past, *S. pneumoniae* and *H.* Influenzae have been quite susceptible to the tetracyclines, but there was concern about occasional resistance, including resistance in S. *pneumoniae* in 5% to 8% of isolates.

2.5.4.3 Pharmacokinetics

Tetracycline is absorbed incompletely from the gastrointestinal tract. According to Lynn (1996: 224) only 60% is absorbed under optimal conditions. Plasma concentrations of doxycycline, however, essentially are equivalent whether given orally or intravenously because the drug's absorption is nearly complete. Once in the serum, the halt-lives of tetracycline and doxycycline are 6-12 hours and 16-18 hours, respectively. The volume of distribution of tetracyclines includes not only that of the extra cellular serous fluid but the tears, saliva, cerebrospinal fluid and amniotic fluid. All tetracyclines are concentrated in the liver and excreted by way of the bile into the intestine. Elimination is through the kidney for tetracycline and through the faeces for doxycycline (Lynn, 1996: 225).

2.5.4.4 Therapeutic uses

The clinical applications of tetracycline and doxycycline in obstetrics and gynecology are the follows as stated by Lynn (1996: 226) and Antimicrobial therapy (2001).

- Acne (inflammatory type) in skin flora.
- Actinomycosis with causative organism *Actinomyces israchi*.
- Cervitis in *Chlamydia trachomatis* and *Neisseria gonorrhoeoae*.
- Endometritis.
- Respiratory tract infections.
- Granuloma inginale (donovanosis).
- Lymphogranuloma venereum with *G.trachomatis*.
- Nongonococcal urethritis.
- Pelvic inflammatory disease.
- Tetracycline is used in chemical pleurodesis, which is an accepted and commonly employed treatment of pneumothorax and pleural effusions (Chaugle *et al.*, 1999: 469).

2.5.4.5 Adverse effects

Tetracyclines as a class of antibiotics are associated with the following adverse effects

- Gastrointestinal irritation with epigastric burning; nausea, vomiting, and diarrhea may occur.
- Skin: erythroderma and photosensitization (Lynn, 1996: 225).
- Discoloration of teeth and depression of bone growth when given to children < 8 years old. *Contraindicated in children < 8 years old and pregnant or nursing women.*
- May elevate blood urea by inhibiting mitochondrial protein synthesis.
- Associated with benign intracranial hypertension.
- Drug interaction with oral contraceptives. This was reported in a retrospective survey, from dermatology-based practices; also reports of 24 pregnancies in oral contraceptive users who concomitantly received therapy with tetracyclines (Dickinson *et al.*, 2001: 853).
- In the nervous system, dizziness, tinnitus, and vertigo have been reported and are completely reversible with tetracycline use (Lynn, 1996: 225).
- Tetracyclines may aggravate uremia in patients with renal disease because, at higher concentrations, the drugs may cause alterations of human protein synthesis (Lynn, 1996: 226).

2.5.5 Chloramphenicol

2.5.5.1 Mechanism of action

Chloramphenicol has a broad spectrum of activity and is primarily bacteriostatic, but may be bactericidal against *Haemophilus influenza, Neisseria meningitis* and *Streptococcus pneumoniae* (Bennett & Brown, 2003: 228).

2.5.5.2 Pharmacokinetics

For oral use, chloramphenicol is available as a capsule to reduce the bitter taste and for intravenous or intramuscular use as the succinate ester, which is soluble. Chloramphenicol succinate is hydrolyzed to the active chloramphenicol and there is much individual variation in the capacity to perform this reaction. It is inactivated by conjugation with glucuronic acid in the liver ($t_{1/2}$ 5 hours in adults). It penetrated well into all tissues, including the cerebral

spinal fluid and brain, even in the absence of meningeal inflammation (Bennett & Brown, 2003: 229).

2.5.5.3 Resistance

In a study of Mills-Robertson (2002: 249) fifty-eight clinical *Salmonella typhi* strains isolated from patients suffering from typhoid fever were obtained whereby each isolate was examined for susceptibility to Chloramphenicol. Ten isolates were resistant to chloramphenicol. Therefore chloramphenicol was considered as an antibiotic in the treatment of typhoid fever.

2.5.5.4 Therapeutic uses

Chloramphenicols should no longer be used, except in very unusual situations such as brain abscess of lung abscess (Hoppe, 1996b: 581). If chloramphenicol is used, serum concentration must be closely monitored. Chloramphenicol is most commonly used topically for bacterial conjunctivitis. Occasionally used to treat haemophilus meningitis and salmonellosis. As stated by Mills-Robertson *et al.* (2002: 249) in their study, chloramphenicol is considered 'first-line' antibiotic in the treatment of typhoid fever. It is a second-line agent in the treatment of meningitis and brain abscess because of its rare but serious toxic effects (Bennett & Brown, 2003: 229);

2.5.5.5 Adverse Effects

The following adverse effects were described in Antimicrobial Therapy, (2001).

- These agents cause bone marrow toxicity which can be fatal.
- "Grey baby syndrome" in newborns: characterized by gastrointestinal and respiratory disturbances; 40% of patients will die. This is caused by high chloramphenicol plasma concentration due to failure of the liver to conjugate, and of the kidney to excrete the drug (Bennett & Browm, 2003: 229).
- Chloramphenicols are associated with idiosyncratic aplastic anemia (rare ~ 1/30,000 dosings) (Bennet & Brown, 2003:229).
- Because of the severe toxicity associated with chloramphenicols, these agents should be used only when infection is not susceptible to less toxic drugs.

2.5.6 Sulphonamides and Trimethoprim

2.5.6.1 Antimicrobial activity

Sulphonamides act by the mechanism of inhibition of nucleic acid sythesis. The enzyme dihydrofolic acid (DHF) synthases converts p-aminobenzoic acid (PABA) to DHF which is subsequently converted to tetrahydric folic acid (THF), purins and DNA (Bennett & Brown, 2003: 231).

Trimethoprim is an inhibitor of dihydrofolate reductase (sensitivity of bacterial enzyme 10,000-fold>mammalian). Its spectrum covers gram-positive and negative strains except pseudomonas.

2.5.6.2 Clinical uses (Gram-positive, Gram-negative)

- Sulphonamides are used for the prevention and treatment of pneumonia due to *Pneumocystis carinii* (PC), a life-threatening infection in immunosuppressed HIV patients (Bartlett *et al.*, 1998: 827), and for the
- Prevention and treatment of toxoplasmosis, and treatment of nocardiasis (Bennett & Brown, 2003: 231).
- Co-trimoxazole may also prevent other opportunistic infections, such as salmonellosis, bacterial pneumonia, nocardiosis and isosporiasis (Crewe-Brown *et al.*, 2004: 440).
- Currently, co-trimoxazole is frequently used in a range of health care settings as a first-line agent, mainly in the treatment of respiratory and urinary tract infections (Crewe-Brown *et al.*, 2004: 441).

2.5.6.3 Adverse effects

The following adverse effects of sulphonamides were described by Bennett and Brown (2003: 232):

- Malaise, diarrhoea, mental depression and rarely cyanosis which latter is due to methaemoglobinaemia and gastrointestinal upset.
- Toxic skin reactions including Steven-Johnson and Lyell (epidermal necrolysis) syndrome (appear to be commoner in HIV/AIDS patients.
- Sulphonamides cause haemolysis in G-6-P deficient patients.
- They can cause macrocytic anaemia due to folate deficiency.
- They can present with teratogenicity (folate deficiency).

- Sulphonamides can interfere with metabolism of other drugs (e.g. warfarin, and phenytoin).
- The wide spread use of co-trimoxazole greatly increase resistance and occurrence of adverse reactions, thus limiting the use.

2.5.7 Quinolones

This class of antibiotics include: ciprofloxacin, sparfloxacin, ofloxacin, levofloxacin, grepafloxacin, moxifloxacin, enoxacin and trovafloxacin. The different quinolones that are currently available on the South African markert are: ciprofloxacin, moxifloxacin, enoxacin, norfloxacin, ofloxacin, levofloxacin, and gatifloxacin (Snyman, 2004: 279-283).

2.5.7.1 Antimicrobial Activity

The quinolones interfere with bacterial DNA synthesis by inhibiting DNA gyrase activity, but differences in the structure of individual agents can determine their specific mode of antibacterial activity (Schentag, 2000: 374). The quinolones are active in vitro against most clinically significant aerobic gram-positive cocci, gram-negative bacilli, *H. influenzae*, *M. catarrhalis*, *Legionella* species, *M. pneumoniae*, and *C. pneuminiae.*

2.5.7.2 Resistance

Resistance of staphylococci to the earlier fluoroquinolones has increased, possibly as a consequence of the modest activity of these compounds. Usually it is the methicillin-resistant strains or S. *aureus* and S. *epidermidis* that develop resistance to ofloxacin or to ciprofloxacin and these strains have diminished susceptibility to all fluoroquinolones (Bartlett *et al.*, 1998: 832). Nevertheless, the more recent compounds do retain some activity against methicillin-resistant strains. The minimum inhibitory concentration $(MIC)_{90}$ values of ciprofloxacin and ofloxacin for these resistant strains can be in excess of 32 mg/l and the MIC_{90} values of levofloxacin, grepafloxacin and sparfloxacin are generally only slightly lower (Appelbaum & Hunter, 2000: 39).

2.5.7.3 Pharmacokinetics

The fluoroquinolones have a remarkably broad spectrum of activity and excellent pharmacokinetics allowing for once-daily dosing and thus improving patient compliance

(Appelbaum & Hunter, 2000: 6). This was supported by Schentag (2000: 376) in his conclusion that the pharmacokinetic characteristics of sparfloxacin, (currently not available in South Africa), unlike those of most other quinolones, support once daily dosing, starting with a 400-mg loading dose on the first day followed by 200mg/d thereafter. The half-life of sparfloxacin plasma after a single 400-mg dose has been determined to be 17.6 hours in healthy volunteers. During the first 52hours after administration, 8.8% of the dose was recovered in the urine as unchanged drug. According to Montay (quoted by Shentag, 2000: 376), urinary excretion accounts for only 28% to 38% of the administered dose of sparfloxacin, and biliary excretion is considered moderate, ranging from 4.6% to 27.1% of sparfloxacin and its metabolite sparfloxacin glucuronide.

2.5.7.4 Therapeutic uses

Quinolones are active in vitro against most clinically significant aerobic gram-positive cocci, gram-negative bacilli, *H. influenzae, M. catarrhalis, Legionella* species, *M. pneumoniae* and *C. pneumonia* (Bartlett *et al.*, 1998: 832).

The early 4-quinolones have a marginal activity against *Mycoplasma* and *Chlamydia* that are pathogens in respiratory tract infections. They also play a great role in urinary tract infections (Gram-negative) that are difficult to treat with other drugs. In some cases ciprofloxacin was used as first-line empiric therapy for upper respiratory tract infections, lower respiratory tract infections, and uncomplicated urinary tract infections (Pickering *et al.*, 1994: 31). Najib *et al.* (2000: 468) in the results of their study showed that sparfloxacin is the most cost-effective antibiotic for community acquired pneumonia (CAP), and is highly effective against common respiratory pathogens, including strains with resistance to several other antibiotics. Lewis (1996: 694) reported in a study of the indications that ciprofloxacion can be used for.

- Infections resistant to all other formulary oral antibiotics (e.g, *pseudomonas aeruginosa*) or as documented by culture and sensitivity report.
- Cystic fibrosis; ciprofloxacin is alternated with other antibiotics such as amoxycillin/clavulanate.
- Osteomyelitis or other infection where intravenous/intramuscular antibiotics are the only other alternative.
- Infections in which patient allergies preclude use of any other formulary antibiotic.
- Prostatitis with systemic symptoms that has not responded to an adequate treatment course with other appropriate antibiotics, such as co-trimoxazole.

- Enterocolitis involving bacterial infections such as *Campylobacter jejuni, Salmonella typhi, Shigella flexneri, Shigella sonnei,* and *Escherichia coli,* as documented by culture and sensitivity report.

2.5.7.5 Adverse Effects

The adverse effects of quinolones include: gastrointestinal upset and allergic reactions (rash, pruritus, arthralgia, photosensitivity and anaphylaxis). Central nervous system effects may develop with dizziness, headache and confusion, and are sufficient to require cautioning the patient against driving a motor vehicle. Convulsions have occurred during treatment. Reversible arthropathy has developed in weight-bearing joints in immature animals exposed to quinolones (Bennett & Brown, 2003: 233).

Sparfloxacin has a few interactions with other drugs because it is a potent liver enzyme inhibitor and impairs the metabolic inactivation of other drugs including warfarin, theophylline and sulphonylureas, increasing their effect. Magnesium-and aluminum-containing antacids impair the absorption of quinolones from the gastrointestinal tract probably through forming a chelate complex; ferrous sulphate and sucralfate also reduce quinolone absorption (Schentang, 2000: 377).

2.5.8 Antimycobacterials

The antimycobacterials include the following drugs: isoniazid (INH), rifampicin, streptomycin, pyrazinamide(PZA), and ethambutol (EMB) (Horgen *et al.,* 1997: 673).

2.5.8.1 Antimicrobial Activity

Antimycobacterial drugs act efficiently against *Mycobacterium avium* complex (MAC) (Horgen *et al.,* 1997: 673). Isoniazid is selectively used against *Mycobacterium tuberculosis* because it prevents the synthesis of components that are unique to mycobacterial cell walls. Rifampicin has bactericidal activity against the tubercle bacillus, comparable to that of isoniazid. It acts by inhibiting RNA synthesis, bacteria being sensitive to this effect at much lower concentrations than mammalin cells; it is particularly effective against mycobacteria that lie semidormant within cells. The action of pyrazinamide is dependent on the activity of intrabacterial pyrazinamidase which converts pyrazinamide (PZA) to the active pyrazinoic acid. Ethambutol is bacteriostatic. Ethambutol, being bacteriostatic, is used in conjunction

with other antituberculosis drugs to delay or prevent the emergence of resistant bacilli (Bennett & Brown, 2003: 252-253).

2.5.8.2 Resistance

Mycobacterium avium complex (MAC) has intrinsic resistance to the majority of common antituberculous drugs as it is impermeable to these agents (Tomioka *et al.*, 2002: 139). The presence of drug resistance is still a major concern and new generation of more effective antimycobacterial agents (antibiotics, fluoroquinolone derivatives) are the subjects of active investigation (Koletar, 1997: 16).

2.5.8.3 Pharmacokinetics

In a study done by Horgen *et al.* (1997: 673) it was reported that antimycobacterial drugs have low minimum inhibitory concentration and body mass index/minimum inhibitory concentration (BMI/MIC) ratios. The results obtained underlined the following values of MIC for rifampicin (28.0 ± 7.6, 62.0 ± 18.5 and 71.0 ± 3.2). It was reported in the same stud that clinical efficacy of these drugs is clearly linked to their pharmacokinetic properties such as higher serum level and /or intracellular concentrations and half-life.

2.5.8.4 Adverse Effects

Antimycobacterial agents present the following adverse effects (Bennet & Brown, 2003: 251-253):

- Isoniazid: In general it is well tolerated. The most severe adverse effect is liver damage which may range from moderate elevation of hepatic enzymes to severe hepatitis and death. It can also cause peripheral neuritis; that is why it is always given with pyridoxine. It also causes Stevens-Johnson Syndrome.

- Rifampicin: It rarely causes any serious toxicity. Adverse reactions include flushing and itching with or without a rash (Bennett & Brown, 2003: 252). Drug interactions with isoniazid and PZA increasing hepatoxicity disorders.

- Pyrazinamide (PZA): Adverse effects of PZA include hyperruricaemia and arthralgia.

- Ethambutol: It is relatively nontoxic. The main problem is optic neuritis (unilateral or bilateral) causing loss of visual acuity, central scotomata, occasionally also peripheral vision loss and red-green colour blindness.

2.5.8.5 Therapeutic Uses

Tuberculosis still remains a serious health problem in many regions of the world, especially in developing nations. Currently, chemotherapy using multiple drug regimens with isoniazid, rifampicin, streptomycin, pyrazinamide, and ethambutol is the recommended treatment for tuberculosis (Georgiev, 1994: 157). Antimycobacterial drugs act efficiently against *Mycobacterium avium* complex MAC) (Tomioka *et al.*, 2002: 139). The treatment of disease caused by *Mycobacterium avium* complex (MAC) in HIV- infected individuals has undergone considerable evolution over the past 15 years. Agents with known antimycobacterial activity such as rifampicin/rifabutin, ethambutol, and clofazimine have all been used with varying degrees of success (Koletar, 1997: 16).

2.5.9 Antifungals

2.5.9.1 Classification

Antifungals site of action in fungal cells are used to categorize them. These classes include (Andriole, 2000: 317-321):

- **Polyenes**: These are fungicidal and have the broadest spectrum of antifungal activity. Examples of this group are: Nystatin, Amphotericin B, Liposomal amphotericin B, and investigational polyenes.

- **Nucleoside analogues**: These include: flucytosine and azoles (The group of azoles include: clotrimazole, miconazole, ketoconazole, fluconazole, itraconazole).

- **Echinocandins:** These are cyclic lipopeptide fungicidal agents and act by preventing cell wall synthesis by inhibition of 1, 3-D-glucan synthase, an enzyme that is absent in mammalian cells. Example LY 303366.

- **Pneumocandins:** These compounds possess activity against *Pneumocystis carinii*, thus the term 'pneumocandins'. They also have activity against *Candida* spp. and *Aspergillus* spp. Example is MK-0991.

- **Pradimicins-benamicins:** These agents are fungicidal compounds that bind, in a calcium-dependent manner, to cell wall mannoproteins, which causes osmotic sensitive lysis, and cell death. This group includes BMS-181184.

- **Nikkomycins:** These are competitive inhibitors of fungal chitin-synthase enzymes that are necessary for fungal cell wall synthesis. Example nikkomycin Z.

- **Allylamines / thiocarbamates:** These are synthetic fungicidal agents that are reversible, non-competitive inhibitors of squalene epoxidase, an enzyme which together with squalene cyclase, converts squalene to lanosterol, which when inhibited prevents the conversion of lanosterol to ergosterol. Examples are naftifine and terbinafine (Lamisil®).

- **Sordarins:** The sordarins are a new class of antifungal agents with a novel mechanism of action because they inhibit protein synthesis, i.e. elongation factor 2, in pathogenic fungi. Investigational sordarin compounds include GM-191519, GM-193663, GM-222712 and GR-135402.

- **Cationic peptides:** These are compounds that bind to ergoterol and cholesterol in fungal cell membranes ultimately leading to cell lysis. They have antifungal activity against *Aspergillus* spp., *Candida* spp., and C. *neoformans* and *Fusarium* spp. The naturally occurring investigational cationic peptides include cecropins, dermaseptins, indilicin, and histatins.

- **Other antifungals:** The search for new antifungal agents has been expanded because progress in molecular biology has led to a better understanding of important and essential pathways in fungal cell growth and multiplication. Those that are under investigation include dication-substituted carbazoles, furans and benzimidazoles.

- **Antifungal targets:** According to Odds *et al.* (2003: 272), there are six new antifungal agents that are currently generating excitement as they pass through the final developmental stages of clinical trials. These are triozole compounds (posanonazole, ravuconazole and voriconazole) and echinocandins (anidulanfungin, caspofungin and cilofungin).

The antifungals that are currently available in South Africa are: polynes (nystatin, amphotericin B); nucleoside analogues (clotrimazole, miconazole, ketoconazole, fluconazole and itraconazole); Allylamines/thiocarbamate (terbinafine).

2.5.9.2. Antimicrobial Activity

- The polyene antifungal agents form a complex with ergosterol and disrupt the fungal plasma membrane resulting in increased membrane permeability, leakage of the cytoplasmic contents and death of the fungal cell (Andriole, 2000: 317; Groll *et al.*, 1998: 348).

- Nucleoside analogues: flucytosine, a fluorinated pyrimidine, interferes with RNA and protein synthesis in the fungal cell (Groll *et al.*, 1998: 370; Andriole, 2000: 318). The azoles inhibit fungal cytochrome P_{450} 3A-dependent C 14-demethylase which is responsible for the conversion of lanosterol to ergosterol, thereby depleting ergosterol in the fungal cell membrane (Andriole, 2000: 318; Groll *et al.*, 1998: 378). Echinocandins are cyclic lipopeptide fungicidal agents and act by preventing cell wall sythesis by inhibition of 1, 3-D-glucagon synthase (Odds *et al.*, 2003: 272; Adriole, 2000: 319).

2.5.9.3 Resistance

There is an increased awareness of the morbidity and mortality associated with fungal infections caused by resistant fungi in various groups of patients. As reported by Canuto and Rodero (2002: 550), epidemiological studies have identified risk factors associated with antifungal resistance. Selection pressure due to the continuous exposure to azoles seems to have an essential role in developing resistance to fluconazole in *Candida* species.

According to Sanglard (2002: 379), the occurrence of resistance of antifungals is dependent on the type of fungal pathogen to be treated and the type of antifungal agents applied.

Sanglard (2002: 379) reported in above study that resistance to azole antifungals rarely develops but ketoconazole resistance has been observed in *C.albicans* in some patients with chronic mucocutaneous candidiasis. The repeated use of azoles (especially Fluconazole) in the treatment of HIV-positive patients with mucosal fungal infections in the period preceding the introduction of highly active antiretroviral therapy has favored the acquisition of azole resistance in several fungal pathogens. These were mostly *Candida* species, including

C.albicans, C. glabrata, C. dubliniensis and *C. tropicalis*, and (less frequently) *Cryptococcus* species. Azole resistance in systemic fungal infections of severely immuno-compromised patients is much less frequent and has been described mainly for *C. albicans* (Marr *et al.*, 1997: 908; Bille, 2000: 331).

2.5.9.4 Pharmacokinetics

Fluconazole has broad-spectrum antifungal activity. Favorable pharmacokinetics, a good safety profile, reliable absorption from the gastrointestinal tract and availability in oral and parenteral formulations makes fluconazole an attractive antifungal agent (Malik *et al.*, 1998: 478).

The absolute bioavailability of oral itraconazole is 55% (± 15%) (De Beule, 1996: 176). Its bioavailability is reduced by 40% when administered under fasting conditions and by 50% when administered together with H_2-antagonists. The mean volume of distribution for itraconazole is 10.7 l/kg and the total clearance is 5.1 ml/kg (renal excretion is negligible). It is highly lipophilic and extensively distributed in tissues (99.8%) protein bound (De Beule, 1996: 177).

2.5.9.5 Clinical Uses

Difficulty in diagnosis, and the poor outcome of those with established fungal infection, has led to the empiric use of antifungal agents in patients with prolonged fever and neutropenia. Empiric therapy with amphotericin B results in defervescence, a reduction in subsequent fungal infections, and a concomitant decrease in mortality from infectious causes (Malik *et al.*, 1998: 478).

Fluconazole is used to treat patients with oro-pharyngeal and esophageal candidiasis, cryptococcal meningitis, and chronic disseminated candidiasis (Malik *et al.*, 1998: 479). Clotrimazole is used for the treatment of oral and vaginal candidiasis (Groll *et al.*, 1998: 378; Adriole, 2000: 318).

Terbinafine is an effective, well tolerated and safe antifungal agent for the treatment of Tinea capitis in children (Filho *et al.*, 1998: 141; De Donker, 1999: S10).

Itraconazole, as stated by De Beule (1996: 175) because of its interesting pharmacokinetic features in terms of its tissue distribution, it is used in short treatment of vaginal candidiasis,

dermatomycosis and onychomycosis, as well as effective oral treatment of several deep mycoses, including aspergillosis, candidiasis, cryptoccoccosis, and histoplasmosis.

2.5.9.6 Adverse effects

As predicted on the basis of its mechanism of action, amphotericin B is toxic to mammalian cells, having a high incidence of potentially serious side effects.
Most patients develop chills and fever, and the development of renal dysfunction and electrolyte imbalance (Malik *et al.*, 1998: 478; Groll *et al.*, 1998: 352).

Serious side effects with Fluconazole are rare and limited to nausea, vomiting, anorexia, rash, and mild elevation of hepatic enzyme levels (Malik *et al.*, 1998: 479).

During short-term itraconazole therapy, adverse effects occurred in 7.0% of patients with superficial mycoses. The most frequently reported events were nausea (1.7%), headache (1.0%) and abdominal/epigastric pain (0.8%) (De Beule, 1996: 175).

2.5.10 Anti-protozoals

The antiprotozoal agents include metronidazole, quinine dihydrochloride, choloroquine, pyrimethamine, tinidazole, halofantrine, mefloquine proguanil (Snyman, 2004: 293-298).

2.5.10.1 Antimicrobial activity

The proposed mechanism of action consists of a four-step process: entry into a target cell, activation, generation of free radicals, and, finally, cell death resulting from damage to DNA (Simms-Cendan, 1996: 153).

2.5.10.2 Pharmacokinetics

Metronidazole can be administered through a variety of routes, including topical, oral, intravenous, rectal and vaginal. The oral bioavailability approximates 100%, with peak serum levels occurring about 1 hour after ingestion. It is distributed in breast milk, with concentration approaching serum concentrations. It passes through the placenta and is found in fatal tissue, cord blood, and amniotic fluid. It is converted in the liver to a hydroxyl metabolite, and a glucuronide derivative. The half-life for metronidazole is 6 to 12 hours if

renal function is normal. The long half-life permits longer dosing intervals (Simms-Cendan, 1996: 154). According to Bennett and Brown (2003: 234) metronidazole is eliminated in the urine, partly unchanged and partly as metabolites. Tinidazole is similar to metronidazole but has a longer half-life of 13 hours.

2.5.10.3 Therapeutic uses

The indications for use for metronidazole and tinidazole as described by Bennett and Brown (2003: 234); Simms-Cendanm (1996: 154-155) are as follows:

- Metronidazole was introduced in 1960 as the first effective cure for trichomoniasis.
- Metronidazole is considered the treatment of choice for amebiasis and giardiasis.
- Metronidazole is as effective as oral vancomycin in the treatment of C *difficile* colitis and is much less expensive.
- Patients with endometritis generally have polymicrobial infections including gram-negative and anaerobes. Metronidazole in combination with an aminoglycoside and penicillin is given to provide broad-spectrum coverage in affected patients.
- It is being used in combination antibiotic therapy for the treatment of peptic ulcer disease due to *Helicobacter pylori*.
- The longer duration of action of tinidazole may be an advantage in the treatment of giardiasis, trichomoniasis and acute ulcerative gingivitis.

2.5.10.4 Adverse effects

The following are the adverse effects of metronidazole: (Bennett and Brown, (2003: 234) and Simms-Cendan, (1996: 155) :

- Many patients have reported a metallic taste after oral administration of metronidazole in doses >2g per day.
- Gastrointestinal effects consisting of mild nausea and diarrhea, vomiting can occur.
- If taken with alcohol patients develop a disilfiram-like reaction.
- Prolonged therapy with high doses leads to Neutropenia in 2% to 4% of patients.
- Central nervous system toxicity has been reported and ranges from paresthesias and peripheral neuropathies to confusion and hallucinations.
- Metronidazole-induced pancreatitis has been reported in three patients treated for bacterial vaginosis and one patient treated for Crohn's disease.

2.5.11 Antivirals

Antiviral agents are divided into two groups: Nonretroviral agents and antiretroviral agents (Hayden, 2001: 1313).

2.5.11.1 Non-retroviral agents

- **Antiherpesvirus agents:** e.g acyclovir, famciclovir, ganciclovir, vidarabin and others,
- **Antiinfluenza agents:** These include amantadine, rimantadine, zanamivir, etc.
- **Other antiviral agents** include: interferon.

2.5.11.2 Antiretroviral (ARV) agents

In combating acquired immunodeficiency syndrome (AIDS) and AIDS related complex (ARC), the search for therapeutic agents possessing activity against human immunodeficiency virus (HIV) has yielded a number of compounds demonstrating potent and selective antiviral activity. Human immunodeficiency virus reverse transcriptase (HIV-RT) remains a primary target for the treatment of HIV infection. As HIV-RT inhibitors, five anti-HIV nucleoside analogs have been approved by the US Food and Drug Administration (FDA) and are currently used clinically (Tan *et al.*, 1999: 118).

2.5.11.2.1 Classification

Bennett and Brown (2003: 259) classify the antiretrovirals (ARVs) as follows:

- **Nucleoside analogue reverse transcriptase inhibitors (NRTIs).** NRTIs were the first antiretroviral agents used to treat HIV infection. Six NRTIs are available in South Africa: Zidovudine (AZT), didanoside (ddI), zalcitabine (ddC), lamivudine (3TC), abacavir and stavudine (d4T) Zidovudine (Retrovir® also known as AZT), as the triphosphate, was the first anti-HIV drug to be introduced and has a high affinity for reverse transcriptase (Snyman, 2004: 298-306).

- **Protease inhibitors (PIs):** These constitute a new class of agent for HIV infection. These have been shown to reduce viral RNA concentration ('viral load'), increase the CD4 count and improve survival when used in combination with other agents. There are

six PIs available in South Africa examples of these are: amprenavir, indanavir, lopinavir, nelfinavir, ritonavir/lopinavir and saquinavir (Snyman, 2004: 298-306).

- **Non-nucleoside reverse transcriptase inhibitors (NNRTIs):** The NNRTIs are structurally different from the NRTIs and act by binding to reverse transcriptase directly, downstream from the active catalytic site, thereby interfering with its transcriptional activity. Three NNRTIs are currently available: nevirapine, delavirdine (not registered for use in South Africa) and efavirenz which has a long duration of action and need be taken only once per day ($t_{1/2}$ 52 hours). Nevirapine is another drug in this group. It is used in combination with at least two other antiretroviral drugs, usually for progressive or advanced HIV infection, although it appears effective also in pregnancy.

2.5.11.2.2 Mechanism of activity of anti-Human Immunodeficiency Virus drugs (anti-HIV)

The anti-HIV drugs act by inhibition of human immunodeficiency virus reverse transcriptase (HIV-RT). The triphosphates of nucleoside analogues produce effects on cellular polymerases, particularly Pol-alpha, which is responsible for cellular DNA synthesis (Bennett & Brown, 2003: 259; Tan *et al.*, 1999: 119).

2.5.11.2.3 Pharmacokinetics

Anti-human immunodeficiency virus nucleoside analogs permeate into cells by both simple diffusion and nucleoside/nucleobase carrier-mediated transportation. Generally, there are extensively distributed throughout the body but with limited penetration into the central nervous systems (CNS), they are rather rapidly cleared from the systemic circulation with apparent half-lives usually less than 3 hours (Tan *et al.*, 1999: 120).

2.5.11.2.4 Resistance

Antiviral drug treatment of infections with the human immunodeficiency virus type 1 (HIV-I) usually leads to a rapid decline in the abundance of plasma virus. The effect of single therapy is often short-lived as the virus readily develops drug-resistant mutants (Nowak *et al.*, 1997: 203). Although clinical use of zidovudine (AZT) is still widely used, it is associated with the development of virus disease resistance and toxicity to the hematopoietic system (Gallicchio & Hughes, 1995: PL265).

2.5.11.2.5 Therapeutic uses

The anti-viral drugs didanoside (ddI) and zidovudine (AZT), synthetic nucleoside analogs, have been used in the treatment of acquired immunodeficiency syndrome (AIDS). Although clinical use of zidovudine (AZT) is still widely used, it is associated with the development of virus disease resistance and toxicity to the hematopoietic system. Alternative nucleoside reverse transcriptase derivatives such as didanoside (ddI) have been developed in order to reduce the incidence of virus disease resistance and hematological toxicity (Bennett & Brown, 2003: 260; Gallicchio & Hughes, 1995: PL265; Tan *et al.*, 1999: 117).

2.5.11.2.6 Adverse effects

Myelosuppressive effects such as neutropenia and anemia are the main clinical adverse effects associated with zidovudine (AZT). Short-term complications such as pancreatitis, cytopenia related to nucleoside reverse transcriptase and other metabolic complications have been reported by Montaner (2001: 94). Peripheral neuropathy is the primary adverse effect associated with didanoside (ddI), zalcitabine (ddc), and stavudine (d4T) (Tan *et al.*, 1999: 120). Zidovudine (AZT) is associated with toxicity to the hematopoietic system (Gallicchio & Hughes, 1995: PL265).

2.6 Chapter summary

In this chapter, antimicrobials were discussed in terms of the principles of drug therapy, resistance and classification according to pharmacological groups.

Health care concepts and approaches will be discussed in Chapter 3.

CHAPTER 3 HEALTH CARE CONCEPTS AND APPROACHES

In this chapter the health care concepts and approaches will be discussed in terms of: primary health care, managed health care, disease management, pharmacoepidemiology, drug utilisation and pharmacoeconomics.

3.1 Primary Health Care

3.1.1 Introduction

The concept of primary health care developed in the 1940s and 1950s, when the governments of several countries were urged to rationalize their highly technical approach to health care and to broaden their coverage by providing better basic services that impact positively on health (Dennill *et al.*, 1999: 1). According to Mullan (1998: 118) the modern concept of primary care providers (PCPs) began in the 1960s as a result of an acute shortage of physicians, particularly in rural and poor inner city areas in the United States. In South Africa, two physicians, Drs Sidney and Kark, started a health centre at Pholela in Zululand and developed a community-oriented primary care program. This model proved so successful that by the end of the decade there were about 40 similar health centers in other rural areas (Dennill *et al.*, 1999: 1).

3.1.2 Concept

The idea of primary care is not tied to an organ system (such as cardiology) or a place (the outside department). It is an idea that describes, by turns, a domain of service, a type of practitioner, or a philosophy of care. To clinicians it is a label that describes certain types of practitioners. To the patients primary care can be the provider who knows them best, giving comprehensive, "high-touch" care over the years, or it can be the designated medical grinch who stands in the way of coveted specialty services (Mullan, 1998: 118). The concept of primary health care encompasses a political philosophy that calls for radical changes in both the design and content of traditional health care services. It advocates an approach to health care based on principles that allow people to receive the

care that enables them to lead socially and economically productive lives (Dennil *et al.*, 1999: 2).

The definition of the concept as determined at Alma-Ata is:

"Primary health care is essential care based on practical, scientifically sound and socially accepted methods and technology, made universally accessible to individuals and families in their community through their full participation and at a cost that the community and country can afford. It forms an integral part both of the countries' health system, of which it is the central function and main focus, and the overall social and economic development of the community" (WHO 1978, as referred to by Pullen et al, 1994: 201).

Mullan (1998: 121) defined primary care as "*an idea that describes, by turns, a domain of service, a type of practitioner, or a philosophy of care.*" He compared and contrasted the "social justice" view of primary care with "industrial efficiency" view of primary health care. Mullin went on to state that the primary care providers (PCPs) see their role as a mission to provide care to the underserved: the poor, rural communities and others who are ignored or abandoned by the mainstream medical establishment, bringing to all those served "competent, comprehensive doctoring to bear-healing in an omnibus sense."

3.1.3 Role of primary care providers (PCP)

Although the concept of primary care has been around for more than 30 years, the role of the primary care providers (PCP) in its iteration is still being defined (Sullivan, 2000: 450). Primary care providers see their role as a mission to provide care to the underserved: the poor, rural communities and others who are ignored or abandoned by the main stream medical establishment, bringing to all those served "*competent, comphrensive doctoring to bear-healing in an omnibus sense*" (Mullan, 1998: 121).

3.1.4 Principles of primary health care

Community-oriented primary care (COPC) is a systematic approach to health care based upon principles derived from epidemiology, primary care, preventive medicine, and

health promotion. Macgregor (1991: 146) and Ochala-Odhiamo, (2003) described the following principles of primary health care:

- Universal coverage of the population, with care provided according to need. It is aimed particularly at children bearing women because they are the most vulnerable.
- Services should not only be curative, but should promote the population's understanding of health and a healthy way of life, reach out towards the root causes of disease with an emphasis upon prevention. Vaccination and population-control programs are important elements in primary health care.
- Services should be effective, culturally acceptable, affordable, and manageable.
- The communities to be served should be actively involved in the development of services so as to promote self-reliance and reduce dependence upon others. An important element is the training of local health care workers chosen by the community.
- The paths taken to deal with ill-health must not be limited to strictly medical intervention because the causes of ill-health are not limited to matters relating directly to health. Areas to be tackled must include education for literacy, income supplementation, clean water and sanitation, improved housing, ecological sustainability, the building of roads, food programs in times of drought and food subsidies.

3.1.5 Strategy for the implementation of primary health care

For a strategy to be determined, first and foremost there must be political commitment to primary health care by the government in power. Priorities must be identified and then detailed plans of action must be set out. As described by Dennill *et al.* (1996: 6 – 9) and Mooney (2003) stated in his keynote address on equity that a successful strategy for implementing health care should be based on the following principles:

- *Equity.* All people should have equal access to basic health care and social services.
- *Accessibility.* Services must be extended to be within the reach of all people in the country. Services must be :

- Geographically accessible; health services should be within a reasonable distance of 5-10 km and transport should be available.
- Financially accessible to the individual and the community.
- Functionally accessible, in that the appropriate type of care be available to meet the needs of the specific community.

- *Affordability.* The level of health care offered should be aligned to what the community can afford. No person should be denied health care because of an inability to pay.
- *Availability.* There should be sufficient and appropriate services to meet the particular health needs of each community.
- *Effectiveness.* The services provided must do what they were intended to do for the specific community. The effectiveness of the service must also be justifiable in terms of the total cost.
- *Efficiency.* The results attained should be proportionate to the input, in terms of effort expended, money spent, resource used and time utilized.

Reorganization of health services

A shift of emphasis of health care is necessary, from curative hospital-based care to community-based primary health care. The overall objective is to deliver health service efficiently and effectively through an infrastructure that covers the needs of communities at ground or district levels, with the necessary support.

Intersectoral collaboration

Primary health care includes such diverse interventions that it cannot be implemented by health workers alone. There should be multisectoral input in determining policy which impacts on health or the environment.

Multidisciplinary approach

The multidisciplinary team must include *"the ordinary individual in the community, be it a patient and his family, or any other concerned individual or group that can assist the*

community in one way or another towards the improvement of their health status." (Mooney, 2003).

Community participation and involvement

Primary health care is a shift of emphasis, from external agencies supplying the health services, to the people of the community becoming active participants in their own health care. Community participation on issues such as policy development is encouraged through committees and community health centers. Community participation is also enhanced through programmes like the tuberculosis (TB) direct observed treatment short-course (DOTS) and the involvement of volunteers and community health workers in home and community based care programmes. This process encourages and allows the community to take responsibility for their own situation, thus empowering them (Ntsaluba, 2003a).

3.1.6 Different approaches to primary health care

Different approaches to primary health care are the following:

3.1.6.1 Comprehensive versus selective primary health care.

Comprehensive primary health care is a strategy for the healthy developing of a community. The emphasis on these comphrensive programs is on change in the community rather than on a programme which can be replicated and instituted in any community. The challenge is to fully staff and equip the facilities so that they can provide a comprehensive health service and lead to more cost-effective service delivery. The critical challenge is the definition and provision of a comphresive package of services. This package should be capable of tackling the leading causes of mortality and morbidity in the country using the most cost-effective strategies (Tshabalala-Msimang, 2003b).

In South Africa, while the philosophy of comprehensive primary health care underpins the restructuring of the health care system under the new political dispensation, care provided at the primary level remains largely biomedical. Furthermore, third generation reforms are visible in the manner in which vertical programmes are being implemented.

Integration, essential for comprehensive care and improving health status through, inter alia, addressing problems in a holistic manner which takes action against diseases and their underlying causes has been implemented in South Africa (Petersen & Swartz, 2002: 1006).

3.1.6.2 Microscopic versus macroscopic or medical versus health model

The microscopic approach is where the focus of both efforts and resources is on the curative side of health care and the patient is a passive recipient. Macroscopic approach is a holistic approach where the emphasis is to create an environment and promote lifestyles which prevent the body from breaking down. This is known as the health model (Dennill *et al.*, 1999: 18).

3.1.7 Indicators

These are methods used at regional, national and international levels to plan and evaluate health care programs. There is an indication or reflection of a given situation. They can be defined as variables which help to measure change. They are important to primary health care because they will indicate the success or failure of programs, as well as give direction to planners to develop the necessary services required to meet the needs of individuals and community. The WHO has provided a list from which countries can choose the categories of indicators which are most relevant to their health needs and socio-economic situations. There are four categories of indicators (Dennill *et al.*, 1999: 20):

- Health policy indicators.
- Social and economic indicators.
- Indicators of the provision of health care.
- Indicators of health status.

3.1.8 Primary health care in South Africa

The South African care health system has evolved from different origins; the two main contributors being Western medicine and the various African cultures with their

traditional tribal medicine. In May 1991 the government's intention to provide primary health care to all the people was made clear in the National Health Service Delivery Plan (Tshabalala-Msimang, 2003a). It stated that during 1990 to 1995 an affordable, comprehensive health service should be developed, which would be planned according to priorities identified by the communities themselves (Dennill *et al.*, 1999: 34).

3.1.9 Strategies for implementation of primary health care in South Africa as compared with strategies set in Section 3.1.5

The strategies determined were as follows, according to Dennill *et al.* (1999: 36); Ochala-Odhiamo, (2003) and Luiz, (1994: 129):

- To make information concerning the prevailing health problems and the methods of preventing and controlling them, available to the population.
- To promote the provision of food, adequate supply of water and basic sanitations, that forms the basis of "health for all".
- To ensure provision of maternal and child health services, including family planning.
- To ensure immunizations against the major infectious diseases so as to improving child survival against measles, tetanus, tuberculosis, poliomyelitis; pertusis and diphtheria, as well as mumps and rubella.
- To appropriately treat common diseases and injuries.

3.1.9.1 Strategies toward greater equity in health care provision

Bloom (1997: June 28 – July 5) argued at the Traveling Seminar on the Attainability and Affordability of Equity in Health Care that, the first step for governments was to recognize their inability to ensure equal access to all health services, so that they could concentrate on measures that yield the greatest benefits. Restructuring of the health sector was the first major task towards equity, which entailed:

- placing equity at the center of strategic plans,
- setting clear objectives improving access to basic health services,
- formulating strategies for best use of available resources, and
- monitoring progress (Bloom, 1997: June 28 – July 5).

3.1.9.2 Monitoring progress towards equity in health care provisions

Development of systems for monitoring and evaluation which specifically identify and monitor change in key aspects of health care inequities were discussed by McCoy and Gilson at a seminar (1997: June 28 – July 5). The following focal points for selecting indicators were identified, including:

- Financial allocation.
- Accessibility.
- Provision of services.
- Quality of care (including assessments of individual health programs).
- Health care decision-making processes and,
- Population trends.

3.1.10 A vision for health in South Africa

The transition from apartheid rule to a new democracy in South Africa has been accompanied by the vision of a national health care system based on the principles of universal primary health care. This vision is now firmly in place in the form of the White Paper for the Transformation of the Health System in South Africa (1997), as referred to by Petersen, (2000: 321). It implies a comprehensive service, which includes the integration of mental health care into the primary health care system. Furthermore, mental health care is conceptualized more broadly than psychiatric care to include care for non-psychiatric mental health problems as well as the promotion of mental health (Petersen, 2000: 321).

3.1.11 Primary health care today: achievements and challenges.

3.1.11.1 Challenges

3.1.11.1.1 Academic Health

Academic health came from a separate academic hospital, departmental-based and research focused on achievement. Its subsequent aim was the formulation of national affordable guidelines for the restructuring of an inefficient, fragmented, inequitable hospital centered health services to an efficient, integrated, decentralized, equitable and comprehensive primary health care system (Van Zyl, 2004: 167). In South Africa, significant changes in academic health have taken place since the first democratic elections in 1994. The role of hospitals was redefined in 1996 to be consistent with primary health care principles. The future challenge focuses on service delivery, research, health education and training, academic health management, professionalism and financial management (Van Zyl, 2004: 169).

3.1.11.1.2 Health Equity

Assessing health equity within a society is another challenge which requires examining inequalities in health (and in its determinants) between more and less socially advantaged groups within the society, focusing for practical reasons on those inequalities likely to be among the most important causes of ill health and also to be relatively avoidable (Braveman & Tarimo, 2002: 1623).

3.1.11.1.3 Adolescents

Health care facilities can play an important role for adolescents in preventing health problems, in promoting sexual and reproductive health and in shaping positive behaviors (Dickson-Tetteh *et al.*, 2001:160). Extensive research has established that South African public health facilities are failing to provide adolescent-friendly health services (Buga *et al.*, 1996: 524). Services are either physically inaccessible or have opening times that

prevent easy access for youth. Staff attitudes can be judgmental or even hostile, and the professional norms of confidentiality and empathy are often neglected.

This a great challenge for the South African primary health system because according to South African census in 2001, there were about 18 million people under the age of 20 (Statistics South Africa, 2001). These young South Africans experience many reproductive health problems, including high rates of sexual transmitted infections (STIs), human immunodeficiency virus (HIV) and unwanted pregnancies. In spite of a high level of awareness of HIV/AIDS among young people, the spread of HIV infection among South African youth (over 750 new infections per day) is one of the fastest growing rates in the world (South Africa, 1998: 76).

3.1.11.1.4 The necessary support services

The users must be confident that systems are in place for speedy referrals where necessary. In particular:

- To work in partnership with other sectors to ensure that at the end of year 2004 all existing and new clinics and community health care facilities have electricity.
- The availability at all times of the drugs on the essential drug list (EDL) for the primary level care facilities.
- Appropriately trained personnel such as primary health care nurses (PHCNs) must be available in all facilities. All primary care facilities to have consistent and visible backup doctors.
- All primary health facilities to run community outreach programmes aimed at galvanizing the energies of communities so that they actively participate in health programmes, in particular the preventive and promotive aspects of health service.

3.1.11.2 Achievements

The following summary reflects the key achievements since 1994 as presented by Ntsaluba (2003b) at the Primary Health Care conference:

- The tabling of the White Paper on the Transformation of the Health System in April 1997.
- The elimination of discriminatory structures and practices in the public health system.

- Consolidation of fourteen fragmented health administrations inherited from the apartheid system into a national and nine provincial health departments.
- Transformation of the public health system from a fragmented, racially divided hospital-centered service to an integrated, comphrensive national service that emphasizes the health needs of disadvantaged people especially those living in rural areas.
- Expansion of the primary care infra-structure:
  - since 1994 more than 700 new clinics have been built or had major upgrading (495 of which were completely newly built) (Tshabalala-Msimang, 2003a)
  - 2298 existing clinics have received new equipment and were upgraded,
  - 124 new visiting points were built, and
  - 125 new mobile clinics were purchased as reported by Nsaluba (2003a) at the PHC conference.
- Launching of the National Drug Policy (NDP) in 1996 and the development of essential drugs lists and standard treatment guidelines for primary health care and hospital levels pediatric and adult levels of care.
- Introduced the World Health Organization - recommended direct observed treatment short-course (DOTS) to combat tuberculosis (TB) in 1996.
- Employment of 402 Cuban and 44 other foreign doctors to strengthen hospital - based care for rural communities and to provide proper support to our primary health system.
- Development of National Adolescent-Friendly Clinic Initiative (NAFCI) to improve the quality of adolescent health services at the primary health care level and strengthen the public sector's ability to respond appropriately to adolescent health needs (Dickson-Tetteh *et al.*, 2001: 161).

3.1.12 Primary health care - programme development

Evaluation of primary health care

At the National Primary Health Care conference (2003a: 25 August), the director general of health, Dr Ntsaluba evaluated South African primary health care reflecting on

achievements of the past nine years in the development and implementations of policies pertaining of primary health care. He observed the following;

- Package of primary health care services which ensures access and free health care for children less than 6 years and pregnant and lactating mothers.
- The roles of provinces and municipalities in funding and rendering primary health care (PHC) services were emphasized.
- Systems to render PHC were established.
- Human resources capacity for PHC was trained both in management and clinical skills.
- Quality: The Batho Pele – which is a government-wide programme, has been implemented.
- Equity/recourse allocation: promoting equity, accessibility and utilization of health services.
- Community participation: Community participation has been strengthened around TB DOTs and home and community based care both through volunteers and community health workers. The HIV and AIDS pandemic has required that health promotion and education be increased through community awareness.

3.1.13 Prime Cure Clinics

3.1.13.1 Overview and services provided

In this study, Prime cure clinic was used as an example of a private health care setting in South Africa. Prime Cure (Pty) Ltd offers primary and occupational healthcare. It is an established healthcare service provider with 50 Medi Centers and more than 700 general practitioners, dentists and optometrists throughout South Africa, offering highly affordable, quality healthcare to a broad spectrum of patients (Prime Cure, 2003a).

3.1.13.2 Evidence-based

Prime Cure's clinical protocols and treatment regimens are in line with the guidelines of the Cochrane Collaboration Database, an international, non-profit evidence-based clinical database with 178 research centers around the world. All treatment protocols as well as

the medicine list are continuously assessed and updated utilizing the Cochrane Database. The strict monitoring of standards of care and adherence to the clinical protocols by Prime Cure practitioners allows for delivery of such cost-effective, yet high quality medical care. Prime cure uses a sophisticated information technology (IT) infrastructure that allows for in-depth reporting on non-adherence to clinical standards as set by the clinical management system (Prime Cure, 2003b).

Primary health care in Zimbabwe

An evaluation of the management of epilepsy by primary health care nurses in Chitungwiza, Zimbabwe was done by Adamolekun *et al.* (2000: 177) with the objective of designing an effective training program for nurses. The results revealed that nurses appeared uncertain as to when to change drug therapy, reduce polytherapy or stop drug therapy in clinically indicated situations. This evaluation provided a basis for planning future training programs for community health care nurses on the treatment of epilepsy (Adamolekun *et al.*, 2000: 180).

3.1.14 Use of antimicrobials in primary health care settings

Antibiotics are one of the most commonly used categories of drugs in modern medicine (Chang *et al.*, 1999: 23). Antibiotic usage tends to be costly, has the potential to cause various side effects and may also result in emergence and increase of bacteria resistance to antibiotics. In addition to the global situation of antibiotic resistance, problems in individual countries need to be monitored and managed locally Primary health care represents the first tier of the health care system. It is therefore necessary to evaluate antimicrobial use in primary health care settings, to ensure rational use of antimicrobials.

Antibiotic usage in primary care units worldwide

To understand the situation of antibiotic usage in primary care units in Taiwan, Chang *et al.* (1999: 23) analyzed prescriptions from outpatients clinics of public health stations located in various parts of Taiwan. Results of the study revealed that antibiotic usage in Taiwan was not well controlled. The use of antibiotics in patients who presented with

common cold which is of viral origin and chronic diseases like diabetes, indicate inappropriate use of these agents.

Antiretroviral therapy in a community public clinic in South Africa

Bekker *et al.* (2003: 459) reported in a study on operational and clinical problems encountered during the first 6 months of a community-based antiretroviral therapy (ART) programme. Conclusions were made that ART could be successfully implemented within a primary care setting. Attention should be given to the diagnosis of tuberculosis during screening and early ART. And incorporating therapeutic counselors into the programme would increase community involvement.

Use of investigations in lower respiratory tract infection in the community

Woodhead *et al* (1996: 1596) reported on a survey done on the impact of the use of investigations on treatment of adult lower respiratory tract infection in the European community. His results revealed a change in initial therapy in 12% cases. Macrolides were the most frequently prescribed second-line and quinolones the most frequently prescribed third-line antibiotics.

Diagnosis and treatment of upper respiratory tract infections in the primary care setting

A study was done by Fendrick *et al.* (2001: 1683) to provide primary care practioners with an accessible combined resource for the management of AECB, Acute otitis media (AOM) and acute bacterial rhinosinutis (ABRS). The antibiotic courses given to these patients were neither necessary nor appropriate because a significant proportion of these infections are caused by viruses or non-bacterial agents, and thus are self limiting. There is need for accurate diagnosis of bacterial and non-bacterial conditions, and patient education on antibiotic use and misuse, thus controlling unnecessary use and subsequent resistance.

Changing provider habits in primary care

Rapid advancement on the science side of medicine has resulted in simple, modern-day treatments for problems that were once uniformly fatal. This has also created new possibilities for treatment that are based on sound principles at the individual level but that are lacking evidence-based proof of overall effectiveness. According to Kinney (2002: 614) sinus infections are common and represent a high cost to the health care centres. Clinical protocols can be used to develop cost-effective treatment strategies of these infections.

Antimicrobial drug use in primary health care centres in India.

Uppal *et al.* (1993: 671) carried out a survey to assess the extent and pattern of use of antimicrobials at two primary health care centres. The results of the study revealed that 20% to 40% of all drugs prescribed were antimicrobials. The most prescribed drugs at both PHCs were sulfa drugs (29%), followed by co-trimoxazole (15%) and penicillins (10%). Antimicrobial prescribing was empirical, or without objective evidence for underlying infection, and there was no way of ascertaining the specific beneficial effect of antimicrobial therapy.

3.2 Managed Health Care

3.2.1 Introduction

Managed care organizations (MCOs) have grown in the United States health care system as a result of rapid growth in health care costs (Kinney, 2002: 614). It was rapidly dominating the health care financing and delivery system in the United States (Fox, 1996: 3). Managed health care organization means a person who has contracted with a medical scheme in terms of regulation 15A to provide a managed health care service (Council for Medical Schemes, 2004).

3.2.2 Concept

Managed care is no longer just a way to finance health care; it also represents a collection of responsibilities that includes patient education, self care, and promotion of wellness, early identification of disease, all aspects of utilization management, and provision of financial incentives to care providers (Fox, 1996: 3). In South Africa, managed health care was instituted more than 5 years ago with varying degrees of success (Booyens & Phil, 2000: 515).

3.2.3 Definition of managed care and managed care organizations

Managed care, within the South African context, is a term used to refer to a diverse range of healthcare organizational strategies aimed at controlling cost, improving access and assuring higher levels of quality of care provided to those covered by medical schemes (Council for Medical Schemes, 2004).

The Regulations promulgated in terms of the Medical Schemes Act, 1998, Act No 131 of 1998 (Council for Medical Schemes, 2004), herein after referred to as the "Act" and the "Regulations", define managed care as "*clinical and financial risk assessment and management of health care, with the view to facilitating appropriateness and cost-effectiveness of relevant health care service within the constraints of what is affordable, through the use of rule-based and clinical management-based programmes.*"

A managed care organization is defined by the regulation as "a *person who has contracted with a medical scheme in terms of regulation 15A to provide a managed-care health service*" (Council for Medical Schemes, 2004).

3.2.4 Goals of managed health care

The central goal of managed care is the identification of ways to achieve both high-quality and cost-effective health care. Efforts to realize these goals have focused on the use of clinical protocols to improve planning, coordination, communication, and evaluation of care (Fox, 1996: 3).

In South Africa, the need to institute managed healthcare principles in private health care industry was emphasized by the country's disproportionately high pharmaceutical and hospitalization costs, the rapid growth of the industry, over servicing (fraud), and government pressure (Booyens & Phil, 2000: 515).

According to Wert (1996: 1369), managed care, through managed care organizations, wants to maintain high-quality care; low costs; have stable, predictable expenditures, and develop strategic alliances. Another strategy being to educate physicians and promote appropriate use of medications for each identified therapeutic class. It is only through appropriate use of medicines, that increased quality and reduced costs can be maintained.

3.2.5 Standards for managed health care

The following standards for managed health care for South Africa as described by the South African Council of Medical Schemes (2004):
If any managed health care is undertaken by the medical scheme itself or by a managed health care organization, the medical scheme must ensure that:

- A written protocol is in place that describes all utilization review activities, including a description of the following:
  - data sources and clinical review criteria used in decision-making,
  - mechanisms to ensure consistent application of clinical review criteria and compatible decisions,
  - data collection processes and analytical methods used in assessing utilisation and price of health services, and
  - the staff position functionally responsible for day-to-day management of the relevant managed health care programs.
- The managed health care programmes use documented clinical review criteria that are based upon evidence-based medicine, taking into account considerations of cost-effectiveness and affordability, and are evaluated periodically to ensure relevance for funding decisions.
- The managed health care programmes use transparent and verifiable criteria for other decision-making factors affecting funding decisions and are evaluated periodically to ensure relevance for funding decisions.

- Qualified health care professionals administer the managed health care programmes and oversee funding decisions, and that the appropriateness of such decisions are evaluated periodically by clinical peers.

3.2.6 Managed care comes of age: 1985 to the present

The last decade has seen a combination of innovation, maturation, and restructuring in the United States, as described by Fox (1996: 9).

In many communities hospitals and physicians have collaborated to form physician-hospital organizations (PHOs), principally as vehicles for contracting with managed care organizations. A second innovation has been the development of carve-outs, which are organizations that have specialized provider networks and are paid on a capitation or other basis for a specific service such as mental health, chiropractic, and dental services. Computer technology in the US was another virtual revolution in the processing of medical and drug claims, which is increasingly being performed electronically rather than by paper submission and manual entry (Fox, 1996: 9).

3.2.7 Trends in managed healthcare in South Africa

After severe initial setbacks, managed healthcare in South Africa is starting to change as reported by Booyens and Phil (2000: 516).

American approach

Managed health care started with an American model. After 3 years, the physicians and specialist groups were hostile about it because of the heavy funding involved. And South Africa is regarded as a developing country, with a significant number of poor citizens.

South African physicians

Physicians reacted to managed care concepts by forming group practices and independent practitioners. In South Africa physicians are regarded as the gateways to cost-effective healthcare and the only persons that can lower the costs of medical services.

Treatment guidelines

Guidelines (consisting of diagnosis, management, and treatment, including algorithms) have been developed for cardiac failure, hyoerlipidemia, stroke, acne, epilepsy chronic pain, arthritis, and osteoporosis.

Networks

Groups of healthcare providers enter into a contractual arrangement with the medical aid's administrator (or managed care organization) to provide certain healthcare services to the members of that medical aid. These networks comprise hospital networks, pharmacy networks, and ambulatory care networks.

Monitoring and auditing

Managed healthcare programs include sophisticated services that monitor and manage hospitalization, monitor hospital procedures, and finally do a careful audit of the account. Pharmaceutical benefit programs monitor the appropriateness of prescribed medicines or identify alternatives that are less expensive but equally effective (Shaw, 2003:115).

3.2.8 Issues faced by managed care in South Africa

Pattinson (2003: 455) discussed in a study challenges in saving babies – avoidable factors, missed opportunities and substandard care in perinatal deaths in South Africa. He concluded that concentration on the remediable priority problems identified (namely labor management, resuscitation of the asphyxiated neonate, and care of the premature neonate) would make the reduction of perinatal mortality in South Africa feasible and inexpensive.

Another logistic challenge was the proposal suggested at a national health research ethics meeting in South Africa in February 2003 that : participants who become HIV-1 infected during HIV-1 vaccine trials to have access to high quality treatment, and moreover, that this should be financed by trial sponsor agencies. This was considered a complex task

especially in resource-poor settings. As urged by Tucker and Slack (2003: 995) this was a practical attempt to address the challenges of long-term, high quality treatment provision.

3.3 Disease Management

3.3.1 Introduction

In the times of dramatic change in health care, there were multiple opportunities and many potential risks for patients, providers, and health care organizations. As health care delivery was being reconfigured, so was role of physicians. Therefore methods to determine and implement optimal practice had also to be developed. Among them was disease management (Ellrodt *et al.*, 1997: 1687). Disease management is often regarded as one of the ways of achieving managed care as stated by Hunter & Fairfield (1997: 50). Disease management (DM), also referred to as disease state management, is a health care management method that attempts to provide an integrated system of prevention and care for patients with specific diseases.

3.3.2 Definition of Disease Management (DM)

Disease management (DM) is a comprehensive approach to preventing and treating disease that: targets patients with specific diseases; provides integrated services across organizational and professional boundaries; utilizes services based on the best scientific evidence available; and focuses on outcomes (Holdford *et al.*, 1998: 328). Its goal is to create population-based, integrated approaches to the provision of ongoing, cost-effective, and clinically efficacious care (Ellrodt *et al.*, 1997: 1687).

3.3.3 Characteristics of disease management

- Disease management targets specific patient populations suffering from a disease.
- It integrates services directed toward the chosen disease by various components of the health care system, providing a seamless system of prevention and care.
- Disease management bases services on consistent application of the best scientific information available concerning treatment and the evaluation of care, with constant

updating and improvement through use of quality improvement through use of quality improvement techniques.

- Disease management links care to the outcomes of interest to consumers of health care, taking into account the multidimensional nature of quality by including clinical, economic, and humanistic outcomes (Holdfold *et al.*, 1998: 329).

3.3.4 Steps for starting a disease management program

The following steps were described by Armstrong (1999: 595); Holdfold *et al.* (1998: 332-335); Hunter & Fairfield (1997: 51) and Ellrodt *et al.* (1997: 1688).

Step 1: Identify a target population

Patient populations with certain diseases are better candidates for community pharmacy-implemented disease management programs than others. Identifying these disease populations consists of answering two questions: which diseases are most responsible to community pharmacy interventions, and which diseases can contribute most to a community pharmacy's profitability.

Step 2: Assess resources

The pharmacist must assess the availability of trained support personnel, as well as of any funds or facilities that might be needed. One way to improve resource capability is to develop alliances with others who have a major role in diseases management.

Step 3: Define key indicators of quality

Pharmacists need measures for assessing how their DM program is progressing and how it can be improved. These measures can be as simple or complex as desired, as long as they give an adequate indication of the program's success.

Step 4: Implementation

The plan should address the program's goal, review what is known and not known about the disease and its treatment, and list implementation strategies:

The program's goals

The goals must address the needs of the various participants, including patients, pharmacists, physicians, and third-party payers.

Review of the disease and its treatment

The pharmacist must have the current scientific information about the disease and how to treat it.

Implementation strategies

Because DM is relatively new to community pharmacy, its implementation should be slow and should take place in stages.

Step 5: Assessment

Although the most exciting aspect of DM is its implementation, follow-up assessment may even be more important, because it gives the pharmacist an opportunity to change aspects of the program that have not been effective.

3.3.5 The disease management process

Disease management must be viewed as a process. This process is illustrated in Figure 3 .1. The process begins with the retrieval of baseline information, then goals and targets are set, guidelines are communicated and behaviour modification. Then redesigning the clinical processes, measuring of outcomes and interventions.

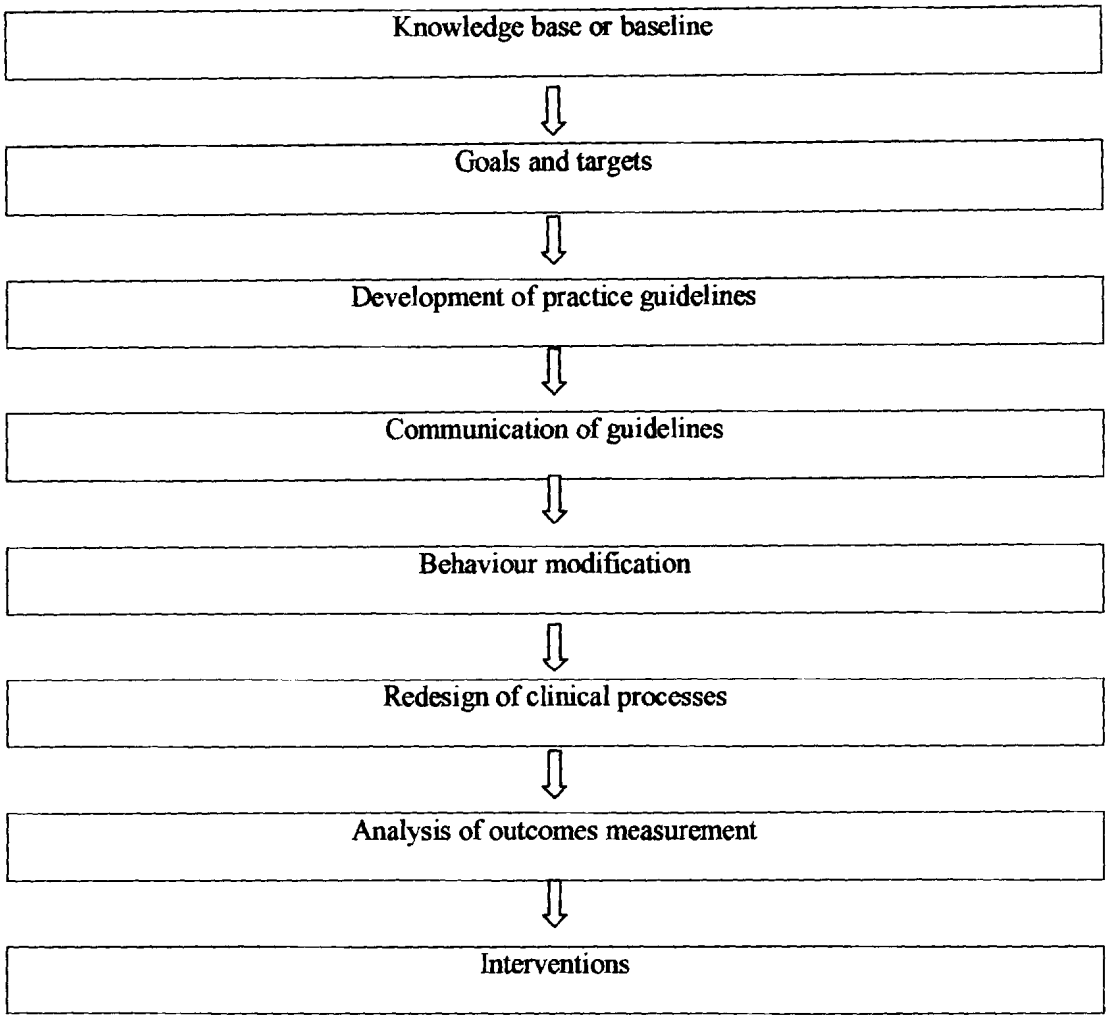

Figure 3.1

The disease management process (Hunter & Fairfield, 1997: 51)

3.3.6 Disease management programs: interventions

According to Armstrong (1999: 593) disease management (DM) programs have become common in health systems, especially in managed care organizations and hospitals. These programs are designed to improve the quality of care and the efficiency of health care delivery and their interventions are: developing educational material for the dissemination of treatment guidelines to primary care and specialty physicians, creation of marketing initiatives within the health system, especially in managed care organizations and assessment of drug formulary products.

3.3.6.1 Application of disease management programs in antimicrobial use

Wert (1996: 1368) reported in a study protocols that were built around eight infectious disease states: tonsillitis/pharyngitis, acute sinusitis, otitis media, bronchitis, urinary tract infections, cellulites and pneumonia. It was recognized that second-line antibiotics were often prescribed when more economic first-line antibiotics would be more effective. There was need to shift attention back to first-line antibiotics.

3.4 Pharmacoepidemiology

3.4.1 Introduction

Pharmacoepidemiology is a relatively new field of study, with concepts, methods and applications that have made increasing contributions to health care as the field has evolved over the past few decades (Einarson *et al* as referred to by Truter, 1999:54). The need for pharmacoepidemiology is increasing, both in developed and in developing countries (Van Boxtel & Wang, 1997: 205).

3.4.2 Definition and scope of pharmacoepidemiology

Pharmacoepidemiology is the study of the use and effects of drugs in large numbers of people, and its need is increasing exponentially both in developed and in developing countries (Van Boxtel & Wang, 1997: 205). According to Porta & Tilson (as referred to by Truter, 1999: 54), pharmacoepidemiology, is the application of epidemiological reasoning, methods and knowledge to the study of the uses and effects (beneficial and adverse) of drugs in human populations. Pharmacoepidemiology therefore aims to describe, explain, control and predict the uses and effects of pharmacologic treatments in a defined time, space and population (Truter, 1999: 54; Truter *et al.*, 2001: 25).

The term pharmacoepidemiology contains two components, namely "pharmaco" and "epidemiology". The core of pharmacoepidemiology lies at the intersection of clinical pharmacology and clinical epidemiology. It is a relatively new applied field, bridging

clinical pharmacology and epidemiology (Truter *et al*, 2001: 27). From clinical pharmacology, pharmacology borrows its focus of inquiry. From epidemiology, pharmacology borrows its methods of inquiry. In other words, it applies the methods of epidemiology to the context area of clinical pharmacology (Truter, 1999: 54).

Pharmacoepidemiology is a new bridge science drawn from the disciplines pharmacology, therapeutics, epidemiology and statistics. Not only does it have a long and cumbersome name, but it is not a clearly demarcated field. It is best characterized by its spans, its overlaps or even by its incursions rather than its borders (Spitzer & Bruppacher, 1996: 364).

3.4.3 Pharmacoepidemiological methods

Pharmacoepidemiology, as mentioned previously, applies the methods of epidemiology to the context area of clinical pharmacology. The methods used in pharmacoepidemiology involve both analytical (that is quantitative) and descriptive (that is qualitative) approaches. Descriptive approaches are aimed at evaluating how drugs are being prescribed and used, and may be used as part of a quality assurance programme. They can thus be directly linked to a disease management and an evidence-based medicine approach, where the focus is also on quality assurance and quality improvement (Truter, 1999: 56).

3.4.4 Pharmacoepidemiological study designs

Pharmacoepidemiological studies utilize experimental as well as observational study designs. These include: experimental studies, such as randomized controlled trials (RCT) (clinical trials, intervention studies) and observational studies such as cohort, case-control and correlation studies (Strom, 1994: 15).

3.4.4.1 Randomized controlled trials

Experimental studies can be performed in humans, where experiments are carried out in a hospital setting with patients (clinical trials) or with healthy individuals in the population to study, for example health effects of dietary changes (intervention studies). This study

type, generally designed as a randomized controlled trial (RCT), allows conclusions regarding whether a measure affects the disease rate directly or should be considered as a marker of another underlying cause affecting disease risk (Van Den Brandt *et al.*, 2002: 319). Experiments are said to be "controlled" when an untreated group or group treated according to a standard method in involved, with the aim of controlling changes in disease incidence occurring independently of changes of exposure.

3.4.4.2 Observational studies

Observational studies, by definition, do not involve intervention and randomization; have a major role in providing evidence on the association between dietary exposure and health effects. Two different types of observational studies can be distinguished: cohort or follow-up studies and case-control studies (Waning & Montagne, 2001: 49).

3.4.4.2.1 Cohort studies

Cohort studies start with a population initially free of the health outcome under study. Exposure is assessed at the start of the study (and is sometimes assessed several times during follow-up) and may include (besides questionnaire/interview data), the collection of biological materials. During *follow-up*, some subjects develop the disease (or other health outcome) and others do not. The risk of developing the disease (defined as cumulative incidence) is related to the exposure, and is generally expressed in terms of *relative risk* or *relative rate*. The main advantage of the cohort design is that at entry, subjects are free of the disease in question. Therefore, the disease will not influence exposure of the subjects (Truter, 1999: 61).

3.4.4.2.2 Case-control studies

In contrast to cohort studies, case-control studies start with a group of patients, or persons known to have the disease or condition. These cases are compared with a control group, selected to represent the population from which the cases arose with respect to the exposure of interest. The exposure information is collected concerning a defined time prior to diagnosis of the disease. An advantage of case-control studies compared to the cohort design is that no long follow-up period is required to obtain the results. Secondly,

for rare diseases, a much smaller sample size is needed, while the odds ratio is a very close approximation of the relative risk. A main disadvantage of this study design is that the disease can influence exposure information by the subjects ("recall bias") or recent exposure really is different from what is used to be , because of the disease (Van Den Brandt *et al.*, 2002: 392).

3.4.4.3 Prospective versus retrospective studies

The word prospective and retrospective often is used to indicate cohort and case-control designs, respectively. In general, prospective studies can be defined as those in which exposure and covariate assessments are made before the cases of illness occur. In a retrospective study these assessments are made after the cases have already occurred. A cohort study can be retrospective when the cohort is identified and assembled on the basis of information recorded in the past and "followed up" to the present time. A case-control study can be prospective by using exposure data that are collected before the diagnosis of disease (Strom, 1994: 25).

3.4.5 Application of pharmacoepidemiological methods in antimicrobial use

A prospective observational cohort study was enrolled in adults and children having acute diarrhea to 1 of 10 academic emergency departments. The objective of the study was to evaluate factors emergency physicians consider in prescribing antibiotics to patients with diarrhea. A conclusion was drawn that physicians in emergency departments were more likely to prescribe antibiotics for diarrhea because they wanted to meet patient expectations, even when antimicrobials were unnecessary (Karras *et al.*, 2003: 535).

Respiratory infections place a heavy burden on patients, providers, employers and health care systems. A retrospective analysis on the economic effect of treating respiratory tract infections with broad-spectrum antibiotics was done. Six managed care health care plans by means of health care claims were used. The results revealed that the costs of treating chronic bronchitis, pneumonia, and acute sinusitis with moxifloxacin, gatifloxacin and nonfluoquinolone broad-spectrum agents were significantly lower that the costs associated with levofloxacin treatment (Coughlin *et al.*, 2003: 34).

In spite of the knowledge that an upper respiratory tract infection (URTI), popularly known as the common cold, is viral in origin, there is evidence that many patients visiting general practitioners receive antibiotics, regardless of efficacy (Wang *et al.*, 1999: 156).

Arrol and Goodyear-Smith (2000: 493) randomly selected in a study 179 general practitioners from a list of Auckland-based practitioners with the aim of assessing general practice description and management of upper respiratory tract infections (URTIs), including conditions under which they prescribe antibiotics. The general practitioners interviewed agreed that most patients presenting with URTI expected antibiotics. These results suggest over-prescribing of antibiotics.

In developing countries, antibiotics are the most common drugs sold, and some data suggest that they are frequently misused. In order to describe the pattern of antibiotic use in a periurban community in Mexico City, 1679 households were randomly-selected in order to describe the pattern of antibiotic use. The results suggest that antibiotics were frequently misused and they support the need to assess the determinants of self-medication, health–seeking behavior and physician prescribing practices. The need for effective educational programs to improve prescribers' decisions is stressed (Calva, 1996: 1121).

An interventional study was performed after assessing the appropriateness of the observed antibiotic prescribing practices using a quasi-experimental study (Perez *et al.*, 2003: 1013). An application of interrupted time series intervention analysis was conducted in three antibiotic groups (aminoglycosides, cephradine/cephalothin, and ceftazidime/cefotaxime) and their hospital weekly rate of incorrect prescriptions before and after the intervention. A conclusion was drawn that a structured antibiotic order form, coupled with graphic and educational intervention, could improve antibiotic use in a university hospital.

Fluconazole is beneficial to HIV/AIDS patients presenting with opportunistic infections like cryptococcal meningitis and oesophageal candidiasis. A retrospective analysis was done of the prescriptions dispensed for fluconazole at Umtata General Hospital pharmacy (South Africa) during a period of one year. The results of the study showed that most prescribers (78%) do not follow the recommended guidelines on the use of fluconazole

and that better information should be disseminated regarding the use of fluconazole in HIV/AIDS patients (Katende-Kyenda & Dambisya, 2003: 65).

3.5 Drug utilisation

3.5.1 Introduction

There are more effective drugs on the market today than ever before. Patients are better educated, have greater expectations from health care and frequently use multiple sources of health care. Yet, drugs are frequently not used to their full potential, or according to generally accepted criteria. All prescribing is not necessarily based patient needs and all patient needs are not necessarily met with drug therapy. Consequently, there is as much concern about inappropriate and expensive prescribing, as there is about under-prescribing. Therefore the development of drug utilisation as a research area made it possible to study drug prescribing and drug usage in scientific and formal manner (Truter, 2001: 3).

3.5.2 Overview of drug utilisation

Medicines are part of everyday life. Yet frequently little is known about how many drugs people take, what sort of drugs are taken, how much the drugs cost, who influences the way drugs are taken and how the drugs are actually taken. Drug utilisation aims to answer these questions (Truter, 2001: 3).

3.5.3 Definition of drug utilisation

Drug utilisation studies are an important application of pharmacoepidemiology. Drug utilization has been defined as "the prescribing, dispensing, administering and ingesting of drugs" (Serradel *et al.*, 1987: 994). The World Health Organization (WHO) expands on this definition by including outcome variables. Drug utilisation is defined by the WHO as: "the marketing, distribution, prescription, and use of drugs in society, with special emphasis on the resulting medical, social, and economic consequences" (Serradell *et al.*, 1987: 994). Tognoni (as referred to by Serradell *et al.*, 1987: 994) stressed the importance of these outcomes by noting that the point of observation in drug utilisation studies is the

act of prescribing the drug, and that quantitative data need to be obtained on the extent and variability in use and costs of drug therapy, from which medical and social qualitative consequences can be extrapolated (Truter, 1999: 68).

3.5.4 Goals of drug utilisation studies

Drug utilisation data are used for a wide variety of pharmacoepidemiologic inquiries and studies, including the use rate for a class of drugs, estimates of the population at risk for the use of a defined casual agent, prescribing rates as an indicator of the prevalence of a non-reportable disease, quantification of the incidence of utilisation drug evaluations (UDEs) and evaluation of shifts in prescribing patterns to document secondary indications for labeling purposes (Bjornson *et al.* as referred to by Truter, 1999: 69).

In general, the following goals of drug utilisation studies can be identified:

- A description of the patterns of drug use in specific populations.
- The identification and definition of likely problems.
- A general analysis of the problem with regard to its importance, cause and consequence.
- The establishment of a weighted basis for decisions on problem-solving, and
- The assessment of the effects of the action taken (Bjornson *et al.* as referred to by Truter, 1999: 69).

3.5.5 Drug utilisation review: Concept

The concept of drug utilisation review was initially developed in hospitals to assess how well drugs were being used. Drug utilisation review (DUR), also referred to as drug utilization evaluation (DUE), is an effective tool for monitoring the appropriateness of physician' prescribing patterns (Olson, 2003: 255). As stated by Spector (2004: 284) drug utilization review allows health care providers to review patient care from perspectives of medical necessity, quality of care, appropriateness of decision-making, place of service, and length of hospital stay.

3.5.6 Drug utilisation review study

Drug utilisation review study is "*an authorized, structured process that reviews, analyzes, and interprets the pattern of drug use in a given healthcare delivery system in relation to explicitly predetermined criteria, guidelines or standards.*" A drug utilisation program introduces educational or regulatory interventions to improve patterns of drug use that are inconsistent with accepted standards of appropriateness (Spooner *et al.*, 1999: 1952).

3.5.7 Types of drug utilisation reviews

There are three broad categories of drug utilisation review namely, retrospective studies, concurrent reviews, and prospective reviews.

3.5.7.1 Retrospective studies

A retrospective drug utilisation study is an approved, systematic process that captures, reviews, analyses, and interprets aggregate medication use data within a specific health care environment. The data are archival in nature. Data are thus collected and analyzed after the events of major interest (the prescription, dispensing, and use of drugs) have occurred (Truter, 2001: 9).

Retrospective drug utilisation review involves assessment of prescription claims after a medication has been dispensed. This type of DUR can be used primarily to describe the medication utilisation of patients and/or the prescribing practices of physicians (Olson, 2003: 256). Retrospective DUR may include interventions, such as mailed letters to prescribers or physician report cards that compare individual physician prescribing patterns with those of a peer physician group (Smith *et al.*, 1998: 1013; Collins *et al.*, 1997: 472). Studies have documented positive effects of retrospective drug utilisation review (rDUR), including reductions in targeted medication use and medication expenditure following an intervention (Collins *et al.*, 1997: 473; Smith *et al.*, 1998: 1014). Retrospective studies are relatively inexpensive, can be conducted rapidly and have easily accessible data (Truter, 2001: 9).

3.5.7.2 Concurrent reviews

Concurrent drug utilisation reviews take place during the period when patients and drug dispensers interact; thus the responsibility of review rests with the pharmacist (Guo *et al.*, 1995: 1175). If a potential problem is discovered, the dispensing function comes to a halt until authorization is received to continue as before or to initiate a modification or dosage correction. These reviews thus prevent therapeutic misadventures. These reviews are more expensive and time consuming than retrospective, but have the potential for much greater pay-offs in preventing problems (Truter, 2001: 10).

3.5.7.3 Prospective reviews

Prospective review is the option closest to the ideal and is a more complete review than a concurrent review. Use of prospective review, based upon a complete drug and medical history obtained from an interview and from historical records, permits the practitioner to evaluate the patient's pre-exiting therapy on a retrospective basis, and prevents interactions by disallowing certain drugs for a patient on the basis of a pre-existing review and by protocols already developed (Truter, 2001: 10). The primary criticism of prospective drug utilisation review programs is the lack of consistency among the criteria used in the development process. These criticisms stem from discrepancies in the scientific literature from which drug-related problems are defined (Soumerai & Lipton, 1995: 1641; Sacristan & Soto, 1994: 300). Other problems associated with prospective drug utilization review (pDUR) include the limited ability to identify underutilisation of essential medications and inappropriate refill denials (Somerai & Lipton, 1995: 1642).

3.5.8 Types of drug utilisation studies and their uses

3.5.8.1 Quantitative

The objective of quantitative study is to quantify the present state, the developmental trends, and the time course of drug usage at various levels of the health care system, whether national, regional, local, or institutional. Routinely compiled drug statistics or drug utilization data that are the result of such studies can be used to estimate drug

utilisation in populations by age, sex, social class, morbidity, and other characteristics, and to identify areas of possible over- or under-utilisation (Lee & Bergman, 1994: 380).

3.5.8.2 Qualitative

These studies assess the appropriateness of drug utilisation, usually by linking prescription data to the reasons for the drug prescribing. Explicit predetermined criteria are created against which aspects of the quality, medical necessity, and appropriateness of drug prescribing may be compared. Drug use criteria may be based upon such parameters as indications for use, daily dose, and length of therapy. Studies like extent of inappropriate prescribing of drugs, in particular antibiotics and the associated adverse clinical, ecologic, and economical consequences can be carried out (Lee & Bergman, 1994: 380).

3.5.9 Drug utilisation reviews of antimicrobial agents

Concern exists regarding the increasing and often inappropriate use of antimicrobial agents. In promoting rational prescribing of optimal antibiotic therapy, health care providers are interested in: ensuring high-quality patient care (promoting healing, avoiding duplication of prescribing, and minimizing drug-related problems (Hoppe, 1996a: 552); curtailing the development of resistant strains of bacteria (Schmader *et al.*, 1994: 1241); and controlling costs.

The following are examples of drug utilisation studies done on antimicrobials

Prescribing patterns of Quinolones (Ciprofloxacin)

Drug utilisation review studies (Hill, 1990: 1120; Lewis, 1996: 694; Pickering *et al.*, 1994: 288; Rovers and Bjornson, 1994: 714) focused solely on the level of appropriateness of prescriptions for ciprofloxacin. The intent to calculate a pooled, weighted mean estimate of appropriate use by applying statistical procedures common to meta-analysis was considered but was considered inappropriate because of heterogenicity in the prescription selection methods, inclusion criteria, measuring instruments applied, and data analysis methods.

Prescription patterns of cephalosporins

Lewis (1994: 694) conducted a drug usage evaluation (DUE) of ciprofloxacin in adult outpatients during a 3-year period in the United States. The results of the study revealed that not all physicians were following rational step prescribing. The outcome of this DUE indicated that an education effort aimed at prescribers to shift the trend of oral ciprofloxacin prescribing to alternative antibiotics. This could reduce the potential for ciprofloxacin resistance developing.

The use of erythromycin with other study drugs was analyzed by De Santis *et al.*, (1994: 502). Discrete erythromycin use was reported, and this DUE determined that 40% of the prescriptions were appropriate (6 of 15 prescriptions).

Prescription of third-generation cephalosporins for upper respiratory tract infections in the Port Elizabeth area

Haupt *et* al. (2002: 275) in a review of cephalosporin prescriptions indicated that these antibacterials were being prescribed in the following ratio to patients in Port Elizabeth, South Africa: first-generation 43%, second-generation 27%, and third generation 30%. This appeared to be in contradiction to the general observation that first-generation cephalosporins are not considered the primary choice for upper respiratory tract infections (URTIs) and other community-acquired infections.

The use of antimicrobial drugs in Nagpur, India

The objective of the study was to determine the patterns of use of antimicrobial drugs in the general population of the large, industrial city of Nagpur, India. Interviews of pharmacists and clients were carried out in a stratified, random sample of 34 pharmacies to determine beliefs and practices in prescribing and self-prescribing of antibiotics by complaint, choice of drug, duration, cost, age and sex of the consumers. The results of the study showed that drugs were dispensed without prescriptions despite prohibition by the Indian Pharmaceutical Act. Proprietary brands of penicillins, co-trimoxazole and tetracyclines were dispensed most often (64.8%) for the common conditions which were

upper respiratory infections, gastrointestinal and nonspecific complaints. The dispenser viewed himself as a businessman rather than a professional and rarely offered unsolicited advice (Dua *et al.*, 1994: 717).

Analysis of antimicrobial agents in private practice in South Africa

Antimicrobial agents are extensively used in medical practice and account for a greater portion of the health system budget. The objective of this study was to establish if there is appropriate usage and cost-effectiveness of these agents in private practice. The results revealed a low % (10.4) of generic prescribing, more drugs being prescribed for medical aid compared to cash patients, and many prescriptions being incomplete. The study highlighted the need to sensitize private practitioners on the safe use of antimicrobials in line with accepted guidelines (Katende-Kyenda *et al.*, 2002: 55).

Usage of antimicrobial agents in a private primary health care setting

Antimicrobials are the most commonly prescribed group of drugs, contributing significantly to the cost of drugs and are claimed worldwide to account for 15% to 30% of the total health budget (Rehana *et al.*, 1998: 175), yet usage of these agents in private primary health care settings is not known. A retrospective, drug utilization study was done on the antimicrobial usage in a private primary health care setting in South Africa for a period of one year. The results showed a high incidence of consultations where antimicrobials (68.9%) were prescribed. This could indicate excessive use of these agents in the private primary health care setting. Also, antimicrobials were prescribed for viral diseases where they do not produce a primary action. Recommendations were made for further investigations to be done on the prescribed protocols of the usage of antimicrobials (Katende-Kyenda *et al.*, 2003: 25).

An investigation on rational use of antibiotics in ten district hospitals in Mashonaland province in Zimbabwe

A retrospective study was done on the rational use of antibiotics in in-patients in district hospitals in Mashonaland, over a period of months (Chikerema & Kasilo, 1994). The results of the study revealed that in all, 99 prescriptions (16.5%) were irrationally

prescribed and 85.86% of these were irrationally indicated and the remainder irrational due to incorrect dosing. A conclusion was drawn that antibiotics were being prescribed irrationally in district hospitals in Mashonaland in Zimbabwe.

Are antimicrobials appropriately used in private primary health care settings in South Africa?

The use of antimicrobials in developing countries is reported to be inappropriate in 20% to 60% of cases. This could be due to: the use of multiple antimicrobials, non-use of first choice of antimicrobials on the basis of provincial diagnosis and the use of irrational and unnecessary antimicrobials. A retrospective drug utilization study (Katende-Kyenda *et al.*, 2003: 16) was done on data obtained from the database of a private primary health care group to determine if antimicrobials are used appropriately in the different diagnoses in private primary health care settings in South Africa. High percentage of antimicrobials (76%) use obtained as compared to 20% to 60% of the results reported by Rehana *et al.* (1998: 175) could indicate that these agents are inappropriately used in developing countries. Therefore the prescribing of antimicrobials in the different diagnoses would indicate overuse of these agents. Amongst the commonest diagnoses presented where antimicrobials were prescribed was acute bronchitis where antibiotics have no primary effect. It was recommended that further investigation be done on the treatment guidelines and antimicrobial guidelines.

3.6 Pharmacoeconomics

3.6.1 Introduction

Pharmacoeconomics is a second important application of pharmacoepidemiology. Corresponding to awareness by the public of rising health care costs has been an increased interest in evaluating drugs' economic as well as clinical benefits (McCloskey, 2001: 143). This interest is readily apparent by the steady growth in the number of pharmacoeconomical studies published in the primary literature since the mid-1999s (Johnson & Coons as referred to by McCloskey, 2001: 143).

Pharmacoeconomics is the area of health care research that evaluates and compares the costs and outcomes associated with drug therapy, and play an increasingly important role in making decisions concerning options regarding drug therapies and pharmaceutical services (Truter *et al.*, 2001: 143; Paladino, 1999: S25).

3.6.2 Perspective of a pharmacoeconomical study

The perspective of a pharmacoeconomical study is the point of view from which it is conducted. A study may be performed from the perspective of a hospital or another health care provider, a payer, a patient, or society in general (Waning & Montagne, 2001: 147).

3.6.3 Pharmacoeconomical study designs

There are four types of pharmaocoeconomical studies that differ in how the outcomes are valued.

3.6.3.1 Cost-minimization analysis (CMA)

This is the most basic of the research methodologies (Freund & Dittus, 1992: 22). It simply compares the cost of two or more alternatives, assuming equal outcomes of each alternative are evaluated. This type of methodology requires that the outcome of the alternatives being evaluated is identical in all aspects, which is often very difficult to demonstrate. For this CMA to be valid, the duration of treatment, efficacy, and toxicity all must be the same for both drugs (McCloskey, 2001: 147; Malek, 1996: 4).

3.6.3.2 Cost–benefit analysis (CBA)

In contrast to a cost-minimization analysis (CMA), in a cost-benefit analysis, the outcomes of the alternatives being studied are not considered to be equal (Malek, 1996: 5). In a CBA, both the costs and the outcomes (benefits) of the alternatives are measured in monetary unit. Whereas a CBA is of limited value in comparing drug therapies, it can be a useful tool that administrative decision makers can use for evaluating the value of

existing services as well as projecting the potential benefits of a proposed service (McCloskey, 2001: 148; Freud & Dittus, 1992: 24).

3.6.3.3 Cost-effectiveness analysis (CEA)

In cost-effectiveness analysis (CEA), the outcomes of the alternatives are not measured in monetary units, but rather in natural or physical units. Although a cost-minimization analysis (CMA) does not assume equal outcomes, it should compare alternatives with similar objectives (e.g. prevention or treatment of same disease). A CEA is primarily used when decisions concerning the relative costs and benefits of alternative therapies are not apparent (McCloskey, 2001: 149; Malek, 1996: 6; Freud & Dittus, 1992: 22).

3.6.3.4 Cost-utility analysis (CUA)

A cost-utility analysis (CUA) is similar to a CEA, but the measured outcomes take into account patient health preferences, or "utilities." Outcome are measured as quality-adjusted life years (QALYs) which consider the fact not each year of life gained from a therapy is valued by a patient equally (McCloskey, 2001: 153; Freud & Dittus, 1996: 23; Malek, 1992: 7).

3.6.5 Pharmacoeconomics of antimicrobial therapy

Pharmacoeconomic analysis of antimicrobials is a relatively recent outgrowth of health economics precipitated by increasing cost controls and an abundance of pharmaceutical products. The value of pharmacoeconomics in determining the cost-effectiveness of a particular therapeutic regimen has grown as institutions seek ways to manage increasing treatment costs (Cooke, 1994: 289). Any measures to increase cost-effectiveness should include improvements in patients' outcome. Examples include individualized therapies to reduce the duration of treatment and therapies that accelerate the rate of bacterial eradication (Paladino, 1999: S25).

Use of pharmacoeconomics in antibiotic treatment

As a result of the large number of infectious diseases and the numerous types of antibiotic treatment available, analyses which can take global prescription criteria into account are required. The pharmacoeconomics of antibacterial treatment is a decision-making tool, as in any other therapeutic field. The ecological implications of treatment for the individual and for society should be considered when assessing the cost and consequences of antibacterial treatment. The development of pharmaco-economics as a decision-making tool should enable the practitioner to prescribe the right antibiotic therapy to the right patient, at the right time (Beresniak & Bouvenot, 2000: 133).

Pharmacy database for tracking drug costs and utilisation

Accurate information on drug costs and utilisation is required for reporting physician prescribing trends, conducting clinically relevant drug-use evaluations and target–drug intervention activities. Chaffee *et al.* (2000: 669) described a pharmacy database for tracking drug costs and physician prescribing trends in the United States of America. Development of a database for tracking drug costs and utilisation allowed a teaching hospital to derive the cost of medications from billing-charge information and to report data to health care professionals on the basis of important facto like clinical service.

Cost of broad-spectrum antibiotic use for acute sinusitis, chronic bronchitis, and pneumonia in a managed care population

Respiratory infections place a heavy burden on patients, providers, employers and health care systems. The economic effect of treating respiratory tract infections with broad-spectrum antibiotics was retrospectively analyzed by means of health care claims data from six managed care health plans in Unites States of America. The costs of treating chronic bronchitis, pneumonia, and acute sinusitis with moxifloxacin, gatofloxacin and nonfluoroquinolone broad-spectrum agents were significantly lower than the costs associated with levofloxacin treatment (Coughlin *et al.*, 2003: 34).

Influence of an infectious disease consulting service on quality and costs of antibiotic prescriptions in a university hospital

In many countries, infectious disease specialists are assisting physicians to diagnose and treat serious infections. Especially in the case of nosocomial infections, the emergence of bacterial resistance has made treatment more difficult and sometimes even impossible (Lemmen *et al.*, 2001: 219). About 30% to 40% of patients in hospitals receive antibiotics and these drugs are among the most expensive medications prescribed by hospitals. The aim of the study was to assess and optimize the quality of antibiotic usage. In addition, the cost reduction was documented to calculate the cost-effectiveness of implementing an infectious disease consulting service in Germany. The data obtained showed that an infectious disease consulting service optimizes antibiotic usage, and is cost-effective as a result of a significant cost reduction in hospitals, while not interfering with the quality of medical care (Lemmen *et al.*, 2001: 220).

Antimicrobial expenditure and usage at four university hospitals

The increasing use of antimicrobial drugs is resulting in enormous hospital expenditure. Careful assessment of inappropriate prescribing and a search for more cost-effective treatment strategies are urgently required. Antimicrobial usage and expenditures at four state university hospitals in Southwestern Germany was done by Kern *et al.* (2001: 127). In two hospitals, the lowest expenditures in either surgery or medicine were associated with active antimicrobial drug use programs suggesting an impact of these programs on drug use and expenditures limited to these services.

Economic justification of antimicrobial management programs: implications of antimicrobial resistance

Antimicrobial drug management in America typically centered on two initiatives: controlling costs and controlling antimicrobial resistance. According to Paladino (2000: S10), selection of therapeutic alternatives without adherence to a well-developed program, or without a rationale based on data from the medical literature, may promote antimicrobial resistance. Attempts to select alternatives can produce cost shifting rather than cost containment. Antimicrobial management programs should be directed at

ensuring the most appropriate use of antimicrobials rather than focusing on limiting choices.

Approaches to drug therapy, formulary, and pathway management in a large community hospital

Health care institutions are challenged by increases in resistance to traditional antimicrobial therapies. Patients with community-acquired pneumonia (CAP) are often treated empirically before culture and susceptibility data are available, and the risk of infection with drug-resistant or multidrug-resistant organism is an important consideration in antimicrobial prescribing (Bartlett *et al.*, 1998: 811). The study analyzed use of a clinical pathway for the management of community-acquired pneumonia (CAP) at a large community hospital in the United States of America, was described. Fluoroquinolone therapeutic interchange and intravenous to oral conversion were part of the pathway. Levofloxacin was chosen as the preferred quinolone. Pharmacists' interventions in antimicrobial prescribing for CAP patients can lead to cost efficiency and positively affect patient outcome (Halley, 2000: S517).

Cost-effectiveness of sparfloxacin compared with other oral antimicrobials in outpatient treatment of community-acquired pneumonia (CAP)

In another study, the cost-effectiveness of commonly prescribed antimicrobials for outpatient treatment of CAP was compared (Najib *et al.*, 2000: 461). One of the selected drugs was sparfloxacin, which is approved for this indication in the United States. Their findings suggest that sparfloxacin for managing CAP is cost-effective relative to other commonly prescribed antibiotics. Sparfloxacin has a better efficacy and costs less than the other drugs.

Outcomes of antimicrobial control program in a teaching hospital

Health care institutions generally strive to promote cost-effective antimicrobial therapy and delay the emergence of antimicrobial resistance. These goals are often sought by establishing antimicrobial control programs (ACPs), placing restrictions on costly broad-spectrum antimicrobial agents, or both (Lesar & Briceland, 1996: 31).

Clinical outcomes and cost-effectiveness of an antimicrobial control program (ACP) were studied in the US. The results of the study revealed that an ACP directed by a clinical pharmacist trained in infectious diseases was associated with improvements in in-patient length of stay and mortality. The ACP decreased intravenous antimicrobial costs and facilitated the approval process for restricted and non-formulary antimicrobial agents (Gentry *et al.*, 2002: 411).

3.7 Chapter summary

In this chapter, health care concepts and approaches were discussed in terms of: primary health care, managed care, disease management, pharmacoepidemiology, drug utilisation and pharmacoeconomics.

The application of the health care concepts to antimicrobials use can be summarized as follows:

Antibiotics are the most commonly used categories of drugs in modern medicine, and primary health care represents the first tier of the health care system. Therefore, to ensure rational use of antimicrobials, it is necessary to evaluate the usage of these agents in primary health care settings.

In this study, the nature of the private primary heath care clinic group used, Prime Cure, uses protocols and treatment guidelines that are in line with the guidelines of the Cochrane Collaboration Database which is evidence-based.

Antimicrobials contribute significantly to the cost of drugs accounting for 15% to 30% of the total health budget worldwide (Rehana *et al.*, 1998: 175). Managed care through managed care organizations will maintain low costs and have stable predictable expenditures on antimicrobials.

Disease management, through its goal of creating population-based, integrated approaches to the provision of care, will also provide ongoing, cost-effective antimicrobial treatments.

Pharmacoepidemiological descriptive approaches are aimed at evaluating how antimicrobials are being prescribed and used, so as to ensure quality assurance programmes.

Drug utilisation as an application of pharmacoepidemiology, its data can be used to review, analyse, and interprete the pattern of antimicrobials use in specified population.

Pharmacoeconomics as a second application of pharmacoepidemiology, its development in antibacterial treatment, is a decision-making tool that enables the practitioners to prescribe the right antibiotic therapy to the right patient, at the right time, and at the most cost-effective manner.

Research methodology will be discussed in Chapter 4.

CHAPTER 4 RESEARCH METHODOLOGY

4.1 Introduction

In this chapter the research methodology will be discussed.

4.2 Research objectives

The research embodies a general research objective with accompanying specific objectives.

4.2.1 General research objective

The general research objective being an analysis and interpretation of the usage and costs associated with the prescribing of antimicrobials in a private primary health care setting in South Africa.

4.2.2 Specific research objectives

The specific research objectives of the literature study (Phase1) are:

- investigate from the literature the usage and prescribing patterns of antimicrobials ;
- determine from the literature what antimicrobial resistance is and its causes are;
- investigate infectious diseases and treatment thereof;
- conceptualise primary health care, its aims and objectives; and
- conceptualise managed health care, disease management, pharmaco-epidemiology, pharmaco-economics and drug utilisation studies as applied to antimicrobials.

The specific research objectives of the empirical study (Phase 2) are:

- determine the prevalence of patients who received antimicrobials in a private primary health care setting;
- determine the prevalence and cost of prescriptions of antimicrobials in a private primary health care setting;

- investigate the influence of age on the prescribing of antimicrobials in a private primary health care setting;
- investigate the influence of gender on the prescribing of antimicrobials in a private primary health care setting;
- investigate the prescribing of antimicrobials and their costs for the different diagnoses;
- determine the use of antimicrobials according to the diagnosis;
- determine if antimicrobial usage in the private primary health care setting was according to the standard treatment guidelines and essential drugs list for South Africa; and
- formulate recommendations regarding the usage of antimicrobials for the different diagnoses.

4.3 RESEARCH METHODOLOGY

The research method of the research project consisted of the following phases:

Phase 1: The literature review:

A literature review has been undertaken to gain the necessary information relating to the study. The specific objectives of the empirical research guided the literature review. The literature review discussed antimicrobials in terms of patterns of usage, whether rational or irrational and the possible causes thereof. Antimicrobial resistance and its causes have been also investigated from the literature. The incidence of infectious diseases in South Africa and the treatment thereof has been discussed.

The last discussion was on health care concepts such as primary health care, managed care, disease management and drug utilisation studies and the application of these concepts to antimicrobials.

Phase 2: The empirical investigation:

The research method of the empirical investigation consisted of several steps, namely:

- The selection of the research design.
- The composition of the research population.
- The selection and application of the criteria and measuring instruments for data analysis.
- Data application and data analysis.
- Reliability and validity of the research instruments.

- The report and discussion of the results of the empirical investigation.
- The conclusions and recommendations based on the results of the empirical investigations as well as the limitations of the study.

4.4.1: Aspects of pharmacoepidemiology, drug utilisation review and pharmacoeconomics used in the empirical study

The aspects of pharmacoepidemiology, drug utilisation review and pharmacoeconomics that were used in the empirical study will be summarized in Table 4.1.

Table 4.1: Aspects of pharmacoepidemiology, drug utilisation review (DUR) and pharmacoeconomics used in the empirical study.

Aspect	Description	Reference
Pharmaco-epidemiology	Aims to describe, explain, control and predict the uses and effects of pharmacologic treatments (Truter, 1999: 205).	Refer to: (3.4.2)
Methods	Retrospective: patterns of drug use were determined after the drug had been dispensed (Strom, 1994: 25).	Refer to: (3.4.4.3)
	Non-experimental: non- involvement of any interventions or any follow-ups (Waning *et al.*, 2001: 49).	(3.4.4.2)

Table 4.1: Aspects of pharmacoepidemiology, drug utilization review (DUR) and pharmacoeconomics used in the empirical study (cont).

Aspect	Description	Reference
Drug utilisation review (DUR)	Description of the patterns of drug use in specific populations (Bjornson as referred by Truter, 1999: 54). An introduction of educational or regulatory interventions to improve patterns of drug use consistent with accepted standards of appropriateness (Spooner *et al.*, 1999: 1952).	Refer to: (3.5.4) (3.5.6)
DUR studies	Retrospective – data are collected and analyzed after the events of major interest (prescription, dispensing, and use of drugs) have occurred (Truter, 2001: 9; Olson, 2003: 256).	Refer to: (3.5.7.3)
	Quantitative–estimate drug utilisation in populations by age and sex to identify areas of possible over- or under-utilization (Lee & Bergman, 1994: 380).	Refer to : 3.5.8.1
Pharmaco-economics	Evaluates and compares the costs and outcomes associated with drug therapy (Paladino, 1999: 525).	Refer to : (3.6.2)
Pharmaco-economic studies	Cost–benefit analysis (CBA): both the costs and outcomes (benefits) of the alternatives are measured in terms of monetary units (McCloskey, 2001: 148).	Refer to: (3.6.4.2)

4.4.2 Research design

The specific objectives of the empirical study (Phase 2) were to review, analyse and interpret patterns of drug utilisation as well as to analyse the costs associated with the prescribing of antimicrobials in a private primary health care setting. The patterns of drug utilisation were determined after the drug had been dispensed. The study did not include intervention activities or any follow-up measures to ascertain whether any changes in drug therapy have occurred. Thus, the research design can be classified as a non-experimental quantitative, retrospective drug utilisation study (Truter, 2001: 9).

4.4.3 The data source used for the empirical study (Phase 2)

The data utilised in this research project were obtained from the central database of a private primary health care service provider namely Prime Cure® Medicentres.
During the research period 42 clinics were operational. Data from 33 clinics were electronically available. Nine clinics that had been in operation for at least one year were randomly selected from the 33 clinics. Data of the selected nine clinics were extracted for the period 1st January to 31st December 2001. The Statistical Analysis System® SAS 8.1®. (SAS Institute Inc., 1999-2000) was used to analyse the data.

4.4.3.1 The database

In creating the database for study purposes, data were extracted and copied from the central database of the private primary health care setting onto diskettes in text format. It was then imported to SAS 8.1® computer package for Windows (SAS for Windows 8.1, 2000).

A schematic representation of the basic structure of the database is given in Figure 4.1. Due to the extent of the database; only the files and fields used in this study will be discussed. Figure 4.1 demonstrates a schematic layout of the database:

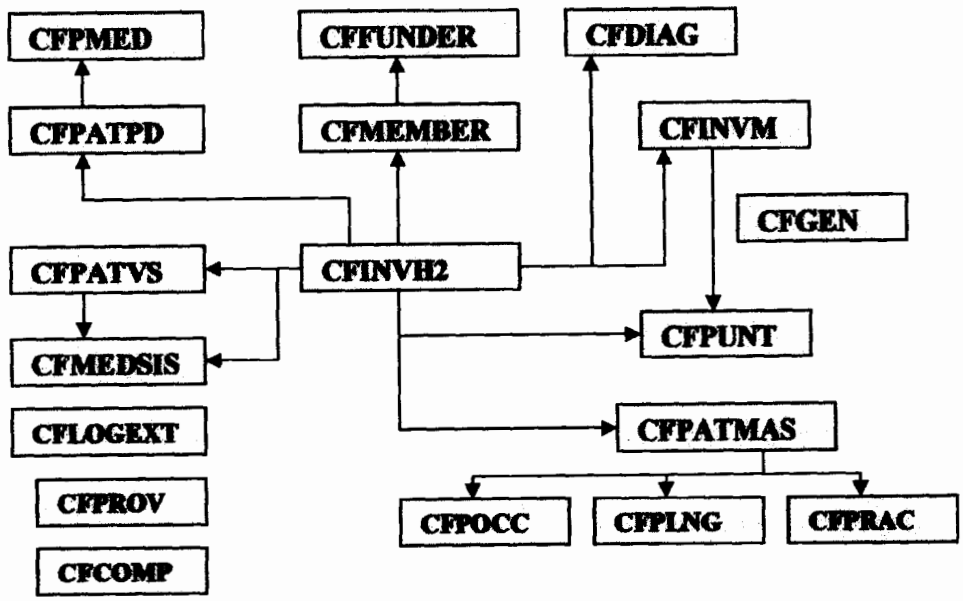

Figure 4.1: Schematic representation of the database

The description of the filenames are given in Table 4.2

Table 4.2: Description of the various files included in the database.

File name	Description
CFCOMP	Company file: describes events in each clinic for management purposes
CFDIAG	Diagnostic information file: contains diagnosis classification and protocol information (e.g. special investigation)
CFFUNDER	Funder information file: capitation information
CFINVH2	History invoice file
CFINVM	Invoice master file
CFLOGEXT	Long extract file: gives time spent in clinic
CFMEDSIS	Medical sister file: information on screening tests, etc.
CFMEMBER	Patient member file: medical aid information for individual patient
CFPATMAS	Patient master file: summary of patient information, e.g. address, language, race, etc.
CFPAPPD	Patient payment detail file
CFPATVS	Patient/visit file: patient number and visit number

The appropriate files and data fields that were used for the purposes of this study are presented in Table 4.3

Table 4.3: Data fields used in this study

File name	Data field name	Description of data field
CFDIAG	Cat	Diagnostic category, e.g. UROG (urology)
	Code	Diagnostic code, e.g. INFECT (infection)
	Desc	Description of diagnosis, e.g. SYPHILIS : ULCER
	Number	Diagnostic number, e.g. 9239
CFINVH2	Visit	Visit number
	Type	Type of transaction, e.g. consultation, special investigation, clinical procedure, or payment
	Date	Date of visit
	Cost	Cost of transaction
	Debtor	Patient number
CFNVM	Desc	Description of medication used
	Stk	Stock code (specific for every medication item)
CFPATMAS	GENDER	Gender of patient
	Bdt	Patient's date of birth
CFGEN	Desc	Generic description of medication

4.4.3.2 Classification systems used for antibiotics

The following classification systems were used to acquire the necessary data for the antimicrobials from the database

4.4.3.2.1 The Nappi code

Every agent on the database has a NAPPI code which is the National Approved Product Pricing Index (Snyman, 2004: 5a). The NAPPI code consists of a series of numbers, which is unique for every agent and which, also distinguishes between different dosage forms of the same agent. The NAPPI codes of the antimicrobials were used to acquire the data from the central database and to run the necessary queries in SAS 8.1® (SAS Institute Inc, 1999-2000).

4.4.3.2.2 Mims™ classification

This classification system classifies medicine according to its pharmacological action. Refer to appendix 2.4.1 for a complete list of this classification (Snyman, 2004: 5a). The MIMS™ classification was used as criterion to classify the antimicrobials according to their pharmacological action. This classification was also used as criterion to run queries in SAS 8.1® (SAS Institute Inc., 1999-2000).

4.4.3.2.3 Active ingredient classification

This classification system classifies medicine according to its active ingredient. Refer to Appendix 2.4.1 for a complete list of this classification.

4.4.3.2.4 ATC classification

This classification system classifies drugs according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Refer to Appendix 2.4.2 for a full description of the classification.

4.4.4 The composition of the study population

The study population was composed from the total patient population of patients who received one or more antimicrobials from the private primary health care setting for the period of 1st January to 31st December 2001.

The criteria for inclusion into the study population were:

- a valid patient record indicating the prescribing of one or more antimicrobial agents, and
- all the cases had to have a cost component.

4.4.5 Data analysis

4.4.5.1 Data application and data analysis

This step consisted of two parts: the first was the application of the criteria to the database. This was achieved by viewing the criteria retrospectively. Any deviations of the criteria were marked either for further review or as potential for intervention. The second part constituted the data analysed by means of SAS 8.1® (SAS Institute Inc., 1999-2000) where the data were viewed and analysed and where the data queries were run.

4.4.5.2 Statistical analysis

For the purpose of the empirical investigation, the following descriptive statistics and calculations were utilised:

4.4.5.2.1 Average value (mean)

The mean or average of observations in data is defined as the sum of all the observations in the data divided by the number of observations (De Wet & Pothas, 2000: 185). The mean is denoted by $\bar{x}$ and is equal to:

$$\bar{x} = \frac{\text{Sum of all observations}}{\text{Number of observations}}$$

4.4.5.2.2 Standard deviation (S)

Standard deviation is a measure of variation and it is defined as the difference/deviation of values from the mean (average) value. It indicates how representive the mean is of the total distribution (Steyn *et al.*, 1996: 130).

The standard deviation is noted as S and is calculated as:

$$S = \sqrt{\frac{\Sigma (x - \bar{x}^2)}{n-1}}$$

Where: S = standard deviation, the difference/deviation of values from the mean value.

x = average value (mean), the sum of all observations in the data divided by the number of observations and n = number of observations.

4.4.5.2.3 Range

The range is a measure of variability. The most obvious advantage of the range is its easy calculation (De Wet & Pothas, 2000: 203).

Range = Maximum - Minimum

4.4.5.2.4 Effect size

Cohen (1988: 3) defines effect sizes as "the degree to which the phenomenon is present in the population". Effect sizes (d-value) can be classified as small, medium and large.

Small: Represented by a d-value of 0.2 or less, with no practical significant difference;

Medium: Represented by a d-value of 0.5, with an effect that is observable and that may be practically significant;

Large: Represented by a d-value of 0.8 or higher, with an effect that is significant and of practical significance.

For the purposes of this study d-values of 0.8 or higher will be assumed to have practical significance. The effect sizes will be utilised in determining whether there are practical significant differences between the average medicine costs.

$$d = \frac{X_a . X_b}{S1}$$

Where:

Xa = the average medicine treatment cost of a.

Xb = the average medicine treatment cost of b.

S1 = the maximum standard deviation between a and b.

4.4.5.2.5 Cost index

The cost index is defined by Serfontein (1989: 180) as follows: It is the percentage cost divided by the percentage frequency.

$$\text{Cost prevalence index} = \frac{\text{Cost \%}}{\text{Prevalence \%}}$$

For the purpose of this study cost index values, equal to or exceeding one will be considered to have a relatively large cost percentage in comparison with the prevalence percentage (Serfontein, 1989: 180).

4.4.6 The selection and application of measuring instruments/criteria for data analysis

In order to achieve the aims set for this study, the following were used as measuring instruments or criteria for data analysis:

4.4.6.1 *Prevalence*

Antimicrobials are the most commonly prescribed group of drugs, leading to their overuse globally. Lemmen *et al.* (2001: 219) reported in a study that 30% to 40% of patients in hospitals receive antibiotics. According to Hooton and Levy (2001: 1087) in a study, 20% to 50% of antibiotic prescriptions in community settings were believed to be unnecessary. Antimicrobials contribute significantly to the cost of drugs and are claimed worldwide to account for 15% to 30% of the total health budget (Rehana *et al.*, 1998: 176). In developing countries, as stated by Gyssens and Kullberg (1995: 163), 30% of all patients received one or more antimicrobial drugs. In view of the above-mentioned statistics the importance of using prevalence as a measuring instrument (Truter *et al.*, 2001: 90) or criteria in the data analysis is made clear.

4.4.6.2 Cost

Marschner *et al.* (1994: 448) reported that about 30% to 40% of patients in hospitals received antibiotics and antibiotics were the most expensive medications prescribed by hospitals. As a group, antimicrobials contribute significantly to the cost of drugs and are claimed worldwide to account for 15% to 30% of the total health budget (Rehana *et al.*, 1998: 175). In developing countries, as stated by Calva (1996: 1121) in a study, antibiotics were the most common drugs sold, accounting for 29% of the drug sales. Guven and Uzun (2003: 91) reported that antimicrobial drug consumption costs more than seven billion US dollars annually in the United States. Antimicrobials account for up to 30% of hospital drug budgets. With reference to the above-mentioned statistics, the importance of the costs of antimicrobials is emphasised and thus costs were used as a measuring instrument or criteria for the data analysis.

4.4.6.3 Age

Antibiotics are among the most commonly prescribed drugs in paediatrics. Van Houten (1998: 161) reported that antibiotics were prescribed at least once for 30% of hospitalised children, although only 12.3% of the patients that received antibiotics had a proven bacterial infection. Infants less than two years received antibiotics more frequently than older children (25% and 11% respectively). Chang *et al.* (1999: 23) stated in a study that patients under the age of 11 years received the highest percentage (>40%) of antibiotic prescriptions. Certain age groups are more vulnerable for certain infections. White *et al.* (1996: 2963) stated that otitis media was the most prevalent disease in children in the United States. It was estimated that 25% of all oral antimicrobials prescribed to children were for otitis media. For this reason the age of the patients was used as a measuring instrument for the analysis of the data.

The following age categories were used for the purpose of this study:

- Age group 1: All patients younger than one month were included in this category.
- Age group 2: All patients older than one month up to and including the age of one year were included in this category.
- Age group 3: All patients older than one year of age up to and including the age of six years were included in this category.
- Age group 4: All patients older than six years of age up to and including the age of twelve years were included in this category.
- Age group 5: All patients older than twelve years of age up to and including the age of twenty were included in this category.
- Age group 6: All patients older than twenty years of age up to and including the age of forty were included in this category.
- Age group 7: All patients older than forty years of age up to and including the age of sixty were included in this category.
- Age group 8: All patients older than sixty years of age were included in this category.

4.4.6.4 Gender

According to Leigh *et al.* (2000: 818) acute uncomplicated urinary tract infection (UTI) is a common condition, particularly among young females. Out of 661 patients randomised for treatment, 90% were females, with a median age of 44 years. Al-Faris and Al-Tawel (1999: 319) in a study done in Saudi Arabia, stated that although more female patients attended the health centres (59%), and consulted more frequently than males, a smaller proportion of them (48%) received prescriptions. It is for this reason that the gender of a patient was used as a measuring instrument for the analysis of the data.

4.4.6.5 Medical conditions / Diseases

According to Naidoo and Wilson (2004: 200) respiratory tract infections are one of the commonest reasons for a visit to a family physician, and many consultations end with an antibiotic prescription. According to Akici *et al.* (2004: 211) upper and lower respiratory-tract

infections (URTIs and LRTIs) are frequently seen during childhood, and inappropriate use of drugs, particularly antibiotics, cause many problems in the treatment of these diseases. Acute respiratory tract infections such as acute exacerbations of chronic bronchitis (AECB), acute otitis media (AOM), and acute bacterial rhinosinusitis (ABRS) account for about 75% of antibiotic prescriptions. Tuberculosis still remains a serious health problem in many regions of the world, especially in developing countries (Georgiev, 1994: 157). In the United States, nosocomial pneumonia is the second most common nosocomial infection and causes the highest rates of morbidity and mortality. Approximately 30% to 50% of deaths among patients with nosocomial pneumonia are directly attributable to the infection (Kashuba *et al.*, 1999: 623). According to Gerbase (as quoted by Wilkinson *et al.* (2001: 517), the WHO estimated that more than 300 million curable STDs occurred each year in South Africa. With reference to the above-mentioned statistics, the importance of medical conditions/diseases was used as a measuring instrument or criteria for the data analysis.

4.4.7 RELIABILITY AND VALIDITY OF THE RESEARCH INSTRUMENTS

The central database of the private primary health care setting was utilised to obtain the data for the study. The data were obtained directly from the central database and thus no direct manipulation of the data by the researcher was possible. Data for the analysis were obtained, from the central database, for a twelve month period thus limiting external validity, implying that results can only be generalized to the specific database used, as well as to the specific study population.

The research was conducted from the viewpoint that all data obtained from the database were correct and accurate. This might be a limitation of the study.

4.4.8 THE REPORT AND DISCUSSION OF THE RESULTS OF THE EMPIRICAL INVESTIGATION

An extensive report, followed by an in-depth discussion of the results acquired through the empirical investigation will be reviewed in Chapter Five.

4.4.9 THE CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

The conclusions and recommendations based on the results of the literature review and the empirical investigation will be discussed, in detail, in Chapter Six. The limitations encountered during the study will be mentioned throughout Chapters Four and Five, with a detailed discussion of the limitations in Chapter Six.

4.5 CHAPTER SUMMARY

In this chapter the empirical investigation was discussed. The discussion included the aims of the empirical investigation, the data source and database in the study, as well as the methodology of the empirical investigation.

The results of the empirical study will be reported and discussed in Chapter 5.

CHAPTER 5 RESULTS AND DISCUSSION

This chapter deals with the results of the empirical study. The results will be presented as follows:

- ♥ Demographic information of patients of each clinic (total number of patients, age and gender distribution).
- ♥ Consultation information.
- ♥ Medicine information.
- ♥ Information regarding antimicrobial agents.
- ♥ Information regarding medical conditions or diagnoses treated with antimicrobials.
- ♥ Cost of antimicrobials.

5.1 DEMOGRAPHIC INFORMATION

Demographic information about the nine clinics (A – I) will be discussed as follows:

- ♣ The total number of patients that visited the nine clinics (Table 5.1).
- ♣ The gender distribution of the patients (Table 5.2).
- ♣ The age distribution of the patients (Table 5.3).
- ♣ The average, minimum and maximum age of patients (Table 5.4).
- ♣ The frequency of patients according to age and gender distribution (Table 5.5).

5.1.1 Total number of patients in the nine clinics

Table 5.1 shows the total number of patients that visited the different clinics during the research period from 1st January to 31st December 2001.

Table 5.1: Total number of patients in each clinic as a percentage of the total number of patients that visited the nine clinics

Clinic	Frequency	% of patients per clinic
A	7576	9.06
B	3549	4.24
C	9250	11.06
D	17362	20.75
E	8358	9.99
F	9993	11.95
G	10480	12.53
H	10311	12.33
I	6776	8.10
Total	**83655**	**100.00**

The total number of patients that visited the nine clinics during the research period was 83655. Clinic D had the highest number (20.75%, n = 17362) of patients that visited the nine clinics during the research period. Clinic B had the lowest number of patients (4.24%, n=3549).

5.1.2 Gender distribution of patients

The results in Table 5.2 show the gender distribution of patients that visited the nine clinics.

Table 5.2: Gender distribution of patients

Clinic	Female	% *	Male	% *	G	Total Z
A	4812	63.56	2759	36.44	5	**7571**
B	1980	55.00	1556	44.00	13	**3536**
C	5639	61.07	3595	38.93	16	**9234**
D	10776	62.33	6513	37.67	73	**17289**
E	4833	58.01	3498	41.99	27	**8331**
F	6421	64.55	3525	35.44	47	**9946**
G	5913	56.45	4561	43.55	6	**10474**
H	5515	53.63	4769	46.37	27	**10284**
I	3883	57.47	2874	42.53	19	**6757**
Total Y	**49772**	**59.50**	**33650**	**40.22**	**233**	**Total Y=83655** **Total Z= 83422**

Total Y: Total number of patients per gender distribution in each of the nine clinics.

Total Z: Total number of patients in each individual clinic.

*% *: Percentage calculations were based on the total number of patients, whose gender was indicated, that visited each specified clinic during the research period.*

G = Number of patients whose gender was not indicated.

During the research period, 1st January to 31st December 2001, female patients visited the clinics more frequently than did their male counterparts. The total number of females that visited the clinics was 49772 (59.50%). The number of male patients who visited the clinics during the same period only accounts for 40.22% (n = 33650). No gender was indicated in 0.28% (n = 233) of the total number of patients (n = 83655) cases.

5.1.3 Age distribution of patients

The age group division was discussed in Chapter 4 Section 4.4.5.3.

Table 5.3: Age distribution of patients

	AGE GROUP																	
Clinic	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**G**	**Total Z**
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	
A	89	24.1	667	18.5	1089	16	545	12.7	605	10.3	2959	8.1	1140	6.18	447	6.8	35	**7541**
B	8	2.2	87	2.4	279	4	231	5.4	291	4.97	1484	4.1	910	4.93	251	3.8	8	**3541**
C	31	8.4	337	9.3	901	1.3	513	11.9	723	12.3	4087	11	1894	10.3	755	11.5	9	**9241**
D	67	18.1	759	21.0	1762	23	681	15.8	933	15.9	7906	22	3692	20	1643	25.0	51	**17311**
E	38	10.3	416	11.5	819	12	384	8.9	578	9.86	4167	11	1535	8.32	406	6.2	15	**8343**
F	63	17.0	499	13.8	989	14	463	10.8	698	11.9	4087	11	2261	12.3	903	13.7	30	**9963**
G	13	3.5	250	6.9	779	11	616	14.3	796	13.6	4671	13	2631	14.3	763	11.6	6	**10474**
H	35	9.5	336	9.3	831	12	521	12.1	688	11.7	4498	12	2678	14.5	716	10.9	8	**10303**
I	26	7.0	260	7.2	516	7.3	346	8.0	548	9.35	2665	7.3	1699	9.21	701	10.6	15	**6761**
Total Y	**370**	**100**	**3611**	**100**	**7965**	**100**	**4300**	**100**	**5860**	**100**	**36524**	**100**	**18440**	**100**	**6585**	**100**	**177**	**83478**
%	**0.45**		**4.36**		**8.47**		**5.19**		**7.07**		**44.06**		**22.25**		**7.95**		**0.21**	**100.0**

Total Y: Total number of patients in each age group in all nine clinics.

Total Z: Total number of patients, whose ages were indicated, of each individual clinic.

%: The percentage was calculated according to the number of patients in each age group in all nine clinics (Total Y).*

%: Percentage calculated according to number of patients in the different age groups in all the nine clinics (n= 83478) (Total Z).

G = Number of patients whose age was not indicated.

As shown in Table 5.3 age group 6 (20-40 years) and 7 (40-60 years) accounts for 66.31% (n = 54964) of patients that visited the clinics. These age groups represents the working and economically active class of the society. It is also likely that a private primary health service provider may have contracts with companies to provide medical care to these patients.

The age group with the smallest number of patients is age group 1 (0 – 1 month), which accounts for 0.45% (n = 370) of the total number of patients that visited the clinics. The age of patients was not indicated in 0.21% (n = 177) cases of the total number of cases recorded during the research period.

5.1.4 Average, minimum and maximum age of patients

Table 5.4 shows the average, minimum and maximum age of the patients that visited the nine clinics during the research period.

Table 5.4: Average, minimum and maximum age of patients visiting the clinics

Clinic	N=83478	Average age (years)	Standard deviation	Minimum age (years)	Maximum age (years)
A	7541	25.7	19.85	0.01	100.2
B	3541	31.2	19.75	0.25	90.9
C	9241	30.9	19.26	0.02	99.3
D	17311	32.2	19.80	0.02	99.6
E	8343	25.9	19.75	0.32	99.7
F	9963	31.4	19.95	0.01	97.1
G	10474	32.3	18.06	0.02	101.2
H	10303	32.4	18.45	0.01	94.2
I	6761	33.5	20.31	0.02	100.1

The averages, minimum and maximum ages were calculated in years. The minimum age of patients varied between 0.01 years (Clinics A, F and H) and 0.32 years (Clinic E). The maximum age of patients varied between 90.9 years (Clinic B) and 101.2 years (Clinic G). The average age of patients varied between 25.7 ± 19.85 years and 33.5 ± 20.31 years in the different clinics. The patients that visited Clinic I had the highest average age of 33.5 ± 20.31 years and the lowest average age was at Clinic A with 25.7 ± 19.85 years.

Statistical d-values as indication of the practical significance differences between the average ages of patients in the different clinics were calculated. The d-values calculated (refer to Chapter

4, Section 4.4.5.2.4) showed that there was no difference of practical significance found between the average age of patients from the different clinics.

5.1.5 Total number of patients according to age group and gender distribution together

The total number of patients according to age groups and gender distribution together is shown in Table 5.5.

As shown in Table 5.5 the distribution of patients according to age group was such that age group 6 (20-40 years) had the highest number of patients in all the nine clinics. The total number of patients in this age group was 36497 (43.79%). The age group with the least number of patients was age group 1 (0-1 month) accounting for 0.44% (n = 370). For the gender distribution of patients, females represented the highest number of patients in all clinics with 12.92% (n = 10770) in Clinic D. The least number of females patients was obtained from Clinic B that was 2.37 % (n = 1978) of the total number of patients. The highest number of patients according to gender and age distribution together was that of females, age group 20-40 years, in Clinic D as shown in the Table 5.5 (with 5161 females representing 6.19 % of the total number of patients).

Table 5.5: Total number of patients according to age groups and gender distribution together in the nine clinics

		CLINIC																		
		A		B		C		D		E		F		G		H		I		
Age group		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	Total Z
1	n	52	37	3	5	11	20	35	32	16	22	38	25	7	6	15	20	9	17	**370**
	%	1.06	1.38	0.15	0.32	0.2	0.56	0.32	0.49	0.33	0.63	0.59	0.71	0.12	0.13	0.27	0.42	0.23	0.59	
2	n	345	322	33	53	149	188	371	388	188	226	238	261	112	138	157	177	126	134	**3606**
	%	7.04	12.1	1.67	3.41	2.64	5.23	3.44	5.96	3.89	6.47	3.71	7.4	1.89	3.03	2.98	3.71	3.25	4.66	
3	n	550	539	135	143		465	784	841	392	426	451	534	368	411	385	445	6.08	278	**7586**
	%	11.2	20.2	6.83	9.2	7.68	12.9	7.28	12.91	8.11	12.2	7.02	15.2	6.22	9.01	6.98	9.33	4.07	9.68	
4	n	291	254	117	112	283	230	350	328	176	206	216	246	318	298	240	276	332	188	**4461**
	%	5.98	9.5	5.92	7.2	5.02	6.4	7.76	5.04	3.04	5.89	3.36	6.98	5.38	6.53	4.35	5.79	8.55	6.54	
5	n	420	185	173	117	448	273	624	304	375	201	452	242	455	341	421	265	332	216	**5844**
	%	8.57	6.92	8.75	7.52	7.94	7.59	5.79	4.67	3.76	5.75	7.04	6.87	7.69	7.48	7.63	5.56	8.25	7.25	
6	n	2169	790	829	652	2659	1426	5161	2736	2612	1551	3008	1074	2634	2037	2507	1988	1624	1040	**36497**
	%	44.3	29.6	41.9	41.9	47.15	39.7	47.92	42.01	54.1	44.4	46.9	30.5	44.6	44.7	45.5	41.7	41.8	36.2	
7	n	736	404	530	380	1151	743	2318	1368	825	707	1395	863	1546	1067	1341	1332	987	710	**18403**
	%	15	15.1	26.8	24.4	20.41	20.7	21.52	21	17.1	20.2	21.7	24.5	26.2	23.4	24.3	27.9	25.4	24.7	
8	n	335	142	158	93	505	250	1127	516	249	156	623	280	473	263	449	266	410	290	**6585**
	%	6.84	5.55	7.99	5.98	8.96	6.95	10.46	7.92	5.15	4.46	9.7	7.94	8	5.77	8.14	5.58	10.6	10.1	
Total Y		**4812**	**2759**	**1978**	**1555**	**5639**	**3595**	**10770**	**6515**	**4833**	**3495**	**6421**	**3525**	**5913**	**4561**	**5515**	**4769**	**3888**	**2873**	**83352**

Total Y: Total number of patients in each gender in the nine clinics.

Total Z: Total number of patients in each age group in each clinic.

%: Percentage calculated according to the number of patients in each gender and age group in each clinic.

5.2 CONSULTATION INFORMATION

The consultations over the one-year research period, in the nine clinics will be discussed under the following headings:

- Total number of consultations and patients in each clinic (refer to Table 5.6)
- Ratio of consultations per total number of patients (refer to Table 5.7)
- Number of consultations per gender distribution (refer to Table 5.8)
- Ratio of consultations per patient according to gender (refer to Table 5.9)
- Number of consultations according to age groups (refer to Table 5.10)
- Ratio of consultations per patient per age group in all nine clinics(refer to Table 5.11)

5.2.1 Total number of consultations in each clinic

The following table (Table 5.6) illustrates the total number of consultations and patients at each clinic during the one year research period.

Table 5.6: Total number of consultations and patients in each clinic

Clinic	Total number of consultations	% *	Total number of patients	% ♦
A	11968	9.03	7576	9.06
B	8713	6.57	3549	4.24
C	13553	10.22	9250	11.06
D	23859	18.00	17362	20.75
E	11463	8.65	8358	9.99
F	15017	11.33	9993	11.95
G	16762	12.64	10480	12.53
H	18671	14.08	10311	12.33
I	12579	9.49	6776	8.10
Total	**132585**	**100.00**	**83655**	**100.00**

** Percentage calculated according to the total number of consultations (N = 132585).*

♦ *Percentage calculated according to the total number of patients (N = 83655).*

As indicated in Table 5.6 a total of 132585 consultations were made by 83655 patients that visited the nine clinics during the one-year research period (refer to Table 5.1). Clinic D had the highest number of consultations (18.00%, n = 23859). This concurs with the results that showed that Clinic D had the highest number of patients that visited the clinic during the research period. Clinic B had the smallest number of consultations (6.57%, n = 8713). This also concurs with the results that showed that Clinic B had the lowest number of patients that visited the clinic (refer to Table 5.1).

5.2.2 Ratio of consultations per total number of patients for the different clinics

The ratio of consultations per total number of patients for the different clinics is illustrated in Table 5.7.

Table 5.7: Ratio of consultations per total number of patients for the different clinics

Clinic	Ratio
A	1.58:1
B	2.46:1
C	1.47:1
D	1.37:1
E	1.37:1
F	1.50:1
G	1.60:1
H	1.81:1
I	1.86:1

As shown in Table 5.7 Clinic B had the highest number of consultations per patient over the year (ratio of 2.46 consultations per patient). Clinics D and E had the least number of consultations per patient at a ratio of 1.37 consultations per patient per year.

5.2.3 Total number of consultations according to gender distribution

(For the purpose of this study a consultation = a patient visit)

The number of consultations per gender distribution is demonstrated in Table 5.8.

Table 5.8: Number of consultations per gender distribution

Clinic	Female	Percentage (%)	Male	Percentage (%)	G	Total Z
A	8010	10.08	3936	7.48	22	**11946**
B	4811	6.05	3879	7.38	23	**8690**
C	8311	10.46	5205	9.90	37	**13516**
D	14704	18.51	9038	7.19	117	**23742**
E	6676	8.40	4733	9.00	54	**11409**
F	9655	12.15	5277	10.03	85	**14932**
G	9707	12.22	7013	13.34	42	**16720**
H	10153	12.78	8394	15.96	124	**18547**
I	7431	9.35	5113	9.72	35	**12544**
Total Y	**79458**	100.00	**52588**	100.00	**539**	**132046**
% ♦	**59.93**		**39.66**		**0.41**	**100.00**

Total Y: Total number of consultations by each gender in the nine clinics.

Total Z: Total number of consultations by patients, whose gender was indicated, in each individual clinic.

%♦: Percentage calculated according to the number of consultations by the each gender in all nine clinics (Total Y).

%: Percentage calculated according to the number of consultations made by the different genders in all nine clinics (n = 132046) (Total Z).

G = Number of consultations by patients where the gender was not indicated.

As shown in Table 5.8 the highest number of consultations according to gender was that of females accounting for 59.93% (n = 79458) as compared to males whose number accounts for 39.66% (n = 52588) of the total number of consultations (n = 132585). Clinic D had the highest number of female consultations representing 18.51% (n = 14704), while Clinic B had the least number of female consultations representing 6.05% (n = 4811). Clinic D had the highest number

of patients and Clinic B the least number of patients as shown in Table 5.1. The gender was not indicated in 539 (0.41%) cases of the total number of consultations (n = 132585).

5.2.4 Ratio of consultation per patient according to gender distribution

Ratio of consultation per patient according to gender distribution in all clinics is shown in Table 5.9.

Table 5.9: Ratio of consultations per patient according to gender distribution

Clinic	Female consultations	Ratio	Male consultations	Ratio
A	8010	1.66:1	3936	1.43:1
B	4811	2.43:1	3879	2.49:1
C	8311	1.47:1	5205	1.45:1
D	14704	1.36:1	9038	1.39:1
E	6676	1.38:1	4733	1.35:1
F	9655	1.50:1	5277	1.50:1
G	9707	1.64:1	7013	1.54:1
H	10153	1.84:1	8394	1.76:1
I	7431	1.91:1	5113	1.78:1
All clinics	**79458**		**52588**	

During the research period, Clinic B had the highest ratio of female consultations represented by 2.43 consultations per female patient for the year. Clinic D had the smallest ratio of female consultations (1.36) per female patient. The total number of consultations made by the females was 60.17% (n = 79458) of the total number of consultations (n = 132046) by patients that visited the nine clinics (refer to Table 5.10). The total number of consultations made by males was 39.83% (n = 52588). The highest ratio for male consultations was obtained from Clinic B. That was 2.49 consultations per male patient. Clinic E had the least ratio of male consultations, i.e. 1.35 consultations per male patient. For both genders Clinic B had the least number of patients that visited that clinic. Clinics D and E, on the other hand, recorded the highest number of patients that visited the clinics.

5.2.5 Total number of consultations according to age groups

The following table (Table 5.10) illustrates the number of consultations according to age groups. As shown in Table 5.10 age group 6 (20-40 years) represented the highest number of consultations (41.64, n = 55211) of the total number of consultations (n = 132585) made in all nine clinics. These results confirm the results in Table 5.3 that showed that age group 6 (20- 40 years) represented the highest number of patients. Since this is the most economically active age group, patients in this age group could afford to visit the private primary health care clinics. The age group with the smallest number of consultations is age group 1 (0-1 month) representing 0.29% (n=389). Again as shown in Table 5.3, this age group represents the least number of patients of the total number of patients in the nine clinics. The age group was not indicated in 398 (0.30%) of the total number of consultations (n = 132585).

Table 5.10: Number of consultations according to age groups

	AGE GROUP																	
	1		2		3		4		5		6		7		8		G	
Clinic	N		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	Total Z
A	95	24.42	1121	22.8	1539	13.91	665	11.53	825	10	4718	8.55	1979	5.81	1004	7.88	22	**11946**
B	12	3.08	142	2.89	567	5.13	433	7.50	477	5.9	3254	5.89	3085	9.06	722	5.67	21	**8692**
C	31	7.97	409	8.31	1190	10.76	654	11.33	949	12	5762	10.4	3229	9.48	1306	10.26	23	**13530**
D	70	17.99	962	19.6	2198	19.87	810	14.04	1138	14	10743	19.5	5330	15.65	2528	19.85	80	**23779**
E	39	10.03	476	9.68	1019	9.21	490	8.49	741	9.2	5672	10.3	2319	6.81	664	5.21	43	**11420**
F	63	16.20	625	12.7	1326	11.99	585	10.14	949	12	5924	10.7	3891	11.42	1595	12.52	59	**14958**
G	13	3.34	328	6.67	1168	10.56	868	15.04	1053	13	6891	12.5	4639	13.62	1760	13.82	42	**16720**
H	36	9.25	467	9.49	1211	10.95	713	12.36	1015	13	7348	13.3	6094	17.89	1689	13.26	98	**18573**
I	30	7.71	389	7.91	845	7.64	552	9.57	893	11	4899	8.87	3494	10.26	1467	11.52	20	**12569**
Total Y	**389**	**100**	**4919**	**100**	**11063**	**100**	**5770**	**100**	**8040**	**100**	**55211**	**100**	**34060**	**100**	**12735**	**100**	**398**	**132187**
% ♦	0.29		3.71		8.34		4.35		6.06		41.64		25.69		9.61		0.30	100

Total Y: Total number of consultations by patients in each age group in all nine clinics.

Total Z: Total number of consultations of patients, whose age group was indicated, that visited each individual clinic.

%: Percentage calculations were based on the total number of consultations by patients in each age group in the nine clinics (Total Y).

%♦: Percentage calculations were based on the total number of consultations in the different age groups in all nine clinics (n = 132187) (Total Z).

G = Number of consultations by patients where age group was not indicated.

5.2.6 Ratio of the number of consultations per patient per age group in all nine clinics

The following table shows the ratio of the number of consultations per patient per age group in all the nine clinics together.

Table 5.11: Ratio of the number of consultations per patient per age group

Age group	Total number of consultations in the nine clinics (n = 132187)	Total number of patients in the nine clinics (n = 83655)	Ratio
1	389	370	1.05:1
2	4919	3611	1.36:1
3	11063	7965	1.39:1
4	5770	4300	1.34:1
5	8040	5860	1.37:1
6	55211	36524	1.51:1
7	34060	18440	1.85:1
8	12735	6585	1.93:1

As shown in Table 5.11 age group 1 (0-1 month) had the lowest ratio of consultations represented by 1.05 consultations per patient. This age group represents the least number of consultations and patients in all the nine clinics.

5.3 INFORMATION ON MEDICINE ITEMS

The following will be discussed with regard to medicine items:

- Total number of medicine items prescribed (Table 5.12)
- Average number of medicine items per consultation (Table 5.13)
- Frequency of the number of medicine items per consultation (Table 5.15).

5.3.1 Total number of medicine items prescribed

The following table shows the total number of medicine items prescribed in the nine clinics. A total of 515976 medicine items were prescribed in all nine clinics over the research period.

Table 5.12: Total number of medicine items prescribed in the nine clinics

Clinic	Frequency (n = 515976)	%
A	46817	9.07
B	30441	5.90
C	47734	9.25
D	93865	18.19
E	41668	8.08
F	74576	14.45
G	60958	11.81
H	60482	11.72
I	59435	11.52
All clinics	**515976**	**100.00**

%: Percentage calculations were based on the total number of medicine items prescribed in all nine clinics.

As shown in Table 5.12 Clinic D had the highest number of medicine items dispensed during the one-year research period, that was 18.19 % (n = 93865) of the total number of medicine items (N = 515976). This concurs with the results obtained in Table 5.1 where Clinic D had the highest number of patients and in Table 5.6 where Clinic D had the highest number of consultations. The lowest number of medicine items were dispensed to Clinic B accounting for 5.90 % (n = 30441) only.

5.3.2 Average number of medicine items prescribed per consultation

The average, minimum and maximum number of medicine items prescribed per consultation is illustrated in Table 5.13.

Table 5.13: Average, minimum and maximum number of medicine items prescribed per consultation in the nine clinics

Clinic	Total number of medicine items	Mean	Standard deviation	Median	Minimum	Maximum
A	46817	3.91	1.34	4	0	11
B	30441	3.49	1.52	3	0	14
C	47734	3.52	1.22	3	0	10
D	93865	3.93	1.27	0	0	19
E	41668	3.63	1.36	0	0	9
F	74576	4.97	1.81	5	0	16
G	60958	3.64	1.56	4	0	12
H	60482	3.24	1.39	3	0	13
I	59435	4.72	1.87	5	0	11

As revealed in Table 5.13, the average number of medicine items prescribed in the clinics varied between 3.24 ± 1.39 (Clinic H) and 4.92 ± 1.87 (Clinic F) per consultation. Clinic D had the maximum number (n = 19) of medicine items prescribed during one consultation. In all the clinics there were also consultations where no medicines were prescribed.

Table 5.14: Statistical d-values as indication of the practical significance differences between the average numbers of medicine items prescribed per consultation between the nine clinics

Clinic	A	B	C	D	E	F	G	H	I
A		0.28	0.29	0.12	0.20	0.58	0.17	0.50	0.43
B	0.28		0.02	0.29	0.09	0.82	0.09	0.16	0.66
C	0.29	0.02		0.32	0.08	0.80	0.08	0.20	0.64
D	0.12	0.29	0.32		0.22	0.57	0.19	0.49	0.42
E	0.20	0.09	0.08	0.22		0.74	0.01	1.29	0.58
F	0.58	0.82	0.80	0.57	0.74		0.85	0.95	0.13
G	0.17	0.09	0.08	0.19	0.01	0.85		0.25	0.58
H	0.50	0.16	0.20	0.49	1.29	0.95	0.25		0.79
I	0.43	0.66	0.64	0.42	0.58	0.13	0.58	0.79	

Difference of practical significance is d>0.8

According to Table 5.14, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there was a difference of practical significance found between the average number of medicine items prescribed per consultation between Clinics H and E with the d-value of 1.29. Then between Clinics G and F with the d-value of 0.85 and between H and F with the value of 0.95. This means that the number of medicine items prescribed in Clinic F was practically significantly higher than those of Clinics G and H.

5.3.3 Frequency of the number of medicine items prescribed per consultation

The frequency of the number of medicine items per consultation are illustrated in Table 5.15.

As shown in Table 5.15 Clinic D had the highest number of medicine items prescribed per consultation. Nineteen medicine items were prescribed during one consultation. Clinic F had 16 medicine items that were prescribed during two consultations. The clinic with the lowest medicine items prescribed per consultation was Clinic E with 9 medicine items prescribed in 11 consultations. These results concur with the results shown in Table 5.12 where Clinic D had the maximum number of medicine items and Clinic B the lowest number of medicine items.

Table 5.15: Frequency of the number of medicine items per consultation over the research period in the nine clinics

	CLINIC																		
	A		B		C		D		E		F		G		H		I		
n		%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total Z
0	7	0.06	3	0.03	4	0.03	4	0.02	5	0.04	5	0.03	3	0.02	47	0.25	2	0.02	80
1	566	4.73	819	9.4	538	3.97	474	1.99	615	5.37	321	2.14	1210	7.22	1893	10.14	854	6.79	7290
2	1040	8.69	1484	17.03	1992	14.7	2390	10	1686	14.7	818	5.45	2807	16.75	3750	20.08	827	6.57	16794
3	2616	21.86	2156	24.74	4306	31.8	5626	23.6	3039	26.5	1611	10.73	4344	25.92	5440	29.14	1458	11.6	30596
4	3977	33.23	2212	25.39	4254	31.4	8289	34.7	3237	28.2	3288	21.9	3916	23.36	4324	23.16	2068	16.4	35565
5	2586	21.61	1290	14.81	1711	12.6	4699	19.7	1949	17	3928	26.16	2474	14.76	2231	11.96	2827	22.5	23695
6	853	7.13	510	5.85	565	4.17	1759	7.37	715	6.24	2552	19.99	1301	7.76	690	3.7	2571	20.4	11516
7	244	2.04	149	1.71	141	1.04	472	1.98	166	1.45	1251	8.33	498	2.97	221	1.18	1313	10.4	4455
9	20	0.17	24	0.28	8	0.06	18	0.08	11	0.1	348	2.32	43	0.26	20	0.11	149	1.18	641
10	2	0.02	8	0.09	1	0.01	7	0.03			142	0.95	16	0.1	3	0.02	42	0.33	221
11	1	0.01	5	0.06			3	0.01			59	0.39	7	0.04			8	0.06	83
12			1	0.01			1				23	0.15	2	0.01					27
13											9	0.06			1	0.01			10
14			1	0.01							2	0.01							3
15											1	0.01							1
16											2	0.01							
17																			
18																			
19							1												1

Total Z: The total frequency of the number of medicine items prescribed per consultation in all the clinics.

%: Percentage calculations were based on the total frequency of the number of medicine items prescribed in all the clinics.

n: number of medicine items prescribed per consultation.

N: frequency of the number of medicine items prescribed per consultation.

5.3.4 Total number of prescriptions where one or more antimicrobials were prescribed

The results in Table 5.16 represent the total number of prescriptions where one or more antimicrobials were prescribed.

Table 5.16: Total number of prescriptions where one or more antimicrobials were prescribed

		N = Number of antimicrobials prescribed per consultation						
Clinic		**1**	**2**	**3**	**4**	**5**	**6**	**Total Y**
A	**N**	6981	1039	214	21			**8255**
	%*	84.57	12.59	2.59	0.25			
B	**N**	3403	384	102	4			**3893**
	%*	87.41	9.86	2.62	0.01			
C	**N**	5414	712	479	5			**6610**
	%*	81.91	10.77	7.25	0.08			
D	**N**	11869	2313	548	36			**14766**
	%*	80.38	15.66	3.71	0.24			
E	**N**	5082	1587	205	2			**6876**
	%*	73.91	23.08	2.98	0.03			
F	**N**	8709	1485	648	19			**10861**
	%*	80.19	13.67	5.97	0.17			
G	**N**	8159	1386	422	44	12	1	**10024**
	%*	81.39	13.83	4.21	0.44	0.12	0.01	
H	**N**	7760	715	370	5	1		**8851**
	%*	87.67	8.08	4.18	0.06	0.01		
I	**N**	5966	1674	269	26			**7935**
	%*	75.19	21.1	3.99	0.33			

Total Y: Total number of prescriptions prescribed at each clinic.

*% *: Percentage calculated according to the total number of prescriptions prescribed during the patients' visits (consultations) to the clinics.*

As illustrated in Table 5.16 Clinic G is the only clinic where 6 antimicrobials (only one case) were prescribed per patient consultation. Clinic H has one case where 5 antimicrobials were prescribed per patient consultation and Clinic G has 12 cases where 5 antimicrobials were prescribed. As indicated in the table patients received a maximum of 6 antimicrobials (only one case) per patient consultation (Clinic G) and a minimum of 1 antimicrobial per patient consultation. The highest percentage of patients received between 1 and 2 antimicrobials per consultation. (Clinic A = 97.13%, Clinic B =97.27%, Clinic C = 92.68%, Clinic D 96.99, Clinic E = 96.99, Clinic F = 93.86, Clinic G = 95.75, Clinic H = 95.75% and Clinic I = 96.29).

5.4 Specific information about antimicrobials

Antimicrobials prescribed over the one-year research period in the nine clinics will be discussed under the following headings:

- Total number of patients for whom antimicrobials were prescribed (refer to Table 5.17.
- Total number of all antimicrobials prescribed (refer to Table 5.18).
- Average, number of antimicrobials prescribed per consultation (refer to Table 5.19).
- Total number of antimicrobials prescribed according to gender (refer to Table 5.21)
- Average number of antimicrobials prescribed according to gender (refer to Table 5.22)
- Total number of antimicrobials prescribed according to age groups (refer to Table 5.23)
- Average number of antimicrobials prescribed according to age groups (refer to Table 5.24).

5.4.1 Total number of patients for whom antimicrobials were prescribed in each clinic

The following table (Table 5.17) shows the total number of patients for which antimicrobials were prescribed in the different clinics during the one-year research period.

Table 5.17: Total number of patients for whom antimicrobials were prescribed in each clinic

Clinic	Total number of patients (n = 83655)	Total number of patients prescribed antimicrobials (n = 54663)	% of patients prescribed antimicrobials (% = 65.34)
A	7576	5773	76.20
B	3549	2227	62.75
C	9250	4749	51.34
D	17362	10952	63.08
E	8358	5184	62.02
F	9993	7915	79.21
G	104780	7201	68.71
H	10311	6056	58.73
I	6776	4606	68.98

%: Percentage calculations were based on the total number of patients for whom antimicrobials were prescribed (n = 54663).

As indicated in Table 5.17 a total of 54663 (65.34%) patients received antimicrobial prescriptions during the one - year research period. Clinic F had the highest number of patients for whom antimicrobials were prescribed (79.21, n = 7915) of the total number of patients. The clinic with the lowest number of patients for whom antimicrobials were prescribed was C with 51.43% (n = 4729) of the total number of patients that visited the clinic.

5.4.2 Total number of antimicrobials prescribed in each clinic

The total number of antimicrobials prescribed in each clinic is shown in Table 5.18.

As indicated in Table 5.18, Clinic A had the highest number of antimicrobials prescribed during the one-year research period (20.90%, n = 9785) of the total number of medicine items prescribed in the specific clinic. The clinic with the lowest number of antimicrobials prescribed was Clinic B with 14.76 % (n = 4493) of the total number of medicine items prescribed in this specific clinic.

Table 5.18: Total number of antimicrobials in each clinic

Clinic	Total number of medicine items (n = 515976)	Total number of antimicrobials (n = 96421)	% of antimicrobials prescribed
A	46817	9785	20.90
B	30441	4493	14.76
C	47734	8295	17.38
D	93865	18283	19.48
E	41668	8879	16.03
F	74576	13699	18.37
G	60958	12439	20.41
H	60482	10325	17.07
I	59435	10223	17.20

% : Percentage was calculated according to the number of medicine items in the nine clinics during the one year research period.

5.4.3 Average, minimum and maximum number of antimicrobials prescribed per consultation

The average, minimum and maximum number of antimicrobials prescribed per consultation over the research period in the nine clinics are illustrated in Table 5.19.

Table 5.19 reveals that the average number of antimicrobials prescribed varied between 1.17 ± 0.48 and 1.54 ± 0.43 antimicrobials per patient consultation. The maximum number of antimicrobials prescribed per consultation was 6 (only one case) in Clinic G. Clinic H had 5 antimicrobials prescribed to the patients per consultation (only 1 case). These results correlate with the results as shown in Table 5.16. All the clinics received the minimum number of antimicrobials (n = 1) prescribed to the patients per consultation.

Table 5.19: Average, minimum and maximum number of antimicrobials prescribed per consultation over the research period in the nine clinics

Clinic	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
A	9785	1.19	0.47	1	1	4
B	4493	1.54	0.43	1	1	4
C	8295	1.25	0.58	1	1	4
D	18283	1.24	0.52	1	1	4
E	8879	1.29	0.52	1	1	4
F	13699	1.26	0.57	1	1	4
G	12439	1.24	0.56	1	1	6
H	10325	1.17	0.48	1	1	5
I	10225	1.29	0.54	1	1	4

Table 5.20: Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed in the nine clinics

Clinic	A	B	C	D	E	F	G	H	I
A		0.74	0.10	0.09	0.19	0.12	0.09	0.04	0.19
B	0.74		0.5	0.58	0.48	0.49	0.54	0.77	0.46
C	0.10	0.5		0.02	0.07	0.02	0.02	0.14	0.07
D	0.09	0.58	0.02		0.09	0.04	0.00	0.13	0.09
E	0.19	0.48	0.07	0.09		0.05	0.09	0.23	0.00
F	0.12	0.49	0.02	0.04	0.05		0.04	**1.16**	0.05
G	0.09	0.54	0.02	0	0.09	0.04		0.13	0.09
H	0.04	0.77	0.14	0.13	0.23	**1.16**	0.13		0.22
I	0.19	0.46	0.07	0.09	0	0.05	0.09	0.22	

Difference of practical significance is d>0.8

According to Table 5.20, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) shows that there was a difference of practical significance found between the average number of antimicrobials prescribed per consultation between Clinics H and F with the d- value of 1.16. This implies that the average cost of antimicrobials prescribed in Clinic H was practically and significantly lower than those prescribed in Clinic F.

5.4.4 Total number of antimicrobials prescribed according to gender

The results in Table 5.21 show the total number of patients that were prescribed antimicrobials according to gender.

Table 5.21: Total number of patients according to gender for whom antimicrobials (one or more) were prescribed

	GENDER					
	Female		Male			
Clinic	N	% ♦	N	% ♦	G	Total Z
A	3762	65.24	2001	34.75	5	**5763**
B	1220	55.00	998	45.00	9	**2218**
C	2972	62.69	1769	37.31	8	**4741**
D	6649	60.96	4258	39.04	45	**10907**
E	2961	57.27	2209	42.73	14	**5170**
F	5124	65.05	2753	34.95	38	**7877**
G	4140	57.52	3057	42.48	4	**7197**
H	4030	66.61	2020	33.39	6	**6050**
I	2724	59.24	1874	40.76	8	**4598**
Total Y	**33582**		**20939**		**137**	**54521**
%	**61.44**		**38.31**		**0.25**	**100**

Total Z: Total number of patients by each gender in each clinic.

Total Y: Total number of patients by gender in the nine clinics.

%♦: Percentage calculated according to the total number of patients, whose gender was indicated, for whom antimicrobials were prescribed during the research period in the specific clinic(Total Y).

%: Percentage calculated according to the number of patients per gender in all nine clinics (n = 54658).
G = No gender was indicated. These numbers indicate the details that have not been recorded in the clinics.
One patient could receive one or more antimicrobials per consultation.

As demonstrated in Table 5.21, the number of female patients that visited the clinics during the research period was more than that of the male patients. The total number of female patients for whom antimicrobials were prescribed was 33582 (61.44%) of the total number of patients who received antimicrobials. The male patients represented 38.31% (n = 20939). These results are supported by the results in Table 5.2, which shows that there were more female patients (n = 49772, 59.66%) than males (33650, 30.34%) who visited the clinics during the research period. Gender was not indicated in 0.25% (n = 137) cases of the total number of patients who received antimicrobials (n = 54658).

5.4.5 Average number of antimicrobials prescribed according to gender

The average, minimum and maximum number of antimicrobials prescribed according to gender are illustrated in Table 5.22.

Table 5.22 reveals that the average number of antimicrobials prescribed for each female patient varied between 1.18 ± 0.48 and 1.33 ± 0.64 antimicrobials. Clinic F had the highest average number of antimicrobials prescribed for females. The average number of antimicrobials prescribed for males varied between 1.09 ± 0.32 and 1.95 ± 0.46. Clinic D had the highest average number of antimicrobials prescribed for males. The maximum number of antimicrobials prescribed for females was 6 and this obtained from Clinic G, as shown in the table. For males the maximum number of antimicrobials prescribed was 5 also represented by Clinic G.

The statistical d-values were calculated to find out if there were practical significance differences between the average numbers of antimicrobials prescribed per gender. The results revealed that there was no difference of practical significance between the different clinics ($d < 0.8$).

Table 5.22: Average, minimum and maximum number of antimicrobials prescribed per gender

Clinic	Gender	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
A	Female	6733	1.23	0.52	1	1	4
	Male	3047	1.09	0.32	1	1	4
B	Female	2446	1.18	0.48	1	1	4
	Male	2034	1.12	0.37	1	1	4
C	Female	5347	1.30	0.67	1	1	1
	Male	2935	1.34	0.37	1	1	4
D	Female	11045	1.27	0.55	1	1	4
	Male	7158	1.95	0.46	1	1	4
E	Female	4993	1.29	0.55	1	1	4
	Male	3848	1.29	0.48	1	1	4
F	Female	9257	1.33	0.64	1	1	4
	Male	4337	1.34	0.37	1	1	4
G	Female	4212	1.29	0.62	1	1	6
	Male	4965	1.19	0.45	1	1	5
H	Female	5671	1.21	0.55	1	1	5
	Male	4615	1.12	0.37	1	1	4
I	Female	6025	1.29	0.54	1	1	4
	Male	4188	1.27	0.54	1	1	4

5.4.6 Total number of antimicrobials prescribed according to age groups

In Table 5.23 the total number of antimicrobials prescribed according to age group is illustrated.

As illustrated in Table 5.23, in all the clinics, the age group that received the highest number of prescriptions of antimicrobials was age group 6 (20-40 years), which represents 47.11% (n = 45420) of the total number of antimicrobials prescribed for all age groups in the nine clinics. This confirms the results in Table 5.3 where age group 6 (20-40 years) presented the highest number of patients. Again as shown in Table 5.8, this age group had the highest number of consultations at the clinics. The age group that received the least number of prescribed antimicrobials was age group 1 (0 – 1 month). As a matter of fact this age group represents the least number of patients in all the clinics.

Table 5.23: Total number of antimicrobials prescribed according to age groups

	AGE GROUP																	
		1		2		3		4		5		6		7		8	G	
Clinic	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	Total Z
A	70	30.6	861	20.8	1421	14.1	552	11.8	707	11.6	4388	9.7	1375	6.8	406	7.5	5	**9780**
B	8	3.5	101	2.4	441	4.4	314	6.7	273	4.5	1975	4.3	1183	5.9	186	3.5	12	**4481**
C	13	5.7	328	7.9	943	9.4	433	9.2	554	9.1	3981	8.8	1568	7.8	466	8.6	9	**8286**
D	40	17.5	879	21.2	2102	20.8	695	14.8	908	14.8	8956	19.7	3552	17.6	1101	20.4	50	**18233**
E	13	5.7	332	8.0	855	8.5	391	8.3	577	9.4	4763	10.5	1570	7.8	359	6.7	19	**8860**
F	49	21.4	649	15.7	1372	13.6	572	12.2	902	14.7	6241	13.7	2895	14.4	938	17.4	81	**13618**
G	8	3.5	288	7.0	1069	10.6	684	14.6	825	13.5	6136	13.5	2813	14.0	600	11.1	16	**12423**
H	14	6.1	368	8.9	1051	10.4	517	11.0	579	9.5	4530	10.0	2714	13.5	533	9.9	19	**10306**
I	14	6.1	335	8.1	830	8.2	529	11.3	795	13.0	4450	9.8	2465	12.2	800	14.8	5	**10218**
Total Y	**229**	**100.0**	**4141**	**100**	**10084**	**100.0**	**4887**	**100**	**6120**	**100**	**45420**	**100**	**20135**	**100**	**5389**	**100.0**	**216**	**96205**
% *	**0.24**		**4.29**		**10.46**		**4.86**		**6.35**		**47.11**		**20.88**		**5.59**		**0.22**	**100**

5.4.7 Average, minimum and maximum number of antimicrobials prescribed according to age groups in the nine clinics during the research period

The average, minimum and maximum number of antimicrobials prescribed according to age groups in each clinic are illustrated in Tables 5.24 (A-I).

The average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic A are illustrated in Table 5.24A.

Table 5.24A: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic A

Age group	Total number of antimicrobials	Mean	Standard Deviation	Median	Minimum	Maximum
1	70	1.05	0.21	1	1	1
2	861	1.05	0.21	1	1	1
3	1421	1.02	0.15	1	1	1
4	552	1.03	0.18	1	1	1
5	707	1.20	0.49	1	1	1
6	4388	1.32	0.59	1	1	1
7	1375	1.22	0.48	1	1	1
8	406	1.04	0.21	1	1	1

Table 5.24A reveals that the average number of antimicrobials prescribed to patients according to age groups varied between 1.02 ± 0.15 (age group 3) and 1.32 ± 0.59 (age group 6). Age group 6 (20-40 years) received the maximum number of prescriptions of antimicrobials as showed in Table 5.24A.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed per age groups in Clinic A were calculated. The d-values calculated (refer to Chapter 4, section 4.4.4.2.4) showed that there was no difference of practical significance found between the average number of antimicrobials prescribed per age groups in Clinic A during the research period ($d<0.8$).

The average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic B are illustrated in Table 5.24B.

Table 5.24B: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic B

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	8	1.14	0.38	1	1	2
2	101	1.02	0.14	1	1	2
3	441	1.02	0.13	1	1	2
4	314	1.05	0.25	1	1	3
5	273	1.10	0.35	1	1	3
6	1975	1.23	0.52	1	1	4
7	1183	1.16	0.45	1	1	4
8	186	1.06	0.26	1	1	3

As shown in Table 5.24B, the average number of antimicrobials prescribed per age group varied between 1.02 ± 0.14 (age groups 2 and 3) and 1.23 ± 0.52 (age group 6). The maximum number of antimicrobials was prescribed for age groups 6 and 7. This number was 4 antimicrobials.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic B. The d-values calculated (refer to Chapter 4, section 4.4.5.2.4) showed that there was no difference of practical significance found between the average number of antimicrobials prescribed between the age groups in clinic B during the research period ($d<0.8$).

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic C are shown in Table 5.24C.

Table 5.24C: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic C

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	13	1.00	0.00	1	1	1
2	328	1.05	0.23	1	1	2
3	943	1.05	0.23	1	1	3
4	433	1.06	0.24	1	1	2
5	554	1.18	0.48	1	1	3
6	3981	1.39	0.70	1	1	4
7	1568	1.28	0.60	1	1	4
8	466	1.12	0.36	1	1	3

The table reveals that the average number of antimicrobials prescribed varied between 1.00 ± 0.00 (age group 1) and 1.39 ± 0.70 (age group 6). The age groups with the maximum number of antimicrobials were 6 and 7 as shown in the table. The maximum number of antimicrobials was 4.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic C were calculated. The d-values calculated showed that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic C ($d<0.8$).

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic D are demonstrated in Table 5.24D.

Table 5.24D: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic D

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	40	1.05	0.23	1	1	2
2	879	1.03	0.18	1	1	2
3	2102	1.03	0.18	1	1	3
4	695	1.07	0.27	1	1	3
5	908	1.22	0.50	1	1	4
6	8956	1.36	0.62	1	1	4
7	3552	1.26	0.53	1	1	4
8	1101	1.09	0.31	1	1	3

As illustrated in the Table 5.24B, the average number of antimicrobials prescribed according to age group varied between 1.03 ● 0.18 (age groups 2 and 3) and 1.36 ± 0.62 (age group 6). The maximum number of antimicrobials (n = 4) was prescribed for age groups 5, 6 and 7.

Statistical d-values as indication of the practical significance differences between the average number of antimicrobials prescribed per age groups in Clinic D are illustrated in Table $5.24D_1$.

As illustrated in Table $5.24D_1$, the d-values calculated show that there was a difference of practical significance found between the average numbers of antimicrobials prescribed for patients in age group 5 and 6, 7 and 8. This implies that the average number of antimicrobials prescribed for patients in age group 5 was the lowest as compared to the average number of antimicrobials prescribed for patients in age groups 6 and 7 (refer to the pink boxes).

Table 5.24D$_1$: Statistical d-values as indication of the practical significance differences between the average number of antimicrobials prescribed per age groups in Clinic D

Age group	1	2	3	4	5	6	7	8
1		0.09	0.09	0.07	0.34	0.50	0.40	0.13
2	0.09		0.00	0.15	0.38	0.53	0.43	0.19
3	0.09	0.00		0.15	0.38	0.53	0.43	0.19
4	0.07	0.15	0.15		0.30	0.47	0.36	0.06
5	0.34	0.38	0.38	0.30		0.97	1.16	0.96
6	0.50	0.53	0.53	0.47	0.97		0.16	0.44
7	0.40	0.43	0.43	0.36	1.16	0.16		0.13
8	0.13	0.19	0.19	0.06	0.96	0.44	0.13	

Difference of practical significance is d>0.8

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic E are illustrated in Table 5.24E.

As illustrated in Table 5.24E, the average number of antimicrobials prescribed according to age group varied between 1.03 ± 0.18 (age group 3) and 1.39 ± 0.58 (age group 6). The maximum number of antimicrobials (n = 4) was prescribed for age groups 6 and 7.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic E were calculated. The d-values calculated showed that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic E (d<0.8).

Table 5.24E: The average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic E

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	13	1.30	0.48	1	1	2
2	332	1.04	0.19	1	1	2
3	855	1.03	0.18	1	1	3
4	391	1.09	0.29	1	1	2
5	577	1.29	0.50	1	1	3
6	4763	1.39	0.58	1	1	4
7	1570	1.34	0.52	1	1	4
8	359	1.27	0.47	1	1	3

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic F are illustrated in Table 5.24F.

As illustrated in Table 5.25F, the average number of antimicrobials prescribed according to age group varied between 1.09 ± (0.29, 0.31, 0.35) for age groups 2, 3, 4, and 8 respectively and 1.38 ± 0.67 (age group 6). The maximum number of antimicrobials (n = 4) was prescribed for age groups 6 and 7.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in clinic F were calculated. The d-values calculated showed that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic F ($d<0.8$).

Table 5.24F: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic F

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	49	1.11	0.32	1	1	2
2	649	1.09	0.29	1	1	3
3	1372	1.09	0.31	1	1	3
4	572	1.09	0.31	1	1	3
5	902	1.23	0.54	1	1	3
6	6241	1.38	0.67	1	1	4
7	2895	1.26	0.56	1	1	4
8	938	1.09	0.35	1	1	3

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic G are illustrated in Table 5.24G.

As shown in Table 5.24G, the average number of antimicrobials prescribed according to age group varied between 1.00 ± 0.00 for patients in age group 1 and 1.34 ± 0.66 for patients in age group. The maximum number of antimicrobials (n = 6) was prescribed for patients age group 6 (20-40 years).

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic G were calculated. The d-values calculated show that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic G ($d<0.8$).

Table 5.24G: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic G

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	8	1.0	0	1	1	1
2	288	1.08	0.27	1	1	2
3	1069	1.07	0.28	1	1	4
4	684	1.07	0.27	1	1	3
5	825	1.18	0.46	1	1	4
6	6136	1.34	0.66	1	1	6
7	2813	1.23	0.54	1	1	5
8	600	1.08	0.30	1	1	3

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic H are illustrated in Table 5.24H.

As illustrated in Table 5.24H, the average number of antimicrobials prescribed according to age group varied between 1.02 ± 0.15 for patients in age group 3 and 1.25 ± 0.57 for patients in age group 6. The maximum number of antimicrobials (n = 5) was prescribed for patients in age groups 7.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic G were calculated The d-values calculated showed that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic H ($d<0.8$).

Table 5.24H: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic H

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	14	1.08	0.28	1	1	2
2	368	1.04	0.20	1	1	2
3	1051	1.02	0.15	1	1	2
4	517	1.03	0.19	1	1	2
5	579	1.09	0.34	1	1	3
6	4530	1.25	0.57	1	1	4
7	2714	1.18	0.51	1	1	5
8	533	1.09	0.33	1	1	3

The average, minimum and maximum number of antimicrobials prescribed per age group in Clinic I are shown in Table 5.24I.

As illustrated in Table 5.24I, the average number of antimicrobials prescribed according to age group varied between 1.00 ± 0.00 for patients in age group 1 and 1.36 ± 0.60 for patients in age group 6. The maximum number of antimicrobials (n = 4) was prescribed for patients in age groups 5, 6 and 7.

Statistical d-values as indication of the practical significance differences between the average numbers of antimicrobials prescribed between the age groups in Clinic I were calculated. The d-values calculated showed that there was no difference of practical significance found between the average numbers of antimicrobials prescribed per age groups in Clinic I.

Table 5.24I: Average, minimum and maximum number of antimicrobials prescribed according to age groups in Clinic I

Age group	Total number of antimicrobials	Mean	Standard deviation	Median	Minimum	Maximum
1	14	1.00	0	1	1	1
2	335	1.06	0.25	1	1	3
3	830	1.08	0.32	1	1	3
4	529	1.10	0.33	1	1	3
5	795	1.26	0.51	1	1	4
6	4450	1.36	0.60	1	1	4
7	2465	1.35	0.57	1	1	4
8	800	1.26	0.46	1	1	3

SUMMARY OF THE RESULTS OF ALL CLINICS

In almost all the nine clinics, the highest average number of antimicrobials was prescribed for age groups 6 (20-40 years) and 7 (40-60 years). The data analyzed also show that these age groups 6 (20-40 years) and 7 (40-60 years) were the age groups that received the maximum number of prescriptions of antimicrobials. In all the clinics these age groups had the highest number of patients that visited the clinics as shown in Table 5.3. This probably explains why these age groups received the highest number of antimicrobials in all clinics as shown in Table 5.23.

Statistical d-values calculated as indication of the practical significance differences between the average numbers of antimicrobials prescribed per gender, showed that there were no differences of practical significance between the different clinics.

However differences of practical significance were observed between the average numbers of antimicrobials prescribed between the age groups in Clinic D only. Clinic D comparatively received the highest number of patients. Hence the highest number of antimicrobials prescribed according to age groups as compared to the rest of the clinics during the one-year research period.

5.4.8 Total number of antimicrobials prescribed according to pharmacological groups and ATC (classification)

The following table will illustrate the list of antimicrobials according to their Pharmacological and Anatomical Therapeutic Chemical (ATC) classification system codes.

Table 5.25: Pharmacological and ATC classification of antimicrobials

Pharmacological group	ATC
Penicillins	J01C
Cephalosporins	J01D
Macrolides	J01F
Aminoglycosides	J01G
Tetracyclines	J01A
Sulphonamides	J01E
Quinolones	J01M
Antifungals	J01X
Antiprotozoals	J01X
Antivirals	J01S

The total number of antimicrobials prescribed according to pharmacological groups

The total number of antimicrobials prescribed according to pharmacological groups in the nine clinics is illustrated in Table 5.26.

According to Table 5.26, the most prescribed antimicrobial in the nine clinics was penicillins accounting for 39.35% (n = 36808) followed by sulphonamides which accounted for 23.18% (n = 21687). The least prescribed antimicrobial according to pharmacological group was cephalosporins accounting for 0.03% (n = 32). Penicillin was prescribed most in Clinic D as much as 42.06% (n = 7690) and Clinic A had the least number of penicillins prescribed, i.e. with 22.13 % (n = 2165). Sulphonamides was mostly prescribed in Clinic F, with 35.4% (n = 4850) and least prescribed in Clinic

B with 17.63% (n = 792). This could be influenced by the type of diagnoses encountered in each clinic (refer to Section 5.6.2).

Table 5.26: Total number of antimicrobials prescribed according to pharmacological groups

Clinic		Penicillins (J01C)	Cephalosporins (J01D)	Antifungals (J01X)	Antiprotozoals (J01X)	Macrolides (J01F)	aminoglycosides (J01G)	Tetracyclines (J01A)	Quinolones (J01M)	Sullphonamides (J01E)	Chlorampenicols (J01B)	Antivirals (J01S)	Total Y
A	N	2165		160	1160	451		1283	462	4104			**9785**
	%	22.13		1.64	11.9	4.61		13.1	4.72	41.94			
B	N	2288		48	346	455	1	357	158	792		48	**4493**
	%	50.92		1.07	7.7	10.1	0.02	7.95	3.52	17.63		1.07	
C	N	3938	11	171	866	536	1	874	667	1164	3	64	**8295**
	%	47.47	0.13	2.06	10.4	6.46	0.01	10.5	8.04	14.03	0.04	0.77	
D	N	7690		397	1747	2485		1824	804	3327		9	**18283**
	%	42.06		2.17	5.56	13.6		9.98	4.4	18.2		0.05	
E	N	2350	1	45	289	41			162	1459	89	1	**4437**
	%	45.39	0.02	0.87	5.58	0.79			3.13	28.18	1.72	0.02	
F	N	3173		259	1562	1122		1854	805	4850		74	**13699**
	%	23.16		1.89	11.4	8.19		13.5	5.88	35.4		0.54	
G	N	5422		216	1075	1267		950	515	2937		57	**12439**
	%	43.59		1.74	8.64	10.19		7.64	4.14	23.61		0.46	
H	N	4981	20	180	806	808		849	593	2020	9	58	**10324**
	%	48.24	0.19	1.74	7.81	7.83		8.22	5.74	19.56	0.09	0.56	
I	N	4801		69	1677	1230	65	1018	331	1034	65	1230	**11520**
	%	46.95		0.67	16.4	12	0.64	9.96	3.24	10.11	0.64	12	

Total Y: Total number of the antimicrobials prescribed according to their pharmacological groups in each clinic.

%: Percentage calculated according to the total number of antimicrobials prescribed in each clinic.

5.4.9 Total number of antimicrobials prescribed according to pharmacological group and gender

The following table (Table 5.27) illustrates the number of antimicrobials prescribed according to pharmacological groups and gender.

Table 5.27: Total number of antimicrobials prescribed according to pharmacological group and gender

Clinic	Gender		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Macrolides (J01F)	Antivirals (J01S)	Cephalosporins (J01D)	Aminoglycosides (J01G)	Tetracyclines (J01A)	Chloramphenicols (J01B)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
A	Female	N	960	13	546	165				109		1872	98	**3763**
		%	25.51	0.3	14.5	4.38				2.9		49.75	2.6	
	Male	N	164	43	20	138				288		1267	85	**2005**
		%	8.18	2.1	1	6.88				14.4		63.19	4.24	
B	Female	N	623	9	91	147	5			34		296	12	**1217**
		%	51.19	0.7	7.48	12.1	0.4			2.79		24.32	0.99	
	Male	N	570	5	18	126	10		1	31		210	27	**998**
		%	57.11	0.5	1.8	12.6	1		0.05	3.11		21.04	2.71	
C	Female	N	1444	15	607	208	27			53		564	54	**2972**
		%	48.59	0.5	20.4	7	0.9			1.78		18.98	1.82	
	Male	N	938	17	52	169	19			54		429	90	**1769**
		%	53.02	1	2.94	9.55	1.1			3.05		24.25	5.09	
D	Female	N	2819	40	622	1060	2			359		1513	234	**6649**
		%	42.4	0.6	9.35	15.9	0			5.4		22.76	3.52	
	Male	N	1898	59	104	717	2			122		1189	167	**4258**
		%	44.57	1.4	2.44	16.8	0			2.87		27.92	3.92	
E	Female	N	1414	14	236	212	12			113	62	858	23	**2960**
		%	47.77	0.5	7.97	7.16	0.4			3.82	2.1	28.99	0.78	
	Male	N	429	31	52	257	29			156	27	600	139	**2208**
		%	19.43	1.4	2.36	11.6	1.3			7.07	1.2	27.17	6.3	
F	Female	N	1906	22	564	375	17			252		2171	309	**5124**
		%	37.2	0.4	11	7.32	0.3			4.92		42.37	6.03	
	Male	N	1522	39	44	275	19			234		1624	89	**2753**
		%	55.29	1.4	1.6	9.99	0.7			8.5		58.99	3.23	
G	Female	N	2543	23	330	414	15			62		1262	128	**4140**
		%	61.43	0.6	7.97	10	0.4			1.5		30.48	3.09	
	Male	N	2413	34	58	347	10			67		958	61	**3057**
		%	78.93	1.1	1.9	11.4	0.3			2.19		31.34	2	
H	Female	N	1224	90	685	406	1	12		519	7	1010	371	**4325**
		%	28.3	2.1	15.8	9.39	0	0.3		12	0.2	23.35	8.58	

Table 5.27: Total number of antimicrobials prescribed according to pharmacological group and gender (cont)

Clinic	Gender		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Macrolides (J01F)	Antivirals (J01S)	Cephalosporins (J01D)	Aminoglycosides (J01G)	Tetracyclines (J01A)	Chloramphenicols (J01B)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
H	Male	N	775	90	120	399		8		329	2	1010	221	**2954**
		%	26.24	3	4.06	13.5		0.3		11.1	0.1	34.19	7.48	
I	Female	N	1224	2	546	385			1	133		413	20	**2724**
		%	44.93	0.1	20	14.1			0.04	4.88		15.16	0.73	
	Male	N	775	3	305	342			1	132		283	33	**1874**
		%	41.36	0.2	16.3	18.2			0.05	7.04		15.1	1.76	
	Total Z		**23989**	**549**	**5000**	**6142**	**168**	**20**	**3**	**3047**	**99**	**17529**	**2161**	**55750**
	*** %**		43.03	0.98	8.97	11.02	0.30	0.04	0.01	5.47	0.18	31.44	3.88	

Total Y: Total number of antimicrobials prescribed according to pharmacological groups in the nine clinics.

Total Z: Total number of antimicrobials prescribed according to gender in each clinic.

%: Percentage was calculated according to the total number of antimicrobials prescribed according to gender.

** %: Percentage calculated according to antimicrobials according to pharmacological group and gender in each clinic.*

Table 5.27 illustrates that female patients received the highest number of antimicrobial prescriptions in the nine clinics accounting for 60.76% (n = 33874) of the total number of antimicrobials. The males received 39.24% (n = 21876). The most prevalent antimicrobial prescribed for both females and males was penicillin accounting for 43.03% (n = 23989) of the total number of antimicrobials prescribed in the nine clinics. Females received 59.87% (n = 14363) and males received 40.13% (n = 9626) penicillins. Sulphonamides were the second most prescribed antimicrobial for both genders accounting for 31.44% (n = 17529). These results were similar to results obtained by Wang *et al.* (1999: 156) in their study, which revealed that the penicillin class of antibiotics remains the most frequently used class of antibiotics, the next being sulphonamides. The least prescribed antimicrobial for this patient population was aminoglycosides accounting for 0.01% (n = 3). Aminoglycosides are recommended for hospitalized patients where patients' plasma levels can be monitored. The reason is concerns regarding ototoxicity and nephrotoxicity of aminoglycosides (Kashuba *et al.*, 1999: 626).

5.4.10 Total number of antimicrobials prescribed according to pharmacological group and age group

The following tables 5.28 (A-I) illustrate the number of antimicrobials prescribed according to pharmacological group and age groups at each clinic.

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic A is illustrated in Table 28A.

Table 5.28A: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic A

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total A
1	N	55	14		3		6		78
	%A	70.51	17.95		3.85		7.69		
	%B	2.33	8.19		0.61		0.14		
2	N	114	60		31		746		951
	%A	11.99	6.31		3.26		78.44		
	%B	4.83	35.10		6.26		16.80		
3	N	138	48		144		1293		1623
	%A	8.50	2.96		8.87		79.67		
	%B	5.84	28.1		19.10		29.20		
4	N	142	36	1	74	4	377		634
	%A	22.40	5.68	0.16	11.67	0.63	59.46		
	%B	6.01	21.10	0.08	15.00	0.15	8.50		
5	N	212	3	103	52	181	248	2	801
	%A	26.47	0.37	12.86	6.49	22.60	30.96	0.25	
	%B	8.98	1.75	8.23	10.50	6.92	5.59	3.99	
6	N	1433	5	916	136	1842	889	384	5605
	%A	25.57	0.09	16.34	2.43	32.86	15.86	6.85	
	%B	60.69	2.92	73.16	27.50	70.40	20.00	69.60	
7	N	223	4	225	54	527	580	119	1732
	%A	12.88	0.23	12.99	3.12	30.43	33.49	6.87	
	%B	9.45	2.34	17.97	10.90	2.37	6.70	4.84	
8	N	44	1	7	1	62	297	27	439
	%A	10.02	0.23	1.59	0.23	14.12	67.65	6.15	
	%B	1.86	0.58	0.56	0.20	2.37	6.70	4.89	
Total Z		**2361**	**171**	**1252**	**495**	**2616**	**4436**	**532**	**11863**
*** %**		**19.87**	**1.44**	**10.54**	**4.17**	**22.01**	**37.33**	**4.65**	

Total Y: Total number of antimicrobials in each age group.

Total Z: Total number of antimicrobials in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

According to Table 5.28A, the most prescribed antimicrobial in Clinic A was sulphonamides followed by tetracyclines and then penicillins. The age group that received the highest number of antimicrobial prescriptions was age group 6 (20-40 years) with 47.17% (n= 5605). Statistically this was the age group with the highest number of patients (Table 5.23). The antimicrobial most prescribed to this age group was tetracyclines accounting for 32.86% (n = 1842) followed by penicillins (n = 1433, 25.57%). This could have been influenced by the clinical diagnoses presented in this age group as will be discussed in Section 5.4.11. Age group 1 (0-1 month) received the lowest number of antimicrobials totalling up 78 (0.59 %). This age group had the smallest number of patients. The antimicrobial most prescribed for this age group was penicillin accounting for 70.51% (n = 55). The majority of patients in Clinic A went to the clinic to be treated of upper respiratory infections. In such cases co-trimoxazole was prescribed for the patients (refer to Clinic A, Table 5.34A). According to Fendrick *et al.* (2001: 1684) antibiotic courses are neither necessary nor appropriate in the treatment of upper respiratory infection because these infections are mostly caused by viruses or other nonbacterial agents, and thus are self-limiting.

The following antimicrobials: antiprotozoals, tetracyclines and quinolones were not prescribed for age groups: 1 (0-1 month), 2 (1 month – 1 year) and 3 (1 year – 6 years). Antiprotozoals (metronidazole) is well known for its role in the treatment of bacterial vaginosis and *Trichomonas vaginalis*, also as a prophylactic agent in general and gynaecologic surgery (Simms-Cendan, 1996: 153). Such conditions do not present in these age groups. Tetracyclines (doxycycline) are contraindicated in ages less than 8 years due to retardation of bone growth and discoloration of teeth (Lynn, 1996: 225). The quinolones (ciprofloxacin) lack paediatric preparations (Appelbaum & Hunter, 2000: 13).

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic B is illustrated in Table 28B.

Table 5.28B: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic B

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Aminoglycosides (J01G)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N	2							1		3
	%A	66.67							33.33		
	%B	0.17							0.20		
2	N	21				18			8		47
	%A	44.68				38.30			17.02		
	%B	1.76				6.55			1.56		
3	N	69	3		1	55			46		174
	%A	39.66	1.72		0.57	31.61			26.44		
	%B	5.77	21.43		6.67	20.00			9.09		
4	N	91	2	2	4	33		1	16		149
	%A	61.07	1.34	1.34	2.68	22.15		0.67	10.74		
	%B	7.61	14.29	1.83	26.67	12.00		1.52	3.16		
5	N	119	1	7		29		6	20	1	183
	%A	65.03	0.55	3.83		15.85		3.28	10.93	0.55	
	%B	5.95	7.14	6.42		10.55		9.09	3.95	2.50	
6	N	528	4	72	6	83	1	38	237	30	999
	%A	52.85	0.40	7.21	0.60	8.31	0.10	3.80	23.72	3.00	
	%B	44.15	28.57	66.06	40.00	30.18	100	57.58	46.84	76.92	
7	N	295	4	28	4	44		19	147	8	549
	%A	53.73	0.73	5.10	0.73	8.01		3.46	26.78	1.46	
	%B	24.67	28.57	25.19	26.67	16.00		28.79	29.05	20.51	
8	N	71				13		2	31		117
	%A	60.68				11.11		1.71	26.50		
	%B	5.94				4.73		3.03	6.13		
Total Z		**1196**	**14**	**109**	**15**	**275**	**1**	**66**	**506**	**39**	**2221**
*** %**		**53.85**	**0.63**	**4.91**	**0.68**	**12.38**	**0.05**	**2.97**	**22.78**	**1.76**	

Total Y: Total number of antimicrobials in each age group.

Total Z: Total number of antimicrobials in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

As illustrated in Table 5.28B, the most prescribed antimicrobial according to pharmacological group in Clinic B was penicillin followed by sulphonamide. The age group that received the highest number of antimicrobials was age group 6 (20-40 years) with a total of 999 antimicrobials (44.98%). The antimicrobial most prescribed according to pharmacological group to this age group was penicillin totalling up to 528 (52.85 %) followed by sulphonamides 237 (23.72 %). This was influenced by the type of clinical diagnoses presented in this age group and will be discussed in section 5.4.11. Age group 1 (0-1 month) received the least number of antimicrobials 3 (0.14 %).

In Clinic B, the diagnoses most frequent were: hypertension followed by viral influenza and amoxycillin was prescribed (refer to Clinic B, Table 5.34B). From the database it was difficult to differentiate medicine items prescribed for individual diagnosis when more than one diagnosis was made during a consultation, so in this case antimicrobials were not prescribed for hypertension but for viral influenza or any possible secondary infection that could be bacterial in origin. Assuming that the antimicrobials were prescribed for viral influenza, this was unnecessary because viral influenza is non-bacterial in origin (Viksveen, 2003: 100). The following antimicrobials were not prescribed for the patients in this clinic: cephalosporins and chloramphenicols. This could be influenced by the type of disease states presented in this clinic as will be discussed later in section 5.6.1. The following antimicrobials were not prescribed for the following age groups: Antifungals (1 and 2), antiprotozoals (1, 2 and 3), antiviral agents 1 and 2), macrolides (1), aminoglycosides (1, 2, 3, 4, 5, 7 and 8), tetracyclines (1, 2 and 3) and quinolones (1 – 4). Aminoglycosides (gentamycin) have been used for over 30 years for the treatment of nosocomial pneumonia caused by gram-negative bacteria in hospitalised patients (Kashuba *et al*., 1999: 623). The type of patients who visit the primary health care clinics present with minor ailments. Macrolides (azithromycin) are used in the treatment of sexually transmitted diseases: chlamydia, chancroid, and gonorrhoea which do not present in the age group 1 (Kremer, 2002: 175). Antifungals (itraconazole) are rarely used in neonates and children unless the potential benefit outweighs the potential risks (De Beule, 1996: 178).

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic C is illustrated in Table 28C.

Table 5.28C: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic C

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N							5		5
	%A %B							100 0.50		
2	N	73				8		69		150
	%A %B	48.67 3.06				5.33 2.12		46.00 6.69		
3	N	186	6	2		60		110		364
	%A %B	51.10 7.80	1.65 18.75	0.55 0.30		16.48 15.92		30.22 11.08		
4	N	146	2	24	2	42	3	43		262
	%A %B	55.73 6.12	0.76 6.25	9.16 0.01	0.76 4.35	16.03 11.14	1.15 2.80	16.41 4.33		
5	N	252	4	36	2	29	8	52	3	386
	%A %B	65.28 10.57	1.04 12.50	9.33 5.46	0.52 4.35	7.51 7.69	2.07 7.48	13.47 5.24	0.78 2.08	
6	N	1102	17	466	33	156	72	379	99	2324
	%A %B	47.42 46.22	0.73 53.13	20.05 70.71	1.42 71.74	6.71 41.38	3.10 67.29	16.31 38.17	4.26 68.75	
7	N	434	3	128	8	65	21	243	38	940
	%A %B	46.17 18.90	0.32 9.38	13.62 19.42	0.85 17.39	6.91 17.24	2.23 19.63	25.85 24.47	4.04 26.39	
8	N	191		23	1	17	3	92	4	331
	%A %B	57.70 8.01		6.95 3.49	0.30 2.17	5.14 4.51	0.91 2.80	27.79 9.26	1.21 2.78	
Total Z		**2384**	**32**	**679**	**46**	**377**	**107**	**993**	**144**	**4762**
*** %**		**50.06**	**0.67**	**14.26**	**0.97**	**7.92**	**2.25**	**20.85**	**3.04**	

Total Y: Total number of antimicrobial in each age group.

Total Z: Total number of antimicrobial in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

As shown in Table 5.28C, the most prescribed antimicrobial according to pharmacological group was penicillin followed by sulphonamides. Age group 6 received mostly penicillin representing 47.42 % (n = 1102). Age group 1 (0-1 month) received the least number of antimicrobials because it was represented by the smallest number of patients.

The most diagnoses presented in this clinic were hypertension; upper respiratory infection and common cold (refer to Clinic C, Table 5.34C). Amoxycillin was mostly prescribed. According to McCaig *et al.* (1995: 214) antimicrobial agents used to treat viral upper respiratory tract infections do not shorten the course of acute illness nor prevent secondary bacterial infections, and this could mean misuse of these agents. No aminoglycosides were prescribed for any age group in this clinic. There are concerns regarding the use of aminoglycosides due to ototoxicity, nephrotoxicity, and uncertain optimal pharmacokinetic and pharmacodynamic targets for efficacy (Kashuba *et al.,* 1999: 626).

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic D is illustrated in Table 28D.

As illustrated in Table 28D, the most prescribed antimicrobial according to pharmacological group was penicillins followed by sulphonamides. Age group 6 received the highest quantity of penicillins (amoxycillin). Age group 1 (0-1 month) received the least antimicrobial prescriptions (n= 6, 0.05%). The commonest diagnoses presented in this clinic were upper respiratory infections followed by acute bronchitis (refer to Clinic D, Table 5.34D). Bronchitis is one of the symptoms of upper respiratory tract of viral origin therefore; there is evidence of lack of efficacy of antibiotic agents in this condition (Viksveen, 2003: 100).

Patients in Clinic D did not receive the following antimicrobials: cephalosporins, aminoglycosides and chloramphenicols prescriptions. This could have been influenced by the disease states presented in this clinic. Aminoglycosides and cephalosporins are prophylactic antimicrobials used by surgery and allied services, in in-patient hospital settings, so their use is limited in private primary health care settings (Srishyla *et al.,* 1994: 284). Chloramphenicol is a 'first-line' antibiotic in the treatment of typhoid fever which is less prevalent in South Africa (Mills-Robertson *et al.,* 2002: 249).

Table 5.28D: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic D

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N	2				4		2		6
	%A	25.00				50.00		25.00		
	%B	0.04				0.11		0.07		
2	N	92				73		160		325
	%A	28.31				22.46		49.23		
	%B	1.95				4.10		5.91		
3	N	456	3	10		236		330		1035
	%A	44.06	0.29	0.97		22.80		31.88		
	%B	9.64	3.03	1.38		13.27		12.20		
4	N	287	6	5		1.1	5	57	1	472
	%A	60.81	1.27	1.06		23.52	1.06	12.08	0.21	
	%B	6.07	6.06	0.69		6.24	1.04	2.11	0.25	
5	N	327	3	42		116	30	110	11	639
	%A	51.17	0.47	6.57		18.15	4.69	17.21	1.72	
	%B	6.91	3.03	5.79		6.52	6.21	4.07	2.74	
6	N	2277	65	487	2	7.9	323	1158	294	5325
	%A	42.76	1.22	9.15	0.04	13.50	6.07	21.75	5.52	
	%B	48.15	65.66	67.08	50.00	40.42	66.87	42.81	73.32	
7	N	940	16	147	2	345	109	631	90	2280
	%A	41.23	0.70	6.45	0.09	15.13	4.78	27.68	3.95	
	%B	19.88	16.16	20.25	50.00	19.39	22.57	23.33	22.44	
8	N	348	6	35		177	16	257	5	844
	%A	41.23	0.71	4.15		20.97	1.90	30.45	0.59	
	%B	7.36	6.06	4.82		9.98	3.31	9.50	1.25	
Total Z		**4729**	**99**	**726**	**4**	**1779**	**483**	**2705**	**401**	**10926**
*** %**		**43.28**	**0.91**	**6.64**	**0.04**	**16.28**	**4.42**	**24.76**	**3.67**	

Total Y: Total number of antimicrobial in each age group in clinic

Total Z: Total number of antimicrobial in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

*%: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic E is illustrated in Table 28E.

Table 5.28E: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic E

Age group		Penicillins (J01C)	Cephalosporins (J01D)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Chloramphenicos (J01B)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N						5			1		6
	%A %B						83.33 1.06			16.67 0.07		
2	N	30					39			83		152
	%A %B	19.74 1.28					25.66 8.28			54.61 5.69		
3	N	99		2	5		130			180		416
	%A %B	23.80 4.21		0.48 4.44	1.20 1.73		31.25 27.60			43.27 12.34		
4	N	141		5	2	1	55	3	3	40		250
	%A %B	56.40 6.00		2.00 11.11	0.80 0.69	0.40 2.44	22.00 11.68	1.20 1.12	1.20 3.37	16.00 2.74		
5	N	201		7	31		27	22	3	80	6	377
	%A %B	53.32 8.55		1.86 15.56	8.22 10.73		7.16 5.73	5.84 8.18	0.80 3.37	21.22 5.48	1.59 3.70	
6	N	1356		20	210	37	147	205	51	686	121	2833
	%A %B	47.86 57.70		0.71 44.44	7.41 72.66	1.31 90.24	5.19 31.21	7.24 76.21	1.80 57.30	24.21 47.02	4.27 74.69	
7	N	417	1	10	39	3	59	36	25	292	27	909
	%A %B	45.87 17.74	0.11 100	1.10 22.22	4.29 13.49	0.33 7.32	6.49 12.53	3.96 13.38	2.75 28.09	32.12 20.01	2.97 16.67	
8	N	106		1	2		9	3	7	97	8	233
	%A %B	45.49 4.51		0.43 2.22	0.86 0.69		3.86 1.91	1.29 1.12	3.00 7.87	41.63 6.65	4.43 4.94	
Total Z		**2350**	**1**	**46**	**289**	**47**	**471**	**269**	**82**	**1459**	**162**	**5176**
*** %**		**45.40**	**0.02**	**0.89**	**5.58**	**0.91**	**9.10**	**5.20**	**1.58**	**28.19**	**3.13**	

Total Y: Total number of antimicrobial in each age group.

Total B: Total number of antimicrobial in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and*

age group.

As shown in Table 5.28E, penicillins are the most prescribed antimicrobials according to pharmacological group followed by sulphonamides. The age group that received the highest quantity of antimicrobials was age group 6 (20-40 years) (n = 2833, 54.77%). In most cases this age group received penicillins prescriptions (n = 1356, 47.86 %). Comparatively, this was the age group in which acute sinusitis was mostly diagnosed (refer to Clinic E, Table 5.34E).

According to Fendrick *et al.* (2001: 1697) sinusitis is classified into five categories based on temporal characteristics of symptoms on which treatment is based. Symptoms associated with a viral infection (for example fever and pharyngitis) usually resolve within 5 days and so such cases do not require antibiotics. The drug treatment for acute sinusitis according to the Department of Health (2004: 246) is amoxycillin oral 8 hourly for 10 days. Patients in age group 1 (0-1 month) did not receive penicillins, cephalosporins, antifungal agents, antiviral agents, antiprotozoals, tetracyclines and chloramphenicols. Tetracyclines are contraindicated in this age group due to retardation of bone growth and discoloration of teeth (Lynn, 1996: 225). Das *et al.* (2002: 60) state that antimicrobials like tetracyclines, chloramphenicol and aminoglycosides are restricted in their indications as first choice drugs due to their toxicity.

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic F is illustrated in Table 28F.

Table 5.28F: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic F

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N					2		32		34
	%A %B					5.88 0.31		94.12 0.84		
2	N	5	3	1		42		323		374
	%A %B	1.34 0.27	0.80 4.84	0.27 0.16		11.23 6.42		86.36 8.50		
3	N	65	19	6		164		537		791
	%A %B	8.22 3.52	2.40 30.65	0.76 0.99		20.73 25.08		67.89 14.13		
4	N	126	13	4	1	80	5	151		380
	%A %B	33.16 6.82	3.42 20.97	1.05 0.66	0.26 2.78	21.05 12.23	1.32 1.03	39.74 3.97		
5	N	198	4	34	3	53	50	203	28	573
	%A %B	34.55 10.72	0.70 6.45	5.93 5.59	0.52 8.33	9.25 8.10	8.73 10.27	35.43 5.34	4.89 7.04	
6	N	1041	16	432	23	213	216	1237	268	3446
	%A %B	30.21 56.36	0.46 25.81	12.54 71.05	0.67 63.89	6.18 32.57	6.27 44.35	35.90 32.55	7.78 67.34	
7	N	304	5	113	5	82	160	903	95	1667
	%A %B	18.24 16.46	0.30 8.06	6.78 18.59	0.30 13.89	4.92 12.54	9.60 32.85	54.17 23.76	5.70 23.87	
8	N	108	2	18	4	18	56	414	7	627
	%A %B	17.22 5.85	0.32 3.23	2.87 2.96	0.64 11.11	2.87 2.75	8.93 11.50	66.03 10.89	1.12 1.76	
Total Z		**1847**	**62**	**608**	**36**	**654**	**487**	**3800**	**398**	**7892**
* %		**23.40**	**0.79**	**7.70**	**0.46**	**8.29**	**6.17**	**48.15**	**5.04**	

Total Y: Total number of antimicrobial in each age group.

Total Z: Total number of antimicrobial in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

Chapter 5: Results and discussion

In Clinic F the antimicrobials most prescribed according to pharmacological group were sulphonamides, followed by penicillin. The least prescribed antimicrobials were antifungal agents. The age group that received the highest number of antimicrobials was 6 (20-40 years). This age group received sulphonamides accounting for 35.90% (n = 1237) followed by penicillins (n = 1041, 30.21%). The commonest diagnosis presented by patients in this clinic was viral influenza in which co-trimoxazole was prescribed (refer to Clinic F, Table 5.33). Viral influenza is one of the symptoms of upper respiratory infections, that is viral in origin. The use of antibiotics in these patients is not only a poor use of health funds but can induce adverse effects and contribute to the development of resistant strains (Arrol *et al.*, 2000: 493). In clinic F, the following antimicrobials were not prescribed: cephalosporins, aminoglycosides and chloramphenicols. This could have been influenced by the types of disease states presented in the clinic. This will be discussed later (refer to Table 5.33). Age groups 1 and 2 did not receive penicillins, anti-fungal agents, antiprotozoals, antiviral agents, tetracyclines and quinolones. The use of antifungal agents (amphotericin B) is complicated by a high incidence of potentially serious side effects. Most patients develop chills and fevers that can be partially controlled with premedication, more serious consequences are the development of renal dysfunction and electrolyte imbalance (Malik *et al.*, 1998: 478). Tetracyclines are contraindicated in patients younger than 8 years because they cause permanent tooth calcification (Lynn, 1996: 225).

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic G is illustrated in Table 28G.

In Clinic G (as shown in Table 5.29G), the most prescribed antimicrobial according to pharmacological group was penicillin followed by sulphonamide. Age group 6 (20-40 years) received the highest number of antimicrobials accounting for 47.83 % (n = 3443). The most prescribed antimicrobial according to age group 6 (20-40 years) was penicillins followed by sulphonamides. Co-trimoxazole was the most prescribed antimicrobial in this clinic in the treatment of colon: non-specific diarrhoea and gastroenteritis (refer to Clinic G, Table 5.33). Calva's (1996: 1121) study showed that 37% of the patients prescribed co-trimoxazole for diarrhoeal episodes could indicate misuses of these agents. Patients in age groups 2 and 3 did not receive antifungals, antiprotozoals, antiviral agents and tetracyclines. These age groups being the smallest of the ages, do not take drugs that lack paediatric preparations (for example, fluoroquinolones) (Appelbaum & Hunter, 2000: 13). Tetracyclines are contraindicated in children because they cause permanent tooth calcification between the ages of 4 months and 8 years (Lynn, 1996: 225). And also contraindicated during pre-birth and fetal stages.

Table 5.28G: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic G

Age group		Penicillins (J01C)	Antifungals (Jo1X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N	3								3
	%A %B	100 0.09								
2	N	48				30		79		157
	%A %B	35.87 1.40				19.11 3.94		50.32 3.56		
3	N	198	1		1	148		204		552
	%A %B	35.87 5.78	0.18 1.75		0.18 4.00	26.81 19.45		36.96 9.19		
4	N	206	5	4		80	3	110		408
	%A %B	50.49 6.01	1.23 8.77	0.98 1.03		19.61 10.51	0.74 2.33	26.96 4.95		
5	N	320	4	16	2	70	6	147	9	574
	%A %B	55.75 9.33	0.70 7.02	2.79 4.12	0.35 8.00	12.20 9.20	1.05 4.65	25.61 6.62	1.57 4.76	
6	N	1627	27	273	17	266	88	1000	145	3443
	%A %B	47.26 47.43	0.78 47.37	7.93 70.36	0.49 68.00	7.73 34.95	2.56 68.22	29.04 45.05	4.21 76.72	
7	N	823	19	90	3	129	23	539	33	1658
	%A %B	49.61 24.01	1.15 33.33	5.42 23.20	0.18 12.00	7.78 16.95	1.39 17.83	32.49 24.28	1.99 17.46	
8	N	204	1	5	2	38	9	141	2	402
	%A %B	50.75 5.95	0.25 1.75	1.24 1.29	0.50 8.00	9.45 4.99	2.24 6.98	35.07 6.35	0.50 1.06	
Total Z		**3428**	**57**	**388**	**25**	**761**	**129**	**2220**	**189**	**7197**
*** %**		**47.63**	**0.79**	**5.39**	**0.35**	**10.57**	**1.79**	**30.85**	**2.63**	

Total Y: Total number of antimicrobials in each age group.

Total Z: Total number of antimicrobials in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the total number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

The total number of antimicrobials prescribed according to pharmacological and age group in Clinic I is illustrated in Table 28I.

Table 5.28I: Total number of antimicrobials prescribed according to pharmacological group and age group in Clinic I

Age group		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Total Y
1	N	1			1		4		6
	%A %B	16.67 0.05			16.67 0.14		66.67 0.57		
2	N	13	2		29		46		90
	%A %B	14.44 0.65	2.22 40.00		32.22 3.98		51.11 6.60		
3	N	65			114	3	82		264
	%A %B	24.62 3.25			43.18 15.66	1.14 1.13	31.06 11.76		
4	N	127		4	104	7	26		268
	%A %B	47.39 6.35		1.49 0.47	38.81 14.29	2.61 2.64	9.70 3.73		
5	N	195		52	80	37	35	5	404
	%A %B	48.27 9.75		12.87 6.11	19.80 10.99	9.16 13.96	8.66 5.02	1.24 9.43	
6	N	927	1	475	224	121	226	32	2006
	%A %B	46.21 46.33	0.05 20.00	23.68 55.82	11.17 30.77	6.03 45.66	11.27 32.42	1.60 60.38	
7	N	465	1	247	142	73	195	14	1137
	%A %B	40.90 23.24	0.09 20.00	21.72 29.02	12.49 19.51	6.42 27.55	17.15 27.98	1.23 26.42	
8	N	208	1	73	34	24	83	2	425
	%A %B	48.94 10.39	0.24 20.00	17.18 8.58	8.00 4.67	5.65 9.06	19.53 11.91	0.47 3.77	
Total Z		**2001**	**5**	**851**	**728**	**265**	**697**	**53**	**4600**
*** %**		**43.50**	**0.11**	**18.50**	**15.83**	**5.76**	**15.15**	**1.15**	

Total Y: Total number of antimicrobials in each age group.

Total Z: Total number of antimicrobials in each pharmacological group.

% A: *Percentage calculated according to the number of antimicrobials in each age group.*

% B: *Percentage calculated according to the total number of antimicrobials in each pharmacological group.*

* %: *Percentage calculated according to the total number of antimicrobials in each pharmacological group and age group.*

As shown in Table 5.28I, penicillins was the most frequently prescribed antimicrobial according to pharmacological group followed by antiprotozoals. The age group that received most antimicrobials was 6 (20-40 years). That group received 43.61 % (n = 2006) of such drugs. Amoxycillin was the most prescribed antimicrobial in arthlagia; acute bronchitis and acute sinusitis (refer to Clinic I, Table 5.34I). Antimicrobials could not have been prescribed for arthlagia but for a possible secondary infection. Colgan and Powers' (2001: 1002) study suggested that sinusitis should only be diagnosed in the presence of the following: prolonged non specific upper respiratory signs and symptoms (for example rhinorrhea and cough without improvement for more than 10 to 14 days). According to that study, antibiotics are not necessary. Antibiotics are almost never necessary for the treatment of common cold or acute bronchitis in otherwise healthy persons (Colgan & Powers, 2001: 1003). Among the few drug families that were not prescribed for patients in the clinics studied were quinolones, cephalosporins and aminoglycosides. Quinolones were not prescribed for patients in age groups 1 to 4 because of their toxic effects in children below 14 years of age. Ciprofloxacin deserves continued monitoring (Srishyla *et al.*, 1994: 266). Aminoglycosides (gentamycin) have a wide gram-negative spectrum including *Pseudomonas aeruginosa* and is the only choice for most cases of hospital-acquired aerobic gram-negative sepsis (Srishyla *et al.*, 1994: 266). Therefore their use is limited in private primary health care settings.

SUMMARY OF THE RESULTS OF ALL CLINICS WITH REFERENCE TO ANTIMICROBIALS PRESCRIBED ACCORDING TO AGE GROUPS

In all nine clinics, the age group for whom the most antimicrobials were prescribed was age group 6 (20-40 years). Probably it is because it was the age group with the highest number of patients in all nine clinics (refer to Section 5.1.3, Table 5.3). Age group 1 (0-1 month) received the smallest number of antimicrobials. This was the age group with the least number of patients in the nine clinics (refer to Section 5.1.3, Table 5.3).

The most frequently prescribed antimicrobials were penicillins followed by sulphonamides. These results are consistent with results obtained by Wang *et al.* (1999: 156) where the penicillin class of antibiotics (specifically, amoxycillin) were the most frequently prescribed, and the next most frequently prescribed were sulphonamides (co-trimoxazole).

It was also noted in this study that some antimicrobials such as cephalosporins, aminoglycosides and chloramphenicols were hardly prescribed in the nine clinics. Cephalosporins and aminoglycosides are antimicrobials used in surgical prophylaxis in in-patient hospital settings and administered parenterally (Srishyla *et al.*, 1994: 266). Chloramphenicol is used in the treatment of typhoid fever (Mills-Robertson *et al.*, 2002: 249), which according to the data of this study was not presented in any of the clinics. In most clinics, patients in age groups 1, 2 and 3 did not receive tetracyclines, quinolones, antifungal agents, antiprotozoals and antiviral agents' prescriptions. Tetracyclines are contraindicated in ages under 8 years due to their toxicity (Lynn, 1996: 224). Some antifungal agents (amphotericin B) also present potential serious side effects according to Malik *et al.* (1998: 478). Quinolones (ciprofloxacin) lacking pediatric preparations (Appelbaum and Hunter, 2000: 13) were another pharmacological drug family that were hardly prescribed for pediatrics patients.

5.4.11 Total number of individual antimicrobials prescribed according to age groups

The following tables (Tables 5.29 (A-I)) show the frequency of the top three individual antimicrobials prescribed according to age groups in each of the nine clinics during the research period.

The top three most prescribed individual antimicrobials according to age groups in Clinic A are illustrated in Table 5.29A.

As illustrated in Table 5.29A, the highest number of antimicrobials was prescribed for patients in age group 6 (20 – 40 years) accounting for 44.87 % (n = 4388). This was the age group with the highest number of patients. The least number of antimicrobials was prescribed for patients in age group 1 (0-1 month). This being the age group with the least number of patients in all age groups.

The top three most prescribed individual antimicrobials for patients in age group 6 and the most frequently diagnosed disease states in the nine clinics are discussed in Tables 5.29(A_1 – I_1).

The top three antimicrobials prescribed for patients in age group 6 (20-40 years) and the most diagnosed states in Clinic A are shown in Table 5.29A$_1$.

Table 5.29A: Top three individual antimicrobials prescribed according to age group in Clinic A

Age group	Antimicrobials Prescribed	Number of individual antimicrobial	% of the total number	Total number antimicrobials prescribed in each age group (n=9780)
1	Amoxycillin 125mg/5ml (J01CA04)	38	63.33	**70**
	Nystatin 100000U/ml (A07AA02)	12	0.20	
	Ampicillin 125mg/5ml (J01CA01)	10	16.67	
2	Co-trimoxazole 240mg/5ml J01EE01)	667	81.74	**861**
	Amoxycillin 125mg/5ml (J01CA04)	97	11.89	
	Nystatin 100000U/ml (A07AA02)	52	6.37	
3	Co-trimoxazole 40mg/5ml)(J01EE01)	1107	84.44	**1421**
	Erythromycin 240mg/5ml (J01FA01)	123	9.38	
	Amoxycillin 125mg/5ml (J01CA04)	81	6.18	
4	Co-trimoxazole 240mg/5ml J01EE01)	265	48.01	**552**
	Erythromycin 240mg/5ml (J01FA01)	50	9.06	
	Co-trimoxazole 240mg/5ml(J01EE01)	47	8.51	
5	Co-trimoxazole 480mg tablets (J01EE01)	239	33.80	**707**
	Ampicillin 250mg capsules (J01CA01)	105	14.85	
	Doxycycline 100mg capsules (J01AA02)	93	13.15	
6	Doxycycline 100mg capsules (J01AA02)	892	20.33	**4388**
	Co-trimoxazole 480mg tablets (J01EE01)	888	20.24	
	Ampicillin 250mg capsules (J01CA01)	775	17.66	
7	Co-trimoxazole 480mg tablets (J01EE01)	576	41.91	**1375**
	Doxycycline 100mg capsules (J01AA02)	260	18.91	
	Metronidazole 200mg tablets (J01XD01)	151	10.98	
8	Co-trimoxazole 480 mg tablets (J01EE01)	295	72.66	**406**
	Doxycycline 100mg capsules (J01AA02)	36	8.87	
	Norfloxacin 400mg tablets (J01MA06)	22	5.42	

Table 5.29A$_1$: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic A

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Doxycycline 100mg (J01AA02)	Pelvic inflammatory disease	180
	Chronic prostatis	95
	Vulvo vaginitis: trichomonas	24
Co-trimoxazole 480mg (J01EE01)	Viral influenza	127
	Upper respiratory infection	47
	Acute sinusitis	39
Ampicillin 250mg (J01CA01)	Antenatal urinary tract infection: cystitis	109
	Antenatal booking visits	18
	Antenatal: vaginal discharge	14

The antimicrobials most prescribed for patients in age group 6 (20-40 years) as shown in Table 5.29A$_1$ were: doxycycline 100mg, co-trimoxazole 480mg and ampicillin 250mg. The diagnoses for which doxycycline were mostly prescribed were: pelvic inflammatory disease, vulvovaginitis: trichomonas and chronic prostatis. This is in line with the recommended treatment for pelvic inflammatory disease as stated by Lynn (1996: 224). Co-trimoxazole 480mg was prescribed for: upper respiratory infection, viral influenza and acute sinusitis. In terms of morbidity and mortality, influenza is clearly the most serious viral airway infection in adults and is associated with seasonal epidemics (Bartlett *et al.*, 1998: 827). Therefore the administration of antibiotics is unnecessary. The use of co-trimoxazole in non-bacterial conditions is a growing concern over increasing resistance, particularly among strains of *S. pneumoniae* and *H. influenzae* (Brown, 2000: 93). Ampicillin was mostly prescribed for: Antenatal: urinary tract infections: cystitis, Antenatal: vaginal discharge and antenatal visits. According to Bailey (1994: 95), the majority of urinary tract infections present as bacterial cystitis in women in the sexually active age group and the most effective drugs used include nitrofurantoin 50mg, trimethoprin 100mg and norfloxacin 200mg given at night. Nevertheless, nitrofurantion is contraindicated in pregnancy (Snyman, 2004: 241), the use of norfloxacin in pregnancy has not been established (Snyman, 2004: 282), and trimethoprin is contraindicated in pregnancy (Snyman, 2004: 276).

The top three antimicrobials prescribed according to age groups in Clinic B will be illustrated in Table 5.29B.

Table 5.29B: Top three individual antimicrobials prescribed according to age group in Clinic B

Age group	Antimicrobials Prescribed	N	%	Total number of antimicrobials prescribed in each age group (n = 4481)
1	Amoxycillin125mg/5ml (J01CA04)	2	25.00	8
	Ampicillin 125mg/5ml (J01CA01)	2	25.00	
	Erythromycin 125mg/5ml (J01FA01)	2	25.00	
2	Amoxycillin 125mg/5ml (J01CA04)	31	30.69	101
	Erythromycin 125mg/5ml (J01FA01)	25	24.75	
	Ampicillin 125mg/5ml (J01CA01)	21	20.79	
3	Amoxycillin 125mg/5ml (J01CA04)	171	38.78	441
	Erythromycin 125mg/5ml (J01FA01)	83	18.82	
	Co-trimoxazole 240mg/5ml (J01EE01)	66	14.97	
4	Amoxycillin 125mg/5ml (J01CA04)	93	29.62	314
	Erythromycin 125mg/5ml (J01FA01)	35	11.15	
	Ampicillin 125mg/5ml (J01CA01)	30	9.55	
5	Amoxycillin 250mg caps (J01CA04)	104	38.10	273
	Erythromycin 250mg caps (J01FA01)	36	13.19	
	Co-trimoxazole 240mg tabs (J01EE01)	29	10.62	
6	Amoxycillin 250mg caps (J01EE01)	617	31.24	1975
	Co-trimoxazole 480mg tabs (J01EE01)	341	17.27	
	Doxycycline 100mg caps (J01AA02)	228	11.54	
7	Amoxycillin 250mg caps (J01EE01)	397	33.56	1183
	Co-trimoxazole 480mg tabs (J01EE01)	262	22.15	
	Doxycycline 100mg caps (J01AA02)	95	8.03	
8	Amoxycillin 250mg caps (J01EE01)	72	38.71	186
	Co-trimoxazole 480mg tabs (J01EE01)	50	26.88	
	Erythromycin 250mg caps (J01FA01)	21	11.29	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As shown in Table 5.29B, patients in age group 6 (20-40 years) received the highest numbers of antimicrobials in this clinic. The commonest antimicrobials prescribed for this age group were: amoxycillin 250mg, co-trimoxazole 480mg and doxycycline 100mg.

The top three individual antimicrobials prescribed for patients in age group 6 (20-40 years) and the most frequently diagnosed disease states in Clinic B are shown in Table $5.29B_1$.

Table $5.29B_1$: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic B

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Amoxycillin 250mg (J01AA04)	Viral influenza	80
	Urinary tract infection	43
	Upper respiratory infection	42
Co-trimoxazole 480mg (J01EE01)	Urinary tract infection	97
	Common cold	13
	Hypertension: new/not controlled	5
Doxycycline 100mg (J01AA02)	Urinary tract infection	25
	STD: bacterial urethritis	20
	STD: urethritis in men	10

As shown in Table $5.29B_1$, amoxycillin was prescribed for viral influenza, urinary tract infection and upper respiratory infection. Amoxycillin is generally viewed as the β-lactam drug of choice for treating infections with penicillin-susceptible strains of *S. pneumoniae* (Bartlett *et al.*, 1998: 831). The use of this drug in viral diseases is inappropriate. Co-trimoxazole 480mg was prescribed for urinary tract infection, upper respiratory infections and "hypertension". It was difficult from the database to differentiate medicine items prescribed for an individual diagnosis when more than one diagnosis was made during a consultation, so in this case antimicrobials were not actually prescribed for hypertension but for a possible secondary infection. Co-trimoxazole is contraindicated in viral diseases as stated by Colgan and Powers (2001: 1000) in a study that antibacterial agents have no effect against a viral disease such as the common cold. However, Crewe-Brown *et al.* (2004: 441) reported in a study that co-trimoxazole was frequently used in a range of health care settings as a first-line agent, mainly in the treatment of respiratory and urinary tract infections. Doxycycline was used in sexual transmitted disease (STD): urethritis in men, STD: bacterial urethritis and urinary tract infection. The use of this drug in STDs is in line with the treatment guidelines as stated by Lynn (1996: 224) that doxycycline is a broad spectrum antibiotic used in the treatment of several sexually transmitted diseases.

The top three antimicrobials prescribed to according to age group in Clinic C are illustrated in Table 5.29C.

Table 5.29C: Top three individual antimicrobials prescribed according to age group in Clinic C.

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n = 8266)
1	Amoxycillin 125mg/5ml (J01CA04)	7	53.85	13
	Co-trimoxazole 240mg/5ml (J01EE01)	5	38.46	
	Nystatin 100000U/ml (A07AA02)	1	7.64	
2	Amoxycillin 125mg/5ml (J01CA04)	147	44.82	328
	Co-trimoxazole 240mg/5ml (J01EE01)	71	21.65	
	Phenoxymethyl penicillin 125mg/5ml (J01CE02)	46	14.02	
3	Amoxycillin 125mg/5ml (J01CA04)	435	46.13	943
	Phenoxymethylpenicillin 125mg/5ml (J01CE02)	150	15.91	
	Co-trimoxazole 240mg/5ml (J01EE01)	120	12.73	
4	Amoxycillin 125mg/5ml (J01CA04)	92	21.25	433
	Amoxycillin 250mg capsules (J01CA04)	56	12.93	
	Phenoxymethyl penicillin 250mg tablets (J01CE02)	46	10.62	
5	Amoxycillin 250mg capsules (J01CA04)	199	35.92	554
	Phenoxymethyl penicillin 250mg tablets (J01CE02)	66	11.91	
	Co-trimoxazole 480mg tablets J01EE01)	64	11.51	
6	Amoxycillin 250mg capsules (J01CA04)	960	24.11	3981
	Doxycycline 100mg capsules (J01AA02)	594	14.92	
	Enoxacin 200mg tablets (J01MA04)	452	11.35	
7	Amoxycillin 250mg capsules (J01CA04)	421	26.85	1568
	Co-trimoxazole 480mg tablets (J01EE01)	288	18.37	
	Doxycycline 100mg capsules (J01AA02)	175	11.16	
8	Amoxycillin 250mg capsules (J01CA04)	192	41.20	446
	Co-trimoxazole 480mg tablets (J01EE01)	110	23.61	
	Metronidazole 400mg tablets (J01XD01)	24	5.15	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As shown in Table 5.29C, patients in age group 6 (20-40 years) received the highest number of antimicrobials accounting for 48.16% (n = 3981) of the total number of antimicrobials in the clinic. Patients in age group 1 (0-1 month) received the lowest number of antimicrobials.

The top three individual antimicrobials prescribed in patients in age group 6 (20-40 years) and the most frequently diagnosed disease states in Clinic C are shown in Table $5.29C_1$.

Table $5.29C_1$: **Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic C**

Antimicrobial prescribed	**Disease states Diagnosed**	**Frequency of disease state**
Amoxycillin 250mg (J01AA04)	Acute bronchitis	92
	Upper respiratory infection	63
	Lower respiratory infection	54
Doxycycline 100mg (J01AA02)	Pelvic inflammatory disease	98
	STI: Lower abdominal pain	56
	STI: Vaginal discharge: non-pregnancy	26
Enoxacin 200mg (J01MA04)	Pelvic inflammatory disease	97
	Lower abdominal pain (Sexual transmitted infection)	51
	Vaginal discharge : non-pregnancy	14

As demonstrated in Table $5.29C_1$, amoxycillin 250mg, enoxacin 200mg and doxycycline 100mg were the most prescribed antimicrobials for patients in age group 6. The commonest diagnoses were: upper respiratory infections, acute bronchitis and common cold for amoxycillin 250mg. The use of an antibiotic in common cold is not recommended unless diagnostic tests have been performed (Woodhead *et al.*, 1996: 1596). Doxycycline was prescribed for patients with pelvic inflammatory disease, STI: lower abdominal pain and STI: vaginal discharge. The use of doxycycline in the diseases is recommended (Lynn, 1996: 224). Enoxacin was used in: pelvic inflammatory disease, sexual transmitted infection (STI): abdominal pain and STI: vaginal discharge: non-pregnancy.

The top three antimicrobials prescribed to according to age group in Clinic D are illustrated in Table 5.29D.

Table 5.29D: Top three individual antimicrobials prescribed according to age group in Clinic D

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n = 18233)
1	Amoxycillin 125mg/5ml (J01CA04)	22	55	**40**
	Ampicillin 125mg/5ml (J01CA01)	6	15	
	Nystatin 100000u/ml (A07AA02)	6	15	
2	Amoxycillin 125mg/5ml (J01CA04)	467	53.13	**879**
	Co-trimoxazole 240 mg/5ml (J01EE01)	180	20.48	
	Phenoxymethyl penicillin 125mg/5ml (J01CE02)	105	11.95	
3	Amoxycillin 125mg/5ml (J01CA04)	788	37.49	**2102**
	Phenoxymethyl penicillin 125mg/5ml (J01CE02)	487	23.17	
	Co-trimoxazole 240mg/5ml (J01EE01)	409	19.46	
4	Amoxycillin 250mg capsules (J01CA04)	138	19.86	**695**
	Phenoxymethyl penicillin 250mg tablets (J01CE02)	112	16.12	
	Amoxycillin 250mg capsules (J01CA04)	110	15.83	
5	Amoxycillin 250mg capsules (J01CA04)	272	29.96	**908**
	Erythromycin 250mg tablets (J01FA01)	146	16.08	
	Co-trimoxazole 480mg tablets (J01EE01)	119	13.11	
6	Amoxycillin 250mg capsules (J01CA04)	2110	23.56	**8956**
	Co-trimoxazole 480mg tablets (J01EE01)	1422	15.88	
	Metronidazole 200mg tablets (J01XD01)	1174	13.11	
7	Amoxycillin 250mg capsules (J01CA04)	930	26.18	**3552**
	Co-trimoxazole 480mg tablets (J01EE01)	779	21.90	
	Erythromycin 250mg tablets (J01FA01)	498	14.02	
8	Amoxycillin 250mg capsules (J01CA04)	363	32.97	**1101**
	Co-trimoxazole 480mg tablets (J01EE01)	304	27.61	
	Erythromycin 250mg tablets (J01FA01)	236	21.44	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As illustrated in Table 5.29D, the patients that received the highest number of antimicrobials were in age group 6 (20-40 years). These patients received mostly: amoxycillin 100mg, co-trimoxazole 480mg and metronidazole 200mg.

The top three individual antimicrobials prescribed in patients in age group 6 (20-40 years) and the most frequent diagnosed disease states in Clinic D are shown in Table 5.29D_1.

Table 5.30D_1: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic D.

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Amoxycillin 250mg (J01AA04)	Upper respiratory infection	277
	Acute bronchitis	260
	Common cold	110
Co-trimoxazole 480mg (J01EE01)	Upper respiratory infection	99
	Cough	79
	Gastroenteritis	67
Metronidazole 200mg (J01XD01)	Pelvic inflammatory disease	363
	Lower abdominal pain: non pregnancy	43
	Vaginal discharge : non-pregnancy	42

As shown in Table 5.29D_1, amoxycillin was mostly prescribed in: upper respiratory tract infection, acute bronchitis and the common cold. All these are mostly viral in origin and the use of an antibiotic is unnecessary as emphasized by Bjerrum *et al.*, (2004: 23) ; Fendrick *et al.* (2001: 1684) in their studies, emphasizing the importance of differentiating between bacterial and non-bacterial infections, choosing an antibiotic based on the likelihood of infection with resistant pathogens, and providing coverage against the predominant pathogens. Co-trimoxazole was prescribed for treating upper respiratory infection, cough and gastroenteritis. Arroll (2000: 493) in his study commented on patient expectations of antibiotics whereby patients sought care with a condition of five days duration of cough. Metronidazole was used for pelvic inflammatory disease, STI (sexual transmitted infection): lower abdominal pain: non-pregnant women. As stated by Simms-Cendan (1996: 153) metronidazole is used in combination with aminoglycoside to provide coverage of anaerobic organisms in patients with polymicrobial pelvic and abdominal infections.

The top three individual antimicrobials prescribed according to age group in Clinic E are illustrated in Table 5.29E.

Table 5.290E: Top three individual antimicrobials prescribed according to age group in Clinic E

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n = 8860)
1	Amoxycillin 125mg/5ml (J01CA04)	5	38.46	**13**
	Nystatin 100000U/ml (A07AA02)	4	30.77	
	Amoxycillin 125mg/5ml (J01CA04)	3	23.08	
2	Amoxycillin 125mg/5ml (J01CA04)	140	42.17	**332**
	Co-trimoxazole 240mg/5ml (J01EE01)	90	27.11	
	Erythromycin 125mg/5ml (J01FA01)	40	12.05	
3	Amoxycillin 125mg/5ml (J01CA04)	355	41.52	**855**
	Co-trimoxazole 240mg/5ml (J01EE01)	196	22.92	
	Erythromycin 125mg/5ml (J01FA01)	145	16.96	
4	Amoxycillin 250mg capsules (J01CA04)	86	21.99	**391**
	Amoxycillin 125mg/5ml (J01CA04)	76	19.44	
	Erythromycin 240mg/5ml (J01FA01)	52	13.30	
5	Amoxycillin 250mg capsules (J01CA04)	162	28.08	**577**
	Co-trimoxazole 480mg tablets (J01EE01)	90	15.60	
	Metronidazole 200mg tablets (J01XD01)	59	10.23	
6	Amoxycillin 250mg capsules (J01CA04)	1150	24.14	**4763**
	Co-trimoxazole 480mg tablets (J01EE01)	790	16.59	
	Doxycycline 100mg capsules (J01AA02)	525	11.02	
7	Amoxycillin 250mg capsules (J01CA04)	363	23.12	**1570**
	Co-trimoxazole 480mg tablets (J01EE01)	348	22.17	
	Metronidazole 200mg tablets (J01XD01)	147	9.36	
8	Co-trimoxazole 480mg tablets (J01EE01)	112	31.20	**359**
	Amoxycillin 250mg capsules (J01CA04)	97	27.02	
	Metronidazole 200mg tablets (J01XD01)	29	8.08	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As shown in Table 5.29E, the age group that received the highest number of antimicrobials was age group 6 (20-40 years). This was the age group with the highest number of patients as shown in Table

5.3. The most prescribed antimicrobial in this age group was amoxycillin 250mg accounting for 53.76 % (n = 4763) followed by co-trimoxazole 480mg and doxycyline 100mg. The age group with the least number of prescribed antimicrobials was one, being the age group with the least number of patients.

The top three individual antimicrobials prescribed in patients in age group 6 (20-40 years) and the most frequent diagnosed disease states in Clinic E are shown in Table $5.29E_1$.

Table $5.29E_1$: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic E

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Amoxycillin 250mg (J01AA04)	Acute sinusitis	185
	Acute bronchitis	83
	Antenatal : urinary tract infection: cystitis	77
Co-trimoxazole 480mg (J01EE01)	Gastroenteritis	64
	Urinary tract infection	64
	Acute cystitis –non-pregnancy	29
Doxycycline 100mg (J01AA02)	STD: urethritis in men	93
	Urethra discharge / cervicitis-female	31
	Urinary tract infection	22

Amoxycillin was most prescribed for acute sinusitis, acute bronchitis and antenatal: urinary tract infection: cystitis as shown in Table $5.29E_1$. According to Garau and Dagan (2003: 1937), acute sinusitis is one of the most common illnesses in primary care and often arises as a complication of an upper respiratory tract infection (URTI) such as common cold which resolves without antibiotic treatment. Guillemot *et al.* (1998: 66) in their study showed that about 40% of antimicrobials may have been inappropriate when prescribed for acute bronchitis, for antimicrobials have never been shown to be of major clinical benefit. Co-trimoxazole was indicated in the treatment of: gastro-enteritis, urinary tract infections and acute cystitis in non-pregnant women. A variety of antimicrobial drugs including co-trimoxazole, achieve good urinary levels and are used for the treatment of uncomplicated urinary tract infection (Leigh *et al.*, 2000: 819). According to Hoppe (1996a: 569) co-trimoxazole is a good antibacterial for the initial empirical treatment of urinary tract infection (UTI), pending the results of culture and sensitivity tests – it is preferred because of its excellent absorption and tissue penetration. Doxycycline was used in the treatment of sexually transmitted disease (STD): urethritis in men, urinary tract infection and urethra discharge/cervicitis in females. The use of doxycycline for the treatment of urinary tract infection is unclear as discussed by Baileys' (1994: 95) study that the most effective drugs

for this condition may include nitrofurantoin 50mg, trimethoprim 100mg and norfloxacin 200mg given at night.

The top three antimicrobials prescribed to according to age group in Clinic F are illustrated in Table 5.29F.

Table 5.29F: Top three individual antimicrobials prescribed according to age group in Clinic F

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n = 13565)
1	Co-trimoxazole 240mg/5ml (J01EE01)	32	65.31	**49**
	Nystatin 100000U/ml (A07AA02)	8	16.33	
	Amoxycillin 125mg/5ml (J01CA04)	7	14.29	
2	Co-trimoxazole 240mg/5ml (J01EE01)	371	57.16	**649**
	Amoxycillin 125mg/5ml (J01CA04)	161	24.81	
	Erythromycin 125/5ml (J01FA01)	57	8.78	
3	Co-trimoxazole 240mg/5ml (J01EE01)	665	48.47	**1319**
	Amoxycillin 125mg/5ml (J01CA04)	292	21.28	
	Erythromycin 125mg/5ml (J01FA01)	254	18.51	
4	Amoxycillin 250mg capsules (J01CA04)	107	18.71	**572**
	Co-trimoxazole 480mg tablets (J01EE01)	101	17.66	
	Co-trimoxazole 125mg/5ml (J01EE01)	76	13.29	
5	Cotrimoxazole 480mg tablet (J01EE01)	242	26.83	**902**
	Amoxycillin 250mg capsules (J01CA04)	170	18.85	
	Doxycycline 100mg capsules (J01AA02)	112	12.42	
6	Co-trimoxazole 480mg tablets (J01EE01)	1593	25.52	**6241**
	Doxycycline 100mg capsules (J01AA02)	1043	16.71	
	Metronidazole 200mg tablets (J01XD01)	1028	16.31	
7	Co-trimoxazole 480mg tablets (J01EE01)	1211	41.83	**2895**
	Doxycycline 100mg capsules (J01AA02)	483	16.68	
	Metronidazole 200mg tablets (J01XD01)	329	11.36	
8	Co-trimoxazole 480mg tablets (J01EE01)	542	57.78	**938**
	Doxycycline 100mg capsules (J01AA02)	128	13.65	
	Amoxycillin 250mg capsules (J01CA04)	122	13.01	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As illustrated in Table 5.29F, patients in age group 6 (20-40 years) received the most antimicrobial prescriptions accounting for 46.01 % (n = 6241) since it had the highest number of patients. The age group with the least numbers of antimicrobial prescriptions was age group 1 accounting for 0.36 % (n = 49). This was the age group with the least number of patients. Age group 6 (20-40 years) received co-trimoxazole 480mg, doxycycline 100mg and metronidazole 200mg.

The top three antimicrobials prescribed to according to patients in age group 6 (20-40 years) and the most diagnosed disease states in Clinic F are shown in Table 5.29F$_1$.

Table 5.29F$_1$: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states disease in Clinic F

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Co-trimoxazole 480mg (J01EE01)	Viral influenza	148
	Acute bronchitis	75
	Gastroenteritis	70
Doxycycline 100mg (J01AA02)	Pelvic inflammatory disease	287
	Vulvo vaginitis: new specific	39
	Viral influenza	34
Metronidazole 200mg (J01XD01)	Pelvic inflammatory disease	158
	Antenatal: vaginal discharge	26
	Acute cystitis: female non-pregnancy	16

As revealed in Table 5.29F$_1$, the diagnoses in which most co-trimoxazole was prescribed were: viral influenza, acute bronchitis and gastroenteritis. Viral influenza and acute bronchitis are respiratory infections caused by viruses; therefore the use of Co-trimoxazole in these conditions is contraindicated (Coughlin *et al.*, 2003: 34). Doxycycline was indicated in pelvic inflammatory disease, vulvovaginitis and viral influenza. Doxycycline is used in the treatment of pelvic inflammatory diseases as stated by Lynn (1996: 224). However, doxycycline is contraindicated in the use of viral influenza because it is viral in origin. Metronidazole was indicated in the treatment of pelvic inflammatory disease, Antenatal: vaginal discharge and sexually transmitted infection (STI): lower abdominal pain in non-pregnancy. Metronidazole in combination with aminoglycosides is used to provide coverage of anaerobic organisms in patients with polymicrobial pelvic and abdominal infections (Simms-Cendan, 1996: 153).

According to Simms-Cendan (1996: 156) recommendations have been to limit the use of metronidazole to the second and third trimester of pregnancy.

The top three antimicrobials prescribed according to age group in Clinic G are illustrated in Table 5.29G.

Table 5.29G: Top three individual antimicrobials prescribed according to age group in Clinic G

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n=12423)
1	Amoxycillin 125mg/5ml (J01CA04)	5	62.50	**8**
	Phenoxymethyl penicillin 125mg/5ml J01CE02)	2	25.00	
	Ampicillin 125mg/5ml (J01CA01)	1	12.50	
2	Co-trimoxazole 240mg/5ml (J01EE01)	98	34.03	**288**
	Phenoxymethyl penicillin 125mg/5ml (J01CA04)	77	22.67	
	Ampicillin 125mg/5ml (J01CA01)	35	12.15	
3	Co-trimoxazole 240mg/5ml (J01CEE01)	291	27.22	**1069**
	Amoxycillin 125mg/5ml (J01CA04)	253	23.67	
	Erythromycin 125mg/5ml (J01FA01)	181	16.93	
4	Amoxycillin 125mg/5ml (J01CA04)	123	17.98	**684**
	Amoxycillin 250mg (J01CA04)	93	13.60	
	Co-trimoxazole 240mg/5ml (J01CEE01)	84	12.28	
5	Amoxycillin 250mg capsules (J01CA04)	237	28.73	**825**
	Co-trimoxazole 480mg tablets (J01CEE01)	174	21.09	
	Erythromycin 250mg capsules (J01FA01)	85	10.30	
6	Co-trimoxazole 480mg tablets (J01CEE01)	1294	21.09	**6136**
	Amoxycillin 250mg capsules (J01CA04)	1248	20.34	
	Doxycycline 100mg capsules (J01AA02)	652	10.63	
7	Co-trimoxazole 480mg tablets (J01CEE01)	743	26.41	**2813**
	Amoxycillin 250mg capsules (J01CA04)	684	24.32	
	Erythromycin 250mg capsules (J01FA01)	217	7.71	
8	Amoxycillin 250 mg capsules (J01CA04)	198	33.00	**600**
	Co-trimoxazole 480mg tablets (J01CEE01)	178	29.67	
	Ampicillin 250mg capsules (J01CA01)	63	10.50	

N = number of individual antimicrobial; % = percentage of the total number in each age group

Table 5.29G demonstrates that patients in age group 6 (20-40 years) received the most antimicrobial prescriptions accounting for 49.41% (n = 6136). This was the age group with the highest number of patients. Patients in age group 1 (0-1 month) received the least number of antimicrobial prescriptions accounting for 0.64% (n = 8). This was the age group with the least number of patients. Co-trimoxazole 480mg, amoxycyllin 250mg and doxycycline 100mg were the most prescribed antimicrobials in age group 6.

The top three antimicrobials prescribed to patients in age group 6 (20-40 years) and the most diagnosed disease states in Clinic G are illustrated in Table 5.29G$_1$.

Table 5.29G$_1$: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic G.

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Co-trimoxazole 480mg (J01EE01)	Gastroenteritis	53
	Colon : non-specific diarrhea	41
	Acute bronchitis	28
Amoxycillin 250mg (J01CA04)	Acute bronchitis	88
	Mild/moderate dental abscess	87
	Upper respiratory infection	44
Doxycycline 100mg (J01AA02)	Pelvic inflammatory disease	65
	STI: vaginal discharge: non pregnancy	46
	STI: lower abdominal pain	40

The diagnoses for which co-trimoxazole was mostly prescribed were: colon: non-specific diarrhoea, gastroenteritis and acute bronchitis. Co-trimoxazole is contraindicated in acute bronchitis because it is a respiratory infection of viral origin. According to the Standard Treatment Guidelines and Essential Drugs List (2003: 25), patients presenting at the primary health care clinics with diarrhoea with complications are to be referred. Amoxycillin was prescribed for mild/moderate dental abscess, upper respiratory infection and acute bronchitis. This drug is contraindicated in diseases that are viral in origin as already discussed. Doxycycline was given for the treatment of pelvic inflammatory disease, vaginal

discharge in non-pregnancy and lower abdominal. This was in line with the treatment guidelines of doxycyline as already discussed.

The top three individual antimicrobials prescribed according to age group in Clinic H are shown in Table 5.29H.

Table 5.29 H: Top three individual antimicrobials prescribed according to age group in Clinic H

Age group	Antimicrobials prescribed	N	%	Total number of antimicrobials prescribed in each age group (n =10306)
1	Amoxycillin 125mg/5ml (J01CA04)	7	50.00	**14**
	Nystatin 100000u/ml (A07AA02)	3	21.43	
	Amoxycillin 125mg/5ml (J01CA04)	2	14.29	
3	Amoxycillin 125mg/5ml (J01CA04)	314	29.88	**1051**
	Co-trimoxazole 240mg/5ml (J01EE01)	253	24.07	
	Ampicillin 125mg/5ml (J01CA01)	158	15.03	
4	Amoxycillin 125mg/5ml (J01CA04)	108	20.89	**517**
	Phenoxymethylpenicillin 250mg (J01CE02)	83	16.05	
	Amoxycillin 125mg/5ml (J01CA04)	70	13.54	
5	Amoxycillin250mg capsules (J01CA04)	181	31.26	**579**
	Co-trimoxazole 4480mg tablets (J01EE01)	81	13.99	
	Ampicillin 250mg capsules (J01CA01)	67	11.57	
6	Amoxycillin 250mg capsules (J01CA04)	874	19.29	**4530**
	Co-trimoxazole 480mg tablets (J01EE01)	732	16.16	
	Ampicillin 250mg capsules (J01CA01)	542	11.96	
7	Amoxycillin 250mg capsules (J01CA04)	601	22.14	**2714**
	Co-trimoxazole 480mg tablets (J01EE01)	575	21.19	
	Ampicillin 250mg capsules (J01CA01)	289	10.65	
8	Co-trimoxazole 480mg tablets (J01EE01)	163	30.58	**533**
	Amoxycillin 250mg capsules (J01CA04)	132	24.77	
	Ampicillin 250mg capsules (J01CA01)	46	8.63	

N = number of individual antimicrobial; % = percentage of the total number in each age group

Table 5.29H shows that patients in age group 6 received the most antimicrobials representing 43.95 % (n = 4530) and age group 1 received the least antimicrobials with 0.14 % (n = 14).
The antimicrobial most prescribed in all age groups was amoxycillin but mostly prescribed in age group 6 representing 19.29 % (n = 874) of the total number of antimicrobials prescribed in this age group. The other antimicrobials prescribed in age group 6 were: co-trimoxazole 480mg and ampicillin 250mg.

The top three antimicrobials prescribed to patients in age group 6 (20-40 years) and the most diagnosed disease states in Clinic H are shown in Table 5.29H_1.

Table 5.29H_1: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic H

Antimicrobials prescribed	Disease states diagnosed	Frequency of disease states
Amoxycillin 250mg (J01CA04)	Acute bronchitis	67
	Upper respiratory infection	48
	Viral influenza	44
Co-trimoxazole 480mg (J01EE01)	Urinary tract infection	39
	Upper respiratory infection	35
	Gastroenteritis	25
Ampicillin 250mg (J01CA01)	Viral influenza	46
	STI: urethritis in men	37
	Urinary tract infection	27

Table 5.29H_1 shows that amoxycillin was prescribed for to treating acute bronchitis, upper respiratory infection and viral influenza. As already discussed these are viral respiratory infections where antibiotic usage is unnecessary. Co-trimoxazole was indicated for upper respiratory infections, urinary tract infection and gastroenteritis. Co-trimoxazole is contraindicated in the treatment of viral diseases like upper respiratory infection. It is however recommended in the treatment of urinary tract infections. Ampicillin was used in viral influenza, sexually transmitted disease: urethritis in men and urinary tract infection. As already discussed the use of ampicillin, is not recommended for the treatment of viral influenza whose aetiology is viral. Neither is the use of ampicillin in urinary tract infection recommended as stated in the Standard Treatment Guidelines and Essential Drugs List for primary health care (2003: 130).

The drug treatment for adults with urinary tract infection is co-trimoxazole 480mg or amoxycillin orally: 250mg 8 hourly for 5 days. According to Leigh *et al.* (2000: 819), a variety of antimicrobial

drugs including sulphonamides, quinolones, and cephalosporins, achieve good urinary levels and are used for the treatment of uncomplicated urinary tract infection (UTI).

The top three individual antimicrobials prescribed according to age group in Clinic I will be illustrated in Table 5.29I.

Table 5.29I: Top three individual antimicrobials prescribed according to age group in Clinic I

Age Group	Antimicrobials prescribed	N	%	Total number of antimicrobials Prescribed in each age group (n =10218)
1	Amoxycillin 125mg/5ml (J01CA04)	7	50	**14**
	Co-trimoxazole 240mg/5ml (J01EE01)	4	28.57	
	Ampicillin 125mg/5ml (J01CA01)	2	14.29	
2	Amoxycillin 125mg/5ml (J01CA04)	224	66.87	**335**
	Co-trimoxazole 240mg/5ml (J01EE01)	53	15.82	
	Erythromycin 125mg/5ml (J01FA01)	36	10.75	
3	Amoxycillin 125mg/5ml (J01CA04)	400	48.19	**830**
	Erythromycin 125mg/5ml (J01FA01)	174	20.96	
	Co-trimoxazole 240mg/5ml (J01EE01)	125	15.06	
4	Amoxycillin 250 mg capsules (J01CA04)	120	22.68	**529**
	Erythromycin 125mg/5ml (J01FA01)	113	21.36	
	Co-trimoxazole 240mg/5ml (J01EE01)	91	17.20	
5	Amoxycillin 250mg capsules (J01CA04)	207	26.04	**795**
	Erythromycin 25omg capsules (J01FA01)	113	14.21	
	Metronidazole 200mg tablets (J01XD01)	86	10.82	
6	Amoxycillin 250mg capsules (J01CA04)	956	21.48	**4450**
	Ampicillin 250mg capsules (J01CA01)	567	12.74	
	Metronidazole 200mg tablets (J01XD01)	476	10.70	
7	Amoxycillin 250mg capsules (J01CA04)	489	19.84	**2465**
	Ampicillin 250mg capsules (J01CA01)	288	11.68	
	Metronidazole 200mg tablets (J01XD01)	288	11.68	
8	Co-trimoxazole 480mg tablets (J01EE01)	202	25.25	**800**
	Ampicillin 250mg capsules (J01CA01)	130	16.25	
	Co-trimoxazole 480mg tablets (J01EE01)	128	16.00	

N = number of individual antimicrobial; % = percentage of the total number in each age group

As shown in Table 5.29l, the age group that received the highest number of antimicrobials was 6 (20-40 years) accounting for 43.55 % (n = 4450) and age group 1 received the least number of antimicrobials accounting for 0.13 % (n = 14). Amoxycillin 250mg, ampicillin 250mg, and metronidazole 200mg were the top 3 antimicrobials prescribed for patients in age group 6.

The top three antimicrobials prescribed for patients in age group 6 (20-40 years) and the most diagnosed disease states in Clinic I are shown in Table 5.29I_1.

Table 5.29I_1: Top three antimicrobials prescribed in age group 6 and the diagnosed disease states in Clinic I

Antimicrobials Prescribed	Disease states diagnosed	Frequency of disease states
Amoxycillin 250mg (J01CA04)	Acute bronchitis	201
	Antenatal follow-up	63
	Acute sinusitis	40
Ampicillin 250mg (J01CA01)	Acute cystitis : non pregnancy	104
	Acute cystitis - male	95
Metronidazole 200mg (J01XD01)	Acute bronchitis	43
	Acute cystitis : non-pregnancy	34
	Uncomplicated gastritis	26

Table 5.29I_1 demonstrates that amoxycillin was prescribed for antenatal follow-ups, acute bronchitis and acute sinusitis. According to Colgan (2000: 1002) the diagnosis of sinusitis is made when there are more severe upper respiratory tract signs and symptoms (for example, fever greater than 39 ° C (degrees Celsius), facial swelling, and /or facial pain). Thereafter a narrow-spectrum agent that is active against the active pathogen can be used. Ampicillin was prescribed for acute cystitis in non-pregnancy and acute cystitis in men. As stated by Chang *et al.* (1999: 29) cystitis can be easily treated with penicillins, cephalosporins or sulphonamides. Metronidazole was prescribed for acute bronchitis, acute cystitis and uncomplicated gastritis. Metronidazole is a nitroimidazole compound active in the treatment of anaerobic protozoan and bacterial infections, therefore is unnecessary in the treatment of a viral disease

like acute bronchitis (Simms-Cendan, 1996: 153). The use of metronidazole for uncomplicated gastritis is recommended as stated by Simms-Cendan (1996: 154) in a study that metronidazole is also considered first-line therapy for the treatment of *C. difficile* pseudomembranous colitis. However the use of metronidazole at primary health care level is not recommenced. For acute uncomplicated cystitis, co-trimoxazole 480mg or amoxycillin 250mg are the recommended treatments (Standard Treatment Guidelines for Primary Health Care, 2003: 130).

SUMMARY OF THE RESULTS OF ALL CLINICS

From these results of the nine clinics, it was observed that age group 6 (20-40 years) was the age group that received the highest number antimicrobials and age group 1 (0-1 month) received the least number of antimicrobials. Age group 6 accounted for the highest number of patients in all the nine clinics and age group 1, the smallest number of patients.

The commonest antimicrobials prescribed for patients in age group 6 in the nine clinics were amoxycillin 250mg, co-trimoxazole 480mg, doxycycline 100mg, metronidazole 200mg and ampicillin 250mg. The commonest disease states for which these antimicrobials were prescribed were: respiratory infections (acute bronchitis, viral influenza, sinusitis, upper respiratory tract infections, and common cold), pelvic inflammatory diseases and urinary tract infections. According to Coughlin *et al.* (2003: 34) respiratory infections place a heavy burden on patients, providers, employer and the health system. Marcfarlane *et al.* (1997: 427) reported in their study that respiratory symptoms are the most common cause of general practitioner (GP) consultation, and hospital-based specialities are often called on to provide management guidelines. As stated by Bjerrum *et al.* (2004: 26) in their study, respiratory tract infections (RTIs) are the most frequent reasons for prescribing antibiotics, the majority of which have a viral aetiology. There was a general trend in the nine clinics of prescribing antibiotics in these conditions, despite the fact that respiratory conditions are caused by viruses. These results are similar to results obtained by Chang *et al.* (1999: 29) in their study performed in primary care units in Taiwan, where they reported a 29.7% of patients with respiratory diseases who received antibiotic treatment. These results suggest that antibiotics were overused in primary care units. This is probably a world-wide phenomenon since Arroll and Goodyear-Smith (2000: 493) also reported that 61% of patients with upper respiratory symptoms were prescribed antibiotics in the United Kingdom.

It was also noted that the patients treated with antimicrobials also presented with chronic diseases such as hypertension. It was not possible from the database to identify which specific drugs were prescribed

for which disease states, in cases where more than one medical problem was diagnosed during the same consultation. This may lead to the fact that antibiotics were prescribed to patients that have hypertension with a secondary infection (refer to limitations of the study, Section 6.3).

It was also observed that there were differences in antibiotic prescribing patterns among the general practitioners for the same conditions. As described by Macfarlane *et al.* (1997: 427) in their study, general practitioners used a wide variety of terms to describe the illness with little consistency. The decision concerning the use and choice of antibiotics and the confidence with which the GP makes that decision is a complex interaction between patient, doctor and disease, being affected not only by clinical features but also by the social and psychological elements of the presenting problem.

5.4.11 The occurrence of the top ten prescribed antimicrobials in the nine clinics

The occurrence of the top ten prescribed antimicrobials in the nine clinics is illustrated in Table 5.30.

Table 5.30: Top ten prescribed individual antimicrobials in each clinic

CLINIC	Co-trimoxazole 240mg/5ml (J01EE01)	Co-trimoxazole 480mg (J01EE01)	Doxycycline 100mg (J01AA02)	Ampicillin 250 mg (J01CA01)	Ampicillin 125mg /5ml (J01CA)1)	Metronidazole 400mg (J01XD01)	Metronidazole 200mg (J01XD01)	Amoxycillin 250mg (J01CA04)	Norfloxacin 400mg (J01MA06)	Amoxycillin 125mg/5ml (J01CA04)	Erythromycin 250mg (J01FA01)	Erythromycin 125mg/5ml (J01FA01)	Phenoxypen 250mg (J01CE02)	Phenoxypen 125mg/5ml (J01CE02)	Oxytetracycline 250mg (J01AA02)	Enoxan 200mg tablets (J01MA04)	Amoxycillin/Clavulanic acid 375mg (J01CR02)	*Total Y*
A	2057	2047	1283	987		744	416	519	417	306	249							**9025**
B		688	347	243	116		264	1225		304	299	147	213					**3846**
C	224	940	826			550		1834		688	420		353	239		608		**6682**
D	663	2664	1392				1747	3854			2057	428	856	673	432			**14766**
E	322	1364	682	659		604	690	1871		582	321					439		**7534**
F	1157	3693	1781	481			1562	1698		530	752	370				672		**12696**
G	491	2446	895		776	497	578	2471			931	307	497					**9889**
H	408	1612	669	981		486		1913	478	545	633		700					**8425**
I		807	778	1081		708	969	1983	895	746	849	336				1719	694	**11565**
TOTAL Z	**5322**	**16261**	**8653**	**4432**		**3589**	**6226**	**17368**		**3701**	**6511**		**2619**					**84428**

Total Y: Total number of the individual antimicrobials in the nine clinics.

Total Z: Total number of the top 10 antimicrobials in each clinic.

As illustrated in Table 5.30, amoxycillin - containing products were the most prescribed antimicrobial accounting for 23.26% (n=17368) of the total number of antimicrobials prescribed in the nine clinics. These results are similar to results obtained by Macfarlane *et al.* (1997: 427) who reported in a study that amoxycillin was the first choice (58% of total) except where the patient had recently received antibiotics. Chang *et al.* (1999: 29) also reported that amoxycillin was the most commonly used antibiotic during their study. This could be explained by the fact that amoxycillin is a newer antibiotic after ampicillin as an approach to the beta-lactamase problem. Ampicillin when first approved by the FDA in 1964 was active against many gram-negative organisms, unfortunately many of the bacterial species are resistant to ampicillin on the basis of beta-lactamase production (Brown, 2000: 94).

The second prescribed antimicrobial in the nine clinics was co-trimoxazole with 16261 (19.26%) of the total number of antimicrobials prescribed in the clinics. These results concur with the results obtained in Table 5.27 where penicillins accounted for the highest number of antimicrobial prescriptions according to pharmacological group and amoxycillin belongs to that group. Again in Table 5.27 penicillins were the most prescribed antimicrobials according to gender. The third most prescribed antimicrobial was doxycycline (10.25%; n = 86530). As shown in Table 5.30 the least prescribed antimicrobial was oxytetracycline 250 mg with 0.51 % (n = 432). This could be influenced by the disease states presented in the clinics as will be discussed in Section 5.6.2.

5.4.11 Ten most frequently prescribed antimicrobials in all the nine clinics.

Percentages of the ten most frequently prescribed antimicrobials in all the clinics are shown in Table 5.31.

The antimicrobial that received the highest number of prescriptions in the nine clinics was amoxycillin accounting for 23.26% (n = 17368) as shown in Table 5.31. Amoxycillin is the first-line antibiotic. According to Bennett and Brown (2003: 219), amoxycillin is better absorbed from the gut (especially after food), and achieves approximately double the plasma concentration. It is preferred than ampicillin because of the bacterial resistance and less side effects, (for example diarrhoea) is less frequent and it has a greater bioavailability and fewer adverse effects. The drug that shows the lowest prescription rate is phenoxymethyl penicillin 250mg (2619, 3.51%). This was influenced by the clinical diagnoses presented in the clinics as discussed in Section 5.6.2. The results obtained in Table 5.31 confirm the results obtained in Table 5.29.

5.5 Information about the disease states diagnosed in the clinics during the research period

In this study, the term "disease states" connotes medical problems.

The information of the disease states diagnosed in the nine clinics will be discussed according to:

- The total number of disease states diagnosed in the clinics (refer to Table 5.32).
- The types of disease states diagnosed in the clinics (refer to Table 5.33).

5.5.1: Total number of disease states diagnosed in each clinic during the research period

The total number of disease states diagnosed in each clinic during the research period are illustrated in Table 5.32.

Table 5.32: Total number of disease states diagnosed in each clinic during the research period

Clinic	Number of disease states	Percentage (%)
A	13668	9.71
B	8877	6.31
C	14159	10.06
D	23682	16.83
E	11251	8.00
F	17808	12.65
G	19719	14.01
H	18670	13.27
I	12889	9.16
Total	**140723**	**100.00**

%: The percentages were calculated according to the total number of disease states diagnosed in each clinic.

As indicated in Table 5.32, the total number of disease states diagnosed over the research period in the nine clinics was 140723. The clinic that diagnosed the highest number of disease states was Clinic D accounting for 16.83% (n = 23682). This is because Clinic D had the highest number of patients as reflected in Table 5.1. The clinic with the least number of disease states as shown in the table was Clinic B accounting for 6.31% (n = 13668). This clinic presented the lowest number of patients that visited the clinics as illustrated in Table 5.1.

5.5.2 The types of disease states in each clinic

The ten most frequently diagnosed disease states in each clinic are listed from the highest to the lowest frequency in Table 5.33.

Table 5.33: The most frequently diagnosed disease states in the nine clinics

	CLINIC A		
	Disease States	N	% *
1	Upper respiratory infection	973	10.96
2	Viral influenza	613	6.91
3	Antenatal: urinary tract infection: cystitis	496	5.59
4	Antenatal follow-up	438	4.93
5	Pelvic inflammatory disease	408	4.60
6	Acute bronchitis	407	4.58
7	Common cold	362	4.08
8	Hypertension : new/ not controlled	335	3.77
9	Tonsillitis	319	3.59
10	Acute cystitis : female	274	3.09
			♠52.10

Table 5.33: The most frequently diagnosed disease states in the nine clinics (cont)

	CLINIC B		
	Disease States	N	% *
1	Hypertension : new/ not controlled stage	771	5.64
2	Viral influenza	734	5.37
3	Urinary tract infection	454	3.32
4	Muscle pains	347	2.54
5	Upper respiratory tract infection	344	2.52
6	Cough	305	2.23
7	Gastroenteritis	201	1.47
8	Hypertension : follow-up controlled	193	1.41
9	Common cold	170	1.24
10	Peptic ulceration	147	1.08
			♠26.82
	CLINIC C		
	Disease States	N	% *
1	Hypertension: new /not controlled : stage	885	6.25
2	Severe tooth cavity	622	4.39
3	Common cold	496	3.50
4	Upper respiratory infection	479	3.38
5	Hypertension: follow-up controlled	428	3.02
6	Acute bronchitis	402	2.84
7	Cough	362	2.56
8	Muscle pains	313	2.21
9	Viral Influenza	307	2.17
10	Osteoarthritis	264	1.86
			♠32.19

Table 5.33: The most frequently diagnosed disease states in the nine clinics (cont)

	CLINIC D		
	Disease States	N	% *
1	Upper respiratory infection	1783	7.53
2	Acute bronchitis	1719	7.26
3	Osteoarthritis	930	3.93
4	Tonsillitis	815	3.44
5	Common cold	729	3.08
6	Amenorrhoea	671	2.83
7	Gastritis: uncomplicated	668	2.82
8	Hypertension : new/not controlled : Stage	579	2.44
9	Fibrositis	514	2.17
10	Pelvic inflammatory disease	511	2.16
			♠37.66
	CLINIC E		
	Disease States	N	% *
1	Acute sinusitis	735	6.53
2	Urinary tract infection	534	4.75
3	Gastroenteritis	478	4.25
4	Severe sinusitis	458	4.07
5	Viral influenza	421	3.74
6	Acute bronchitis	341	3.03
7	Antenatal booking visit	251	2.23
8	Gastritis: uncomplicated	238	2.12
9	Fibrositis	232	2.06
10	Antenatal follow-up	219	1.95
			♠35.73

Table 5.33: The most frequently diagnosed disease states in the nine clinics (cont)

	CLINIC F		
	Disease States	N	% *
1	Viral influenza	1265	7.10
2	Acute bronchitis	1063	5.97
3	Gastroenteritis	761	4.16
4	Hypertension : new/not controlled stage	740	4.16
5	Pelvic inflammatory disease	719	4.04
6	Osteoarthritis	709	3.98
7	Upper respiratory infection	637	3.58
8	Weakness	604	3.39
9	Gastritis	482	2.71
10	Infection acute cystitis	381	2.14
			♠41.27
	CLINIC G		
	Disease States	N	% *
1	Hypertension : new/not controlled stage	928	4.71
2	Hypertension: follow – up controlled	715	3.63
3	Arthralgia	583	2.96
4	Deep burns	548	2.78
5	Viral Influenza	537	2.72
6	Mild/ moderate dental abscess	501	2.54
7	Diffuse Myalgia	459	2.33
8	Infection bronchitis acute	426	2.16
9	Upper respiratory infection	418	2.12
10	Acute sinusitis	399	2.02
			♠27.97

Table 5.33: The most frequently diagnosed disease states in the nine clinics (cont)

	CLINIC H		
	Disease States	N	% *
1	Viral influenza	1370	7.34
2	Upper respiratory infection	1022	5.44
3	Hypertension: new/controlled stage	606	3.25
4	Acute bronchitis	529	2.83
5	Sever tooth cavity	487	2.61
6	Common cold	465	2.49
7	Muscle pains	409	2.19
8	Gastro-enteritis	375	2.01
9	Deep burns	362	1.94
10	Gastritis: uncomplicated	334	1.79
			♠31.92
	CLINIC I		
	Disease States	N	% *
1	Acute bronchitis	1247	9.67
2	Arthralgia	1166	9.05
3	Acute sinusitis	892	6.92
4	Osteoarthritis	632	4.90
5	Viral influenza	560	4.34
6	Gastritis : uncomplicated	545	4.23
7	Acute cystitis : female	506	3.93
8	Hypertension: new/not controlled stage	323	2.51
9	Antenatal follow-up	292	2.27
10	Hypertension : follow-up controlled release	266	2.06
			♠49.08

●: *Percentages were calculated according to the total number of disease states diagnosed per clinic during the research period (refer to Table 5.33).*

♠: *For percentages that the top ten disease states represent the total number of disease states diagnosed in each clinic (refer to Table 5.33).*

According to Table 5.33, one form of a respiratory tract infection or another was diagnosed under the top five disease states in the nine clinics. According to the International Classification of Diseases (ICD-9-CM) diagnostic codes, the following diagnoses: acute

bronchitis, viral influenza, common cold, cough, acute sinusitis, acute pharyngitis, acute laryngitis, and acute upper respiratory tract infection are classified as respiratory tract infections (Wang *et al.*, 1999: 156). Coughlin *et al.* (2003: 34) stated that respiratory infections place a heavy burden on patients, providers, employer and health care systems. Thomas and Walker (as referred to by Rugg and Loader, 2000: 7114) reported the unnecessary visits of patients with upper respiratory tract infections to the already over-stretched general medical practitioner services.

5.5.3 Disease states diagnosed and individual antimicrobials used for them

The following Tables 5.34 (A – I) show the ten most prevalent diagnosed disease states in each clinic and the antimicrobials prescribed for them.

The ten most frequently diagnosed disease states and antimicrobials prescribed for them in Clinic A is demonstrated in Table 5.34A.

According to Table 5.34A, the diagnoses in which antimicrobials were mostly prescribed was the upper respiratory infection. These results concur with the results obtained in the study by Mlynarczyk *et al.* (2001: 497) where it is reported that respiratory infections are the most frequent reason for primary health care consultation. It is evident from the table that co-trimoxazole was the highest used antimicrobial in treating different disease states. These results tally with the results in Table 5.31 which show that the most prescribed antimicrobial according to individual pharmacological group in this clinic was co-trimoxazole. The other antimicrobials commonly used in this clinic were penicillins and tetracyclines. It is also evident that in this clinic there were disease states where antimicrobials were contraindicated in their management. For example, upper respiratory tract infection, viral influenza, common cold and acute bronchitis. Regardless of the age of the patient, viruses are the micro-organisms most frequently involved in respiratory tract infections (Garcia *et al.*, 1996: 74). Therefore the use of antimicrobials is less beneficial to these patients (Mainous *et al.*, 2003: 1910). An antimicrobial should only be used after the knowledge of the pathogen most frequently associated with the infection (Garcia *et al.*, 1996: 77; Holmes *et al.*, 2001: 177).

Table 5.34A: Ten most frequently diagnosed disease states and individual antimicrobials prescribed in Clinic A

Top ten diagnoses	Frequency of antimicrobials	Top three antimicrobials used
1. Upper respiratory infection	637	Co-trimoxazole 240mg/5ml ((J01EE01) Co-trimoxazole 480mg ((J01EE01) Amoxycillin 125mg /5ml (J01CA04)
2. Viral influenza	513	Co-trimoxazole 480mg ((J01EE01) Co-trimoxazole 240mg/5ml (J01EE01) Amoxycillin 250mg/Clavulanic acid 125mg(J01CR02)
3. Antenatal : urinary tract infection :cystitis	415	Ampicillin 250mg (J01CA01) Amoxycillin 250mg (J01CA04) Metronidazole 200mg (J01XD01)
4. Antenatal follow up	393	Ampicillin 250mg (J01CA01) Amoxycillin 250mg (J01CA01) Metronidazole 200mg (J01XD01)
5. Pelvic inflammatory disease	317	Doxycycline 100mg (J01AA02) Metronidazole 200mg (J01XD01) Enoxacin 100mg (J01MA04)
6. Acute Bronchitis	311	Co-trimoxazole 480mg (J01EE01) Co-trimoxazole 240mg/5ml (J01EE01) Doxycycline 100mg (J01AA02)
7. Common Cold	252	Amoxycillin 250mg (J01CA01) Co-trimoxazole 240mg (J01EE01) Co-trimoxazole 240mg (J01EE01)
8. Tonsillitis	219	Co-trimoxazole 240mg/5ml (J01EE01) Co-trimoxazole 480mg (J01EE01) Erythromycin 250mg (J01FA01)
9. Chronic prostatitis	191	Doxycycline 100mg (J01AA02) Co-trimoxazole 480mg (J01EE01) Norfloxacin 400mg (J01MA06)
10. Urinary tract infection	159	Co-trimoxazole 480mg (J01EE01) Norfloxacin 400mg (J01MA06) Ampicillin 250mg (J01CA01)

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic B will be illustrated in Table 5.34B.

The diagnosis in which the most antimicrobials were mostly prescribed was hypertension: new/not controlled as demonstrated in Clinic B, Table 5.34B. It is not possible from the database to identify which specific drugs were prescribed for which disease states in cases where more than one medical problem was diagnosed during the same consultation. This suggests that antibiotics were prescribed to patients that had chronic diseases like hypertension and antenatal visit follow-ups revealing related infections and or complications. Therefore it is assumed that antibiotics were prescribed for another infection most likely to be of bacterial origin and therefore likely to respond to antibiotics (Wang *et al.*, 1999: 156). In Table 5.25B, the antimicrobial mostly used was amoxycillin. Again there was mismanagement of disease states for example upper respiratory infection, viral influenza, common cold and coughs. As already discussed there are respiratory tract infections of viral origin and do not require antibiotic treatments. According to the South African Standard Treatment Guidelines and Essential Drugs List for primary health care (2003: 243) the treatment used in otitis media in Clinic B was according to the treatment guidelines. Although amoxycillin and co-trimoxazole are usually used as first-line agents, there are many variables to consider when choosing antimicrobials for acute otitis media (AOM) (Hoppe & Johnson, 1998: 1894).

Table 5.34B: Ten most commonly diagnosed disease states and the individual antimicrobials prescribed for them in Clinic B

Top ten diagnoses	Frequency of antimicrobials	Top three antimicrobials used
1. Hypertension new/not controlled	578	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Ampicillin 250mg (J01CA01)
2. Upper respiratory infection	33	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Amoxycillin 125mg/5ml (J01CA04)
3. Muscle pains	246	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Erythromycin 250mg (J01FA01)

Table 5.34B: Ten most commonly diagnosed disease states and the individual antimicrobials prescribed for them in Clinic B (cont)

Top ten diagnoses	Frequency of antimicrobials	Top three antimicrobials used
4. Viral influenza	554	Amoxycillin 250mg (J01CA04) Erythromycin 250mg (J01FA01) Ampicillin 250mg (J01CA01)
5. Common cold	167	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Amoxycillin 125mg/5ml (J01CA04)
6. Cough	278	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Erythromycin 250mg (J01FA01)
7. Urinary tract infection	367	Metronidazole 400mg (J01XD01) Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04)
8. Gastroenteritis	162	Co-trimoxazole 480mg (J01EE01) Metronidazole 200mg (J01XD01) Amoxycillin 250mg (J01CA04)
9. Peptic ulceration	117	Amoxycillin 125mg/5ml (J01CA04) Co-trimoxazole 480mg (J01EE01) Metronidazole 400mg (J01XD01)
10. Otitis media	117	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250 mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04)

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic C are illustrated in Table 5.34C.

Table 5.34C: Ten most frequently diagnosed disease states and the individual antimicrobials prescribed *for them in Clinic C*

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
1.Hypertension new/not controlled	363	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Doxycycline 100mg (J01AA02)
2. Upper respiratory infection	379	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04) Ampicillin 250mg J01CA01)
3. Hypertension : follow- up	229	Amoxycillin 250mg (J01CA04) Erythromycin 250mg (J01FA01) Ampicillin 250mg (J01CA01)
4. Viral influenza	214	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Amoxycillin 125mg/5ml (J01CA04)
5. Cough	192	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Phenoxymethyl penicillin 250mg (J01CE02)
6.Mild/moderate dental abscess	186	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Phenoxymethyl penicillin 125mg(J01CE02)
7. Muscle pains	181	Doxycycline 100mg (J01AA02) Enoxacin 200mg (J01MA04) Co-trimoxazole 480mg (J01EE01)
8. Common cold	340	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Phenoxymethyl penicillin 125mg (J01CE02)
9. Acute bronchitis	335	Amoxycillin /clavulanic acid 375mg (J01CR02) Amoxycillin 125mg/5ml J01CA04) Amoxycillin 250mg (J01CA04)
10. Lower respiratory infection	200	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250 mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04)

In Table 5.34C, it is observed that antibiotics were prescribed for hypertension and muscle pains. As already stated, it was not possible to differentiate from the database which antibiotics were prescribed for which specific diagnoses. Especially in the case of patients

who presented multiple diagnoses at any one visit. Therefore it was assumed that the diagnostic code accurately reflected the infection most likely to be of bacterial origin and likely to respond to antibiotics. It is observed that there was mismanagement of some disease states like: respiratory tract infections. Acute bronchitis was one of the diagnoses in which most antimicrobials were used. Antibiotics have not been shown to be useful in the treatment of acute uncomplicated bronchitis. According to Naidoo and Wilson (2004: 200) most cases of acute bronchitis are preceded by a viral upper respiratory tract infection. As such, the illness tends to be self-limiting and benign. As pointed out Hooton & Levy (2001: 1087) antimicrobials intended for the treatment of bacterial infections should not be used to manage viral illnesses. In this light local resistance trends may be used to guide prescribing decisions.

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic D are illustrated in Table 5.34D.

In Clinic D the diagnosis where most antimicrobials were prescribed was upper respiratory infection as being the most diagnosed disease state in this clinic as shown in Table 5.34D. Respiratory infections are one of the leading public health problems in developing countries (Garcia *et al.*, 1996: 73). The main causes of respiratory tract infections in children are viruses and most common types are upper respiratory tract infections: common cold, pharyngitis, otitis media and sinusitis (Mlynarczyk *et al.*, 2001: 497). It is shown that antimicrobials were used to treat common colds. Common colds are self-limiting viral conditions, which begin to clear within three days (South African Standard Treatment Guidelines and Essential Drugs List for primary health care, 2003: 206). Antibiotics are of no value for the common cold and could have serious side effects. It is also indicated from the table that antibiotics were prescribed for acute bronchitis, despite them having little or no effect on disease progression (Nasrin *et al.*, 2002: 91). Ochoa *et al.* (2000: 73) concluded in a study done in Spain that was excessive use of antimicrobial drugs in acute respiratory infections, and the majority were for viral infections. There is need to educate patients over the value of antibiotics for specific conditions. Glasziou (as referred to by Marchetti *et al.*, 2004: 293), antibiotic treatment of AOM provides only marginal benefits. As stated by Sanz *et al.* (2004: 42) non-antibiotic therapy with analgesics and decongestants will result in clinical cure in a large majority of the children diagnosed with AOM.

Table 5.34D: Ten most frequently diagnosed disease states and the individual antimicrobials prescribed for them in Clinic D

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
1. Amenorrhoea	641	Amoxycillin 250mg (J01CA04) Metronidazole 200mg (J01XD01) Doxycycline 100mg (J01AA02)
2.Common cold	646	Erythromycin 250mg (J01FA01) Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04)
3. Antenatal follow-up	406	Metronidazole 200mg (J01XD01) Erythromycin 250mg (J01FA01) Amoxycillin 250mg (J01CA04)
4. Gastritis : uncomplicated	527	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Metronidazole 200mg (J01XD01)
5. Osteoarthritis	804	Amoxycillin 250mg (J01CA04) Erythromycin 250mg (J01FA01) Co-trimoxazole 480mg (J01EE01)
8. Upper respiratory infection	1680	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CE04)
7. Follicular tonsillitis	809	Phenoxymethyl penicillin 125mg/5ml (J01CE02) Phenoxymethyl penicillin 250mg (J01CE02) Erythromycin 250mg (J01FA01)
8. Acute bronchitis	1557	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Co-trimoxazole 480mg (J01EE01)
9. Fibrositis	443	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04) Erythromycin 250mg (J01FA01)
10. Gastroenteritis	409	Co-trimoxazole 480mg (J01EE01) Co-trimoxazole 240mg/5ml (J01EE01) Metronidazole 200mg (J01XD01)

In Clinic D the diagnosis in which most antimicrobials were prescribed was upper respiratory infection. This diagnosed disease state apparently was the most prevalent in this clinic as

shown in Table 5.34D. Respiratory infections, according to Garcia *et al.* (1996: 73) are one of the leading public health problems in developing countries. The main causes of respiratory tract infections in children are viruses and most common types are upper respiratory tract infections: common cold, pharyngitis, otitis media and sinusitis (Mlynarczyk *et al.*, 2001: 497). The findings of this study show that antimicrobials were used to treat common colds. Common colds are self-limiting viral conditions, which begin to clear within three days (South African Standard Treatment Guidelines and Essential Drugs List for primary health care, 2003: 206). Antibiotics are of no value for the common cold and could have serious side effects. It is also indicated from the table that antibiotics were prescribed for acute bronchitis, despite them having little or no effect on disease progression (Nasrin *et al.*, 2002: 91). Ochoa *et al.* (2000: 73) concluded in a study done in Spain that was excessive use of antimicrobial drugs in acute respiratory infections, and the majority were for viral infections. There is need to educate patients over the value of antibiotics for specific conditions.

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic E are illustrated in Table 5.34E.

The diagnosis in which most antimicrobials were prescribed was acute sinusitis as is illustrated in Table 5.34E. Sinusitis is one of the common types of upper respiratory tract infections (Mlynaarczyk *et al.*, 2001: 497). The antibiotics used in this condition were appropriate. Amoxycillin is an appropriate agent for most patients with uncomplicated acute sinusitis. It is well tolerated, effective, reasonably priced and achieves an overall cure rate of 80% (Hoppe, 1996a: 566; Venter, 1997: 236). For penicillin-allergic patients co-trimoxazole is given (Department of Health, 2003: 246). Most adults who present with sinusitis-like symptoms do not require antibiotics. Antimicrobials are contraindicated in the treatment of respiratory tract infections as already discussed. Antenatal follow-up was one of the multiple diagnoses where in another infection was also diagnosed.

Table 5.34E: Ten most frequently diagnosed disease states and the individual antimicrobials prescribed for them in Clinic E

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
1. Antenatal : booking visits	243	Ampicillin 250mg (J01CA01) Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04)
2. Viral influenza	322	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250 mg (J01CA04) Co-trimoxazole 240mg/5ml (J01EE01)
3. Acute sinusitis	564	Co-trimoxazole 480mg (J01CA04) Amoxycillin 250 mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04)
4. Severe sinusitis	373	Ampicillin 250mg (J01CA01) Ampicillin 125mg/5ml (J01CA01) Metronidazole 200mg (J01XD01)
5. Upper respiratory infection	402	Doxycycline 100mg (J01AA02) Enoxacin 200mg (J01MA04) Co-trimoxazole 480mg (J01EE01)
6. Infection bronchitis acute	292	Amoxycillin 125mg (J01CA04) Amoxycillin 250mg (J01CA04) Metronidazole 200mg (J01XD01)
7. Gastroenteritis	354	Co-trimoxazole 240mg/5ml (J01EE01) Co-trimoxazole 480mg (J01EE01) Metronidazole 200mg (J01XD01)
8. Antenatal : follow-up	212	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Ampicillin 250mg (J01CA01)
9. Fibrositis	184	Co-trimoxazole 480mg (J01EE01) Amoxycillin 250mg (J01CA04) Metronidazole 400mg (J01XD01)
10. Gastritis uncomplicated	142	Co-trimoxazole 480mg (J01EE01) Co-trimoxazole 240mg/5ml (J01EE01) Metronidazole 200mg (J01XD01)

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic H will be illustrated in Table 5.34H.

Table 5.34H: Ten most diagnosed disease states and the individual antimicrobials prescribed for them in Clinic H

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
1. Severe dental abscess	235	Phenoxymethyl penicillin 250mg (J01CE02) Erythromycin 250mg (J01FA01) Phenoxymethyl penicillin 125mg/5ml (J01CE02)
2. Antenatal follow-up Visits	217	Erythromycin 250mg (J01FA01) Amoxycillin 250 mg (J01CA04) Ampicillin 250mg (J01CA01)
3. Muscle trauma	212	Cloxacillin 250mg (J01CF02) Amoxycillin 250 mg (J01CA04) Ampicillin 250mg (J01CA01)
4.Upper respiratory infection	816	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04 Co-trimoxazole 480mg (J01EE01)
5. Muscle pains	246	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Doxycycline 100mg (J01AA02)
6. Viral influenza	661	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Phenoxymethyl penicillin 250mg (J01CE02)
7. Tonsillitis	242	Amoxycillin 25omg (J01CA04) Phenoxymethyl penicillin 125mg/5ml (J01CE02) Phenoxymethyl penicillin 250mg (J01CE02)
8. Common cold	456	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Co-trimoxazole 480mg (J01EE01)

Table 5.34H: Ten most diagnosed disease states and the individual antimicrobials prescribed for them in Clinic H (cont)

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
9. Infection bronchitis acute	431	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Phenoxymethyl penicillin 250mg (J01CE02)
10. Gastroenteritis	276	Metronidazole 200mg (J01XD01) Co-trimoxazole 480mg (J01EE01) Co-trimoxazole 240mg/5ml (J01EE01)

As shown in Table 5.34H, the diagnosis in which most antimicrobials were prescribed most for was upper respiratory infection. The antimicrobial mostly used was amoxycillin. There was an inappropriate use of antimicrobials in severe dental abscess. According to the Department of Health (2003: 9) the recommended drug treatment for severe dental abscess is amoxycillin 250mg oral 8 hourly for 5 days. Therefore the use of phenoxymethyl penicillin 250mg noted at this clinic was inappropriate. For penicillin-allergic patients, erythromycin oral 6 hourly can be used for 5 days and metronidazole oral for 5 days. The data analysed show that antibiotics were used in gastroenteritis. Gastrointestinal disturbances present themselves as one of the adverse effects of antibiotics (Kali & Swingler, 2003: 509). Since the use of these agents for gastroenteritis would worsen the adverse effects in patients. Viral influenza, upper respiratory infection, acute bronchitis are all respiratory tract infections that do not necessitate the use of antimicrobials to treat as already discussed. From the database it was difficult to differentiate medicine items prescribed for individual diagnosis when more than one diagnosis was made during a consultation. It appears in this case in this case antimicrobials were not prescribed for muscle pains but for a possible secondary infection.

The ten most diagnosed disease states and individual antimicrobials used for them in Clinic I will be illustrated in Table 5.34I.

Table 5.34I: Ten most frequently diagnosed disease states and the individual antimicrobials prescribed for them in Clinic I

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
1. Osteoarthritis	554	Ampicillin 250mg (JO1CA01) Metronidazole 200mg (J01XD01) Amoxycillin 250mg (J01CA04)
2. Atopic dermatitis uncomplicated	233	Erythromycin 250mg (J01FA01) Erythromycin 125mg/5ml (J01FA01) Oxytetracycline 250mg (J01AA06)
3. Peptic ulceration	230	Oxytetracycline 250mg (J01AA06) Amoxycillin 250mg (J01CA04) Metronidazole 200mg (J01XD01) Metronidazole 400mg (J01XD01)
4. Arthralgia	1158	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Erythromycin 250mg (J01FA01)
5. Gastritis : uncomplicated	532	Amoxycillin 250mg (J01CA04) Co-trimoxazole 480mg (J01EE01) Erythromycin 250mg (J01FA01)
6. Acute sinusitis	880	Amoxycillin 250mg / clavulanic acid 125mg (J01CR02) Amoxycillin 250mg (J01CA04) Erythromycin 250mg (J01FA01)
7. Bronchitis acute	1200	Amoxycillin 25omg (J01CA04) Amoxycillin 125mg (J01CA04) Amoxycillin 250mg / clavulanic acid 125mg (J01CR02)
8. Viral influenza	474	Amoxycillin 250mg (J01CA04) Amoxycillin 125mg/5ml (J01CA04) Co-trimoxazole 240mg /5ml (J01EE01)

Table 5.34I: Ten most frequently diagnosed disease states and the individual antimicrobials prescribed for them in Clinic I (cont)

Top ten diagnoses	Frequency of antimicrobials used	Top three antimicrobials used
9. Antenatal follow up	291	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Metronidazole 200mg (J01XD01)
10. Hypertension : follow-up controlled	229	Amoxycillin 250mg (J01CA04) Ampicillin 250mg (J01CA01) Erythromycin 250mg (J01FA01)

As shown Table 5.34I, acute bronchitis was the most common diagnosis for which antimicrobials were used. The second most frequent diagnosis was arthralgia. As already discussed it was not possible to differentiate from the database medicine items prescribed for individual diagnosis when more than one diagnosis was made during a consultation. That being the case, in this instance, antimicrobials were not prescribed for arthralgia as a primary infection but for a possible secondary infection. The same applies to patients with hypertension who could have presented a primary infection for which antimicrobials were prescribed. As stated in the Standard Treatment guidelines of the Department of Health (2003: 71), hypertension is managed through a step-wise treatment.

SUMMARY OF THE RESULTS OF ANALYSIS OF DATA FROM ALL CLINICS

The analysis of the data obtained from all the clinics shows that respiratory tract infections were the highest diagnosed disease states in all the clinics. Such respiratory tract infections include: acute exacerbations of chronic bronchitis, acute otitis media, common cold, viral influenza, upper respiratory infection. In all the respiratory tract infections antimicrobials were prescribed. These findings were similar to those obtained by Fendrick *et al.* (2001: 1684) in a study performed in the primary health care setting in USA. Fendrick and others reported that approximately 75% of all outpatient antibiotic use (>80 million antibiotic courses) each year was attributable to the treatment of acute respiratory tract infections. Many of these antibiotic courses are neither necessary nor appropriate because a significant proportion of these infections are caused by viruses or other nonbacterial agents. Such infections being self-limiting will not respond to such drugs. If so, the use of antimicrobials in

such cases is inappropriate and may be implicated as a factor in the development of resistance among the causative pathogens of respiratory tract infections.

It was also noted that there were variations in the management of infectious diseases in all the clinics. According to Guillemot *et al.* (1998: 66) these types of variations may be explained by several factors: difficulty of diagnosing bacterial versus viral aetiology in circumstances such as pharyngitis or otitis; difficulty of predicting bacterial complications in viral infection; variability in medical knowledge; psychosocial factors involved in medical decision making; and lack of simple and clear recommendations for the dose and treatment duration. Appropriate antibiotic prescriptions should rely on scientific objective criteria (Tremolieres, 2003: 73).

As was illustrated in the tables, some patients presented multiple diagnoses which included chronic diseases like hypertension and osteoarthritis, and follow-up visits for antenatal. In their visits these patients were given antibiotic prescriptions. Since it was difficult to distinguish from the database which specific diagnoses antibiotics were prescribed from any others, it was assumed that the diagnostic code accurately reflected the infection most likely to be of bacterial origin and therefore likely to respond to antibiotics.

5.6 Information on cost

Point of information about the minimum costs recorded as R 0.00: All the minimum costs of antibiotics that were less than R 0.01, the computer read such costs as R 0.00

The cost will be discussed under the following headings:

- Average medicine cost per consultation prescribed in the different clinics (refer to Table 5.35).
- Average cost of all medicine items prescribed (refer to Table 5.37).
- Average cost of all antimicrobials in the clinics (refer to Table 5.38).
- Average cost of individual antimicrobials prescribed according to pharmacological groups (refer to Table 5.39).
- Cost/prevalence index of the most prescribed antimicrobials according to pharmacological groups (refer to Table 5.40).
- Average cost of individual antimicrobials prescribed according to gender (refer to Table 5.42).
- Average cost of individual antimicrobials prescribed according to age groups (refer to Table 5.43).

- Average cost of individual antimicrobials prescribed in individual diagnosis (refer to Table 5.44).

5.6.1 Average medicine cost per consultation prescribed in the nine clinics

The average, minimum and maximum medicine cost per consultation will be shown in Table 5.35.

Table 5.35: The average, minimum and maximum medicine cost per consultation prescribed in the nine clinics during the research period

Clinic	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
A	127813.42	10.68	8.85	8.14	0	81.81
B	135636.46	15.57	26.59	8.39	0	1293.39
C	176119.62	12.99	40.42	8.64	0	3886.67
D	253129.00	10.61	8.52	8.80	0	222.87
E	134874.65	11.77	11.59	9.34	0	366.81
F	235127.24	15.66	14.61	11.39	0	431.39
G	221242.70	13.19	36.57	9.15	0	4350.51
H	220513.00	11.81	14.65	7.58	0	543.16
I	211862.25	16.84	19.89	11.99	0	202.29

The average, minimum and maximum medicine costs are calculated in Rands. As Table 5.35 reveals the average medicine cost per consultation varied between R10.61± R8.52 (lowest Clinic D) and R16.84 ± R19.89 (highest Clinic I). The maximum medicine cost per consultation varied between R81.81 (Clinic A) and R4350 (Clinic G) in the different clinics. The minimum medicine cost per consultation was zero which indicates that the patients received no medication during the consultation.

Statistical d-values as indication of practical significance differences between the medicine cost per consultation between the different clinics

The d-values calculated (refer to Chapter 4, Section 4.4.4.2.4) showed that there was no practical significance difference found between the average medicines costs per consultation among the different clinics.

5.6.2 Average cost of all medicine items – total clinic

The average, minimum and maximum cost of all medicine items in all the clinics are illustrated in Table 5.36.

As illustrated in Table 5.36, Clinic D presented the highest percentage of the total medicine cost and was also the clinic with the highest number of medicine items as shown in table 5.12. As shown in this table, the average cost of all medicine items varied between R2.69 ± R4.03 (lowest Clinic D) and R4.46 ± R12.89 (highest Clinic B). The maximum cost of all the medicine items varied between R69.49 (clinic A) and R4303.80 (Clinic G).

Table 5.36: Average, minimum and maximum cost of all medicine items

Clinic	Total cost (R)	Percentage of total cost (%)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
A	127813.42	7.44	2.73	4.28	1.44	0	69.49
B	135636.46	7.90	4.46	12.89	1.66	0	1268.40
C	176119.62	10.26	3.69	21.34	1.58	0	3865.19
D	253129.56	14.75	2.69	4.03	1.58	0	200.90
E	134874.65	7.86	3.24	5.59	1.61	0	348.14
F	235127.24	13.69	3.15	5.73	1.58	0	423.20
G	221242.70	12.89	3.63	18.78	1.81	0	4303.80
H	220513.00	12.85	3.64	7.02	1.60	0	395.54
I	211862.25	12.34	3.56	8.84	1.59	0	175.50

Statistical d-values as indication of the practical significance differences between the costs of all medicine items.

The d-value calculated (refer to Chapter 4, section 4.4.4.2.4) showed that there was no difference of practical significance found between the average cost of all medicine items among the different clinics.

5.6.3 Average, minimum and maximum cost of all antimicrobials prescribed in the nine clinics

The average, minimum and maximum cost of all antimicrobials prescribed in the nine clinics during the research period will be shown in Table 5.37.

Table 5.37: Average, minimum and maximum cost of all antimicrobials prescribed in the nine clinics

Clinic	Total cost ®	% of the total cost	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
A	40858.94	31.97	4.18	5.10	2.19	0	37.44
B	21814.42	16.08	4.86	5.22	2.99	0	90.41
C	582121.41	33.05	7.02	8.66	4.57	0	343.05
D	89436.12	35.33	4.89	4.36	4.49	0	149.15
E	47582.04	35.28	5.36	5.02	4.53	0	82.74
F	71170.14	30.27	5.19	5.99	3.74	0	149.87
G	58985.29	26.66	4.74	4.91	3.29	0	171.50
H	52759.62	23.93	5.11	6.35	3.56	0	183.02
I	80380.00	37.94	7.86	17.52	4.49	0	175.50

As shown in Table 5.37, the maximum cost of the antimicrobials varied between R37.44 (Clinic A) and R343.05 (Clinic C). The average cost of the antimicrobials varied between R4.18 ± R5.10 for Clinic A and R7.86 ± 17.52 for Clinic I. Clinic I had the highest average cost of antimicrobials of R7.86 ± 17.52, on the other hand Clinic A had the lowest mean cost of 4.18 ± 5.10. Clinic I had the highest % (37.94) of antimicrobials of the total cost of medicine items prescribed in the nine clinics. Clinic B accounting for the lowest percentage (16.08%) of the total cost of antimicrobials prescribed in all the nine clinics.

Statistical d-values as indication of the differences of practical significance between the average costs of all antimicrobials prescribed in the nine clinics.

The d-values calculated (refer to Chapter 4, section 4.4.5.2.4) showed that there was no difference of practical significance found among he average cost of all antimicrobials prescribed in the nine clinics.

5.6.4 Total cost of individual antimicrobials prescribed according to pharmacological groups.

The following table (Table 5.38) shows the total cost of all antimicrobials prescribed according to their pharmacological groups in the nine clinics.

As illustrated in Table 5.38, the individual antimicrobials that had the highest medicine cost was penicillins accounting for 37.76% (n = R188 918.50) of the total cost of antimicrobials in the nine clinics. The total amount of penicillin prescriptions in the nine clinics was 36808. These results concur with the results in Table 5.26 where penicillins represented the highest number of the total number of antimicrobials in the nine clinics. Aminoglycosides had the minimum medicine cost of the total cost of all antimicrobials prescribed in the nine clinics.

5.7 The cost/prevalence index of the most prescribed antimicrobials according to pharmacological group in the nine clinics

The cost/prevalence index of the most prescribed antimicrobials prescribed according to pharmacological groups in the nine clinics is shown in Table 5.39.

Table 5.39: Cost/prevalence index of the antimicrobials prescribed according to pharmacological groups in the nine clinics

Antimicrobial	Cost/prevalence index
Penicillins (J01C)	1.54
Antifungals (J01X)	5.47
Antiprotozoals (J01X)	0.68
Macrolides (J01F)	2.64
Tetracyclines (J01A)	1.77
Sulphonamides (J01E)	0.78
Quinolones (J01M)	0.48
Antivirals (J01S)	5.83
Aminoglycosides (J01G)	1.00
Chloramphenicols (J01B)	1.33

As shown in Table 5.39, the cost index values calculated (refer to Chapter 4, Section 4.4.5.2.5) shows that the following antimicrobials : penicillins, antifungals, macrolides, tetracyclines, antivirals, aminoglycosides and chloramphenicols with index values equal to or exceeding 1, have relatively large costs percentages in comparison with their prevalence percentages (Serfontein, 1989: 180).

Table 5.38: Total cost of individual antimicrobials according to pharmacological groups

Clinic		Penicillins (J01C)	Antifungals (J01X)	Antiprotozoals (J01X)	Antivirals (J01S)	Macrolides (J01F)	Tetracyclines (J01A)	Sulphonamides (J01E)	Quinolones (J01M)	Aminoglycosides (J01G)	Chloramphenicols (J01B)	Total Y
A	N	2165	160	1160		451	1283	4140	462			**9821**
	Cost	12503.39	3188.53	1240.71		3389.97	6917.12	8514.61	5104.6			
B	N	2288	48	346	48	455	357	792	158	1	3	**4445**
	Cost	9797.39	1186.48	416.52	849.03	3436.82	2097.74	1762.1	2265.7	2.31	9.57	
C	N	3938	171	866	64	536	874	1164	667	1		**8281**
	Cost	28566.38	4040.07	1775.45	1211.45	5612.8	5317.6	3018.89	8589.82	2.31		
D	N	7690	397	1747	9	2485	1824	3327	804		125	**18408**
	Cost	32480.33	7064.33	1948.18	243.34	21473	9129.54	7538.62	9557.94		598.03	
E	N	3604	138	1305	65	566	721	1686	662			**8747**
	Cost	20286	2536	1831.38	1666.3	3690.55	5020	4049.18	7736.63			
F	N	3173	259	1562	74	1122	1854	4850	805			**13699**
	Cost	65.81	149.87	23.95	84.64	26.27	23.35	10.5	91.51			
G	N	5422	216	1075	57	1267	950	2937	515		9	**12448**
	Cost	23812.68	2620.98	1277.64	877.92	11818	6016.38	6663.76	5897.9		37.92	
H	N	4981	180	806	58	808	849	2020	593			**10295**
	Cost	24028.52	4295.34	1659.75	996.55	6971.74	4417.93	4179.43	6048.41			
I	N	4801	69	1677		1230	1018	1034	331	65		**10225**
	Cost	37378.03	1596.51	2022.28		10341.4	5895	2395.82	20650.9	100.61		**96369**
Total Z		**188918.5**	**28156.11**	**21579.86**	**5929.23**	**75229.6**	**53281.7**	**55942.9**	**70478.4**	**171.23**	**645.52**	**500333**

Total Y: The total number of individual antimicrobials in each clinic.

Total Z: The total cost of the individual antimicrobials in the nine clinics.

5.7.1 Average cost of the top ten individual antimicrobials in each clinic

The following Tables 5.40 (A – I) shows the average cost of the top ten individual antimicrobials prescribed in each clinic.

The average, minimum and maximum costs of the top ten individual antimicrobials prescribed in Clinic A are shown in Table 5.40A.

Table 5.40A: Average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic A

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Co-trimoxazole 240mg/5ml (J01EE01)	2057	4427.99	2.15	0.93	1.95	0.01	7.24
Co-trimoxazole 480mg Tablets (J01EE01)	2047	4086.62	1.99	0.66	1.87	0	6.23
Doxycycline 100mg capsules (J01AA02)	1283	6917.12	5.93	2.73	5.65	0	12.38
Ampicillin 250mg capsules (J01CA01)	987	4130.75	4.19	1.55	4.09	0	10.28
Metronidazole 400mg tablets (J01XD01)	744	879.66	1.18	0.34	1.19	0	3.22
Amoxycillin 250mg capsules (J01CA04)	519	2166.60	4.17	1.93	4.49	0.03	12.62
Metronidazole 200mg tablets(J01XD01)	416	361.04	0.87	0.29	0.81	0.05	3.27
Amoxycillin 125mg/5ml (J01CA04)	249	1018.77	4.09	1.84	4.57	0	13.71
Erythromycin 250mg tablets (J01FA01)	214	1922.40	8.98	4.17	8.75	0.17	24.52
Erythromycin 125mg/5ml (J01FA01)	206	1153.10	5.59	1.01	5.57	0	12.18

As demonstrated in Table 5.40A, the minimum cost of the antimicrobials was zero. The maximum cost of the individual antimicrobials varied between R3.22 for metronidazole 400mg (744 prescriptions) and R24.52 for erythromycin 250mg (214 prescriptions). The average cost of the individual antimicrobials varied between R0.87 ± R0.29 and R8.98 ± 4.17. Erythromycin 250mg tablets had the highest average cost of R8.98 ± R4.17 and the lowest average cost was for metronidazole 200mg tablets at R0.87 ± R0.29 for 416 prescriptions.

Table 5.40A$_1$: Statistical d-values as indication of practical significance differences between the costs of the top ten individual antimicrobials in Clinic A.

Antimi-Crobial	Co-trim 240mg (J01EE01	Co-trim 480mg (J01EE01)	Doxy 100mg (J01AA02	Amp 250mg (J01CA01)	Metro 400mg (J01XD01	Amoxy 250mg (J01CA04)	Metro 200mg (J01XD01)	Amoxy 125mg (J01CA04	Erythr 250mg (J01FA01)	Erythr 125mg (J01FA01
Co-trim 240mg		0.17	1.19	1.32	1.04	1.05	1.38	1.05	1..64	3.70
Co-trim 480mg	0.17		1.25	1.42	1.23	1.13	1.70	1.14	1.68	3.86
Doxy 100mg	1.19	1.25		0.44	1.54	0.45	1.66	0.48	0.86	0.18
Amp 250mg	1.32	1.42	0.44		1.94	0.01	2.14	0.05	1.15	1.10
Metro 400mg	1.04	1.23	1.54	1.94		1.55	0.91	1.58	1.87	4.66
Amoxy 250mg	1.05	1.13	0.45	0.01	1.15		1.17	0.04	1.15	0.89
Metro 200mg	1.38	1.70	1.66	2.14	0.91	1.17		1.75	1.94	4.97
Amoxy 125mg	1.05	1.14	0.48	0.05	1.58	0.04	1.75		1.17	1.78
Erythr 250mg	1.64	1.68	0.86	1.15	1.87	1.15	1.94	1.17		1.91
Erythr 125mg	3.70	3.86	0.18	1.10	4.66	0.89	4.97	1.78	1.91	

Abbreviations:

Co-trim = Co-trimoxazole, Doxy = doxycycline, Amp = ampicillin, Metro = metronidazole, Amoxy = amoxycillin, Erythr = erythromycin

Difference of practical significance is d>0.8

As shown in Table 5.40A$_1$, the d-values calculated (refer to chapter 4, section 4.4.5.2.4) show that there were differences of practical significance among the costs of individual

antimicrobials prescribed in Clinic A. From the results there were differences of practical significance between erythromycin 480mg and the rest of the antimicrobials. This implies that erythromycin 480mg had the highest average cost of all antimicrobials prescribed in Clinic A (refer to the grey boxes as indication of practical significance).

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic B is shown in Table 5.40B.

Table 5.40B: Average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic B

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation	Median (R)	Minimum (R)	Maximu (R)
Amoxycillin 250mg (J1CA04)	2225	3642.37	2.97	2.41	2.34	0	58.65
Co-trimoxazole 480mg (J01EE01)	688	1452.07	2.11	0.86	1.87	0	7.49
Doxycycline 100mg (J01AA02)	347	2058.95	5.93	4.72	5.62	3.89	90.41
Amoxycillin 125mg/5ml (J01CA04)	304	1876.44	6.17	2.32	4.57	0	11.90
Metronidazole 200mg (J01XD01)	264	278.44	1.05	0.72	0.97	0.01	11.28
Erythromycin 250mg (J01FA01)	299	2343.80	7.84	5.00	8.76	0	35.03
Ampicillin 250mg (J01CA01)	243	916.89	3.77	1.37	3.59	0	10.28
Phenoxymethyl penicillin 250mg (J01CE02)	213	1313.25	6.17	3.69	6.12	0	12.24
Enoxacin 200mg (J01MA04)	132	1628.79	12.34	5.33	12.20	6.10	64.58
Ampicillin 125mg/5ml (J01CA01)	116	513.12	4.42	1.09	4.46	0	8.92

As shown in Table 5.40B, the minimum cost of the individual antimicrobials in Clinic B was R0.00 for most of the antimicrobials. The maximum cost of the antimicrobials varied between

R7.49 for co-trimoxazole 480mg (688 prescriptions) and R90.41 for doxycycline 100mg (347 prescriptions). The average cost of the antimicrobials varied between R1.05 ± R0.72 and R12.34 ± R5.33. Enoxacin 200mg had the highest average cost of R12.34 ± R5.33 for 132 prescriptions and metronidazole 200mg had the lowest average cost of R1.05 ± R0.72 for 264 prescriptions. Enoxacin 200mg accounted for 7.47% of the total cost of medicine items prescribed in the nine clinics.

Statistical d-values as indication of practical significance differences between the costs of individual antimicrobials in Clinic B

Statistical d-values as indication of practical significance differences between the costs of individual antimicrobials in Clinic B are shown in Table 5.40B_1.

Table 5.40B_1: Statistical d-values as indication of practical significance differences between the cost of individual antimicrobials in Clinic B

Antimicrobial	Amoxy 250mg (J01CA04	Co-trim 480mg (J01EE01	Doxy 100mg (J01AA02	Amoxy 125mg/5ml (J01CA04)	Metron 200mg (J01XD01	Erythr 250mg (J01FA01)	Amp 250mg (J01CA01)	Phen 250mg (J01CE02)	Enoxac 200mg (J01MA04)	Amp 125mg (J01CA01
Amoxy 250mg		0.38	0.63	1.33	0.80	0.97	0.33	0.87	1.67	0.60
Co-trim 480mg	0.38		0.64	0.66	0.50	0.73	0.44	0.66	0.83	0.52
Doxy 100mg	0.63	0.64		0.05	1.03	0.38	0.46	0.05	1.20	0.32
Amoxy 125mgl	1.33	0.66	0.05		2.21	0.33	1.03	0.00	1.16	0.75
Metro 200mg	0.80	0.50	1.03	2.21		1.36	1.99	1.39	2.12	3.09
Erythr 250mg	0.97	0.73	0.38	0.33	1.36		0.81	0.33	0.83	0.68
Amp 250mg	0.33	0.44	0.46	1.03	1.99	0.81		0.65	1.61	0.47
Phen 250mg	0.87	0.66	0.05	0.00	1.39	0.33	0.65		1.16	0.33
Enoxac 200mg	1.67	0.83	1.20	1.16	2.12	0.83	1.61	1.16		1.49
Amp 125mg	0.60	0.52	0.32	0.75	3.09	0.68	0.47	0.33	1.49	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metron = metronidazole, Amp = ampicillin, Phenoxy = phenoxymethyl penicillin, Enoxac = enoxacin

Difference of practical significance is d>0.8

As illustrated in Table 5.40B$_1$, the d-value calculated (refer to Chapter 4, Section 4.4.5.2.4) shows that there were differences of practical significance found among the average costs of individual antimicrobials prescribed in Clinic B. There were differences of practical significance found between enoxacin 200mg and the other individual antimicrobials prescribed in the Clinic B. Enoxacin had the highest average cost of all antimicrobials prescribed in Clinic B (refer to the grey boxes as indication of practical significance).

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic C.

The average, minimum and maximum costs of the top ten individual antimicrobials prescribed in Clinic C are shown in Table 5.40C.

As shown in Table 5.40C, the minimum cost of the individual antimicrobials in Clinic C was R0.00 The maximum cost of the individual antimicrobials varied between R6.70 for phenoxymethyl penicillin 250mg (353 prescriptions) and R343.05 for 1834 prescriptions of amoxycillin 250mg capsules. This was because amoxycillin represented the highest number (n = 1834) of the total number of antimicrobial prescriptions in Clinic C. The average cost of the individual antimicrobials varied between R1.49 ± R0.73 and R12.49 ± R6.30. Enoxacin 200mg (608 prescriptions) had the highest average cost of R12.49 ± R6.30 while metronidazole 200mg had the lowest average cost of R1.49 ± 0.73 for 316 prescriptions

Table 5.401C: Average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic C.

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	1834	8173.42	4.46	8.15	4.49	0	343.05
Co-trimoxazole 480mg (J01EE01)	940	2252.93	2.39	0.87	2.20	0	13.12
Doxycycline 100mg (J01AA02)	826	5178.66	6.27	6.18	5.61	0	92.63
Amoxycillin 125mg/5ml (J01CA04)	688	4431.64	6.44	7.65	4.57	0	196.94
Enoxacin 200mg (J01MA04)	608	7475.31	12.29	6.30	12.20	0.06	122.01
Metronidazole 400mg (J01XD01)	550	1302.35	2.37	9.34	1.79	0	128.12
Erythromycin 250mg (J01FA01)	420	4884.85	11.63	5.71	10.12	0	47.82
Phenoxymethyl penicillin 250mg (J01CE02)	353	2766.44	7.84	3.14	6.12	1.20	12.24
Metronidazole 200mg (J01XD01)	316	473.09	1.49	0.73	1.99	0.01	2.88
Phenoxymethyl penicillin 125mg (J01CE02)	239	1407.68	5.89	1.36	6.58	0	6.70

Statistical d-values as indication of the practical significance differences between the average costs of the individual antimicrobials prescribed in Clinic C are shown in Table 5.40C_1

Table 5.40C_1: Statistical d-values as indication of the practical significance differences between the average costs of the individual antimicrobials prescribed in Clinic C

Antimi-crobial	Amoxy 250mg (J01CA04	Co-trim 480mg (J01EE01	Doxy 100mg (J01AA02	Amoxy 125mg (J01CA04	Enoxac 200mg (J01MA04	Erythr 250mg (J01FA01	Amp 250mg (J01CA01	Phen 250mg (J01CE02	Metro 200mg (J01XD01	Phen 125mg (J01CE02
Amoxy 250mg		0.25	0.22	0.24	0.96	0.22	0.88	0.41	0.36	0.18
Co-trim 480mg	0.25		0.63	0.53	1.57	0.00	1.62	1.74	1.03	2.57
Doxy 100mg	0.22	0.63		0.02	0.96	0.42	0.87	0.25	0.77	0.06
Amoxy 125mg	0.24	0.53	0.02		0.76	0.44	0.66	0.18	0.65	0.07
Enoxac 200mg	0.96	1.57	0.96	0.76		1.06	0.10	0.71	1.71	1.02
Metro 400mg	0.22	0.00	0.42	0.44	1.06		0.99	0.59	0.09	0.38
Erythr 250mg	0.88	1.62	0.87	0.66	0.10	0.99		0.62	1.78	0.87
Phen 250mg	0.41	1.74	0.25	0.18	0.71	0.59	0.62		2.02	0.62
Metro 200mg	0.36	1.03	0.77	0.65	1.71	0.09	1.78	2.02		3.24

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Amp = ampicillin, Phen = phenoxymethyl penicillin, Enoxac = enoxacin, Erythr = erythromycin

Difference of practical significance is d>0.8

As illustrated in Table 5.40C$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were differences of practical significance found among the average costs of the different antimicrobials prescribed in Clinic C. This was mostly noted with enoxacin 200mg. This means that enoxacin had the highest average cost as compared to the rest of the antimicrobials prescribed in Clinic C (refer to the grey boxes as indication of practical significance).

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic D are shown in Table 5.40D.

As illustrated in Table 5.40D, the minimum cost of the individual antimicrobials in Clinic D was zero for most of the antimicrobials. The maximum cost of the individual antimicrobials varied between R5.43 for procaine penicillin and R95.26 for metronidazole 200mg (1747 prescriptions) and phenoxymethyl penicillin 250mg (1392 prescriptions). The average cost of the individual antimicrobials varied between R1.12 ± 2.29 and R11.77 ± R2.83. Enoxacin

200mg had the highest average cost of R11.17 ± R2.83 for 794 prescriptions while metronidazole 200mg had the lowest average cost of R1.12 ± R2.29. Enoxacin 200mg belongs to the group of quinolones that are newer and more expensive than metronidazole 200mg which is an older and cheaper antibiotic.

Table 5.40D: Average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic D

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	3854	133394.07	3.48	1.53	3.0	0	19.68
Co-trimoxazole 480mg (J01EE01)	2664	5266.09	1.98	1.00	1.87	0	20.68
Erythromycin 250mg (J01FA01)	2057	18432.42	8.96	3.04	8.76	0	36.78
Metronidazole 200mg (J01XD01)	1747	1948.18	1.12	2.29	1.23	0.05	95.26
Amoxycillin 125mg/5ml (J01CA04)	1424	7831.95	3.48	1.53	3.00	0	9.14
Phenoxymethyl penicillin 250mg (J01CE02)	1392	8290.49	5.96	2.79	5.59	0	95.26
Doxycycline 100mg (J01AA02)	856	5157.72	6.03	1.98	6.12	0	12.24
Enoxacin 200mg (J01MA04)	794	9346.42	11.77	2.83	12.20	0	13.61
Phenoxymethyl penicillin 125mg (J01CE02)	673	4010.40	5.96	1.54	6.58	1.65	9.78
Procaine penicillin (J01CE09)	514	746.18	1.45	1.03	1.56	0.10	5.43

Statistical d-values as indication of practical significance differences between the average costs of individual antimicrobials prescribed in Clinic D are illustrated in Table 5.40D_1

Table 5.40D$_1$: Statistical d-value as indication of practical significance differences between the average costs of individual antimicrobials prescribed in Clinic D.

Antimicrobial	Amoxy 250mg (J01CA04	Co-trim 480mg (J01CEE01	Erythr 250mg (J01FA01	Metro 200mg (J01XD01	Amoxy 125mg (J01CA04	Doxy 100mg (J01AA02	Phen 250mg (J01CE02	Enoxac 200mg J01MA04	Phen 125mg (J01CE02	Proc pen (J01CE09
Amoxy 250mg		0.98	1.80	1.03	0.00	0.89	1.29	2.93	1.61	1.33
Co-trim 480mg	0.98		2.30	0.38	0.98	1.43	2.05	3.46	2.58	0.51
Erythr 250mg	1.80	2.30		2.58	1.80	0.99	0.96	0.92	0.99	2.47
Metro 200mg	1.03	0.38	2.58		1.03	1.73	2.16	3.76	2.11	0.14
Amoxy 125mg	0.00	0.98	1.80	1.03		0.89	1.29	2.93	1.61	1.33
Doxy 100mg	0.98	1.43	0.99	1.73	0.89		0.03	2.05	0.00	1.62
Phen 250mg	1.29	2.05	0.96	2.16	1.29	0.03		2.03	0.04	2.31
Enoxac 200mg	2.93	3.46	0.92	3.76	2.93	2.05	2.03		2.83	3.65
Phen 125mg	1.61	2.58	0.99	2.11	1.61	0.00	0.04	2.05		2.89
Proc Pen	1.33	0.51	2.47	0.14	1.33	1.62	2.31	3.65	2.89	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Phen = phenoxymethyl penicillin, Enoxac = enoxacin, Proc pen = procaine penicillin, Erythr = erythromycin

Difference of practical significance is d>0.8.

As shown in Table 5.40D$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significance differences found among the average costs of individual antimicrobials in Clinic D.

The practical significance differences were mostly noted with enoxacin 200mg and erythromycin 250mg. This means that these two drugs present the highest average costs of all antimicrobials prescribed in Clinic D (refer to the gray boxes as indication of practical significance).

The average, minimum and maximum costs of the top ten individual antimicrobials prescribed in Clinic E are shown in Table 5.40E.

Table 5.40E: The average, minimum and maximum costs of the top ten individual antimicrobials prescribed in Clinic E

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	1871	8735.88	4.67	1.60	4.49	0	16.72
Co-trimoxazole 480mg (J01EE01)	1364	3226.21	2.37	1.16	4.62	0	13.10
Metronidazole 200mg (J01XD01)	690	743.91	1.08	0.39	0.96	0	2.56
Doxycycline 100mg (J01AA02)	682	4868.25	7.14	2.97	6.44	0	61.99
Ampicillin 250mg (J01CA01)	659	3586.05	5.44	1.54	5.76	2.05	14.39
Metronidazole 400mg (J01XD01)	604	713.19	1.18	0.57	1.19	0.43	6.44
Amoxycillin 125mg/5ml (J01CA01)	582	3907.29	6.71	2.38	4.57	1.58	18.28
Enoxacin 200mg (J01MA04)	439	5409.31	12.32	3.51	12.20	6.10	61.00
Co-trimoxazole 240mg/5ml (J01EE01)	322	822.97	2.56	1.34	1.81	0.91	7.24
Erythromycin 250mg (J01FA01)	321	2704.78	8.43	4.08	6.40	0	36.14

The minimum cost of the individual antimicrobials was zero as illustrated in Table 5.40E. The maximum cost varied from R2.56 for metronidazole 200mg (690 prescriptions) and R61.99 for 682 prescriptions of doxycycline 100mg. The average cost of the antimicrobials varied between R1.08 ± R0.39 and R12.32 ± R3.51. Enoxacin 200mg had the highest average cost of R12.33 ± R3.15 for 439 prescriptions and metronidazole 200mg had the lowest average cost of R1.08 ± R0.39 for 690 prescriptions. The total cost for enoxacin was the second highest accounting for 11.37% (R5409.31) and metronidazole 200mg accounting for 1.56% (R743.91) of the total cost of antimicrobials prescribed in Clinic E.

Table 5.40E$_1$: Statistical d-values as indication of practical significance differences between the average costs of individual antimicrobials prescribed in Clinic E

Antimi-crobial	Amoxy 250mg (J01CA04	Co-trim 480mg (J01EE01	Metro 200mg (J01XD01	Doxy 100mg (J01AA02	Amp 250mg (J01CA01	Metro 400mg (J01XD01	Amoxy 125mg (J01CA04	Enoxac 200mg (J01MA04	Co-trim 240mg (J01EE01	Erythr 250mg (J01FA01
Amoxy 250mg		1.44	2.24	0.83	0.48	2.18	0.86	2.18	1.32	0.92
Co-trim 480mg	1.44		1.11	1.61	1.99	1.03	1.82	2.83	0.14	1.49
Metro 200mg	2.24	1.11		2.04	2.83	0.18	2.37	3.20	1.10	1.80
Doxy 100mg	0.83	1.61	2.04		0.58	2.03	0.15	1.48	1.56	0.32
Amp 250mg	0.48	1.99	2.83	0.58		2.77	0.56	1.96	1.87	0.73
Metro 400mg	2.18	1.03	0.18	2.03	2.77		2.32	3.17	1.03	1.78
Amoxy 125mg	0.86	1.82	2.37	0.15	0.56	2.32		1.60	1.18	0.42
Enoxac 200mg	2.18	2.83	3.20	1.48	1.96	3.17	1.60		2.78	0.95
Co-trim 240mg	1.32	0.14	1.10	1.56	1.87	1.03	1.18	2.78		1.44
Erythr 250mg	0.92	1.49	1.80	0.32	0.73	1.78	0.42	0.95	1.44	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Phenoxy = phenoxymethyl penicillin, Enoxac = enoxacin, Erythr = erythromycin, Amp = ampicillin

Difference of practical significance is d>0.8.

As shown in Table 5.40E$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significance differences found among the average medicine costs of the antimicrobials prescribed in Clinic E. The differences of practical significance were mostly observed with enoxacin 200mg followed by erythromycin 250mg. This implies that enoxacin 200mg had the highest average cost of all antimicrobials, followed by erythromycin 250mg in Clinic E (refer to the grey boxes for indication of practical significance).

The average, minimum and maximum costs of the top ten individual antimicrobials prescribed in Clinic F are shown in Table 5.40F.

Table 5.40F: The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic F

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Co-trimoxazole 480mg (J01EE01)	3693	8718.44	2.36	0.92	1.87	0	8.42
Doxycycline 100mg (J01AA02)	1781	10895.22	6.12	1.74	5.65	0.39	23.35
Amoxycillin 250mg (J01CA04)	1698	7581.71	4.47	1.79	4.49	0	14.25
Metronidazole 200mg (J01XD01)	1562	2064.95	1.32	0.77	1.13	0	23.95
Co-trimoxazole 240mg/5ml (J01EE01)	1157	3112.85	2.69	1.27	2.18	0	10.86
Erythromycin 250mg (J01FA01)	752	8578.94	11.41	5.57	10.35	0	26.27
Enoxacin 200mg (J01MA04)	672	7990.61	11.89	4.76	12.26	6.10	91.51
Amoxycillin 125mg/5ml (J01CA04)	530	2770.95	5.23	1.72	4.57	1.58	18.28
Ampicillin 250mg (J01CA01)	481	147.18	4.57	1.48	4.32	0	8.29
Erythromycin 125mg/5ml (J01FA01)	370	2511.04	6.79	2.42	5.59	2.57	12.02

The minimum cost of the individual antimicrobials was zero. The maximum cost varied from R8.29 for co-trimoxazole 480mg (3693 prescriptions) and R91.51 for enoxacin 200mg (672 prescriptions). The average cost of other antimicrobials varied between R1.32 ± R0.77 and R11.89 ± R4.76. Enoxacin 200mg had the highest average cost of R11.89 ± R4.76 accounting for 11.22% of the total cost of antimicrobials in Clinic F, and metronidazole 200mg (1562 prescriptions) had the lowest average cost of R1.32 ± R0.77 accounting for 2.90% of the total cost of antimicrobials prescribed in Clinic F.

Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic F are shown in Table $5.40F_1$.

Table 5.40F$_1$: Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic F

Antimi-crobial	Co-trim 480mg (J01EE01	Doxy 100mg (J01AA02	Amoxy 250mg (J01CA04	Metro 200mg (J01XD01	Co-trim 240mg (J01EE01	Erythro 250mg (J01FA01	Enoxac 200mg (J01MA06	Amoxy 125mg (J01CA04	Amp 250mg (J01CA01	Erythr 125mg (J01FA01
Co-trim 480mg		2.16	1.18	1.13	0.26	1.62	2.00	1.67	1.49	1.83
Doxy 100mg	2.16		0.92	2.76	1.97	0.95	1.21	0.50	0.87	0.28
Amoxy 250mg	1.18	0.92		1.76	0.99	1.25	1.56	0.42	0.06	0.96
Metro 200mg	1.13	2.76	1.76		0.51	0.88	0.89	0.75	0.71	0.81
Co-trim 240mgl	0.26	1.97	0.99	0.51		1.57	1.93	1.48	1.27	1.69
Erythro 250mg	1.26	0.95	1.25	0.88	1.57		0.09	1.11	1.23	0.83
Enoxac 200mg	2.00	1.21	1.56	0.89	1.93	0.09		1.40	1.54	1.07
Amoxy 125mg	1.67	0.50	0.42	0.75	1.48	1.11	1.40		0.38	0.64
Amp 250mg	1.49	0.87	0.06	0.71	1.27	1.23	1.54	0.38		0.92
Erythro 125mg	1.83	0.28	0.96	0.81	1.69	0.83	1.07	0.64	0.92	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Amp = ampicillin, Erythr = erythromycin, Enoxac = enoxacin

Difference of practical significance is d>0.8.

As shown in Table 5.40F$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were differences of practical significance found among the average costs of various antimicrobials prescribed in Clinic F. The highest average cost of an antimicrobial was that of enoxacin 200mg. The next highest average cost of such medicines was that of erythromycin 250mg. Enoxacin belongs to the group of quinolones and erythromycin to the group of macrolides. Both are second line antibiotics that are more expensive than the first-line antibiotics (refer to the gray boxes as indication of practical significance). Considering what they cost, they are supposed to be used a lot more sparingly.

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic G.

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic G will are shown in Table 5.40G.

As shown in Table 5.40G, the minimum cost of the antimicrobials was zero. The maximum cost varied from R5.59 for metronidazole 400mg (497 prescriptions) and R85.41 for doxycycline 100mg (895 prescriptions). The average cost of the antimicrobials varied between R1.04 ± 2.89 and R10.54 ± R3.92. Erythromycin 250mg (931 prescriptions) had the highest average cost of R10.54 ± R3.92. On the other hand, metronidazole 200mg (578 prescriptions) had the lowest average cost of R1.36 ± R0.56. Erythromycin 250mg accounted for 16.63% while metronidazole 400mg accounted for 1.15% of the total cost of antimicrobials prescribed in Clinic G.

Table 5.40G: Average, minimum and maximum cost of the top 10 individual antimicrobials prescribed in Clinic G

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	2471	8884.93	3.59	1.40	3.15	0	16.03
Co-trimoxazole 480mg (J01EE01)	2446	5442.54	2.23	0.95	1.87	0	15.08
Erythromycin 250mg (J01FA01)	931	9809.99	10.54	3.92	8.75	0	55.83
Doxycycline 100mg (J01AA02)	895	5833.93	6.52	4.01	5.78	0	85.41
Ampicillin 240mg/5ml (J01CA01)	776	2984.87	3.85	1.22	3.59	1.09	8.04
Metronidazole 200mg (J01XD01)	578	601.28	1.04	2.89	0.81	0	62.11
Metronidazole 400mg (J01XD01)	497	676.37	1.36	0.56	1.19	0.09	5.59
Phenoxymethylpenicillin 250mg (J01CE02)	495	2083.56	4.21	1.67	3.09	0.29	15.30
Co-trimoxazole 240mg/5ml (J01EE01)	491	1221.22	2.49	1.49	2.25	0	14.80
Erythromycin 125mg/5ml (J01FA01)	307	1807.96	5.88	2.54	5.56	0.11	16.50

Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic G.

Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic G are shown in Table 5.40G_1.

Table 5.40G_1: Statistical d-values as indication of practical significance differences Between the individual antimicrobials prescribed in Clinic G

Antimi-robial	Co-trim 480mg (J01EE01	Doxy 100mg (J01AA02	Amoxy 250mg (J01CA04	Metro 200mg (J01XD01	Co-trim 240mg (J01EE01	Erythr 250mg (J01FA01	Metro 400mg (J01XD01	Amoxy 125mg (J01CA04	Amp 250mg (J01CA01	Erythr 125mg (J01FA01
Co-trim 480mg		2.16	1.18	1.13	0.26	1.62	2.00	1.67	1.49	1.83
Doxy 100mg	2.16		0.92	2.76	1.97	0.95	1.21	0.50	0.87	0.28
Amoxy 250mg	1.18	0.92		1.76	0.99	1.25	1.56	0.42	0.06	0.96
Metro 200mg	1.13	2.76	1.76		0.51	0.88	0.89	0.75	0.71	0.81
Co-trim 240mg	0.26	1.97	0.99	0.51		1.57	1.93	1.48	1.27	1.69
Erythr 250mg	1.26	0.95	1.25	0.88	1.57		0.09	1.11	1.23	0.83
Metro 400mg	2.00	1.21	1.56	0.89	1.93	0.09		1.40	1.54	1.07
Amoxy 125mg	1.67	0.50	0.42	0.75	1.48	1.11	1.40		0.38	0.64
Amp 250mg	1.49	0.87	0.06	0.71	1.27	1.23	1.54	0.38		0.92
Erythr 125mg	1.83	0.28	0.96	0.81	1.69	0.83	1.07	0.64	0.92	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Amp = ampicillin, Erythr = erythromycin

Difference of practical significance is d>0.8.

As shown in Table $40G_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were differences of practical significance found among the average costs of the antimicrobials prescribed in Clinic G. The d-values obtained were significantly higher in the case of erythromycin 250mg and doxycycline 100mg.

Given the findings of this study, erythromycin 250mg had the highest average cost as compared to most of the other antimicrobials. The second highest antimicrobial in terms of average cost was doxycycline 100mg (refer to the grey boxes as indication of practical significance).

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic H

The average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic H are shown in Table 5.40H.

As shown in Table 5.40H, the minimum cost of the individual antimicrobials is zero. The maximum cost varied from R7.24 for co-trimoxazole 240mg/5ml (408 prescriptions) and R183.02 for norfloxacin 400mg (488 prescriptions). The average cost of the antimicrobials varied between R1.61 ± R8.26 and R9.78 ± R7.53. While metronidazole 400mg (478 prescriptions) had the highest average cost of R9.78 ± R7.53 accounting for 8.86%, norfloxacin 400mg (488 prescriptions) had the lowest average cost of R1.61 ± R8.26 accounting for only 1.46% of the total cost of antimicrobials prescribed in Clinic H.

Table 5.40H: Average, minimum and maximum cost of the top ten individual antimicrobials prescribed in Clinic H

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	1913	7043.82	3.68	1.32	4.49	0	11.96
Co-trimoxazole 480mg (J01EE01)	1612	3417.16	2.12	0.86	1.87	0	13.10
Ampicillin 250mg (J01CA01)	981	3178.40	3.24	1.76	2.92	0	10.99
Phenoxymethyl penicillin 250mg (J01CE02)	700	3022.45	4.32	1.84	4.59	0	12.24
Doxycycline 100mg (JOAA02)	669	3968.89	5.93	3.44	5.64	0	85.41
Erythromycin 250mg (J01FA01)	633	5742.51	9.07	6.01	8.76	0	72.28
Amoxycillin 125mg/5ml (J01CA04)	545	2685.42	4.93	1.56	4.57	0	11.90
Norfloxacin 400mg (J01MA04)	488	783.78	1.61	8.26	1.19	0	183.02
Metronidazole 400mg (J01XD01)	478	4675.75	9.78	7.53	8.81	0	57.48
Co-trimoxazole 240mg/5ml (J01EE01)	408	762.28	1.87	1.18	1.81	0	7.24

Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic H.

Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic H are shown in Table 5.40H$_1$.

Table 5.40H$_1$: Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic H.

Antimi-Crobial	Amoxy 250mg (J01CA04	Co-trim 480mg (J01EE01	Erythr 250mg (J01FA01)	Doxy 100mg (J01AA02	Amp 250mg (J01CA01	Metro 200mg (J01XD01	Metro 400mg (J01XD01	Phen 250mg (J01CE02	Co-trim 125mg (J01EE01	Erythr 125mg (J01FA01
Amoxy 250mg		0.97	1.77	0.73	0.19	0.88	1.59	0.37	0.74	0.90
Co-trim 480mg	0.97		2.12	1.07	1.33	0.41	0.92	1.19	0.17	1.44
Erythr 250mg	1.77	2.12		1.00	1.71	2.42	2.34	1.61	2.05	1.19
Doxy 100mg	0.73	1.07	1.00		0.67	1.37	1.29	0.58	1.00	0.16
Amp 250mg	0.19	1.33	1.71	0.67		0.99	2.04	0.22	0.91	0.80
Metro 200mg	0.88	0.41	2.42	1.37	0.99		0.11	1.10	0.50	1.67
Metro 400mg	1.59	0.92	2.34	1.29	2.04	0.11		1.71	0.76	1.78
Phen 250mg	0.37	1.19	1.61	0.58	0.22	1.10	1.71		1.03	0.66
Co-trim 240mg	0.74	0.17	2.05	1.00	0.91	0.50	0.76	1.03		1.33
Erythr 125mg	0.90	1.44	1.19	0.16	0.80	1.67	1.78	0.66	1.33	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Amp = ampicillin, Erythr = erythromycin, phenyl = phenoxymethyl penicillin

Difference of practical significance is d>0.8.

As demonstrated in Table 5.40H$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show there were differences of practical significance found among the average costs of the antimicrobials prescribed in Clinic G. Difference of practical significance was shown to be more significant in the case of the following drugs: erythromycin 250mg and metronidazole 400mg.

Comparatively, erythromycin had the highest average cost of all antimicrobials prescribed in that clinic. Metronidazole 400mg was the next highest prescribed antimicrobial. (see the grey boxes for details).

Table 5.40I: Average, minimum and maximum cost of the top 10 individual Antimicrobials prescribed in Clinic I

Antimicrobial	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg (J01CA04)	1983	7837.00	3.95	1.49	4.49	0.03	11.96
Ampicillin 250mg (J01CA01)	1081	4958.63	4.59	1.69	4.09	0.93	10.28
Metronidazole 200mg (J01XD01)	969	993.40	1.02	0.47	0.81	0.05	10.74
Erythromycin 250mg (J01FA01)	849	7807.95	9.19	3.17	8.76	0.62	24.52
Co-trimoxazole 480mg (J01EE01)	807	1793.46	2.22	1.31	1.87	0.50	11.76
Doxycycline 100mg (J01AA02)	778	5114.36	6.57	2.29	5.60	0	22.88
Amoxycillin 125mg/5ml (J01CA04)	746	3793.04	5.08	2.08	4.57	0	11.90
Metronidazole 400mg (J01XD01)	708	1028.88	1.45	0.51	1.29	0.43	5.78
Amoxycillin 250mg / Clavulanic acid 125mg (J01CR02)	694	19290.30	27.79	7.29	26.14	17.43	67.05
Erythromycin 125mg/5ml (J01FA01)	336	2258.13	6.72	3.39	5.64	0.11	14.44

As revealed in Table 5.40I$_1$, the minimum cost of the individual antimicrobials was zero The maximum cost varied from R5.78 for metronidazole 400mg (708 prescriptions) and R67.05 for amoxycillin 250mg/clavulanic acid 125mg (694 prescriptions). The average cost of the antimicrobials varied between R1.02 ± R0.47 and R27.79 ± R7.29. Amoxycillin 250m/clavulanic acid 125mg had the highest average cost of R27.79 ± R7.29 and metronidazole 200mg had the lowest average cost of R1.45 ± R0.51.

Amoxycillin 250mg/clavulanic acid 125mg (Augmaxcil® 375mg) presented the highest percentage (23.99) and metronidazole 200mg presented the lowest percentage (1.24) of the total cost of antimicrobials prescribed in Clinic I.

Table 5.40I$_1$: Statistical d-values as indication of practical significance differences between the individual antimicrobials prescribed in Clinic I.

Antimi-crobial	Amoxy 250mg (J01CA04	Amp 250mg (J01CA01	Metro 400mg (J01XD01	Erythr 250mg (J01FA01	Co-trim 480mg (J01EE01	Doxy 100mg (J01AA02	Amoxy 125mg (J01CA04	Metro 200mg (J01XD01	Amoxy 250mg/clav 125mg (J01CR02)	Co-trim 240mg (J01EE01
Amoxy 250mg		0.38	1.97	1.65	1.16	1.14	0.54	1.68	3.27	0.82
Amp 250mg	0.38		2.11	1.45	1.40	0.86	0.24	1.86	3.18	0.63
Metro 400mg	1.97	2.11		2.58	0.92	2.42	1.95	0.84	3.67	1.68
Erythr 250mg	1.65	1.45	2.58		2.20	0.83	1.30	2.44	2.55	0.73
Co-trim 480mg	1.16	1.40	0.92	2.20		1.90	1.38	0.59	3.51	1.33
Doxy 100mg	1.14	0.86	2.42	0.83	1.90		0.65	2.24	2.91	0.04
Amoxy 125mg	0.54	0.24	1.95	1.30	1.38	0.65		1.75	3.12	0.48
Metro 200mg	1.68	1.86	0.84	2.44	0.59	2.24	1.75		3.61	1.55
Amoxy 250mg/ Clav 125mg	3.27	3.18	3.67	2.55	3.51	2.91	3.12	3.61		2.89
Co-trim 240mg	0.82	0.63	1.68	0.73	1.33	0.04	0.48	1.55	2.89	

Abbreviations:

Amoxy = amoxycillin, Co-trim = Co-trimoxazole, Doxy = doxycycline, Metro = metronidazole, Amp = ampicillin, Erythr = erythromycin, Amoxy/clav = amoxycillin/clavulanic acid (Augmaxcil)

Difference of practical significance is d>0.8.

As demonstrated in Table 5.40I$_1$, the d-values calculated (refers to Chapter 4, Section 4.4.5.2.4) show that there was difference of practical significance found among the average costs of antimicrobials prescribed in Clinic I. The d-values obtained show that the following drugs contributed more significantly to the overall average cost of antimicrobials in that clinic

than did the others: amoxycillin 250mg/clavulanic acid 125mg (Augmaxcil® 375mg) and erythromycin 250mg. Amoxycillin 250mg/clavulanic acid 125mg (Augmaxcil® 375mg) had the highest average cost followed by erythromycin 250mg (refer to the grey boxes in Table 5.411I, as indication of practical significance).

SUMMARY OF THE RESULTS OF THE NINE CLINICS WITH REFERENCE TO THE AVERAGE COSTS OF ANTIMICROBIALS

From the results of the data analysed from all the nine clinics, it can be noted that there were practical significant differences observed in the average costs of individual antimicrobials prescribed in the nine clinics. These differences were noted in the following antimicrobials drugs: erythromycin 250mg, erythromycin 125mg, enoxacin 200mg, metronidazole 200mg and amoxycillin 250mg/clavulanic acid 125mg. All these drugs had the highest average costs of all antimicrobials prescribed in the nine clinics.

It was observed from this study that quinolones presented the highest average cost of all antimicrobials, followed by macrolides. These are newer and therefore more expensive than the other antimicrobials prescribed in the clinics. Both groups have a broad spectrum of activity.

There were differences in the average costs of the antimicrobials in the different clinics. This could have been influenced by the different amounts of the different antimicrobials prescribed, depending on the different disease states presented in the different patients. The differences in the disease states noted in the nine clinics might be attributed to the differences in geographic locations of these clinics

5.7.2 Average cost of top ten antimicrobials prescribed according to gender in each clinic

The average, minimum and maximum cost of the ten most prescribed antimicrobials according to gender in each clinic are shown Tables 5.41 (A – I).

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic A are illustrated in Table 41A.

Table 5.41A: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic A.

Antimicrobial	Gender	N	Total Cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Co-trimoxazole	F	1010	2141.40	2.12	0.91	1.89	0.37	7.24
240mg/5ml (J01EE01)	M	1045	2283.41	2.19	0.94	1.95	0.01	6.38
Co-trimoxazole 480mg	F	1459	2811.07	1.93	0.52	1.87	0	5.62
(J01EE01)	M	587	1272.94	2.17	0.89	1.87	0.55	6.23
Doxycycline 100mg	F	811	4159.04	5.13	2.26	5.60	0	12.38
(J01AA02)	M	472	2758.07	5.84	3.35	7.78	0	12.38
Ampicillin 250mg	F	921	3902.02	4.24	1.54	4.31	0	10.28
(J01CA01)	M	65	226.42	3.48	1.58	3.06	0	7.18
Metronidazole 400mg	F	702	830.44	1.18	0.34	1.19	0	3.22
(J01XD01)	M	42	49.22	1.17	0.37	1.19	0	2.39
Amoxycillin 250mg	F	442	1837.21	4.16	1.76	4.50	0.03	11.70
(J01CA04)	M	77	329.39	4.28	2.69	3.07	0.03	12.62
Metronidazole 200mg	F	382	327.16	0.86	0.25	0.89	0.05	1.72
(J01XD01)	M	34	33.89	0.99	0.50	1.86	0.05	3.27
Amoxycillin 125mg/5ml	F	123	528.15	4.29	1.97	4.57	0.46	13.71
(J01CA04)	M	126	490.62	3.89	1.67	4.57	0	11.90
Erythromycin 250mg	F	144	1305.28	9.06	3.99	8.76	0.17	24.52
(J01FA01)	M	70	617.11	8.81	4.53	8.75	0.60	20.70
Erythromycin 25mg/5ml	F	97	546.32	5.63	0.80	5.61	0.75	6.75
(J01FA01)	M	109	606.78	5.57	1.18	5.57	0	12.18

As shown in Table 5.41A, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials according to gender varied between R1.72 for metronidazole 200mg and R24.52 for erythromycin 250mg prescribed for females and R2.39 for metronidazole 400mg and R20.70 for erythromycin prescribed for males. The average cost of antimicrobials prescribed according to gender varied between R0.86 ± 0.25 and R9.06 ● 3.99 for females and R0.99 ● 0.50 and R8.81 ± 4.53 for males. Metronidazole 200mg had the lowest average cost and erythromycin 250mg the highest average cost for both genders. The quantity of erythromycin 250 mg prescribed for female

patients that received erythromycin was more (n = 144) at a total cost of R1305.28 as compared to male patients (n = 70) at a total cost of R617.11. For metronidazole 200mg, the quantity that female patients received was more (n = 382) at a total cost of R327.16 as compared to the male patients (n = 34) at a total cost of R 33.89.

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic A were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender in Clinic A.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic B are illustrated in Table 41B.

Table 5.41B shows that the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R7.49 for co-trimoxazole 480mg and R64.58 for enoxacin 200mg for females, and R4.49 for co-trimoxazole 480mg and R90.41 for doxycycline 100mg for males. The average cost of the antimicrobials prescribed according to gender varied from R1.08 ● 0.87 and R12.96 ± R6.25 for females and R1.01 ● R0.11 and R11.36 ● R 3.33 for males. Metronidazole 200mg had the lowest average cost for both genders and enoxacin 200mg had the highest average for both genders. The quantity of enoxacin received by female patients was 80 prescriptions at a higher total cost of R1036.77 as compared to the male patients who received 51 prescriptions at a lower total cost of R579.11. Same applied to the high quantities of metronidazole received (182 prescriptions) a total cost of R195.76, as compared to 80 prescriptions for metronidazole at a lower total cost of R81.06. According to Appelbaum and Hunter (2000: 6), enoxacin belongs to the newer group of fluoroquinolones that have a number of characteristics that have led to their increased use. Consequently, it is more expensive than metronidazole, an antiprotozoal.

Table 5.41B: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic B

Antimicrobial	Gender	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg	F	654	1902.77	2.91	1.74	2.34	0	14.29
(J01CA04)	M	596	173.94	3.05	2.99	2,34	0	58.65
Co-trimoxazole 480mg	F	388	822.27	2.12	0.86	2.32	0	7.49
(J01EE01)	M	300	629.79	2.09	0.85	1.87	0	4.49
Doxycycline 100mg	F	198	1127.75	5.69	1.50	5.59	3.89	11.39
(J01AA02)	M	147	921.72	6.27	7.04	5.68	3.89	90.41
Amoxycillin 125mg/5ml	F	150	946.16	6.31	2.27	4.57	0	11.90
(J01CA04)	M	154	930.28	6.04	2.37	4.57	0	11.90
Erythromycin 250mg	F	171	1313.49	7.68	4.68	8.76	0	35.03
(J01FA01)	M	127	1021.56	8.04	5.44	8.76	0	28.80
Metronidazole 200mg	F	182	195.76	1.08	0.87	0.97	0.01	11.28
(J01XD01)	M	80	81.06	1.01	0.11	0,97	0.62	11.29
Ampicillin 250mg	F	119	453.04	3.81	1.26	3.59	1.49	8.07
(J01CA01)	M	123	460.89	3.75	1.48	2.97	0	10.28
Phenoxymethyl	F	117	708.23	6.05	3.97	6.12	0	12.24
penicillin 250mg	M	96	605.02	6.30	3.35	6.12	0	12.24
(J01CE02)								
Enoxacin 200mg	F	80	1036.77	12.96	6.25	12.20	6.10	64.58
(J01MA04)	M	51	579.11	11.36	3.33	12.20	6.46	25.83
Erythromycin 25mg/5ml	F	52	227.59	4.38	1.07	4.46	0	8.92
(J01FA01)	M	63	281.07	4.47	1.13	4.46	0	8.92

Statistical d-values as indication of practical significance differences between the costs of antimicricrobials in Clinic B were calculated. The d-values obtained show that there were no differences of practical significance found among the average costs of antimicrobials prescribed according to gender in Clinic B.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic C are illustrated in Table 41C.

Table 5.41C: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic C

Antimicrobial	Gender	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg	F	1122	4800.96	4.28	2.05	4.49	0	14.25
(J01CA04)	M	709	3362.88	4.74	12.85	4.49	0	343.25
Co-trimoxazole 480mg	F	573	1360.74	2.37	0.91	2.20	0.40	13.12
(J01EE01)	M	367	892.19	2.43	0.82	2.62	0	8.82
Doxycycline 100mg	F	623	3931.93	6.31	6.71	5.78	0.36	92.63
(J01AA02)	M	202	1240.95	6.14	4.19	5.61	0	61.69
Amoxycillin 125mg/5ml	F	323	2031.24	6.29	2.42	4.57	0	11.90
(J01CA04)	M	263	2391.26	6.59	10.29	5.57	0	196.04
Enoxacin 200mg	F	485	6036.17	12.45	6.92	12.20	0.06	122.01
(J01MA04)	M	123	1439.14	11.70	2.92	12.20	0.12	26.47
Metronidazole 400mg	F	496	1218.45	2.46	9.83	1.79	0	128.11
(J01XD01)	M	53	82.70	1.56	0.56	1.29	0.43	3.59
Erythromycin 250mg	F	244	2717.96	11.14	4.67	8.86	0	32.94
(J01FA01)	M	176	2166.89	12.31	6.86	10.35	0	47.82
Phenoxymethyl penicillin 250mg	F	245	1961.80	8.00	3.11	6.12	1.22	12.24
(J01CE02)	M	108	804.64	7.45	3.19	6.12	1.20	12.24
Metronidazole 200mg	F	275	418.81	1.52	0.75	2.10	0.10	2.88
(J01XD01)	M	41	54.29	1.32	0.53	1.09	0.05	2.10
Phenoxymethyl penicillin 125mg/5ml	F	128	748.92	5.85	1.35	6.58	2.42	6.70
(J01CE02)	M	110	1961.80	5.93	1.39	6.58	0	6.70

As illustrated in Table 5.41C, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R2.88 for metronidazole 200mg and R128.11 for metronidazole 400mg for females, and R2.10 for metronidazole 200mg and R343.05 for amoxicillin 250 mg for males. The average cost of the antimicrobials prescribed according to gender varied from R1.52 ± 0.75 and R12.45 ± R6.92 for females and R1.32 ± R0.53 and R12.31 ± R 6.86 for males. Metronidazole 200mg had the lowest average cost for both genders and enoxacin 200mg had the highest average for females and erythromycin 250 mg for males. The female patients received 275 prescriptions of metronidazole 200mg at a total cost of R418.81, while males received 41 prescriptions of metronidazole at a total cost of R54.29. Whereas enoxacin was

prescribed in bigger quantities for female patients (485 prescriptions) at a total coat of R6036.17 it was prescribed in lesser quantities (n = 123) for males at a lesser total cost of R1439.14.

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic C were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic D are illustrated in Table 41D.

In Table 5.41D, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R5.43 for procaine penicillin and R95.26 for metronidazole 200mg and doxycycline 100mg for females, and R5.43 for procaine penicillin and R36.78 erythromycin 250 mg for males. The average cost of the antimicrobials prescribed according to gender varied from R1.11 ± 2.49 and R8.86 ± R2.99 for females and R1.08 ● R0.44 and R11.74 ± R 2.93 for males. Metronidazole 200mg had the lowest average cost for both genders and enoxacin 200mg had the highest average for males and erythromycin 250 mg for females. The quantity of metronidazole 200mg (n = 1463) was prescribed for females at a total cost of R1638.44 as compared to 273 prescribed for males at a lower total cost of R295.47.

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic D were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender prescribed in Clinic D.

Table 5.41D: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic D

Antimicrobial	Gender	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg	F	2363	8097.23	3.43	1.52	2.99	0	12.11
(J01CA04)	M	1473	5237.21	3.56	1.54	3.02	0	19.68
Co-trimoxazole 480mg	F	1515	3031.99	3.36	1.36	3.62	0	20.68
(J01EE010	M	1138	2214.20	3.49	1.42	3.62	1.10	8.23
Erythromycin 250mg	F	1229	10886.50	8.86	2.99	7.59	0	26.27
(J01FA01)	M	822	7493.44	9.11	3.11	8.76	0	36.78
Metronidazole 200mg	F	1463	1638.44	1.11	2.49	1.13	0.05	95.26
(J01XD01)	M	273	295.47	1.08	0.44	1.13	0.05	5.76
Amoxycillin 125mg/5ml	F	650	3592.47	5.53	1.91	4.57	0	9.14
(J01CA04)	M	770	4212.06	5.47	1.89	4.57	0	9.14
Doxycycline 100mg	F	958	5732.66	5.98	3.22	5.59	0	95.26
(J01AA02)	M	429	2524.53	5.88	1.47	5.59	0	23.95
Phenoxymethyl	F	563	3399.14	6.04	1.89	6.12	0	12.24
penicillin 250mg	M	288	1730.89	6.02	2.13	6.12	0	12.24
(J01CE02)								
Enoxacin 200mg	F	483	5671.42	5.88	1.47	5.59	0.08	13.61
(J01MA04)	M	308	3640.98	11.74	2.93	12.20	0.01	13.61
Phenoxymethyl	F	336	1981.90	5.89	1.58	6.58	1.65	9.87
penicillin 125mg/5ml	M	331	1999.38	6.04	1.46	6.58	2.69	9.87
J01CE02)								
Procaine penicillin	F	240	307.71	1.28	0.88	1.16	0.10	5.43
(J02CE09)	M	274	538.47	1.60	1.13	1.16	0.12	5.43

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic E are illustrated in Table 41E.

As illustrated in Table 5.42E, the minimum cost of the antimicrobials prescribed according to gender is zero. The maximum cost of the antimicrobials prescribed according to gender varied from R7.24 for co-trimoxazole 240mg/5ml and R61.99 for doxycycline 100mg for females and, and R2.06 for metronidazole 200mg and R40.40 for enoxacin 200mg for males.
The average cost of the antimicrobials prescribed according to gender varied from R0.39 ± 0.96 and R4.63 ± R8.86 for females and R0.39 ± R1.02 and R7.47 ± R8.87 for males. Metronidazole 200mg had the lowest average cost for both genders and metronidazole 400mg

had the highest average for males and erythromycin 250 mg for females. However female patients received more of the metronidazole (n = 411) at the total cost of R644.78 as compared to the males (n = 276) at a total cost of R433.12.

Table 5.41E: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic E

Antimicrobial	Gender	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximu (R)
Amoxycillin 250mg	F	1191	5693.67	4.78	1.68	4.53	0	16.72
(J01CA04)	M	672	3016.68	4.49	1.43	4.89	0	14.25
Co-trimoxazole 480mg	F	840	1880.11	2.24	1.08	2.62	0	13.10
(J01EE01)	M	522	1342.65	2.57	1.27	2.62	0	13.10
Metronidazole 200mg	F	411	644.78	1.06	0.39	0.96	0	31.03
(J01CD01)	M	276	433.12	1.11	0.39	1.02	0	2.06
Doxycycline 100mg	F	318	2401.15	7.58	3.78	7.52	0	61.99
(J01AA02)	M	364	2458.10	6.75	1.92	5.78	0	16.33
Ampicillin 250 mg	F	395	2161.49	5.47	1.61	5.76	2.05	14.39
(J01CA01)	M	259	1403.13	5.41	1.43	5.82	2.51	10.28
Metronidazole 400mg	F	126	1152.23	9.14	4.63	8.86	5.98	26.62
(J01XD01)	M	91	1030.97	11.32	7.47	8.87	5.98	35.89
Amoxycillin 125mg/5ml	F	272	1845.41	6.78	2.43	4.57	2.30	18.28
(J01CA04)	M	310	2061.88	6.65	2.33	4.57	1.58	13.71
Enoxacin 200mg	F	203	2537.71	12.50	4.47	12.20	6.10	61.00
(J01MA04)	M	236	2871.60	12.17	2.39	12.20	6.10	40.40
Co-trimoxazole240mg/5ml	F	141	351.47	2.49	1.15	1.81	0.99	7.24
(J01EE01)	M	181	471.50	2.60	1.47	1.81	0.91	7.24
Erythromycin 250mg	F	141	1135.19	8.05	4.54	6.40	0	36.14
(J01FA01)	M	177	1550.71	8.76	3.66	6.40	0	19.20

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic E were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender in Clinic E.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic F are illustrated in Table 41F.

Table 5.41F: Average, minimum and maximum cost of individual antimicrobials Prescribed according to gender in Clinic F

Antimicrobial	Gender	N	Total Cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Co-trimoxazole 480mg	F	2274	5321.17	2.34	0.87	1.87	0	7.49
(J01EE01)	M	1415	3389.79	2.39	1.00	1.87	0	8.24
Doxycycline 100mg	F	1328	8187.81	6.17	1.82	5.75	0.69	23.35
(J01AA02)	M	44	2676.32	5.99	1.48	5.65	0.38	12.38
Amoxycillin 250mg	F	1291	5875.62	4.55	1.77	4.86	0	14.24
(J01CA04)	M	398	1668.27	4.19	1.85	4.86	0	14.24
Metronidazole 200mg	F	1373	1802.33	1.31	0.78	1.13	0	23.95
(J01XD01)	M	159	223.85	1.40	0.69	1.39	0.10	4.51
Co-trimoxazole	F	543	1465.25	2.69	1.24	2.13	0	8.72
240mg/5ml (J01EE01)	M	611	1637.05	2.67	1.29	1.18	0	10.86
Erythromycin 250mg	F	496	5657.86	11.40	3.29	5.39	0	10.35
(J01FA01)	M	233	2705.70	11.61	5.38	6.04	0	10.35
Enoxacin 200mg	F	544	6551.90	12.04	5.03	12.26	6.10	91.51
(J01MA04)	M	128	1438.70	11.24	3.29	12.26	6.10	27.16
Amoxycillin	F	250	1343.87	5.38	1.96	4.57	1.58	18.28
125mg/5ml (J01CA04)	M	278	1413.37	5.08	1.44	4.57	2.12	11.90
Ampicillin 250 mg	F	432	1968.48	4.56	1.44	4.32	2.87	10.28
(J01CA01)	M	48	225.11	4.69	1.81	5.14	0	10.06
Erythromycin	F	161	1110.37	6.89	2.49	5.62	2.57	12.02
125mg/5ml (J01FA01)	M	208	1395.53	6.71	2.38	5.59	3.00	12.02

Table 5.41F shows that the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R7.49 for co-trimoxazole 480mg and R91.51 for enoxacin 200mg for females and, R4.51 for metronidazole 200mg and R27.16 for enoxacin 200mg for males. The average cost of the antimicrobials prescribed according to gender varied from R1.31 ± 0.78 and R12.04 ± R5.03 for females and R1.40 ± R0.69 and R7.47 ± R11.61 for males. Metronidazole 200mg had the lowest average cost for both genders and enoxacin 200mg had the highest average for females and erythromycin 250 mg for males. Enoxacin had the highest average

cost for females because of the high numbers of prescriptions for females (n = 544) at the highest total cost of R 6551.90 as compared to males who received only 128 prescriptions at a total cost of R1438.

Statistical d-values as indication of practical significance differences among the costs of antimicrobials in Clinic F were calculated. The d-values obtained showed that there were no differences of practical significance found among the average costs of antimicrobials prescribed according to gender in Clinic F.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic G are illustrated in Table 41G.

As shown in Table 5.41G, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R5.59 for metronidazole 400mg to R62.11 for metronidazole 200mg for females and, and R5.59 for metronidazole 400mg and R85.41 for doxycycline 100mg for males. The average cost of the antimicrobials prescribed according to gender varied from R1.33 ± 0.52 and R10.40 ± R3.95 for females and R0.98 ± R0.69 and R10.72 ± R3.88 for males. Metronidazole 200mg had the lowest average cost for both genders and erythromycin 250mg had the highest average for both gender. Female patients received more prescriptions for metronidazole 200mg (n = 399) at a total cost of R821.24 than male patients who received (n = 179) at a total cost of R425.76. Erythromycin 250mg was more prescribed for females (n = 516) at a total cost of R5367.06 than males (n = 413) at a total cost of R4426.63. This could have been influenced by the disease states presented in both genders.

Table 5.41G: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic G

Antimicrobial	Gender	N	Total cost (R)	Average (R)	Standard Deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg	F	1418	5032.89	3.55	1.39	3.11	0	16.03
(J01CA04)	M	1049	3839.42	3.66	1.41	3.56	0	14.25
Co-trimoxazole 480mg	F	1450	3253.49	2.24	0.88	1.88	0	12.06
(J01EE01)	M	993	2183.41	2.19	1.04	1.87	0.22	15.08
Erythromycin 250mg	F	516	5367.06	10.40	3.95	8.76	0	55.83
(J01FA01)	M	413	4426.63	10.72	3.88	10.34	0	47.29
Doxycycline 100mg	F	641	4221.44	6.59	4.38	5.78	0	85.41
(J01AA02)	M	254	1612.49	6.35	2.88	5.78	2.79	30.67
Ampicillin 250 mg	F	481	1818.52	3.78	1.18	3.59	2.15	8.04
(J01CA04)	M	295	1166.34	3.95	1.28	3.59	1.09	7.71
Metronidazole 200mg	F	399	821.24	1.07	3.48	0.81	0	46.54
(J01XD01)	M	179	425.76	0.98	0.38	0.97	0.05	62.11
Metronidazole 400mg	F	432	574.95	1.33	0.52	1.19	0.86	5.59
(J01XD01)	M	65	101.42	1.56	0.77	1.43	0.09	5.14
Phenoxymethyl	F	292	1251.19	4.28	1.81	1.81	3.09	15.18
penicillin250mg	M	203	832.37	4.10	1.44	1.44	3.09	9.18
(J01CE02)								
Co-trimoxazole	F	252	634.92	1.66	2.25	2.25	0	14.80
240mg/5ml (J01EE01)	M	238	585.19	1.30	2.33	2.33	0.01	7.40
Erythromycin	F	154	931.98	2.81	5.56	5.56	0.11	16.50
125mg/5ml (J01FA01)	M	153	875.98	2.23	5.50	5.50	0.11	13.78

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic G were calculated. The d-values obtained showed that there were no differences of practical significance found among the average costs of antimicrobials prescribed according to gender in Clinic G.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic H are shown in Table 5.41H.

Table 5.41H: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic H

Antimicrobial	Gender	N	Total Cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximu (R)
Amoxycillin 250mg	F	1037	3816.84	3.68	1.27	4.49	0	7.12
(J01CA04)	M	869	3203.25	3.69	1.38	4.49	0	11.96
Co-trimoxazole 480mg	F	824	1741.33	2.11	0.83	1.87	0	7.49
(J01EE01)	M	782	1664.78	2.13	0.89	1.87	0	13.10
Ampicillin 250 mg	F	528	1711.93	3.24	1.57	2.92	0	10.28
(J01CA01)	M	447	1443.16	3.22	1.95	2.87	0	10.99
Phenoxymethyl	F	330	1424.45	4.32	1.97	4.72	0	12.24
penicillin 250mg	M	365	1577.98	4.33	1.70	3.06	0	7.08
(J01CE02)								
Doxycycline 100mg	F	421	2456.36	5.83	1.66	5.76	0.42	12.38
(J01AA02)	M	247	1507.06	6.10	5.23	5.65	0	85.41
Erythromycin 250mg	F	322	2878.37	8.94	6.39	8.76	0	72.28
(J01FA01)	M	309	2841.18	9.19	5.61	8.76	0	26.27
Amoxycillin	F	244	1270.07	5.21	1.72	4.57	0	11.90
125mg/5ml J01CA04)	M	298	1401.64	4.70	1.38	4.57	0	11.84
Norfloxacin 400mg	F	296	2885.53	9.75	6.98	8.81	0	53.23
(J01MA06)	M	181	1783.50	9.85	8.38	8.81	0	57.48
Metronidazole 400mg	F	437	717.62	1.64	8.71	1.19	0	183.02
(J01XD01)	M	49	66.16	1.35	0.46	1.19	0.43	2.57
Co-trimoxazole	F	186	358.37	1.81	1.17	1.81	0	7.24
240mg/5ml (J01EE01)	M	220	399.05	2.11	0.83	1.87	0	7.24

As demonstrated in Table 5.41H, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R7.24 for co-trimoxazole 240mg/5ml for both genders and R183.02 for metronidazole 400mg for females and R85.41 for doxycycline 100mg prescribed for males. The average cost of the antimicrobials prescribed according to gender varied from R1.64 ± 8.71 and R9.75 ± R6.98 for females and R2.11 ± R0.83 and R9.85 ± R8.38 for males. Co-trimoxazole 240mg/5ml had the lowest average cost for both genders and norfloxacin 400mg had the highest average for both genders. Co-trimoxazole 240mg/5ml was prescribed less for females (186 prescriptions) at a total cost of R358.37 as compared to 220 prescriptions to

males at a total cost of R399.05. Female patients received more of norfloxacin (296 prescriptions) at a total cost of R28885.53 while males received 181 prescriptions at a total cost of R1783.50.

Statistical d-values as indication of practical significance differences among the costs of antimicrobials in Clinic H were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender in Clinic H.

The average, minimum and maximum cost of the most frequently prescribed antimicrobials according to gender in Clinic I are shown in Table 5.41I.

As illustrated in Table 5.41I, the minimum cost of the antimicrobials prescribed according to gender was zero. The maximum cost of the antimicrobials prescribed according to gender varied from R4.79 for metronidazole 400mg and R67.05 for amoxycillin 250mg/clavulanic acid 125mg prescribed for females and R3.15 for metronidazole 200mg and R67.05 for amoxycillin 250mg/clavulanic acid 125mg prescribed for males. The average cost of the antimicrobials prescribed according to gender varied from R1.02 ± 0.52 and R28.03 ± R8.06 for females and R1.03 ± R0.39 and R27.48 ± R6.13 for males. Metronidazole 200mg had the lowest average cost for both genders and amoxycillin 250mg/clavulanic acid 125mg had the highest average cost for both genders. The quantity of metronidazole prescriptions (648) for females was more than what the male patients received (n = 321) at a total cost of R662.22 for females and R331.19 for males. Amoxycillin 250mg/clavulanic acid 125mg was prescribed more for females (n = 455) at a total cost of R11100.72 than for males (n = 298) at a total cost of R8189.58.

Table 5.41I: Average, minimum and maximum cost of individual antimicrobials prescribed according to gender in Clinic I

Antimicrobial	Gender	N	Total Cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amoxycillin 250mg	F	1195	4693.16	3.93	1.52	4.87	0.03	11.96
(J01Ca04)	M	786	3131.84	3.98	1.44	4.89	0.03	11.96
Ampicillin 250 mg	F	814	3731.79	4.58	1.72	4.09	0.93	10.28
(J01CA01)	M	267	1226.84	4.59	1.64	4.09	1.22	10.28
Metronidazole 200mg	F	648	662.22	1.02	0.52	10.81	0.55	10.74
(J01XD01)	M	321	331.19	1.03	0.39	10.81	0.14	3.15
Erythromycin 250mg	F	446	3946.91	8.85	2.87	7.53	0.62	21.46
(J01FA01)	M	402	3853.88	9.59	3.43	8.76	1.27	24.52
Co-trimoxazole 480mg	F	511	1048.18	2.05	1.23	1.87	0.50	11.76
(J01EE01)	M	294	740.67	2.52	1.40	1.87	0.50	10.82
Doxycycline 100mg	F	441	2864.17	6.49	2.31	5.60	0	22.88
(J01AA02)	M	337	2250.19	6.68	2.27	5.60	0	12.94
Amoxycillin 125mg/5ml	F	332	1706.37	5.14	2.17	4.57	0	11.90
(J01CA04)	M	413	2080.72	5.03	2.01	4.57	0	11.90
Metronidazole 400mg	F	455	641.71	1.41	0.41	1.29	0.43	4.79
(J01XD01)	M	253	387.17	1.53	0.65	1.29	1.01	5.78
Amoxycillin 250mg/	F	396	11100.72	28.03	8.06	26.14	17.43	67.05
clavulanic acid 125mg	M	298	8189.58	27.49	6.13	26.14	26.14	67.05
(J01CR02)								
Erythromycin	F	149	986.38	6.62	3.57	5.72	0.11	14.44
125mg/5ml (J01FA01)	M	185	1253.61	6.78	3.25	5.64	0.11	14.44

Statistical d-values as indication of practical significance differences between the costs of antimicrobials in Clinic I were calculated. The d-values obtained showed that there were no differences of practical significance found between the average costs of antimicrobials prescribed according to gender in Clinic I.

SUMMARY OF THE RESULTS OF THE AVERAGE COSTS OF ANTIMICROBIALS PRESCRIBED ACCORDING TO GENDER IN NINE CLINICS

In summary, the results of the average costs of individual antimicrobials prescribed according to gender in the nine clinics showed that female patients received more antimicrobials than males did. This may be because there were more female patients than male patients that visited all nine clinics during the research period. This resulted in higher average costs for antimicrobials prescribed for females than males.

It was also observed from the study that the following antimicrobials had the highest average costs: erythromycin 250mg, enoxacin 200mg, metronidazole 400mg, norfloxacin 400mg and amoxycillin 250mg/clavulanic acid 125mg. From these drugs: enoxacin 200mg and norfloxacin 400mg had the highest average costs. These belong to the group of fluoroquinolones that are newer and more expensive agents than the macrolides and anti-protozoal agents.

The higher average costs of specific antimicrobials prescribed according to gender in different clinics could be influenced by the different disease states presented in the different genders in the different clinics. The different disease states could be influenced by the fact that the nine clinics are located in the different geographical areas of South Africa.

The statistical d-values calculated between the average costs of antimicrobials prescribed according to gender showed that there was no difference of practical significance observed between the average costs of antimicrobials prescribed according to gender in the nine clinics.

5.7.3 Average cost of antimicrobials according to age groups in each clinic

The following tables 5.42(A – I) illustrate the average, minimum and maximum costs of the top three antimicrobials prescribed according to age groups in each clinic.

The average, minimum and maximum costs of co-trimoxazole 240mg/5ml prescribed according to age groups in Clinic A are shown in Table $5.42A_1$.

Table 5.42A$_1$: Average, minimum and maximum cost of co-trimoxazole 240mg/5ml prescribed according to age groups in Clinic A

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1	6	9.34	1.56	0.40	1.66	1.07	2.11
2	667	1158.11	1.74	0.50	1.74	0.37	5.81
3	1107	2484.60	2.24	0.97	1.98	0.01	4.95
4	265	736.73	2.78	1.03	2.81	0.31	6.38
5	7	22.98	3.28	0.78	3.51	2.13	4.22
6	1	7.24	7.24	0.00	7.24	7.24	7.24
7	1	2.69	2.69	0.00	2.69	2.69	2.69
8	1	3.13	3.12	0.00	3.13	3.13	3.13

Table 5.42A$_1$ shows that the minimum cost of co-trimoxazole 240mg/5ml was R0.01 for patients in age groups 3. The maximum cost varied between R2.11 for patients in age group 1 and R7.24 for patients in age group 6. The average cost varied between R1.56 ± R0.40 (age group 1) and R7.24 ± 0.00 (age group 6). There were a few prescriptions (n = 6) for co-trimoxazole 240mg/5ml prescribed for patients in age group 1 (0-1 month). According to Hoppe (1996: 561), co-trimoxazole is contraindicated in infants younger than 2 months of age because of competition at bilirubin binding-sites.

Co-trimoxazole 240mg/5ml was prescribed for the following disease states: upper respiratory tract infections, viral influenza, acute bronchitis, tonsillitis and urinary tract infections (refer to Clinic A, Table 5.35A). As already discussed in section 5.4.11 antimicrobials are contraindicated in non-bacterial diseases (Bartlett *et al.*, 1998: 827). According to Garau and Dagan (2003: 1936), inappropriate use of antibiotics for the treatment of viral upper respiratory tract infections has contributed to the development of resistant micro organisms.

Table 5.42A$_{11}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 240mg/5ml prescribed according to age groups in Clinic A

Age group	1	2	3	4	5	6	7	8
1		0.36	0.70	1.18	2.21	14.20	2.83	3.90
2	0.36		0.52	1.01	1.97	11.00	1.90	2.76
3	0.70	0.52		0.52	1.33	5.15	0.46	0.91
4	1.18	1.01	0.52		0.49	4.33	0.09	0.33
5	2.21	1.97	1.33	0.49		5.08	0.76	0.21
6	14.20	11.00	5.15	4.33	5.08			
7	2.83	1.90	0.46	0.09	0.76			
8	3.90	2.76	0.91	0.33	0.21			

Difference of practical significance is d>0.8

According to Table 5.42A$_{11}$, the d-values calculated (refer to chapter 4, section 4.4.5.2.4) showed that there were practical significant differences observed between the average cost of co-trimoxazole 240mg/5ml prescribed for patients in age groups 1 and 2. This means that the average costs of co-trimoxazole 240mg/5ml prescribed in age groups 1 and 2 were lower than the average costs of co-trimoxazole 240mg/5ml prescribed in other age groups. The lowest number of co-trimoxazole 240mg/5ml was prescribed for patients in age groups 1 and 2 as compared to patients in age group 3 and 4 (refer to Table 5.42A$_1$).

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic A are shown in Table 5.42A$_2$.

Table 5.42A$_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic A

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	47	50.49	1.07	0.36	1.87	0.86	2.23
5	239	428.83	1.79	0.71	1.87	0.52	5.62
6	888	1833.44	2.06	0.69	1.87	0.15	6.23
7	576	1177.62	2.04	0.56	1.87	0.27	5.61
8	295	591.77	2.00	0.58	1.87	0	5.61

The table shows that no co-trimoxazole 480mg was prescribed for patients in age groups 1, 2 and 3 because of the high dosage and solid dosage form which are not appropriate for paediatric patients. The minimum cost of co-trimoxazole 480mg was R0.15 prescribed for patients in age group 6. The maximum cost varied between R1.86 for patients in age group 3 and R6.23 for patients in age group 6. The average cost varied between R1.07 ± R0.36 and R2.06 ± R0.69. The minimum average cost for co-trimoxazole was prescribed for patients in age group 4 at R1.07 ± R0.36 and patients in age group 6 received prescriptions of co-trimoxazole 480mg at the highest average cost of R2.06 ± R0.69. Co-trimoxazole 480mg was mostly prescribed for patients in age group 6 (n = 88).

Co-trimoxazole 480mg was prescribed for urinary tract infection; upper respiratory infection and hypertension (refer to Clinic A, Table 5.35A). According to the Department of Health (2003: 129) the recommended drug treatment for urinary tract infection is co-trimoxazole 480mg. Colgan and Powers (2001: 1000) have argued that antibacterial agents have no effect against viral diseases like upper respiratory tract infection. Patients who presented with multiple diseases including chronic diseases like hypertension, it was assumed that the antibiotic was prescribed for those likely to be of bacterial origin, because of the difficulty to identify from the database which specific drugs were prescribed for specific disease states.

Table 5.42A$_{21}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg according to age groups in Clinic B.

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					1.01	1.43	1.73	1.60
5				1.01		0.38	0.35	0.30
6				1.43	0.38		0.03	0.09
7				1.73	0.35	0.03		0.07
8				1.60	0.30	0.09	0.07	

Difference of practical significance is d>0.8

According to Table 5.42A$_{21}$, the d-values calculated (refer to chapter 4, section 4.4.5.2.4) showed that there were practical significant differences found between the average cost of co-trimoxazole 480mg prescribed for patients in age groups 4 and 5, 6, 7 and 8. This means that the average cost of co-trimoxazole 480mg was lower in patients in age group 4 than the rest of the age groups. The lowest number of co-trimoxazole 480mg prescribed for patients was in age group 4.

The average, minimum and maximum cost of doxycycline 100mg prescribed according to age group in Clinic A are shown in Table 5.42A$_3$

Table 5.42A$_3$: Average, minimum and maximum cost of doxycycline 100mg prescribed according to age group in Clinic A

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	2	2.91	1.45	2.03	1.45	0.02	2.89
5	93	498.333	5.36	3.46	5.63	0	12.38
6	892	4883.89	5.48	2.63	5.72	0	12.38
7	260	1347.25	5.18	2.78	5.62	0	12.38
8	36	184.83	5.13	2.59	5.59	0.29	8.25

The table shows that no doxycycline 100mg was prescribed for to patients in age groups 1, 2 and 3 because of contraindication of the drug to patients younger than 8 years. This drug is hardly prescribed for that age group due to retardation of bone growth and discoloration of teeth (Lynn, 1996: 225). The minimum cost of doxycycline 100mg was zero. The maximum cost varied between R2.89 for patients in age group 4 and R12.38 for patients in age groups 5, 6 and 7. The average cost varied between R1.45 ± R2.03 and R5.48 ± R2.63. The minimum average cost for doxycycline 100mg was R1.45 ± R2.03 prescribed for patients in age group 4. Patients in age group 6 received prescriptions of doxycycline 100mg at highest average cost of R5.48 ± R2.63. There were only 2 prescriptions for doxycycline 100mg for patients in age group 4 while patients in age group 5 received 892 prescriptions for doxycycline 100mg.

Doxycycline was prescribed to treat acute bronchitis (refer to Clinic A, Table 5.34A). As already discussed in section 5.5.3 antimicrobials are contraindicated in respiratory tract infections of viral origin.

Table 5.42A$_{31}$: Statistical d-values as indication of the practical significance differences between the average cost of doxycycline 100mg prescribed according to age groups in Clinic A

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					1.13	1.53	1.34	1.42
5				1.13		0.05	0.06	0.09
6				1.53	0.05		0.11	0.13
7				1.34	0.06	0.11		0.02
8				1.42	0.09	0.13	0.02	

Difference of practical significance is d>0.8

Although the results in Table 5.42$_{31}$ indicated that there were differences of practical significance observed between the average cost of doxycycline 100mg prescribed for patients in age group 4 and other age groups, it should be noticed that doxycycline 100mg was only prescribed in two cases for patients in age group 4.

The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age group in Clinic B are shown in Table 5.42B$_1$.

Table 5.42B$_1$: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age group in Clinic B

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	3	7.59	2.53	0.25	2.67	2.24	2.67
4	28	65.37	2.33	0.50	2.34	0	2.99
5	104	331.19	3.18	2.37	2.51	0	12.25
6	617	1792.40	2.91	1.79	2.34	0	14.29
7	397	1255.69	3.16	3.33	2.67	0	58.65
8	72	182.95	2.54	1.04	2.34	0	5.94

The table shows that no amoxycillin 250mg was prescribed for age groups 1 and 2 because this drug should be taken in higher dosages. Both its required dosages and its solid dosage form are not appropriate for paediatric patients. The minimum cost of amoxycillin 250mg was zero. The maximum cost varied between R2.67 for patients in age group 3 and R58.65 for patients in age group 7. The average cost varied between R2.33 ± R0.50 and R3.18 ± R2.37. Patients in age group 4 received amoxycillin 250mg at the minimum average cost of amoxycillin 250mg at R2.33 ± R0.50 and patients in age group 5 received the antibiotic at the highest average cost of R3.18 ± R2.37.

Amoxycillin 250mg was prescribed for urinary tract infection cystitis; viral influenza and upper respiratory infection (refer to Clinic B, Table 5.35B). The prescribing of amoxycillin 250mg in urinary tract infection is recommended by the Department of Health, (2003: 129). The use of the same drug in viral diseases is contraindicated as already discussed in section 5.5.3.

Statistical d-values as indication of the practical significance differences between the average cost of amoxycillin 250mg prescribed according to age groups in Clinic B were calculated. The findings of this regard show that there was no practical significant differences observed between the average cost of amoxycillin 250mg prescribed in the different age groups in Clinic B.

The average, minimum and maximum cost of co-trimoxazole 480 mg prescribed according to age group in Clinic B are shown in Table $5.42B_2$

Table $5.42B_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age group in Clinic B

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	5	5.39	1.07	0.31	0.94	0.79	1.49
5	29	55.46	1.91	0.79	1.87	0	3.93
6	341	745.02	2.18	0.91	2.32	0	7.49
7	262	544.21	2.08	0.84	1.87	0	7.49
8	50	100.13	2.00	0.59	1.87	0	3.74

Table $5.42B_2$ shows that no co-trimoxazole 480mg was prescribed for patients in age groups 1, 2 and 3 because of this drugs' higher dose requirements and solid dosage forms which are not appropriate for paediatric patients. Patients in age group 4 (only 5 cases) received the minimum quantities of co-trimoxazole 480mg which led to a lower cost minimum rated at R0.79. The patients in this age group received the minimum amount of co-trimoxazole 480mg. The maximum cost varied between R1.49 prescribed for patients in age group 4 and R7.49 for patients in age group 6 and 7. The average cost varied between R1.07 ± R0.31 and R2.18 ± R0.91. The minimum average cost of co-trimoxazole 480mg prescribed for patients in age group 4 was R1.07 ± R0.31 and patients in age group 6 (n = 341) received co-trimoxazole 480mg at the highest average cost of R2.18 ± R0.91.

The disease states where co-trimoxazole 480mg was prescribed were: common cold, urinary tract infection, muscle pains (reason already discussed in Section 5.6.2) and peptic ulceration. As already discussed, co-trimoxazole is contraindicated in common cold and muscle pains (refer to Section 5.5.3).

Co-trimoxazole is not recommended in peptic ulceration. According to Ferrero *et al.* (2000: 247) the first line recommended therapy for peptic ulceration is the combination of amoxycillin, clarithromycin and omeprazole. From the database it was difficult to differentiate between medicine items prescribed for individual diagnoses when more than one diagnosis was made during a consultation, so in this case co-trimoxazole 480mg could not possibly be prescribed for peptic ulceration. As already discussed co-trimoxazole is recommended in the treatment of urinary tract infections.

Table 5.42B$_{21}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic B

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					1.06	1.22	1.20	1.58
5				1.06		0.30	0.19	0.10
6				1.22	0.30		0.11	0.20
7				1.20	0.19	0.11		0.10
8				1.58	0.10	0.20	0.10	

Difference of practical significance is d>0.8

Although the results in Table 5.42B$_{11}$ indicated that there were differences of practical significance observed between the average cost of co-trimoxazole 480mg prescribed to patients in age group 4 and the rest of the age groups, it should be noticed that co-trimoxazole 480mg was only prescribed in five cases for patients in age group 4.

The average, minimum and maximum cost of doxycycline 100mg prescribed according to age group in Clinic B are shown in Table 5.42B$_3$.

Table 5.42B$_3$: Average, minimum and maximum cost of doxycycline 100mg prescribed according to age group in Clinic B

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	2	11.26	5.63	0.06	5.63	5.59	2.68
5	14	76.63	5.47	0.61	5.74	3.99	5.78
6	228	1318.75	5.78	1.37	5.62	3.89	111.39
7	95	612.91	6.45	8.77	5.59	3.89	90.41
8	7	33.80	4.83	0.88	5.45	3.89	5.78

It is shown that in Table 5.42B$_3$ no doxycycline 100mg was prescribed for patients in age groups 1, 2 and 3. Doxycycline is contraindicated in ages below 8 years. The minimum cost of doxycycline 100mg was R3.89 for age groups 5, 6, 7 and 8. The maximum cost varied between R2.68 for patients in age group 4 and R111.39 for patients in age group 6. Patients in age group 4 received the minimum number of prescriptions whereas patients in age group 6 received the maximum number of items as shown in the table. The average cost varied between R4.83 ± R0.88 and R6.45 ± R8.77. The minimum average cost of doxycycline prescribed to patients in age group 8 was R4.83 ± R0.88 and patients in age group 7 were prescribed doxycycline 100mg at the highest average cost of R6.45 ± R8.77.

In Clinic B, doxycycline was prescribed for treatment of the following disease states: urethritis in men, sexual transmitted disease: bacterial urethritis and urinary tract infections (refer to Clinic B, Table 5.34B). According to Lynn (1996: 224) the use of this drug in sexual transmitted diseases is recommended. However, according to the Department of Health, (2003: 129) the use of doxycycline in urinary tract infections is not recommended.

Table 5.42B$_{31}$: Statistical d-values as indication of the practical significance differences between the average cost of doxycycline 100mg prescribed according to age groups in Clinic B

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					0.26	0.11	0.09	0.91
5				0.26		0.23	0.11	0.73
6				0.11	0.23		0.08	0.11
7				0.09	0.11	0.08		0.18
8				0.91	0.73	0.11	0.18	

Difference of practical significance is d>0.8

According to table 5.42B$_{31}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there was practical significance difference of d-value 0.91 in the average cost of doxycycline 100mg prescribed for patients in age groups 4 and 8. This means that the average cost of doxycycline 100mg prescribed for patients in age group 8 was higher than the average cost of doxycycline 100mg prescribed for patients in age group 4. However, it should be remembered that only two patients in age group 4 received doxycycline 100mg.

The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age group in Clinic C are illustrated be shown in Table 5.42C$_1$.

Table 5.42C$_1$: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic C

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	4	12.74	3.19	0.93	2.99	2.28	4.49
4	56	165.84	2.96	1.34	2.27	0.06	7.12
5	199	796.16	4.00	1.71	4.49	0.06	12.20
6	960	4550.46	4.74	11.13	4.49	0	343.05
7	421	1832.48	4.35	1.97	4.49	0	14.25
8	192	810.65	4.22	1.24	4.49	0.06	11.96

The table shows that no amoxycillin 100mg was prescribed for patients in age groups 1 and 2 because of the solid dosage form and high dose not being appropriate for these age groups. Patients in age groups 4, 5 and 8 received amoxycillin 250mg at a minimum cost of R0.06. The maximum cost varied between R4.49 for patients in age group 3 and R343.05 for patients in age group 6. Patients in age group 3 received the minimum number of amoxycillin 250mg and patients in age group 6 the maximum number of the antibiotic as illustrated in the table. The average cost varied between R2.96 ± R1.34 and R4.74 ± R11.13. Patients in age group 4 were prescribed amoxycillin at the minimum average cost of R2.96 ± R1.34 and the highest average cost of amoxycillin 250mg were prescribed for patients in age group 6 at R4.74 ± R11.13. This was because patients in age group 4 received the minimum prescribed items (n = 56) as compared to patients in age group 6 who received the maximum number of items (n = 960).

In Clinic C, amoxycillin 250mg was prescribed for the following disease states: upper respiratory infection, acute bronchitis and lower respiratory tract infection due to common cold (refer to Clinic C, Table 5.34C). According to Woodhead *et al.* (1996: 1596), the use of antibiotics in lower respiratory infection due to a common cold that is viral in aetiology is neither effective nor recommended.

Table 5.42C$_{11}$: Statistical d-values as indication of the practical significance differences between the average costs of individual antimicrobials prescribed according to age groups in Clinic C

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.17	0.47	0.14	0.59	0.83
4			0.17		0.61	0.16	0.71	0.94
5			0.47	0.61		0.06	0.18	0.13
6			0.14	0.16	0.06		0.04	0.05
7			0.59	0.71	0.18	0.04		0.07
8			0.83	0.94	0.13	0.05	0.07	

Difference of practical significance is d>0.8

According to Table 5.42C$_{11}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there were practical significance differences observed between the average cost of amoxycillin 250mg prescribed for age groups 3, 4 and 8. This means that patients in age group 8 received prescriptions of amoxycillin 250mg at a higher average cost (R = 4.22) than that prescribed for patients in age groups 3 and 4 at R3.19 and R2.96 respectively.

The average, minimum and maximum costs of co-trimoxazole 480mg prescribed according to age group in Clinic C are shown in Table 5.42C$_2$.

Table 5.42C$_2$: Average, minimum and maximum cost of Co-trimoxazole 480mg prescribed according to age groups in Clinic C

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	2	2.81	1.40	0.66	1.40	0.93	1.87
4	28	45.86	1.64	0.60	1.87	0.56	2.81
5	64	149.06	2.33	0.83	1.87	0.94	4.41
6	448	1099.88	2.46	0.96	2.62	0	13.12
7	288	693.12	2.41	0.81	2.20	0.40	7.49
8	110	262.21	2.38	0.62	2.62	0.40	4.41

According to Table 5.42C$_2$, no co-trimoxazole 480mg was prescribed for patients in age groups 1 and 2 because these are paediatric patients who cannot be given such a high dosage and solid dosage form. The minimum cost of co-trimoxazole 480mg was zero prescribed for patients in age group 6. The maximum cost varied between R1.87 for patients in age group 3 and R13.12 for patients in age group 6. The average cost varied between R1.40 ± R0.66 and R2.46 ± R0.96. Patients in age 3 received prescriptions of co-trimoxazole 480mg at the minimum average cost of R1.40 ± R0.66 and patients in age group 6 received prescriptions of co-trimoxazole 480mg at the highest average cost of R2.46 ± R0.96 Patients in age group 3 received the minimum number (n = 2) of co-trimoxazole 480mg and the highest number (n = 448) of the antibiotic was prescribed for patients in age group 6 as shown in Table 5.42C$_2$.

Co-trimoxazole was used in Clinic C for the treatment of muscle pains, lower respiratory infection and viral influenza. As already discussed in section 5.6.3, according to Hooton and Levy, (2000: 1087) antimicrobials intended for the treatment of bacterial infections should not be used to manage viral illnesses like lower respiratory infections and viral influenza.

Table 5.42C$_{21}$: Statistical d-values as indication of the practical significance differences between the average cost of individual antimicrobials prescribed according to age groups in Clinic C.

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.15	0.40	0.43	0.42	0.41
4			0.15		0.83	0.85	0.95	1.19
5			0.40	0.83		0.14	0.10	0.06
6			0.43	0.85	0.14		0.05	0.08
7			0.42	0.95	0.10	0.05		0.04
8			0.41	1.19	0.06	0.08	0.04	

Difference of practical significance is d>0.8

According to Table 5.42C$_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significance differences observed between the average cost of co-trimoxazole 480mg prescribed to age group 4 and the rest of the age groups. The d-value was more significant between patients in age group 4 and 8. This means that the average cost of co-trimoxazole 480mg prescribed to patients in age group 8 was higher than that prescribed to patients in age group 4.

The average, minimum and maximum cost of doxycycline 100mg prescribed according to age group in Clinic C are demonstrated in Table 5.42C$_3$.

Table 5.42C$_3$: Average, minimum and maximum cost of doxycycline 100mg prescribed according to age groups in Clinic C

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	3	10.66	3.55	2.78	4.79	0.36	5.51
5	33	212.97	6.45	3.37	5.59	4.72	23.95
6	594	3746.42	6.31	6.39	5.78	0.42	92.63
7	175	1095.77	6.26	6.29	5.61	0	85.41
8	20	107.06	5.35	1.00	5.59	1.43	5.78

The table shows that no doxycycline 100mg was prescribed for age groups 1, 2 and 3 because doxycycline is contraindicated in patients below the age of 8 years. Doxycycline was prescribed for patients in age group 4 at a minimum cost of R0.36. The maximum cost for doxycycline 100mg in Clinic C varied between R5.51 for patients in age group 4 and R92.63 for patients in age group 6. Patients in age group 4 received the minimum quantity of doxycycline 100mg and the maximum quantity of doxycycline 100mg was prescribed for patients in age group 6. The average cost varied between R3.55 ± R2.78 and R6.45 ± R3.37. Patients in age group 4 received prescriptions of doxycycline at a minimum average cost of R3.55 ± R2.78 and the highest average cost for the antibiotic was prescribed for patients in age group 5 at R6.45 ± R3.37.

Patients with pelvic inflammatory disease in Clinic C received doxycycline 100mg prescriptions. Other disease states where doxycycline was used were: sexually transmitted disease: lower abdominal pains and sexually transmitted disease: vaginal discharge (refer Clinic C, Table 5.34C). As stated by Lynn (1996: 224), the use of doxycycline in sexually transmitted diseases is recommended. The Department of Health (2003: 150) recommends the drug treatment for non-pregnant females with a vaginal discharge to be doxycycline 100mg 12 hourly for 7 days plus other antibiotics.

Table 5.42C$_{31}$: Statistical d-values as indication of the practical significance differences between the average costs of individual antimicrobials prescribed according to age groups in Clinic C

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					0.86	0.43	0.43	0.65
5				0.86		0.02	0.03	0.46
6				0.43	0.02		0.01	0.15
7				0.43	0.03	0.01		0.14
8				0.65	0.46	0.15	0.14	

Difference of practical significance is d>0.8

According to Table 5.42C3$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there was practical significance difference observed between the average cost of doxycycline 100mg prescribed to patients in age group 4 and 5. This means that the average cost of doxycycline 100mg prescribed to patients in age group 5 was higher than that of the average cost of the same antibiotic prescribed for age group 4. Patients in age group 5 received more of the doxycycline 100mg (n = 33) than patients in age group 4 (n = 3) as shown in Table 5.42C3$_1$.

The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age group in Clinic D are illustrated in Table 5.42D$_1$.

Table 5.42D$_1$: The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic D

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	36	87.45	2.43	0.85	2.26	0.03	5.40
4	138	338.69	2.45	0.86	2.26	0.03	4.56
5	272	913.34	3.36	1.37	2.99	0	7.56
6	2110	7391.54	3.50	1.58	3.01	0	19.68
7	930	3307.64	3.56	1.49	3.03	0.03	9.02
8	363	1341.15	3.69	1.53	4.49	0	10.69

As illustrated in Table 5.42D$_1$, no amoxycillin 250mg was prescribed for patients in age groups 1 and 2. These age groups belong to paediatric patients for whom prescribed lower dosages should be lower and in solution forms. Amoxycillin 250mg was prescribed for patients in age groups 5, 6 and 8 at a minimum cost of zero. The maximum cost varied between R4.56 for patients in age group 4 and R19.68 for patients in age group 6. The average cost varied between R2.43 ± R0.85 and R3.69 ± R1.53. Amoxycillin was prescribed for patients in age group 3 at a minimum average cost of R2.43 ± R0.85 and prescribed for patients in age group 8 at a highest average cost of R3.69 ± R1.53.

Amoxycillin 250mg was prescribed for the following disease states: common cold, uncomplicated gastritis, osteoarthritis, upper respiratory infection and acute bronchitis (refer to Clinic D, Table 5.35D). Amoxycillin as already discussed is not recommended for viral diseases like viral influenza, common cold and upper respiratory tract, since these are self-limiting (Department of Health, 2003: 206).

Table 5.42D$_{12}$: Statistical d-values as indication of the practical significance differences between the average cost of amoxycillin 250mg prescribed according to age groups in Clinic D

Age group	1	2	3	4	5	6	7	8
1								
2								
3						0.68	0.76	0.82
4			0.02			0.66	0.74	0.81
5			0.68			0.09	0.13	0.22
6			0.68				0.04	0.12
7			0.76			0.04		0.08
8			0.82	0.81		0.12	0.08	

Difference of practical significance is d>0.8

According to Table 5.43D$_{12}$ the d-values calculated (refer to chapter 4, section 4.4.5.2.4) show that there were practical significance differences between the average cost of amoxycillin 100mg prescribed for patients age groups 3 with 8, then age group 4 with 8. This means that the average cost of amoxycillin prescribed to patients in age group 8 was higher than the average costs of amoxycillin 250mg prescribed for patients in age groups 3 and 4. As shown in the Table 5.43D$_1$, patients in age groups 3 and 4 received minimum quantities of amoxycillin 250mg as compared to patients in age group 8.

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age group in Clinic D will be shown in Table 5.42D$_2$

Table 5.42D$_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic D

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	3	2.72	0.91	0.05	0.94	0.85	0.94
4	30	34.53	1.15	0.49	0.94	0.28	1.87
5	119	225.93	1.89	0.78	1.87	0.32	3.74
6	1422	2865.68	2.02	1.04	1.87	0	20.68
7	778	1525.16	1.96	1.01	1.87	0	8.23
8	304	598.60	1.97	0.91	1.87	0.03	8.42

The table shows that no co-trimoxazole 480mg was prescribed for patients in age groups 1 and 2 because of the high dose and dosage form of drug not being appropriate for these ages. Co-trimoxazole 480mg was prescribed to patients in age group 6 and 7 at a minimum cost of zero. The maximum cost varied between R0.94 for patients in age group 2 and R20.68 for patients in age group 6. The average cost varied between R0.91 ± R0.05 and R2.02 ± R1.04. Patients in age group 3 received co-trimoxazole 480mg prescriptions at a minimum average cost of R0.91 ± R0.05 and patients in age group 6 received co-trimoxazole 480mg at the highest average cost of R2.02 ± R1.04. As illustrated in Table 5.42$_{32}$ patients in age group 3 received the minimum number of co-trimoxazole 480mg and patients in age group 6 received the maximum number of co-trimoxazole 480mg prescriptions.

The commonest diagnoses for which co-trimoxazole 480mg was prescribed were: uncomplicated gastritis, acute bronchitis, fibrosis and gastroenteritis (refer to Clinic D, Table 5.34D). As already discussed antibiotics are not recommended for patients suffering from gastroenteritis because they worsen the condition (Kali & Swingler, 2003: 509).

Table 5.42D$_{21}$: Statistical d-values as indication of the practical significance differences between the average costs of co-trimoxazole 480mg prescribed according to age groups in Clinic D

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.49	1.26	1.07	1.04	1.16
4			0.49		0.95	0.84	0.80	0.90
5			1.26	0.95		0.13	0.07	0.09
6			1.07	0.84	0.13		0.06	0.05
7			1.04	0.80	0.07	0.06		0.01
8			1.16	0.90	0.09	0.05	0.01	

Difference of practical significance is d>0.8

According to table 5.42D$_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significance differences found between the average cost of co-trimoxazole prescribed for patients in age groups 3, 4 and 5, 6, 7 and 8. This means that the average cost of amoxycillin 250mg prescribed to patients in age groups 3 and 4 is lower than the average cost of co-trimoxazole 480mg prescribed to patients in groups 5, 6, 7, and 8. Patients in age groups 3 and 4 received the minimum number of amoxycillin 250mg prescriptions as compared to patients in age groups 5, 6, 7 and 8.

The average, minimum and maximum cost of erythromycin 250mg prescribed according to age group in Clinic D are illustrated in Table 5.42D$_3$.

Table 5.42D$_3$: The average, minimum and maximum cost of erythromycin 250mg prescribed according to age groups in Clinic D

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	5	36.64	7.33	0.82	7.12	6.78	8.76
4	61	489.95	8.03	1.29	7.59	4.49	13.14
5	146	1440.10	9.86	3.97	8.76	0.38	26.27
6	1107	10136.83	9.16	3.09	8.76	0	26.27
7	498	4392.39	8.82	3.06	7.59	0	36.78
8	236	1901.55	8.06	1.97	7.45	0	17.52

As shown in Table 5.42D$_3$, no erythromycin 250mg was prescribed for age groups 1 and 2 for the same reason of high dose and dosage form. The minimum cost of erythromycin 250mg was zero. The maximum cost varied between R8.76 for patients in age group 3 and R36.78 for patients in age group 7. Patients in age group 3 received the minimum number of erythromycin 250mg prescriptions. The average cost of erythromycin 250mg varied between R7.33 ± R0.82 and R9.86 ± R3.97. Erythromycin 250mg was prescribed for patients in age group 3 at a minimum cost of R7.33 ± R0.82 and prescribed for patients in age group 5 at the highest average cost of R9.86 ± R3.97.

In Clinic D erythromycin 250mg was prescribed for the treatment of common cold, osteoarthritis fibrositis (refer to Clinic D, Table 5.34D). As already discussed it was difficult to identify from the database which antimicrobials were prescribed for specific cases of patients presenting multiple disease states. So it in this regard it was assumed that antimicrobials were not prescribed for fibrositis but diseases likely to be bacterial. Otherwise antibiotics are contraindicated in a common cold.

Statistical d-values as indication of the practical significance differences between the average costs of erythromycin 250mg prescribed according to age groups in Clinic D were calculated. The d-values obtained show that there were no differences of practical significance found between the average costs of erythromycin 250mg prescribed for different patients in different age groups in Clinic D.

The average, minimum and maximum costs of amoxycillin 250mg prescribed according to age group in Clinic E are shown in Table 5.42E$_1$.

Table 5.42E$_1$: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic E

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	7	26.73	3.82	2.90	2.56	2.24	10.12
4	86	273.83	3.18	1.33	2.29	2.24	7.12
5	162	796.59	4.92	1.79	4.52	1.81	14.25
6	1150	5534.95	4.81	1.61	4.53	0	14.25
7	363	1655.55	4.56	1.41	4.94	0	16.72
8	97	428.71	4.42	1.00	4.94	2.24	7.12

As demonstrated in Table 5.42E$_1$, no amoxycillin 250mg was prescribed for patients in age groups 1 and 2 because of the solid dosage form and high dose. The minimum cost of amoxycillin 250mg was zero. The maximum cost varied between R7.12 for patients in age groups 4 and 8 and R16.72 for patients in age group 7. The average cost varied between R3.18 ± R1.33 and R4.92 ± R1.79. The minimum average cost for amoxycillin 250mg was prescribed for patients in age group 4 at R3.18 ± R1.33 and patients in age group 5 received amoxycillin 250mg with the highest average cost of R4.92 ± R1.79.

In Clinic E the commonest diagnoses in which amoxycillin 250mg was prescribed included: viral influenza, acute sinusitis, acute bronchitis (refer to Clinic E, Table 5.34E). Viral influenza and acute bronchitis are symptoms of respiratory tract infections that do not require antibiotics. According to Hoppe (1996a: 566) amoxycillin 250mg is recommended as a drug treatment for acute sinusitis.

Statistical d-values as indication of the practical significance differences between the average costs of amoxycillin 250mg prescribed according to age groups in Clinic E were calculated. The d-values obtained show that there were no differences of practical significance found between the average costs of amoxycillin 250mg prescribed to different patients in different age groups in Clinic E.

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age group in Clinic E are demonstrated in Table 5.42E$_2$.

Table 5.42E$_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic E

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	22	35.43	1.61	0.68	1.87	0.56	2.62
5	90	198.02	2.20	1.00	2.62	0	5.61
6	790	1830.74	2.32	1.22	2.62	0	13.10
7	348	877.92	2.52	1.12	2.62	0	7.86
8	112	281.59	2.51	0.96	2.62	0	7.49

As shown in Table 5.43E$_2$, no co-trimoxazole 480mg was prescribed for patients in age groups 1, 2 and 3 because of the high dosage requirements and the dosage form of that drug. The minimum cost of co-trimoxazole 480mg was zero. The maximum cost varied between R2.62 for patients in age group 4 and R13.10 for patients in age group 6. Patients in age group 4 received the minimum number of co-trimoxazole 480mg prescriptions while the maximum number of co-trimoxazole

480mg prescriptions was prescribed to patients in age group 6 as illustrated Table 5.42E$_2$. The minimum average cost was for patients in age group 4 at R1.61 ± 0.68 and patients in age group 7 received co-trimoxazole 480mg prescriptions at the highest average cost of R2.52 ± R1.12.

The commonest diagnoses in which co-trimoxazole was prescribed were respiratory tract infections that are viral in origin (refer to Clinic E, Table 5.35E).

Table 5.42E$_{21}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic E

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					0.59	0.58	0.81	0.94
5				0.59		0.10	0.29	0.32
6				0.58	0.10		0.16	0.16
7				0.81	0.29	0.16		0.01
8				0.94	0.32	0.16	0.01	

Difference of practical significance is d>0.8

According to Table 5.42E$_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were significant practical differences observed between the average cost of co-trimoxazole 480mg prescribed for patients in age groups 4, 7 and 8. This means that the average cost of co-trimoxazole 480mg prescribed for patients in age groups 7 and 8 were higher than that of the average cost of co-trimoxazole 480mg prescribed for patients in age group 4. Patients in age group 7 and 8 received more co-trimoxazole 480mg prescriptions than patients in age group 4 as illustrated in Table 5.43E$_{21}$.

The average, minimum and maximum cost of metronidazole 200mg prescribed according to age group in Clinic E will be shown in Table 5.42E $_3$.

Table 5.42E$_3$: Average, minimum and maximum cost of metronidazole 200mg prescribed according to age groups in Clinic E

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	5	2.63	0.53	0.17	0.56	0.28	0.73
4	27	19.09	0.71	0.17	0.81	0.41	0.87
5	59	61.44	1.04	0.42	0.96	0.09	1.98
6	422	462.34	1.09	0.39	0.98	0	2.06
7	147	168.01	1.14	0.38	1.17	0.41	2.26
8	29	28.84	0.99	0.46	0.84	0.41	1.67

As shown in Table 5.42E$_3$, patients in age groups 1 and 2 did not receive metronidazole 200mg because of the high dosage requirement and dosage form for that drug. Metronidazole was prescribed to patients in age group 5 at the minimum cost of R0.09. The maximum cost for metronidazole 200mg varied between R0.73 for patients in age group 3 and R2.26 for patients in age group 7. The average cost varied between R0.53 ± R0.17 and R1.14 ± R0.38. Metronidazole was prescribed for patients in age group 3 at the minimum average cost of R0.53 ± 0.17 and patients in age group 7 received metronidazole 200mg at the highest average cost at R1.14 ± R0.38.

The commonest diagnoses in which metronidazole 200mg was prescribed were: sinusitis, acute bronchitis, gastroenteritis and uncomplicated gastritis (refer to Clinic E, Table 5.34E). Metronidazole is a protozoan agent contraindicated in the treatment of viral diseases like acute bronchitis.

Table 5.42E$_{32}$: Statistical d-values as indication of the practical significance differences between average cost of metronidazole 200mg prescribed according to age groups in Clinic E

Age group	1	2	3	4	5	6	7	8
1								
2								
3				1.06	1.21	1.44	1.61	1.00
4			1.06		0.79	0.97	1.13	0.61
5			1.21	0.79		0.12	0.24	0.11
6			1.44	0.97	0.12		0.13	0.22
7			1.61	1.13	0.24	0.13		0.33
8			1.00	0.61	0.11	0.22	0.33	

Difference of practical significance is d>0.8

According to Table 5.42E$_{32}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences observed between the average cost of metronidazole 200mg prescribed to patients in age groups 3 and 4. This means that patients in age group 4 received metronidazole at an average cost higher than metronidazole 200mg prescribed for patients in age group 3. Patients in age group 3 received the minimum number of metronidazole 200mg as indicated in Table 5.43E$_3$.

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age group in Clinic F are illustrated in Table 5.42F$_1$.

Table 5.42F$_1$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic F

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	2	6.08	3.04	3.64	3.04	0.49	5.61
4	101	140.41	1.39	0.60	1.31	0	3.74
5	242	544.89	2.25	0.82	1.87	0.94	7.49
6	1593	3928.05	2.47	0.98	1.87	0	8.42
7	1211	2870.33	2.37	0.88	1.87	0.14	7.49
8	542	1224.18	2.26	0.82	1.87	0.94	7.49

As illustrated in Table 5.42F$_1$, age groups 1 and 2 did not receive co-trimoxazole 480mg prescriptions because of its high dosage requirements and dosage form. The minimum cost of co-trimoxazole 480mg was zero prescribed for patients in age groups 4 and 6. The maximum cost varied between R3.74 for patients in age group 4 and R8.42 for patients in age group 6. Patients in age group 6 received the maximum number of co-trimoxazole 480mg prescriptions as compared to patients in age group 4. The average cost for co-trimoxazole 480mg varied between R1.39 ± R0.60 and R3.04 ± R3.64. The minimum average cost for co-trimoxazole was R1.39 ± 0.60 prescribed for patients in age group 4 and the highest average cost for co-trimoxazole 480mg was R3.04 ± R3.64 prescribed for patients in age group 4.

The diagnoses for which most co-trimoxazole 480mg was prescribed were: viral influenza, gastroenteritis and acute bronchitis (refer to Clinic F, Table 5.29F$_1$). As already discussed the use of co-trimoxazole 480mg in these diseases is contraindicated (Garan & Dagan, 2003: 1936).

Table 5.42F$_{12}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic F

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.45	0.22	0.16	0.18	0.21
4			0.45		1.05	1.10	1.11	1.06
5			0.22	1.05		0.22	0.14	0.01
6			0.16	1.10	0.22		0.10	0.21
7			0.18	1.11	0.14	0.10		0.13
8			0.21	1.06	0.01	0.21	0.13	

Difference of practical significance is d>0.8

According to Table 5.42F$_{12}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences observed between the average cost of co-trimoxazole 480mg prescribed for patients in age group 4 with 5, 6, 7 and 8. This means that patients in age group 4 received co-trimoxazole 480mg prescriptions at an average cost lower than that of co-trimoxazole 480mg prescribed for patients in age groups 5, 6, 7 and 8. Patients in age group 4 received less co-trimoxazole 480mg as compared to patients in age groups 5, 6, 7 and 8 as illustrated in Table 5.42F$_1$.

The average, minimum and maximum costs of doxycycline 100mg prescribed according to age group in Clinic F are shown in Table 5.42F$_2$.

Table 5.42F$_2$: Average, minimum and maximum cost of doxycycline 100 mg prescribed according to age groups in Clinic F

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	12	54.25	4.52	1.55	4.68	1.99	7.52
5	112	697.09	6.22	1.89	5.78	2.83	12.38
6	1043	6477.10	6.21	1.87	5.72	0.69	23.35
7	483	2910.78	6.01	1.51	5.65	0.72	11.71
8	128	747.98	5.84	1.07	5.65	0.38	11.18

As demonstrated in Table 5.42F$_2$, no doxycycline 100mg was prescribed to age groups 1, 2 and 3 because it is contraindicated in patients below the age of 8 years. Patients in age group 8 received doxycycline 100mg at a minimum cost of R0.38. The maximum cost varied between R7.52 for patients in age group 4 and R23.35 for patients in age group 6. The average cost varied between R4.52 ± R1.55 and R6.21 ± R1.87. Patients in age group 4 received doxycycline 100mg at a minimum average cost of R4.52 ± 1.55 and patients in age group 6 received doxycycline 100mg at the highest average cost of R6.21 ± R1.87. As shown in the Table 5.43F$_2$, patients in age group 4 received the minimum number of doxycycline 100mg prescriptions while patients in age group 6, received the maximum number of doxycycline 100mg prescriptions.

The commonest diagnoses in which doxycycline 100mg was prescribed in Clinic F were: pelvic inflammatory disease, vulvovaginitis and viral influenza (refer to Clinic F, Table 5.33). As already discussed the use of doxycycline in the treatment of pelvic inflammatory disease is recommended (Lynn, 1996: 224). Nevertheless its use in viral influenza is contraindicated.

Table 5.42F$_{21}$: Statistical d-values as indication of the practical significance differences between he average cost of doxycycline 100mg prescribed according to age groups in Clinic F

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					0.90	0.90	0.96	0.85
5				0.90		0.01	0.11	0.20
6				0.90	0.01		0.11	0.20
7				0.96	0.11	0.11		0.11
8				0.85	0.20	0.20	0.11	

Difference of practical significance is d>0.8

According to Table 5.42F$_{21}$, the d-value calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there was practical significant differences observed between the average cost of doxycycline 100mg prescribed in age group 4 and 5, 6, 7 and 8. This means that patients in age group 4 were prescribed doxycycline 100mg at an average cost lower than in other age groups. Patients in age group 4 received the minimum number of doxycycline 100mg prescriptions as compared to patients in other age groups.

The average, minimum and maximum costs of amoxycillin 250mg prescribed according to age groups in clinic F are shown in Table 5.42F$_3$.

Table 5.42F$_3$: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic F

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	5	18.87	3.77	1.52	3.56	2.29	5.34
4	107	304.85	2.85	0.97	2.46	0	6.28
5	170	747.87	4.39	1.69	4.49	0.90	11.96
6	962	4650.12	4.74	1.80	4.49	0	14.25
7	325	1414.33	4.35	1.78	4.49	0.47	14.25
8	122	509.07	4.17	1.62	4.49	1.55	11.96

As shown in Table 5.42F$_3$, patients in age groups 1 and 2 did not receive amoxycillin 250mg because these are paediatric patients that require lower doses and liquid dosage forms. Patients in age group 7 received amoxycillin 250mg at a minimum cost of R0.47. The maximum cost varied between R5.34 for patients in age group 3 and R14.25 for patients in age groups 6 and 7. The average cost varied between R2.85 ± R0.97 and R4.74 ± R1.80. The minimum average cost for amoxycillin 250mg was prescribed for patients in age group 4 at R2.85 ± R0.97 and patients in age group 6 received amoxycillin 250mg at the highest average cost of R4.74 ± R1.80. Patients in age group 6 received the maximum number of amoxycillin 250mg prescriptions as compared to patients in other age groups.

Amoxycillin was mostly prescribed for: severe sinusitis, acute bronchitis and viral influenza. According to Mlynaarczyk *et al.* (2001: 497), amoxycillin 250mg is recommended in the treatment of severe sinusitis. As already stated viral diseases do not require antibiotics.

Table 5.42F$_{31}$: Statistical d-values as indication of the practical significance differences between the average cost of amoxycillin 250mg prescribed according to age groups in Clinic F

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.61	0.37	0.54	0.33	0.25
4			0.61		0.91	1.05	0.84	0.81
5			0.37	0.91		0.91	0.02	0.13
6			0.54	1.05	0.91		0.22	0.32
7			0.33	0.84	0.02	0.22		0.10
8			0.25	0.81	0.13	0.32	0.10	

Difference of practical significance is d>0.8

According to Table 5.42F$_{31,}$ the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average cost of amoxycillin 250mg prescribed in patients in age group 4 with 5, 6, 7 and 8. This implies that in the average cost of amoxycillin 250mg prescribed for patients in age group 4 was lower than the average cost of amoxycillin 250mg prescribed for patients in age groups 5, 6, 7 and 8.

The average, minimum and maximum cost of ampicillin 250mg prescribed according to age group in Clinic G are illustrated in Table 5.42G$_{1.}$

Table 5.42G$_1$: The average, minimum and maximum cost of ampicillin 250mg prescribed according to age groups in Clinic G

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	7	16.41	2.34	1.41	2.25	2.24	6.75
4	93	264.45	3.34	0.99	2.36	0.46	8.01
5	237	791.60	3.63	1.23	2.99	0	14.25
6	1248	4527.34	3.69	1.39	3.48	0	16.03
7	684	2530.09	3.75	1.44	3.56	0	14.25
8	198	742.62	4.46	1.53	3.56	4.46	4.46

As illustrated in Table 5.42G$_1$, patients in age groups 1 and 2 did not receive ampicillin 250mg because of the drug's high dose requirement and the solid dosage form that are not appropriate for paediatric prescribing. The minimum cost of ampicillin 250mg was R0.46 for patients in age group 4. The maximum cost varied between R4.46 for patients in age group 8 and R16.03 for patients in age group 6. The average cost varied between R2.34 ± R1.41 and R4.46 ± R1.53. Patients in age group 3 received ampicillin 250mg at the minimum average cost of R2.34 ± 1.41 and the patients in age group 8 received ampicillin 250mg prescriptions at the highest average cost of R4.46 ± R1.53. As illustrated in the table, patients in age group 3 received the minimum number of ampicillin 250mg prescriptions as compared to the rest of the age groups in Clinic G.

Statistical d-values as indication of the practical significance differences between the average costs of ampicillin 250mg prescribed according to age groups in Clinic G are illustrated in Table 5.42G$_{12}$.

Table 5.42G$_{12}$: Statistical d-values as indication of the practical significance differences between the average costs of ampicillin 250mg prescribed according to age groups in Clinic G

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.71	0.91	0.96	0.98	1.39
4			0.71		0.24	0.25	0.28	0.73
5			0.91	0.24		0.04	0.08	0.54
6			0.96	0.25	0.04		0.04	0.50
7			0.98	0.28	0.08	0.04		0.46
8			1.38	0.73	0.54	0.05	0.46	

Difference of practical significance is d>0.8

According to table 5.42G$_{12}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences observed between the average cost of ampicillin prescribed for patients in age group 3 and other age groups. This means that the average cost for ampicillin 250mg prescribed for patients in age 3 was lower than the average costs of ampicillin prescribed for patients in the rest of the age groups because patients in this age group received the minimum number of ampicillin 250mg prescriptions.

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic G are demonstrated in Table 5.42G$_2$.

Table 5.42G$_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic G

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	4	6.59	1.65	0.91	1.40	0.94	2.85
4	50	78.21	1.56	0.55	1.87	0.82	2.81
5	174	367.74	2.11	0.88	1.87	0.24	11.23
6	1294	2948.25	2.28	1.05	1.87	0	15.08
7	743	1633.08	2.19	0.84	1.88	0.32	12.92
8	178	403.03	2.26	0.66	1.99	0.90	5.63

This table shows that no co-trimoxazole 480mg was prescribed to age groups 1 and 2 because these are paediatric patients that need low doses and liquid dosage forms. Co-trimoxazole 480mg was prescribed at the minimum cost of zero for patients in age group 6. The maximum cost varied between R2.81 for patients in age group 4 and R15.08 for patients in age group 6. The average cost varied between R1.56 ± R0.55 and R2.28 ± R1.05. Co-trimoxazole 480mg was prescribed at a minimum average cost of R1.56 ± 0.55 for patients in age group 4 and the highest average cost for co-trimoxazole was R2.28 ± R1.05 prescribed for patients in age group 6. Patients in age group 6 received the maximum number of co-trimoxazole 480mg prescriptions as compared to other age groups.

In Clinic G the most frequent diagnoses in which co-trimoxazole was prescribed were: non-specific diarrhoea, gastroenteritis and acute bronchitis (refer to Clinic G, Table 5.29G$_1$). As already stated antibiotics are not recommended in the treatment of these diseases.

Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic G are demonstrated in Table 5.42G$_{21}$.

Table 5.42G$_{21}$: Statistical d-values as indication of the practical significance differences between the average costs of co-trimoxazole 480mg prescribed according to age groups in Clinic G

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.10	0.51	0.60	0.59	0.67
4			0.10		0.63	0.69	0.75	1.06
5			0.51	0.63		0.16	0.09	0.17
6			0.60	0.69	0.16		0.09	0.02
7			0.59	0.75	0.09	0.09		0.08
8			0.67	1.06	0.17	0.02	0.08	

Difference of practical significance is d>0.8

According to Table 5.42G$_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there was a practical significant difference found between the average cost of Co-trimoxazole 480mg prescribed for patients in age group 4 and 8 with d-value of 1.06. This means that the average cost for co-trimoxazole 480mg prescribed for patients in age group 4 was lower (R1.65) than that of co-trimoxazole 480mg prescribed for patients in age group 8 (R2.26). Patients in age group 4 received smaller amount of co-trimoxazole 480mg as compared to what patients in age group 8 received as shown in Table 5.43G$_2$.

The average, minimum and maximum cost of erythromycin 250mg prescribed according to age groups in Clinic G are illustrated in Table 5.42G$_3$.

Table 5.42G$_3$: Average, minimum and maximum cost of erythromycin 250mg prescribed according to age groups in Clinic G

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	2	15.30	7.65	1.06	7.65	6.90	8.40
4	28	243.77	8.71	2.59	8.24	6.57	16.47
5	85	886.67	10.43	6.21	8.40	6.57	55.83
6	542	5915.39	10.91	3.72	10.35	0	47.29
7	217	2233.60	10.92	3.46	8.76	1.20	24.19
8	55	498.96	9.07	2.86	8.40	0	17.52

According to Table 5.42G$_3$, no erythromycin 250mg was prescribed for age groups 1 and 2 because patients in this age group require low doses and liquid dosage forms. Erythromycin 250mg was prescribed at the minimum cost of zero to patients in age groups 6 and 8. The maximum cost of erythromycin 250mg varied between R8.40 for patients in age group 3 and R55.83 for patients in age group 5. The average cost varied between R7.65 ± R1.06 and R10.92 ± R3.46. The minimum average cost was for age group 3 at R7.65 ± 1.06 and patients in age group 7 received erythromycin 250mg prescriptions at the highest average cost of R10.92 ± R3.46. Patients in age group 3 received the minimum number of erythromycin 250mg prescriptions as compared to the other age groups.

Statistical d-values as indication of the practical significance differences between average cost of erythromycin 250mg prescribed according to age groups in Clinic G are shown in Table 5.42G$_{32}$.

Table 5.42G$_{32}$: Statistical d-values as indication of the practical significance differences between average costs of erythromycin 250mg prescribed according to age groups in Clinic G

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.41	0.45	0.88	0.76	0.50
4			0.41		0.28	0.59	0.47	0.13
5			0.45	0.28		0.88	0.02	0.22
6			0.88	0.59	0.88		0.17	0.53
7			0.76	0.47	0.02	0.17		0.53
8			0.50	0.13	0.22	0.53	0.53	

Difference of practical significance is d>0.8

According to Table 5.42G$_{32}$ the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences observed between the average cost of erythromycin 250mg prescribed for patients in age groups 3 and 6 with a d-value of 0.88, then between age groups 5 and 6 with the d-value of 0.88. This means that the average cost of erythromycin 250mg prescribed for patients in age group 6 was higher (R10.91) than the average costs of erythromycin 250 mg prescribed for patients in age groups 3 (R7.65) and 5 (R10.43) respectively.

The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic H are shown Table 5.42H$_1$.

Table 5.42H$_1$: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic H

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	11	34.66	3.15	2.08	2.67	1.11	8.97
4	108	274.73	2.54	0.83	2.26	0	7.12
5	181	634.77	3.51	1.28	2.99	0	8.97
6	874	3305.48	3.78	1.29	4.49	0	11.96
7	601	2261.17	3.76	1.29	4.49	0	8.36
8	132	512.27	3.88	1.42	4.49	0	11.96

This table shows that no amoxycillin 250mg was prescribed for age groups 1 and 2 because of the high dose and these age groups require liquid dosage forms. Amoxycillin 250mg was prescribed at a minimum cost of R1.11 for patients in age group 3. The maximum cost varied between R7.12 for patients in age group 4 and R11.96 for patients in age groups 6 and 8. The average cost varied between R2.54 ± R0.83 and R3.88± R1.42 Amoxycillin 250mg was prescribed at a minimum average cost of R2.54 ± R0.83 to patients in age group 4 and prescribed for patients in age group 6 at the highest average cost of R4.49. Patients in age group 6 received the maximum number of amoxycillin 250mg prescriptions.

In Clinic H the most frequent diagnoses where amoxycillin 250mg was prescribed were: muscle pains, muscle trauma and respiratory tract infections (refer to Clinic H, Table 5.34H). As already stated the use of antibiotics in muscle pains and trauma is inappropriate (Department of Health, 2003: 265) (refer to limitation of the database Section 6.3).

Statistical d-values as indication of the practical significant differences between the average costs of amoxycillin 250mg prescribed according to age groups in Clinic H are demonstrated in Table 5.42H$_{11}$.

Table 5.42H$_{11}$: Statistical d-values as indication of the practical significance differences between the average cost of amoxycillin 250mg prescribed according to age groups in Clinic H

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.29	0.17	0.30	0.29	0.35
4			0.29		0.76	0.96	0.95	1.04
5			0.17	0.76		0.21	0.19	0.26
6			0.30	0.96	0.21		0.02	0.07
7			0.29	0.95	0.19	0.02		0.08
8			0.35	1.04	0.26	0.07	0.08	

Difference of practical significance is d>0.8

According to Table 5.42H$_{11}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) shows that there were practical significant differences found between the average cost of amoxycillin 250mg prescribed for patients in age groups 4 and age groups 6, 7 and 8. This implies that the average cost of amoxycillin 250mg prescribed for patients in age groups 6, 7 and 8 were higher than the average cost of amoxycillin 250mg prescribed to patients in age group 4. Patients in age group 4 received the minimum number of amoxycillin 250mg prescriptions as compared to patients in age group 6, 7 and 8.

The average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic H are shown in Table 5.42H$_2$.

Table 5.42H$_2$: Average, minimum and maximum cost of co-trimoxazole 480mg prescribed according to age groups in Clinic H

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	2	3.74	1.87	0	1.87	1.87	1.87
4	56	76.77	1.37	0.61	1.31	0	3.74
5	81	154.99	1.91	0.73	1.87	0	3.74
6	732	1554.59	2.12	0.79	1.87	0	7.49
7	575	1274.30	2.22	0.97	1.87	0	13.10
8	163	347.14	2.13	0.76	1.87	0	4.21

According to Table 5.42H$_2$, no co-trimoxazole 480mg was prescribed to age groups 1 and 2 because of paediatric patients require lower doses and liquid dosage forms. Co-trimoxazole was prescribed at the minimum cost of zero. The maximum cost varied between R1.87 for patients in age group 3 and R13.10 for patients in age group 7. The average cost varies between R1.37 ± R0.61 and R2.22 ± R0.97. The minimum average cost for co-trimoxazole 480mg was R1.37 ± 0.61 prescribed for patients in age group 4, and patients in age group 7 received co-trimoxazole 480mg prescriptions at the highest average cost of R2.22 ± R0.97.

Co-trimoxazole 480mg was prescribed for the treatment of common cold, and gastroenteritis (refer to Clinic H, Table 5.34H). As stated by Kali and Swingler (2003: 509), the use of antibiotics in gastroenteritis worsens the condition because gastrointestinal disturbance presents itself as one of the adverse effects of antibiotics. The use of co-trimoxazole 480mg for the common cold as already discussed is contraindicated.

Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic H

Table 5.42H$_{21}$: Statistical d-values as indication of the practical significance differences between the average cost of co-trimoxazole 480mg prescribed according to age groups in Clinic H

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.82	0.05	0.32	0.36	0.34
4			0.82		0.74	0.95	0.88	1.00
5			0.05	0.74		0.27	0.32	0.29
6			0.32	0.95	0.27		0.10	0.01
7			0.36	0.88	0.32	0.10		0.09
8			0.34	1.00	0.29	0.01	0.09	

Difference of practical significance is d>0.8

According to Table 5.42H$_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average cost of co-trimoxazole 480mg prescribed for patients in age groups 3 and 4 and then age groups 4 and 6, 7 and 8. This means that the average cost of co-trimoxazole 480mg prescribed for patients in age groups 4 was lower than that of co-trimoxazole 480mg prescribed to patients in age groups 3, 6, 7 and 8.

The average, minimum and maximum cost of ampicillin 250mg prescribed according to age group in Clinic H are shown in Table 5.42H$_3$.

Table 5.42H$_3$: Average, minimum and maximum cost of ampicillin 250mg prescribed according to age groups in Clinic H

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	4	11.82	2.95	0.16	2.87	2.87	3.20
4	29	86.74	2.99	1.35	2.92	0.03	5.75
5	67	204.61	3.05	1.44	2.87	0	7.18
6	542	1695.61	3.13	1.69	2.92	0	10.28
7	289	993.31	3.44	1.98	2.92	0	10.99
8	46	173.05	3.76	1.51	2.92	0	7.18

As demonstrated in Table 5.42H$_3$, no ampicillin 250mg was prescribed for age groups 1 and 2 because these are paediatric patients that require low dosages and liquid dosage forms. The minimum cost of ampicillin 250mg was R0.03 prescribed for patients in age group 4. The maximum cost varied between R3.20 for patients in age group 3 and R10.99 for patients in age group 7. The average cost varied between R2.95 ± R0.16 and R3.76 ± R1.51. The minimum average cost of ampicillin was prescribed for patients in age group 3 at R2.95 ± 0.16 and patients in age group 8 were prescribed ampicillin 250mg at the highest average cost of R3.76 ± R1.51. Patients in age group 3 received the minimum number of ampicillin 250mg prescriptions as compared to patients in other age groups.

Patients in Clinic H that presented mostly with common cold, muscle pains and trauma (refer to limitations of the study section 6.3) and acute bronchitis were prescribed ampicillin 250mg prescriptions (refer to Clinic H, Table 5.34H). The use of this antibiotic in these disease states is contraindicated as already discussed (Department of Health, 2003: 265).

Statistical d-values as indication of the practical significance differences between the average costs of ampicillin 250mg prescribed according to age groups in Clinic H were calculated. The d-values obtained showed that there were no practical significant differences observed between the average costs of ampicillin 250mg prescribed for patients in the different age groups.

The average, minimum and maximum cost of amoxycillin 250mg prescribed according to age group in Clinic I are shown in Table 5.43I_1.

Table 5.42I_1: Average, minimum and maximum cost of amoxycillin 250mg prescribed according to age groups in Clinic I

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	7	19.69	2.81	0.51	2.79	5.25	3.72
4	120	325.78	2.71	1.03	2.27	0.08	6.46
5	207	805.35	3.89	1.56	4.49	2.24	11.96
6	956	3848.09	4.02	1.47	4.49	0.06	11.96
7	489	2036.26	4.16	1.49	4.49	0.03	11.96
8	202	789.05	3.91	1.46	4.49	0.22	11.96

According to Table 5.42I_1, patients in age groups 1 and 2 did not receive amoxycillin 250mg due to the fact that these require paediatric low dosages and liquid preparations. The minimum cost of amoxycillin 250mg was R0.03 prescribed for patients in age group 7. The maximum cost varied between R3.72 for patients in age group 3 and R11.96 for patients in age groups 5, 6, 7 and 8. The average cost varied between R2.71 ± R1.03 and R4.16 ± R1.49. The minimum average cost for amoxycillin was R2.71 ± R1.03 prescribed for patients in age group 4 and patients in age group 7 were prescribed amoxycillin 250mg at the highest average cost of R4.16 ± 1.49.

The most frequent disease states for which amoxycillin 250mg was prescribed were: Arthralgia, uncomplicated gastritis, acute bronchitis and viral influenza. According to the Department of Health (2003: 251) arthralgia should be treated with analgesics and not antibiotics (refer to the limitations of the data problem Section 6.3). Neither should acute bronchitis nor viral influenza be treated with antibiotics.

Table 5.42I$_{12}$: Statistical d-values as indication of the practical significance differences between the average cost of amoxycillin 250mg prescribed according to age groups in Clinic I.

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.10	0.69	0.82	0.91	0.75
4			0.10		0.76	0.89	0.97	0.82
5			0.69	0.76		0.08	0.17	0.01
6			0.82	0.89	0.08		0.09	0.07
7			0.91	0.97	0.17	0.09		0.17
8			0.75	0.82	0.01	0.07	0.17	

Difference of practical significance is d>0.8

According to this Table 5.42I$_{12}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average cost of amoxycillin 250mg prescribed for patients in age groups 3 and 4. Patients in age groups 3 and 4 were received amoxycillin prescriptions at average costs that were lower than the average cost of amoxycillin 250mg prescribed in age groups 6, 7 and 8. Patients in age group 3 and 4 received the smaller numbers of amoxycillin 250mg prescriptions as compared to patients in age groups 6, 7 and 8.

The average, minimum and maximum cost of ampicillin 250m prescribed according to age groups in Clinic I are illustrated in Table 5.42I$_2$.

Table 5.42I$_2$: Average, minimum and maximum cost of ampicillin 250mg prescribed according to age groups in Clinic I

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3	3	9.88	3.29	0.72	2.88	2.87	4.12
4	19	70.64	3.72	0.89	3.59	2.87	5.73
5	74	364.01	4.92	1.93	5.07	2.87	10.28
6	567	2570.18	4.53	1.71	4.09	1.22	10.28
7	288	1356.34	4.71	1.71	4.09	0.93	10.28
8	130	587.59	4.52	1.54	4.09	2.87	10.28

The table shows that no ampicillin 250mg was prescribed for age groups 1 and 2 because these are paediatric patients that require low doses and liquid preparations. Ampicillin 250mg was prescribed at a minimum cost of 0.93 for patients in age group 7. The maximum cost varied between R4.12 for patients in age group 3 and R10.28 for patients in age groups 5, 6, 7 and 8. The average cost varies between R3.29 ± R0.72 and R4.92 ± R193. Ampicillin 250mg was prescribed at the minimum average cost of R3.72 ± 0.89 for patients in age group 4 and patients in age group 5 were prescribed ampicillin 250mg at the highest average cost of R4.92 ± R1.93.

Ampicillin was used in the following disease states: osteorthritis, arthralgia, hypertension and antenatal follow-up visits (refer to Clinic I, Table 5.34I). As stated earlier on the antibiotics prescribed for patients with multiple diseases including chronic diseases like hypertension and osteoarthritis, it was assumed that antibiotics were prescribed for those diseases that are bacterial because it was difficult from the database to identify which specific diseases for which antibiotics were prescribed. The management of arthalgia does not require antibiotics but analgesics.

Statistical d-values as indication of the practical significance differences between the average costs of ampicillin 250mg prescribed according to age groups in Clinic I are demonstrated in Table $5.42I_{21}$.

Table 5.42_{21}: Statistical d-values as indication of the practical significance differences between the average cost of ampicillin 250mg prescribed according to age groups in Clinic I.

Age group	1	2	3	4	5	6	7	8
1								
2								
3				0.48	0.84	0.73	0.83	0.80
4			0.48		0.62	0.47	0.58	0.52
5			0.84	0.62		0.20	0.11	0.21
6			0.73	0.47	0.20		0.11	0.01
7			0.83	0.58	0.11	0.11		0.11
8			0.80	0.52	0.21	0.01	0.11	

Difference of practical significance is d>0.8

According to Table $5.42I_{21}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there practical significant differences found between the average cost of ampicillin prescribed for patients in age group 3 and 5, then between 3 and 7. This implies that the average cost of ampicillin prescribed for patients in age group 3 was lower than the average cost of ampicillin prescribed to patients in age groups 5 and 6. Patients in age group 3 received the minimum number of ampicillin 250mg prescriptions as compared to patients in other age groups.

The average, minimum and maximum cost of metronidazole 200mg prescribed according to age group in Clinic I are illustrated in Table $5.42I_3$.

Table 5.42I$_3$: Average, minimum and maximum cost of metronidazole 200mg prescribed according to age groups in clinic I

Age group	Total number of antimicrobials prescribed	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
1							
2							
3							
4	8	5.06	0.63	0.28	0.54	0.48	1.31
5	86	84.78	0.99	0.45	0.81	0.48	3.14
6	476	490.71	1.03	0.35	0.81	0.48	2.63
7	388	303.32	1.05	0.66	0.81	0.71	10.74
8	111	109.54	0.99	0.35	0.81	0.48	3.15

As shown in Table 5.42I$_3$, no metronidazole 200mg was prescribed for age groups 1, 2 and 3 because of the high dose and dosage form. The minimum cost of metronidazole 200mg was prescribed for patients in age groups 4, 5, 6 and 8 at R0.48. The maximum cost varied between R1.31 for patients in age group 4 and R10.74 for patients in age group 7. The average cost varied between R0.63 ± R0.28 and R1.05 ± R0.66. The minimum average cost of metronidazole 200mg prescribed for patients in age group 4 was R0.63 ± 0.28 and patients in age group 7 were prescribed metronidazole at the highest average cost of R1.05 ± R0.66.

Patients in Clinic I received metronidazole prescriptions in the treatment of uncomplicated gastritis (refer to Clinic I, Table 5.34I). As stated by Simms-Cendan (1996: 153) the use of metronidazole in uncomplicated gastritis is recommended.

Statistical d-values as indication of the practical significance differences between the average costs of metronidazole 200mg prescribed according to age groups in Clinic I are demonstrated in Table 5.42$_{32}$

Table 5.42I$_{32}$: Statistical d-values as indication of the practical significance differences between the average cost of metronidazole 200mg prescribed according to age groups in Clinic I.

Age group	1	2	3	4	5	6	7	8
1								
2								
3								
4					0.80	1.14	0.64	1.03
5				0.80		0.09	0.09	0.00
6				1.14	0.09		0.03	0.11
7				0.64	0.09	0.03		0.09
8				1.03	0.00	0.11	0.09	

Difference of practical significance is d>0.8

According to Table 5.42I$_{32}$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were significant practical differences observed between the average cost of metronidazole 200mg prescribed for patients in age groups 4 and 6, then 4 and 8. This implies that the average cost of metronidazole prescribed for patients in age group 4 was lower than the average costs of metronidazole prescribed for patients in age groups 6 and 8. Patients in age group 4 received the minimum number of metronidazole 200mg prescriptions as compared to patients in age group 6 and 8.

SUMMARY OF THE RESULTS OF ALL CLINICS

The results obtained from the average costs of the top three individual antimicrobials prescribed according to the different age groups in the nine clinics can be summarised as follows: The commonest individual antimicrobials prescribed in the nine clinics were: Co-trimoxazole 480mg, amoxycillin 250mg, doxycycline 100mg, ampicillin 250mg and metronidazole 200mg. This trend in prescriptions was influenced by the disease states presented in the different age groups of the different clinics.

There was a general trend observed in the nine clinics that those antimicrobials whose costs was R 0.01, their minimum costs was zero. It was also observed that the minimum average costs of any antimicrobial corresponded to patients in age groups that received the minimum number of that antimicrobial prescriptions, for example age groups 3 or 4 received the minimum numbers of prescriptions and age groups 6, 7 and 8 the highest numbers of antimicrobial prescriptions. Patients in age groups 3 and 4 presented themselves to the clinics in small numbers as compared to patients in age groups 6, 7 and 8. This resulted in these patients getting smaller numbers of the antimicrobial prescriptions. That explains the lower average costs of drug prescriptions in these age groups as compared to patients in age groups 6, 7 and 8. Furthermore patients in age groups 3 and 4 were paediatric patients for who are prescribed lower dosages and suspension dosage forms. Correspondingly this makes the costs of antimicrobials for these age groups cheaper as compared to patients in age groups 6, 7 and 8. The latter groups are adult patients and are receive higher doses and higher quantities in forms of tablets and capsules, making the total costs of their drugs more costly.

The most common diagnoses in which most antimicrobials were prescribed in the nine clinics were respiratory tract infections.

There were practical significant differences observed between the average costs of individual antimicrobials prescribed for patients in the different age groups in the nine clinics. Significant practical differences were observed between the patients that were prescribed antimicrobials for which average costs were lower (age groups 3 and 4) and those for which average costs were highest (age groups 6, 7 and 8).

5.7.4 The average costs of antimicrobials prescribed for the top ten individual diagnoses in each clinic

The following tables 5.43(A-I) illustrate the average, minimum and maximum cost of antimicrobials prescribed for the different diagnoses in each of the nine clinics.

The discussion of this section will not include the following disease states: hypertension, antenatal follow-ups, chronic prostatitis, muscle pains, muscle trauma, peptic ulceration, fibrositis, osteoarthritis, and acute cystitis in pregnancy because of the following limitation of the study. From the database it was not possible to differentiate medicine items prescribed for individual diagnosis when more than one diagnosis was made during a consultation. However, it was assumed that

antimicrobials were not prescribed for any of the above mentioned diagnoses but for secondary infections.

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic A are illustrated in Table 5.43A.

As shown in Table 5.43A, the minimum cost of the antimicrobials prescribed in individual diagnosis was zero for pelvic inflammatory disease and viral influenza. The maximum cost varied between R26.07 for the common cold and R34.54 for upper respiratory infection. The average cost varied between R3.08 ± R4.34 and R7.44 ± R5.21. The diagnosis for which antimicrobials were prescribed with the minimum average cost was upper respiratory infection at R3.08 ± R4.34. On the other hand, urinary tract infection had the highest average cost of antimicrobials prescribed at R6.91 ± R9.01.

Table 5.43A: Average, minimum and maximum cost of antimicrobials prescribed in individual diagnoses in Clinic A

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Pelvic inflammatory disease	317	2358.30	7.44	5.21	6.79	0	29.69
Upper respiratory infection	637	1930.74	3.08	4.34	1.89	0.01	34.54
Urinary tract infection	159	1085.12	6.91	9.01	2.88	0.05	33.73
Viral Influenza	513	1620.58	3.26	5.05	1.87	0	33.73
Tonsillitis	217	942.74	4.38	3.56	3.57	0.64	32.55
Common Cold	252	742.74	3.09	3.15	1.95	0.31	26.07
Acute bronchitis	311	971.02	3.15	4.36	1.87	0.10	34.49

According to Table 5.43A$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average costs of antimicrobials prescribed in individual diagnoses in Clinic A. Differences of practical significance were observed between the pelvic inflammatory diseases and urinary tract infections with d-value 0.84. Between pelvic inflammatory disease and upper respiratory infection, d-value at 0.83, whereas between pelvic inflammatory diseases and acute bronchitis acute, d-value was 0.82. This implies that the average cost of antimicrobials prescribed in pelvic inflammatory diseases was higher than the average cost of antimicrobials prescribed in upper respiratory infection and acute bronchitis. On the whole the number of antimicrobials prescribed in pelvic inflammatory diseases was the highest. Consequently the cost of such drugs turned out to be the highest adding up to R2358.30. The commonest antimicrobial prescribed in pelvic inflammatory diseases in Clinic A was doxycycline 100mg. Whereas antimicrobials prescribed for upper respiratory disease and acute bronchitis were co-trimoxazole 480mg and amoxycillin 250mg (refer to Clinic A, Table 5.35A).

Table 5.43A$_1$: Statistical d-values as indication of practical significance differences between the average costs of individual diagnosis in Clinic A

Diagnosis	PID	URI	UTI	Viral Influenza	Tonsillitis	Common cold	Acute bronchitis
PID		0.84	0.10	0.46	0.59	0.83	0.82
URI	0.84		0.43	0.04	0.30	0.00	0.02
UTI	0.10	0.43		0.41	0.28	0.42	0.42
Viral Influenza	0.46	0.04	0.41		0.22	0.03	0.02
Tonsillitis	0.59	0.30	0.28	0.22		0.36	0.28
Common cold	0.83	0.00	0.42	0.03	0.36		0.01
Acute bronchitis	0.82	0.02	0.42	0.02	0.28	0.01	

Abbreviations:
PID: pelvic inflammatory disease
UTI: urinary tract infection
URI: upper respiratory infection
URT: upper respiratory tract

Difference of practical significance is d>0.8

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic B will be illustrated in Table 5.44B.

Table 5.43B: The average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic B

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Upper respiratory infection	339	1079.08	4.23	3.34	3.56	0	25.99
Viral influenza	554	1294.00	3.77	3.16	2.67	0	27.56
Common Cold	167	604.76	4.41	3.68	2.67	0.11	28.06
Cough	278	793.77	4.29	2.84	3.62	0	21.67
Urinary tract Infection	367	1629.81	4.53	5.95	2.62	0	64.58
Gastro-Enteritis	162	190.98	4.06	2.69	3.62	0	13.78
Otitis Media	117	802.16	7.22	3.89	8.76	0	14.29

Table 5.44B reveals that the minimum cost of the antimicrobials prescribed in individual diagnosis was zero. The maximum cost varied between R13.78 for gastroenteritis and R64.58 for urinary tract

infections. The average cost varied between R3.77 ± R3.16 and R7.22 ± R3.89. The minimum average cost of antimicrobials prescribed for viral influenza was at R3.77 ± R3.16 and the highest average cost was at R7.22 ± 3.89 for antimicrobials prescribed for otitis media.

Table 5.43B$_1$: Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic B

Diagnosis	URTI	Viral influenza	UTI	Common cold	Cough	GE	Otitis media
URTI		0.14	0.05	0.02	0.05	0.05	0.77
Viral influenza	0.14		0.17	0.16	0.13	0.09	0.89
Common Cold	0.05	0.17		0.03	0.02	0.10	0.72
Cough	0.02	0.16	0.03		0.04	0.08	0.75
URI	0.05	0.13	0.02	0.04		0.08	0.45
GE	0.05	0.09	0.10	0.08	0.08		0.81
Otitis Media	0.77	0.89	0.72	0.75	0.45	0.81	

Abbreviations:

URTI: upper respiratory infection
UTI: urinary tract infection
GE: gastroenteritis

Difference of practical significance is d>0.8

According to Table 5.43$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average costs of antimicrobials prescribed in viral influenza and otitis media with d-value of 0.89 and gastroenteritis (GE) and otitis media with d-value of 0.81. The average cost of antimicrobials prescribed in otitis media was higher than the average costs of antimicrobials prescribed in viral influenza and gastroenteritis. The most frequently antimicrobial prescribed for otitis media in Clinic B was co-trimoxazole 480mg and amoxycillin was prescribed in viral influenza and gastroenteritis (refer to Clinic B, Table 5.35B).

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic C are illustrated in Table 5.43C.

Table 5.43C: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic C

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Upper respiratory infection	379	2436.03	6.92	8.07	4.46	0.11	34.55
Viral influenza	214	332.83	5.74	7.63	4.46	0.90	52.29
Cough	192	653.95	7.03	5.41	4.57	0.40	26.15
Mild/mod: dental abscess	186	790.15	4.97	5.35	4.49	0.05	67.46
Common Cold	181	884.63	7.49	6.09	6.58	0.11	33.73
Acute bronchitis	335	2168.29	6.69	6.68	4.50	0.11	52.29
Lower respiratory tract infection	200	1194.30	6.00	6.30	4.49	0	1194.30

The minimum cost of the antimicrobials prescribed in individual diagnosis was zero for lower respiratory tract infections. The maximum cost varied between R26.15 for antimicrobials prescribed for cough and R1194.30 for antimicrobials prescribed for lower respiratory tract infection. The average cost varied between R5.74 ± 7.63 and R9.70 ± R9.59. The minimum average cost of antimicrobials prescribed for mild/moderate dental abscess was R4.97 ± 5.35 and common cold had the highest average cost of antimicrobials prescribed at R9.70 ± R9.59.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic C were calculated. The d-values calculated (refer to Chapter 4, Section 4.4.4.2.3) shows that there was no practical significance differences found between the average costs of antimicrobial prescribed in individual diagnoses in Clinic C.

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic D will be illustrated in Table 5.43.

Table 5.43D: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic D

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Amenorrhoea	641	682.40	4.27	3.15	2.71	0.06	20.15
Common Cold	646	3061.52	4.97	3.17	4.57	0.03	32.53
Gastritis uncomplicated	527	399.23	3.95	2.98	2.67	0.54	14.55

Table 5.43D: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic D (cont)

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Upper respiratory infection	1680	7079.35	4.27	4.07	3.02	0	42.17
Follicular tonsillitis	809	5868.39	7.25	4.37	6.58	0	43.77
Acute bronchitis	1557	8357.73	5.39	3.36	4.57	0	36.19
Fibrositis	443	264.82	4.20	3.46	2.67	1.13	18.79
Gastro-Enteritis	409	1229.86	3.67	3.19	2.75	0	31.40

According to Table 5.437D, the minimum cost of antimicrobials prescribed in individual diagnosis was zero. The maximum cost of antimicrobials prescribed varied between R14.55 for gastritis uncomplicated and R43.77 for follicular tonsillitis. The average cost varied between R3.67 ± R3.19 and R7.25 ± R4.37. The diagnosis with the minimum average cost of antimicrobials prescribed was gastroenteritis at R3.67 ± R3.19 and follicular tonsillitis had the highest average cost of antimicrobials prescribed at R7.25 ± R4.37.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic D.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic D are shown in Table 5.43D$_1$.

Table 5.43D$_1$: Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic D

Diagnosis	Ameno-rrhoea	CC	Gastritis Un-Comp	URI	Follicular tonsillitis	Acute bronchitis	Fibrositis	GE
Ameno-rrhoea		0.22	0.10	0.00	0.68	0.33	0.02	0.19
Common cold.	0.22		0.32	0.17	0.52	0.13	0.22	0.41
Gastritis Un-comp	0.10	0.32		0.08	0.76	0.43	0.07	0.09
URI	0.00	0.17	0.08		0.68	0.28	0.02	0.15
Follicular tonsillitis	0.68	0.52	0.76	0.68		0.43	0.70	0.82
Acute bronchitis	0.33	0.13	0.43	0.28	0.43		0.24	0.09
Fibrositis	0.02	0.22	0.07	0.02	0.70	0.24		0.15
GE	0.19	0.41	0.09	0.15	0.82	0.09	0.15	

Abbreviations:
CC: Common cold
un –comp: uncomplicated
URI: upper respiratory infection
GE: gastro-enteritis

Difference of practical significance is d>0.8

According to Table 5.43D$_1$, the d-values calculated (refer to chapter 4, section 4.4.5.2.4) show that there were practical significant differences found between the average cost of antimicrobials prescribed in gastroenteritis and follicular tonsillitis with d-value 0.82. This means that the average

cost of antimicrobials prescribed in gastroenteritis was lower than the average cost of antimicrobials prescribed for follicular tonsillitis. This also reflects the high total cost and the number of antimicrobials prescribed for follicular tonsillitis as reflected in Table 5.47D. The antimicrobials prescribed for gastroenteritis were Co-trimoxazole 480mg and metronidazole, while phenoxymethyl penicillin 250mg was prescribed for follicular tonsillitis (refer to Clinic D, Table 5.35D).

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic E are illustrated in Table 5.43E.

Table 5.43E: The average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic E

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Viral Influenza	243	567.64	3.78	3.71	2.67	0	26.07
Acute Sinusitis	564	3354.57	6.02	3.36	5.13	0	33.73
Severe Sinusitis	373	2451.66	6.63	4.44	6.67	0.11	66.96
Upper respiratory infection	402	3085.75	7.91	7.11	4.66	0	61.00
Acute Bronchitis	292	1484.01	5.15	2.83	4.57	0.11	31.25
Gastro-Enteritis	354	656.45	2.77	2.92	1.87	0	29.01
Fibrositis	184	66.69	3.51	2.08	2.62	0.87	8.44
Gastritis : Uncomplicated	250	104.00	4.16	4.22	2.62	0	20.07

Table 5.43E shows that the minimum cost of antimicrobials was zero. The maximum cost varied between R8.44 for antimicrobials prescribed for fibrosis and R66.96 for antimicrobials prescribed for severe sinusitis. The average cost varied between R2.77 ± 2.92 and R7.91 ± R7.11. The diagnosis in which antimicrobials were prescribed at the minimum average cost was gastroenteritis. That was R2.77 ± R2.92 whereas antimicrobials prescribed for upper respiratory infection had the highest average cost of R7.91 ± R7.11.

Table 5.43E$_1$: Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed for individual diagnosis in Clinic E

Diagnosis	Viral influenza	Acute sinusitis	Severe Sinusitis	UTI	Acute bronchitis	GE	Fibrositis	Gastritis un-comp
Viral Influenza		0.60	0.64	0.58	0.37	0.27	0.07	0.10
Acute Sinusitis	0.60		0.14	0.27	0.24	0.90	0.69	0.44
Severe Sinusitis	0.64	0.14		0.18	0.33	0.87	0.70	0.59
UTI	0.58	0.27	0.18		0.21	0.39	0.49	0.59
Acute bronchitis	0.37	0.24	0.33	0.21		0.82	0.58	0.23
GE	0.27	0.90	0.87	0.39	0.82		0.25	0.33
Fibrositis	0.07	0.69	0.70	0.49	0.58	0.25		0.15
Gastritis un-comp	0.10	0.44	0.59	0.59	0.23	0.33	0.15	

Abbreviations:
UTI: upper tract infection
GE: gastroenteritis
Un-comp: uncomplicated

Difference of practical significance is d>0.8

According to Table 5.43E$_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were differences of practical significance found between the average cost of antimicrobials prescribed for gastroenteritis and severe and acute sinusitis and acute bronchitis with d-values of 0.90, 0.87 and 0.82 respectively. This means that the average cost and total costs of antimicrobials prescribed for gastroenteritis were lower than the average costs and total costs of antimicrobials prescribed for acute and severe sinusitis and acute bronchitis (refer to Table 5.44E). The antimicrobials prescribed for gastroenteritis were co-trimoxazole 480mg, while amoxycillin 250mg was prescribed for acute sinusitis; ampicillin 250mg prescribed for severe sinusitis and amoxycillin 250mg prescribed for acute bronchitis (refer to Clinic E, Table 5.34E).

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic F are demonstrated in Table 5.43F.

As illustrated in Table 5.43F, antimicrobials were prescribed at the minimum cost of zero. The maximum cost varied between R34.38 for antimicrobials prescribed for bronchopneumonia and R42.58 for antimicrobials prescribed for pelvic inflammatory disease. The average cost varied between R3.36 ± 4.31 and R16.21 ± R7.78. Antimicrobials were prescribed for gastroenteritis at the minimum average cost of R3.36 ± R4.31 and antimicrobials were prescribed for pelvic inflammatory diseases at the highest average cost of R16.21 ± R7.78.

Table 5.43F: The average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic F

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Pelvic inflammatory disease	518	8330.35	16.21	7.78	19.09	0	42.58
Upper respiratory infection	418	1809.74	4.44	5.01	3.62	0	35.94
Viral Influenza	876	3116.22	3.64	3.54	2.13	0	41.31
Acute Bronchitis	289	3049.66	3.89	3.28	2.62	0	35.68
Infection *bronchopneumonia*	289	1486.60	5.22	5.75	3.74	0.93	34.38
Gastroenteritis	516	1432.34	3.36	4.31	2.13	0	34.39
Weakness	276	1012.87	6.75	8.14	3.74	0	35.60

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed for individual diagnosis in Clinic F are illustrated in Table $5.43F_1$.

According to Table $5.43F_1$, the d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) show that there were practical significant differences found between the average costs of antimicrobials prescribed for pelvic inflammatory diseases and the rest of the individual diagnoses. This means that the average cost and total cost of antimicrobials prescribed for pelvic inflammatory diseases were higher than the average costs of antimicrobials prescribed for other individual diagnoses.

As indicated in Table 5.30F$_1$, doxycycline was the most frequently antimicrobial prescribed for pelvic inflammatory disease.

Table 5.43F$_1$: Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed for individual diagnosis in Clinic F

Diagnosis	PID	URI	Viral influenza	AB	Broncho-pneumonia	GE	Weakness
PID		1.51	1.62	1.58	1.41	1.65	1.16
URI	1.51		0.16	0.11	0.14	0.22	0.28
Viral influenza	1.62	0.16		0.07	0.27	0.06	0.38
Acute bronchitis	1.58	0.11	0.07		0.23	0.12	0.35
Broncho-pneumonia	1.41	0.14	0.27	0.23		0.32	0.19
Gastro-enteritis	1.65	0.22	0.06	0.12	0.32		0.42
Weakness	1.16	0.28	0.38	0.35	0.19	0.42	

Abbreviations:
PID: pelvic inflammatory disease
GE: gastroenteritis
URI: upper respiratory infection
AB: acute bronchitis
Difference of practical significance is d>0.8

The average, minimum and maximum cost of antimicrobials prescribed for individual diagnosis in Clinic G are illustrated in Table 5.43G.

Table 5.43G: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic G

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Severe dental abscess	472	1300.72	4.53	4.46	3.04	0	50.49
Upper respiratory infection	306	1161.11	3.88	3.84	3.48	0	51.26
Viral Influenza	368	1276.56	4.16	2.64	3.59	0.03	27.03
Acute Tonsillitis	221	1048.46	4.83	2.44	4.31	0.03	15.77
Common Cold	238	814.52	3.88	2.30	3.00	0.02	16.47
Acute bronchitis	330	1564.75	4.79	3.71	4.50	0.02	49.68

As shown in Table 5.43G, the minimum cost of the antimicrobials in individual diagnosis was zero. The maximum cost for antimicrobials prescribed for individual diagnoses between R15.77 and R51.26 for antimicrobials prescribed for upper respiratory infection. The average cost varied between R3.88 ± 3.84 and 2.30 for upper respiratory infection and common cold respectively and R4.83 ± R2.44 for acute tonsillitis.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed for individual diagnosis in Clinic G were calculated. The d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there was no difference of practical significance found between the average cost of antimicrobials prescribed for the different diagnoses in Clinic G.

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic H are illustrated in Table 5.43H.

Table 5.43H: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic H

Diagnosis	N	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Severe dental abscess	235	610.59	3.18	2.36	3.06	0	33.05
Upper respiratory infection	816	2389.89	4.16	4.53	3.00	0	47.11
Viral influenza	661	1839.19	4.49	4.69	3.20	0	40.41
Tonsillitis	242	1220.18	5.04	3.10	4.57	0	28.78
Common Cold	456	1808.84	4.17	3.41	3.02	0.03	40.41
Acute bronchitis	431	2565.21	6.08	6.58	4.49	0	40.41
Gastroenteritis	276	414.22	2.84	4.67	1.87	0.01	32.20

As illustrated in Table 5.43H, the minimum cost of antimicrobials prescribed for individual diagnosis was zero. The maximum cost varied between R28.78 for tonsillitis and R47.11 for upper respiratory infection. The average cost varied between R2.84 ± 4.67 and R6.08 ± R6.58. The diagnosis for which antimicrobials were prescribed at the minimum average cost was gastroenteritis at 2.84 ± R4.67 and acute bronchitis acute had the highest average cost of antimicrobials prescribed at R6.08 ± R6.58.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed for individual diagnosis in Clinic H were calculated. The d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there was no difference of practical significance found between the average cost of antimicrobials prescribed for the different diagnoses in Clinic H.

The average, minimum and maximum cost of antimicrobials prescribed in individual diagnosis in Clinic I are demonstrated in Table 5.43I.

Table 5.43I: Average, minimum and maximum cost of antimicrobials prescribed for the top ten individual diagnoses in Clinic I

Diagnosis	Total cost (R)	Average (R)	Standard deviation (R)	Median (R)	Minimum (R)	Maximum (R)
Uncomplicated atopic dermatitis	1844.95	10.42	14.33	7.15	0.11	175.50
Uncomplicated gastritis	2584.69	7.83	12.71	4.26	0.48	175.50
Acute Sinusitis	7606.48	9.98	9.36	7.09	0.09	63.75
Acute bronchitis	13769.04	11.55	19.89	5.49	0	175.50
Viral Influenza	1037.74	4.24	3.75	3.23	0.06	34.97

Table 5.43I reveals that the minimum cost of the antimicrobials was zero. This was prescribed acute bronchitis. The maximum cost varied between R34.97 for antimicrobials prescribed for viral influenza and R175.50 for antimicrobials prescribed for uncomplicated atopic dermatitis, uncomplicated gastritis and acute bronchitis. The average cost varied between R4.24 ± 3.75 for antimicrobials prescribed for viral influenza and R11.55 ± R19.89 for antimicrobials prescribed for acute bronchitis.

Statistical d-values as indication of practical significance differences between the average costs of antimicrobials prescribed in individual diagnosis in Clinic I were calculated. The d-values calculated (refer to Chapter 4, Section 4.4.5.2.4) showed that there was no difference of practical significance found between the average cost of antibiotics prescribed for the different diagnosis in Clinic I.

SUMMARY OF THE RESULTS OF ALL CLINICS

From the results of the nine clinics it was evident that differences of practical significance were observed between the average costs of antimicrobials prescribed for the different diagnoses. These differences were observed in diagnoses where average costs of antimicrobials prescribed were highest. For example, pelvic inflammatory disease for which doxycycline 100mg was prescribed, otitis media in which co-trimoxazole 480mg was prescribed. The others were: follicular tonsillitis for which phenoxymethyl penicillin 250mg were prescribed, acute sinusitis, severe sinusitis and acute bronchitis, for which amoxycillin 250mg was prescribed.

5.8 CHAPTER SUMMARY

In this chapter the results of the empirical study of the nine clinics were discussed in terms of: demographic information of patients of each clinic, consultation information, regarding medicine items prescribed in each clinic. This chapter also discussed specific information about antimicrobials and information regarding the types of disease states as well as their treatments in each clinic. It also dealt with information on costs of antimicrobials.

Conclusions and recommendations will be discussed in Chapter 6.

CHAPTER 6 CONCLUSIONS AND RECOMMENDATIONS

The conclusions and recommendations will be based on the discussions of the results of the specific objectives of the literature reviewed and the empirical investigation that was conducted.

6.1 LITERATURE REVIEW

The specific objectives of the literature review will be discussed in sections 6.1.1 to 6.1.5

6.1.1 The usage and prescribing patterns of antimicrobials (irrational and cause)

The first objective of the literature review was to investigate the usage and prescribing patterns of antimicrobials in the literature.

It was established from the literature review that antimicrobials are one of the most commonly used categories of drugs in modern medicine. As a result they tend to be overused globally (Chang *et al.*, 1999: 23). The increasing overuse of these agents significantly contributes to the enormous hospital expenditure on drugs and account for 15% to 30% of the total worldwide health budget (Rehana *et al.*, 1998: 175).

Hooton and Levy (2001: 1088) reported in a study that 20% to 50% of antibiotic prescriptions in community settings were believed to be unnecessary. The irrational use of these agents could be attributed to the use of multiple antimicrobials, non-use of first choice antimicrobials on the basis of provisional diagnosis, and the use of irrational and unnecessary antimicrobials. There is empirical evidence confirming the use of antimicrobials without corroborative culture and sensitivity (Das *et al.*, 2002: 59). Therefore educational programmes and careful assessment of inappropriate prescribing and a search for more cost-effective treatment strategies are urgently required.

6.1.2 Antimicrobial resistance and its causes

The second objective of the literature review was to determine what antimicrobial resistance is and its causes.

Antimicrobial resistance occurs when microbes adapt to survive the use of medications meant to kill or weaken them – making the infection more difficult or even impossible to treat.

Someone infected with a germ that is resistant to a certain medicine can pass on that resistant microbe to others, allowing a hard-to-treat illness to spread from person to person. It is the germ itself – not the person who is infected - that develops a resistance to specific drugs (Department of Health and Human Services, 2001).

It was established from the literature reviewed that overuse or "inappropriate" use of antimicrobials is a risk factor for the emergence of antimicrobial resistant bacteria (Naidoo & Wilson, 2004: 200; Von Gottberg, 2004: 189; Crew-Brown *et al.*, 2004: 441; Hooton & Levy, 2001: 1088; Hemming & Harvey, 1999: 1). Factors that contribute to the spread of antimicrobial resistance are: doctors prescribing antibiotics too frequently or inappropriately, patients not completing the prescribed course of an antibiotic, making it more likely that surviving microbes will contribute to the emergence of resistant germs that can infect people and through international trade and travel, resistant microbes can spread quickly worldwide. There is a need to monitor accurately the spread of resistance, limiting this by appropriate antimicrobial usage, infection control strategies, and surveillance data to be returned timeously to the prescribers and the committees that formulate treatment guidelines.

6.1.3 **Infectious diseases and treatment thereof**

The third objective of the literature review was to investigate infectious diseases and treatment thereof.

The literature survey revealed that in developing countries there is a high incidence of infectious diseases that are caused by a multitude of micro-organisms which can either be bacterial or viral and these are the leading causes of patients' trips to the doctors' clinics (Liu, 1999: 539). In South Africa infectious diseases account for at least 14 % of potential years of life lost and perinatal conditions contribute 17% (Bourne as quoted by Bloom & McIntyre, 1998: 1529). These conditions are due to poor living conditions and inadequate basic health services. It has been documented in the existing literature on the subject that respiratory tract infections are one of the commonest reasons for a visit to a family physician. Consequently many consultants ultimately are led to an antibiotic prescription (Naidoo & Wilson, 2004: 200). Antimicrobial agents commonly used to treat viral respiratory tract infections do not shorten the course of acute illness nor prevent secondary bacterial infections. As stated by Ochoa *et al.* (2000: 73) the excessive and inappropriate use of antibiotics in viral respiratory tract infections leads to antibiotic resistance

among the respiratory tract pathogens and adds an unnecessary economic burden to the health care system.

6.1.4 Primary health care, its aims and objectives

The fourth objective of the literature review was to conceptualise primary health care, its aims and objectives and its application to antimicrobials.

Primary health care is an essential care based on practical, scientifically sound and socially accepted methods and technology, made universally accessible to individuals and families in their community through their full participation at a cost that the community and country can afford.

The aim of primary health care is to address the main health problems in the community, by addressing the socio-economic causes of poor health and making provision for basic health needs by providing promotive, preventive, curative and rehabilitative services accordingly.

The South African Institute of Medical Research expressed concerns on antibiotic use in communities. The report stated inappropriate prescribing of antibiotics in terms of unknown optimal doses and duration of therapy of many infections (Bell, 2004: 2). There is need to educate both doctors and patients about the appropriate use of antibiotics.

6.1.5 Managed health care, disease management, pharmacoepidemiology, pharmacoeconomics and utilisation studies as applied to antimicrobials

The fifth objective was to conceptualise managed health care, disease management, pharmacoepidemiology, pharmacoeconomics and drug utilisation studies as applied to antimicrobials.

As established from the literature reviewed managed care within the South African context is a diverse range of healthcare organizational strategies aimed at controlling cost, improving access and assuring higher levels of quality of care provided to those covered by medical scheme (Council for medical schemes, 2004).

The literature reviewed suggests that disease management is a thorough analysis of a particular disease process that may include its prevention, treatment, and follow-up care approaches to the provision of ongoing, cost-effective, and clinically efficacious care. Wert (1996: 1368) reported

the application of disease management programmes in antimicrobial use. In the light of the findings there is need to shift attention back to first-line antibiotics in the treatment of infectious diseases.

Pharmacoepidemiology, as presented in medical literature, is the study of the use and effects of drugs in large numbers of people and its need is increasing exponentially both in developed and developing countries. Pharmacoepidemiological methods used in evaluating how drugs like antimicrobials are being prescribed and used are experimental and observational, and these methods may be used as part of a quality assurance programme (Truter, 1999: 56).

As an important application of pharmacoepidemiology, drug utilisation is the marketing, distribution, prescription, and use of drugs in society, with special emphasis on the resulting medical, social, and economic consequences. Drug utilisation reviews are used to analyse and interpret the patterns of drug use in a given healthcare delivery system in relation to explicitly predetermined criteria, guidelines or standards. For example in promoting rational prescribing of optimal antibiotic therapy, ensuring high-quality patient care, curtailing the development of resistant strains of bacteria and controlling cost (Hoppe, 1996a: 552).

It was also noted from the literature reviewed that pharmacoeconomics is the second important application of pharmacoepidemiology. It is the area of health care research that evaluates and compares the costs and outcomes associated with drug therapy, and play an increasingly important role in making decisions concerning options regarding drug therapies and pharmaceutical services. The pharmacoeconomics of antibacterial treatment is a decision making tool which enables the practitioner to prescribe the right antibiotic therapy to the right patient, at the right time (Beresniak & Bouvenot, 2000: 133).

6.2 EMPIRICAL REVIEW

The specific objectives of the empirical review will be discussed in sections 6.2.1 to 6.2.7

6.2.1 Demographic information of patients (age, gender distribution)

The first objective of the empirical review was to determine the prevalence of patients who received antimicrobials in a private primary health care setting during the research period.

The total number of patients who visited the nine clinics was 83655 (refer to Section 5.1.1, Table 5.1). The gender distribution was 59.50% females and 40.22% males. In 0.28% of the cases reported gender not indicated .The age group distribution of patients was illustrated in Table 5.3, Section 5.1.2. The age group 6 (older than 20 years and younger than 40 years) and 7 (older than 40 years and younger than 60 years) represented the highest number of patients of 65.72% (n = 54964) that visited the nine clinics. The age group with the smallest number of patients was 1 (0 – 1 month). The average age of patients varied between 25.7 ± 19.75 years for patients in Clinic A and 33.20 ± 20.31 years for patients in Clinic I (refer to Section 5.1.4, Table 5.4). There was no difference of practical significance observed between the average ages of patients from the different clinics (refer to Section 5.1.4).

A total of 132585 consultations were made by 83655 patients that visited the nine clinics during the one-year research period (refer to Section 5.2.1, Table 5.6). Clinic B had the highest number of consultations per patient standing at a ratio of 2.46 consultations per patient (refer to section 5.2.1, Table 5.7). Of this number of consultations made during that period (59.93%), were made by female patients and only (39.66%) of that number of consultations was made by male patients. No gender was indicated in 0.41% of the recorded cases (refer to Section 5.2.3, Table 5.8). Age group 6 (20-40 years) came out as the highest number of consultations made in all the nine clinics. This is the most economic and active age group that could afford to visit the private primary health clinics. Age group 1 (0-1 month) came out as the smallest number of consultations (refer to Section 5.2.5, Table 5.10).

The total number of medicine items prescribed to patients per consultation in the nine clinics was 515976 (refer to Section 5.3.1, Table 5.12).The average number of medicine items prescribed per consultation in the nine clinics varied between 3.24 ± 1.39 medicine items for Clinic H and 4.72 ± 1.87 medicine items for Clinic I. The maximum number of medicine items prescribed during one consultation was 19 relating to patients in Clinic D (refer to Section 5.3.2, Table 5.13 and Section 5.3.3, Table 5.15). There were differences of practical significance observed between the average number of medicine items prescribed per consultation in Clinics H and E, G and F and H and F. This means that the average number of medicine items prescribed per consultation in Clinic F was practically and significantly higher than those prescribed in Clinic G and H (refer to Section 5.3.2, Table 5.14 and Section 5.3.3, Table 5.15).

6.2.2 **Specific information about antimicrobials.**

The second specific objective of the empiric review was to determine the prevalence of prescriptions of antimicrobials as well as the total costs associated with such prescriptions in a private primary health care setting.

Antimicrobials were prescribed to approximately 65% of all patients that visited the nine clinics during the research period (refer to Section 5.4.1, Table 5.17). The antimicrobials represented 18.69% (n = 96421) of the total number of medicine items prescribed during the research period (refer to Section 5.4.2, Table 5.18). The average number of antimicrobials prescribed per patient consultation (visit) varied between 1.17 ± 0.48 for patients in Clinic H and 1.54 ±0.43 antimicrobials prescribed to patients in Clinic B (refer to Section 5.4.3, Table 5.19). The maximum number of antimicrobials prescribed was six (only one case) and the minimum number of antimicrobials was one antimicrobial (refer to Section 5.4.3, Table 5.16 and Section 5.4.3, Table 5.19). There was a significant difference observed between the average number of antimicrobials prescribed per consultation in Clinics H and F. This implies that the average number of antimicrobials prescribed per consultation to patients in clinic H was the lower than those of Clinic F (refer to Section 5.4.3, Table 5.20).

In all the nine clinics, age group 6 (20 – 40 years) received the highest number of antimicrobials, accounting for 47.21% (n = 45420) of the total number of antimicrobials prescribed according to age groups. In all the nine clinics, there was no difference of practical significance observed between the numbers of antimicrobials prescribed according to the different age groups in the nine clinics.

The most prescribed antimicrobial according to pharmacological group was penicillins accounting for 39.35% (n = 36808), followed by sulphonamides with 23.18% (n = 21687). The total cost of all antimicrobials prescribed in the nine clinics was R1 045 108.00. The maximum cost of the antimicrobials varied between R37.44 for antimicrobials prescribed in Clinic A and R343.05 for antimicrobials in Clinic C. The average cost of antimicrobials varied between R4.18 ± 5.10 for antimicrobials prescribed to patients in Clinic A and R7.86 ± 17.52 for antimicrobials prescribed to patients in Clinic I (refer to Section 5.6.3, Table 5.37). There was no difference of practical significance observed between the average costs of all antimicrobials prescribed in the

nine clinics during the research period. This could perhaps strengthen the allegations of general misuse of antimicrobials across the board and not only by certain clinics.

6.2.3 The influence of age on the prescribing of antimicrobials in a private primary health care setting

The forth objective of the empirical study was to investigate the influence of age on the prescribing of antimicrobials in a private primary health care setting.

The results revealed that the highest number of antimicrobials was prescribed to patients in age group 6 (20-40 years) on the one hand. On the other hand, patients in age group 1 (0-1 month) received the least number of antimicrobials. This significant difference in the studied prescriptions may be attributed to the fact that patients in age group 6 (20-40 years) are the most econonomically active groups of patients. This group of patients could afford to come to the private primary health care clinics. The most antimicrobial prescribed according to age group was penicillin followed by sulphonamides. The most frequent individual antimicrobials prescribed to age group 6 (20-40 years) were amoxycillin 250mg, co-trimoxazole 480mg, doxycycline 100mg, metronidazole 200mg and ampicillin 250mg. Antimicrobials less prescribed according to pharmacological and age group were cephalosporins, aminoglycosides, and chloranmphenicols. This was influenced by the types of disease states presented by patients. Quinolones and tetracyclines were not prescribed to patients in age groups 1 to 3 (0-1 month to 1 year–6 years) because these antimicrobials are contraindicated in patients with these age groups.

6.2.4 The influence of gender on the prescribing of antimicrobials in a private primary health care setting.

The forth objective of the empirical review was to investigate the influence of gender on the prescribing of antimicrobials in private primary health care setting

The prescribing of antimicrobials according to gender was such that female patients received more antimicrobials with n = 33874 (60.764%) and males received 21786 (39.24%). The average number of antimicrobials prescribed per gender varied between 1.18 ± 0.48 and 1.33 ± 0.64 antimicrobials prescribed to females. The average number of antimicrobials prescribed to males varied between 1.09 ● 0.32 and 1.95 ± 1.12 antimicrobials. There was no difference of practical significance found between the average numbers of antimicrobials prescribed for males and females in the nine clinics. Male patients received less prescriptions of antimicrobials (39.24%) as

compared to female patients with 60.76%. The evidence gathered showed that males received (21786) 39.24% of the total number of antimicrobials prescribed according to pharmacological and gender groups.

The most prevalent antimicrobial prescribed according to pharmacological group and gender was penicillins (n = 23989, 43.03%) of which females received 14363 (59.87%) and males received 9626 (40.13%) (refer to Section 5.4.9, Table 5.27). From this study it can be deduced that since the gender distribution in the nine clinics is such that there were more females than males, inevitably females received the higher number of antimicrobials than the males.

6.2.5 Antimicrobials prescribed in the different medical conditions or disease states and their costs for the different diagnoses

The fifth objective of the empirical review was investigate antimicrobials prescribed in the different medical conditions and their costs for the different diagnoses

The total number of medical conditions or disease states diagnosed in the nine clinics was 140723 (refer to Section 5.5, Table 5.32). The clinic with the highest number of disease states recorded was Clinic D. The most frequent disease states presented in patients that visited the nine clinics are summarised in Table 5.33.

One form or another of a respiratory tract infection was one of the top five disease states. These were: upper respiratory infection, viral influenza, acute bronchitis, common cold, cough, acute sinusitis. The ten most diagnosed disease states and individual antimicrobials prescribed for them in the nine clinics are summarised in Tables 5.34 (A-I). In all the respiratory tract infections antimicrobials were prescribed. This could indicate overuse and inappropriate use of antimicrobials because many of these infections are caused by viruses or other nonbacterial agents, and thus are self-limiting, therefore the use of antibiotic courses are neither necessary nor appropriate in these conditions.

The variations in the management of these infectious diseases could be attributed to the following factors: difficulty of diagnosing by doctors bacterial versus viral aetiology, difficulty of predicting bacterial complications in viral infections; variability in medical knowledge; psychosocial factors involved in medical decision making; and lack of simple and clear recommendations for the dose and treatment duration.

The highest medicine cost was for penicillin accounting for 37.76% (n = R188 918.50) of the total cost of antimicrobials prescribed according to pharmacological groups in the clinics (refer to Section 5.6.4, Table 5.38).

The average costs of the top ten individual antimicrobials prescribed to patients in the nine clinics is illustrated in Tables 5.40 (A – I). From the tables it could be summarised that there were practical significant differences observed between the average costs of the following antimicrobials: erythromycin 250mg, erythromycin 125mg, enoxacin 200mg, metronidazole 200mg and amoxycillin 250mg/clavulanic acid 125mg in comparison with the following drugs: co-trimoxazole 480mg, co-trimoxazole 240mg/5ml, amoxycillin 250mg, amoxycillin 125mg/5ml, ampicillin 250mg, doxycycline 100mg, metronidazole 400mg, phenoxymethyl penicillin 250mg and phenoxymethyl penicillin 125mg/5ml. It can therefore be concluded that these drugs had the highest average cost of all antimicrobials prescribed in the clinics. From the results a prediction can be made of the use of newer, more expensive and broader-spectrum drugs such as enoxacin, amoxycillin/clavulanic acid, replacing the older, cheaper, effective and available drugs such as ampicillin, amoxycillin and co-trimoxazole. Such trends increase health care costs and lead to antimicrobial resistance (Lesar & Briceland, 1996: 31).

The average costs of antimicrobials prescribed according to gender are shown in Tables 5.41 (A – I). From the tables the following antimicrobials had the highest average costs: erythromycin 250mg, enoxacin 200mg, metronidazole 400mg, norfloxacin 400mg and amoxycillin/clavulanic acid. There were no differences of practical significance found between the average costs of antimicrobial prescribed according to gender in the nine clinics.

The average costs of antimicrobials prescribed according to age groups are illustrated in Tables 5.42 (A–I). The minimum average costs corresponded to antimicrobials prescribed to patients in age groups 1 to 4. The patients in these age groups received the minimum number of antimicrobials (refer to Section 5.7.3, Clinics (B-I), Tables 5.42 (B-I)) . The maximum average costs corresponded to antimicrobials prescribed to patients in age groups 6 (20-40 years) for these patients received the maximum number of antimicrobials ((refer to Section 5.7.3, Clinics (B-I), Tables 5.42 (B-I)). There were practical significant differences observed between the average costs of individual antimicrobials prescribed for patients in age groups 3 and 4 and patients in age groups 6 or 7. Therefore the average costs of antimicrobials prescribed for patients in the lower

age groups were the lowest as compared to the average costs of antimicrobials prescribed for patients in higher age groups.

6.2.6 The prescribing of antimicrobials and their costs for the different diagnoses

The sixth objective of the empirical review was to investigate the prescribing of antimicrobials and their costs for the different diagnoses.

The ten most prescribed antimicrobials in the nine clinics during the research period were: amoxycillin 250mg, co-trimoxazole 480mg, doxycycline 100mg, erythromycin 250mg, metronidazole 200mg, co-trimoxazole 240mg/5ml, ampicillin 250mg, amoxycillin 125mg/5ml, metronidazole 400mg and phenoxymethyl penicillin 250mg (refer to Table 5.31).

The average costs of antimicrobials prescribed for the top ten individual diagnoses are illustrated in tables 5.43 (A – I). The diagnoses with the minimum average costs of antimicrobials were: upper respiratory infection, viral influenza and gastroenteritis. The diagnoses with the highest average cost of antimicrobials were pelvic inflammatory disease, urinary tract infection, otitis media, common cold, follicular tonsillitis, acute bronchitis, and acute and severe sinusitis. There were differences of practical significance found between the average costs of antimicrobials used in individual diagnoses presented with patients in the different clinics.

6.2.7 Antimicrobial usage according to the standard treatment guidelines and essential drug list for South Africa.

The seventh objective of the empirical review was to determine antimicrobial usage according to the standard treatment guidelines and essential drug list for South Africa.

It was established from the results chapter that most prescribers in private primary health do not follow the treatment guidelines of some diseases diagnosed to their patients. There is a lot of prescribing of antibiotics in respiratory tract infections like the common colds, acute bronchitis, viral influenza, acute sinusitis and otitis media. According to the Standard Treatment Guidelines and Essential Drugs List for Primary Health Care in South Africa 2003, antibiotics are not recommended for the treatment of viral diseases. Therefore, it is considered that the following as inappropriate indications for antibiotics: non-specific upper respiratory infection, the common cold, acute bronchitis, acute sinusitis, viral influenza and otitis media (unless there is a possibility of secondary infection). There are factors other than clinical condition that influence antibiotic

prescribing. Such factors include lack of certainty of diagnosis, heavy workload and inadequate time for each patient, fear of litigation for not treating a bacterial infection, the belief that antibiotics are innocuous, social and psychological characteristics of the patient, and perceived pressure from patients to prescribe (Wang *et al.*, 1999: 159).

6.3 LIMITATIONS OF THE STUDY

The following limitations of the study must be considered when evaluating the results and conclusions:

- It was difficult to identify from the database the specific antimicrobials that were prescribed for specific diseases especially in cases where the patients presented with multiple diagnoses including chronic diseases like hypertension, osteoarthritis, and antenatal follow-ups at the time of the visit. Therefore, it was assumed that the diagnostic code accurately reflected the infection most likely to be of bacterial origin. The kind that is likely to respond to antibiotics.
- The previous reason describe the problem with multiple diagnoses – different codes were provided but it was not possible to differentiate on the database which drug was prescribed for which diagnoses.
- There was no direct manipulation of the data by the researcher since the data were obtained directly from the central database. It was assumed that all diagnoses, drugs and costs on the database were considered to be correct.
- The combined data of the nine clinics collectively was not possible to obtain because the nine clinics are located in different geographical areas of South Africa.
- The patterns of antimicrobial utilisation were determined after the antimicrobials had been dispensed, therefore no interventional activities were done.
- Certain information of patient history (e.g. smoking and drinking habits, occupation and sport involvement) was not included in the database and could be considered in the analysis.
- It was assumed that physicians' diagnoses and protocols on the database were correct and accurate. Physians may diagnose certain conditions as bronchitis, sinusitis, or otitis media to justify antibiotic prescriptions. This would lead to an underestimate of inappropriate antimicrobial prescribing.
- Seasonal variations were not evaluated in the occurrence of respiratory tract infections.

- ♠ The research performed in this study was limited to the medicine treatment costs and did not include tests (e.g. culture tests) and procedures performed.

6.4 RECOMMENDATIONDS

Based on this study the following recommendations aimed at improving appropriate prescribing of antimicrobials and thereof management of infectious diseases in private primary health care settings in South Africa are made:

- ♥ Physicians in private primary health care settings should be familiar with the clinical situations in which they should provide antibiotics and those in which such drugs need not be prescribed.
- ♥ Physicians should understand the motivations of patients who are seeking antibiotics and wisely provide education, empathy and alternative treatments.
- ♥ The physician should address the social aspects of the illness and explain to the patient that antibacterial drugs are not effective in viral infections and emphasize that those unnecessary antibiotics can be harmful in several ways. They should also educate patients on simple measures that may reduce transmission of infection in the household and community, such as hand washing, food hygiene, etc. and the importance of preventative measures, such as immunizations.
- ♥ An infectious disease consulting service to evaluate and improve antibiotic prescription patterns in private primary health care settings in South Africa should be established.
- ♥ Standard Treatment Guidelines for the most common bacterial infectious in primary health care settings be implemented, with recognition of the existence of the potential obstacles to rational antibiotic prescribing.
- ♥ Finally, the physician should actively manage symptoms with analgesics, antipyretics and decongestants, where appropriate.

The following recommendations for further research can be formulated:

- ♣ Perform studies on the factors that influence antibiotic prescribing in private primary health care settings in South Africa.
- ♣ Perform studies on antibiotic resistance in primary health care settings.
- ♣ Carry on a prospective study on antimicrobial use and thereafter interventional strategies accordingly depending on the results.

- ♣ Conduct studies to investigate the seasonal variation in the occurrence of respiratory tract infections.
- ♣ Perform studies on the prescription patterns of antimicrobials and prescribing behaviours of the physicians in private primary health care settings in South Africa.

6.5 CHAPTER SUMMARY

This chapter focused on the conclusions drawn from the findings of this study. Given such findings, this chapter inter alia presented recommendations aimed at improving management of infectious diseases in private primary health care practice (refer to Section 6.4). In addition, this chapter presented some of the limitations (refer to Section 6.3) the researchers encountered in pursuit for answers the study sought to provide to the identified problem in primary health care practice. Lastly, the chapter suggested possible issues for further research in this section. Thereby the objectives of this study were met and discussed.

ABSTRACTS ACCEPTED FOR PRESENTATIONS AT CONFERENCES FOR YEARS 2003 AND 2004

Usage of Antimicrobial Agents in a Private Primary Health Care Setting : A drug Utilisation Study.

N L Katende-Kyenda[1], M S Lubbe[2], J H Serfontein[3], and I Truter[4]

Dept of Pharmacology, University of Transkei[1]; Pharmacy Practice, University of Potchefstroom[2-3] ; Dept of Pharmacy, University of Port Elizabeth[4]. South Africa. (E-mail: Kyendanorah@yahoo.com)

Background and Aim: Antimicrobials are most commonly prescribed, contributing significantly to the cost of drugs and are claimed worldwide to account for 15 to 30% of total health budget (Harmeet S R et al, 1998), yet usage of these agents in a private primary health care setting is unknown. The aim of this study was to investigate antimicrobial usage in a private primary health care setting in South Africa. **Methods:** A retrospective, non-experimental quantitative method was used. Data were obtained from a central database of a private primary health care service provider. Antimicrobials were classified according to their pharmacological groups. The study population consisted of all patients who visited the clinic (N=11968) for a period of 1 year, from 1st January – 31st December 2001. Antimicrobial usage was analyzed according to : number of patients, consultations, age groups, gender, diagnosis and cost of treatment. **Results:** The results of the study revealed that the total medicine items prescribed were 46817 at a total cost of R 127813. Of these, antimicrobials represented 20.9% (N = 9785) at a cost of R 40858 (31.97%). The total number of consultations (N = 11968) of which antimicrobials were prescribed accounted for 68.9% (N = 8255). The most prescribed antimicrobials were sulfonamides N = 4104 (41.94%) at a cost of R 8514 (20.84%). The most important diagnoses (N = 13668) where antimicrobials were prescribed were: Upper respiratory infection, Viral: Influenza, Antenatal: U.T.I cystitis, Antenatal follow-up, Pelvic Inflammatory Disease and Infection: Bronchitis: Acute. **Conclusions:** High incidence of consultations where antimicrobials were prescribed could indicate excessive use of these agents in a private primary health care setting. It is recommended that further investigation on the prescribed protocols of antimicrobials be done.

Are Antimicrobials Appropriately Used in Private Primary Health Care Settings In South Africa?

N L Katende-Kyenda*[1], M S Lubbe[2], J H Serfontein[3], and I Truter[4]
*Dept of Pharmacology, University of Transkei[1]; Pharmacy Practice, Potchefstroom University[2-3]; Dept of Pharmacy, University of Port Elizabeth[4], South Africa (e-mail: Kyendanorah@yahoo.com)

The aim of this non-experimental, quantitative, retrospective study was to determine if antimicrobials were used appropriately in different diagnoses in six private primary health care clinics.
Data were obtained from a central database of a private primary health care provider. The study population consisted of all patients (N=55463) who visited the six clinics situated in different geographical areas of South Africa, from 1st January-31st December 2001. Antimicrobial usage was analyzed according to: number of patients, age, gender, disease states, pharmacological groups and treatment cost.
A total of 220927 medicine items costing R1115691 were prescribed, of these, 18% (N=38670) were antimicrobials costing 30% (R329568). The total number of diagnoses (76634), where antimicrobials were prescribed accounted for 76% (N=58168). The most frequently used antimicrobials according to pharmacological groups were: Penicillins(39.2%), Sulphonamides(28.8%), Tetracyclines(8%), and Anti-protozoals(2%). The commonest diagnoses where antimicrobials were prescribed were:

Diagnosis	Frequency of diagnoses (N=76634)	Antimicrobials Prescribed	Cost of antimicrobial treatment (R329568)
Viral influenza	4.4%(n=3410)	Penicillins, Sulphonamides	2.8%(R9312)
URT	4.2%(n=3225)	Penicillins, Sulphonamides	3.6%(R11842)
Bronchitis;Acute	2.4%(n=1886)	Penicillins, Sulphonamides	2.4%(R7832)
PID	1.1%(n=870)	Cephalosporins	3.2%(R10688)

Antibiotics have no primary effect against viral diseases such as Influenza, and don't significantly shorten the duration of illness in Acute Bronchitis. The study recommends further investigation on standard treatment guidelines and antimicrobial guidelines.

ANTIMICROBIAL USAGE IN DIFFERENT AGE GROUPS IN PRIVATE PRIMARY HEALTH SETTINGS IN SOUTH AFRICA

[1]Katende-Kyenda N L, [2]Lubbe M S, [3]Serfontein J H P and [4]Truter I.
Dept of Pharmacology, University of Transkei[1]; Pharmacy Practice, North West University[2-3]; Dept of Pharmacy, University of Port Elizabeth[4]. South Africa. (E-mail: Kyendanorah@yahoo.com)

Aim
The aim of this retrospective, drug-utilization study was to analyze antimicrobial usage in different age-groups in private primary health care settings in South Africa.

Methods
Data were obtained from a central database of a private primary health care group. The study population consisted of all patients (N=83655) who visited nine clinics situated in different geographical areas of South Africa, from 1st January to 31st December 2001. Antimicrobial usage in different age groups was analyzed according to: number of patients, gender, pharmacological groups, diagnoses, dosages and cost of treatment.

Results
A total of 515976 medicine items costing R1 716 318.90 were prescribed. Of these, 18.69% (n=94008) were antimicrobials costing 60.89% (R1 045 108.00). Of the total number of patients, 65.34% (n=54663) were prescribed antimicrobials. The most frequently used antimicrobials according to pharmacological groups were: Penicillins (39.46%) and Sulphonamides (23.25%). The commonest diagnoses for antimicrobials prescribing according to age-groups were: upper respiratory infection (0-1month & >6yrs-12yrs), acute bronchitis (>1month-1yr; >1yr-6yrs; >20-40yrs; >40-60yrs & >60yrs and over) and Viral Influenza (>12-20yrs).

Conclusions
Antimicrobial use in non-bacterial infections indicate misuse of antimicrobials that could result in an increase of bacterial resistance to antibiotics, various side-effects and increasing costs without impacting positively on patient outcomes. The study recommends improvement in prescribing habits in order to reduce unnecessary usage of antibiotics.

The Influence of Age on the Prescribing and Cost of Antimicrobials in Private Primary Health Care Setting in South Africa.

Norah L Katende-Kyenda*[1], Martie S Lubbe[2], J H P Serfontein[3], and Ilse Truter[4].

[1]Dept of Pharmacology, University of Transkei; [2-3]Pharmacy Practice, North West University; [4]Dept of Pharmacy, University of Port Elizabeth, South Africa

Aim:

The aim of this non-experimental, quantitative, retrospective study was to determine the influence of age on the prescribing and cost of antimicrobials in nine private primary health care clinics.

Methods:

Data were obtained from a central database of a private primary health care service provider. The study population consisted of all patients (N=83655) who visited the nine clinics situated in different geographical areas of South Africa, from 1st January – 31st December 2001.Antimicrobial usage was analysed according to: the number of patients, age, gender, disease states, pharmacological groups and treatment costs.

Results:

A total of 515976 medicine items costing R1 716 318.90 were prescribed, of these, 18.69%, (N=96423) were antimicrobials costing 60.89%, (R1 045 108.00). Of the total number of patients that visited the nine clinics, 65.34% (N=54663) were prescribed antimicrobials The total number of diagnoses (140723), where antimicrobials were prescribed accounted for 68.52% (N=96421).

The most prescribed antimicrobials according to pharmacological and age groups were: penicillins followed by sulphonamides and tetracyclines. The diagnoses with the most prescribed antimicrobials were the respiratory tract infections (viral influenza, acute bronchitis and upper respiratory tract infection) and pelvic inflammatory disease.

Patients in age groups 6 (20-40 years) and 7 (40-60 years) were prescribed the highest number of antimicrobials at maximum average costs. Patients in age groups 3 (1-6 years) and 4 (6-12years) received the minimum number of antimicrobials at the lowest average costs.

Conclusions:

Antibiotic courses are neither necessary nor appropriate in viral infections. The highest number of antimicrobials and therefore higher average costs were prescribed to adult patients while the paediatric patients received the minimum number of antimicrobials at minimum average costs.

Prevalence of infectious disease states and treatments in private primary health care settings in South Africa

N.L. Katende-Kyenda*[1], M.S. Lubbe[2], J.H.P. Serfontein[3], and I. Truter[4].

[1]Dept of Pharmacology, University of Transkei; [2-3]Pharmacy Practice, North West University; [4]Dept of Pharmacy, University of Port Elizabeth, South Africa (e-mail: kyendanorah@yahoo.com).

The aim of this non-experimental, quantitative, retrospective study was to analyse the incidence of disease states in private primary health care settings and their treatments.

Data were obtained from the central database of a private primary health care provider. The study population consisted of all patients who visited nine clinics situated in different geographical areas of South Africa, from 1st January to 31st December 2001. Disease states were analysed according to: number of patients, gender, age groups and treatments.

A total of 140723 disease states were diagnosed of 83655 patients. A total of 515976 medicine items costing R1716318.90 were prescribed, of which 18.69%, (N = 96423) were antimicrobials costing 60.89%, (R1045108.00). The most frequently diagnosed disease states were: upper respiratory infection, viral influenza, acute bronchitis, common cold, cough and acute-severe sinusitis. One form of respiratory tract infection was one of the top five disease states. Antibiotic treatments prescribed were penicillins (amoxycillin), sulphonamides (co-trimoxazole) and tetracyclines (doxycycline).

Antibiotics prescribed in respiratory tract infections were neither necessary nor appropriate because most of these infections are caused by viruses and thus are self-limiting. This could indicate overuse and inappropriate use of antibiotics and

these are factors often implicated in the development of resistance among causative pathogens of respiratory tract infections.

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3TC	Lamividine
ABRS	Acute bacterial rhinosinutis
ACPs	Antimicrobial control programs
AECB	Acute exarbations chronic bronchitis
AIDS	Acquired immuno-defiency syndrome
Anti-HIV	Anti human immunodeficiency virus
AOM	Acute otitis media
ARC	Aids related complex
ART	Antiretroviral therapy
ARVS	Antiretrovirals
ATC	Anatomical Therapeutic Chemical
AZT	Zidovudine (Retrovir)
BMC/MIC	Body mass index/minimum inhibitory concentration
CAP	Community acquired pneumonia
CBA	Cost benefit analysis
CEA	Cost effectiveness analysis
CMA	Cost minimisation study
CNMs/CMs	Certified nurse-midwives/certified midwives
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
COPC	Community-oriented primary care
CSF	Cerebral spinal fluid
CUA	Cost utility analysis
D4T	Abacavir and Stavudine
ddC	Zalcitabine
DDD	Defined daily dose
ddI	Didanoside
DECB	Acute exarbations of chronic bronchitis
DM	Disease management
DNA	Deoxynucleic acid
DOTS	Direct observed treatment short-courses
DUE	Drug utilisation evaluation
DUR	Drug utilisation review
EDL	Essential drug list
FDA	Food and drugs administration
GP	General Practitioners

HIV	Human immunodeficiency virus
HIV-RT	Human immunodeficiency virus reverse transcriptase
IV/IM	Intravenous/intramuscular
MAC	Mycobacterium avium
MCO	Managed care organization
MIC	Minimum inhibitory concentration
MIMS	Medicines Index Medical Specialities
NAFCI	National adolescent-friendly clinic initiative
NAPPI	National approved product pricing index
NDP	National drug policy
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTIs	Nucleoside analogue reverse transcriptase inhibitors
PCPs	Primary care providers
PHC	Primary health care
PHCNs	Primary health care nurses
PHOs	Physician hospital organizations
PID	Pelvic inflammatory disease
PIs	Protease inhibitors
PZA	Pyrazinamide
QALYs	Quality adjusted life years
RCT	Randomised controlled trials
RNA	Ribonucleic acid
SAS	Stastical analysis system
STD	Sexual transmitted disease
STI	Sexual transmitted infection
TB	Tuberculosis
TGCs	Third-generation cephalosporins
UDEs	Utilisation drug evaluations
URI	Upper respiratory infection
USA	United States of America
UTI	Urinary tract infection
WHO	World Health Organisation