AN EDUCATION INTERVENTION ON PRESCRIBING PATTERNS OF DRUGS FOR ACID-RELATED DISORDERS IN A CLINIC SETTING: A CASE STUDY

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“So we make it our goal to please Him, whether we are at home, in the body or away from it.” 2 Corinthians 5:9

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Abstract

Title: **An education intervention on prescribing patterns of drugs for acid-related disorders in a clinic setting: a case study.**

Key words and phrases: *Rational drug use; standard treatment guidelines; essential drugs list; acid-related disorders; peptic ulcer; intervention, effective prescribing.*

The South African national drug policy (NDP) was implemented in 1994 to ensure the availability and accessibility of essential drugs to all citizens. The NDP also hoped to ensure the safety, efficacy and quality of drugs as well as to promote the concepts of individual responsibility for health, preventative care and informed decision making. However, drug utilisation studies performed after the implementation of the national drug policy showed that South Africa's pharmaceutical sector was characterised by indiscriminate and irrational drug use, high drug prices and polypharmacy.

A retrospective study that was done in 2001 in the clinics supplied by Evander Hospital showed that only 11.9% of prescriptions for acid-related disorders complied with the standard treatment guidelines (STG). It became evident that there was need for an intervention.

The general objective of this study was to determine the effect of an education intervention, implemented in 2003, on the prescribing patterns of drugs for acid-related disorders in the Govan Mbeki municipal clinics serviced by Evander Hospital.

An empirical pre–intervention and post–intervention study using primary data obtained from patient files at the clinics was done. A quantitative survey of the use of the drugs included in the study (magnesium trisilicate, aluminium hydroxide/magnesium trisilicate combination tablets, cimetidine or omeprazole) was conducted.

To determine a baseline, all prescriptions where the drugs selected for this study were prescribed from 1 July 2001 to 31 December 2001 were collected. For the period 1 January 2002 to 31 December 2002 retrospective data was collected in the form of all prescriptions where the relevant drugs were prescribed. Additional retrospective data was collected for the period January 2002 to 30 June 2003 to determine the outcome of treatment given.

The phi coefficient was calculated, and although statistical correlation could not be proven, important tendencies could be detected in the data.

Only 8% of the prescriptions adhered to the STG before the presentation of the face to face education intervention. In the first six months following the intervention, STG compliance increased to 15.2%. In the following six-month period, the STG compliance decreased to 14.1%.

The assumption was made that patients were cured if they did not return with the same complaint. Based on this assumption the conclusion was drawn that, before the intervention, 50.2% of the patients were cured. In the first six months after the intervention had taken place the percentage patients who did not return increased from 50.2% to 60.6%. In the second six months after the intervention the percentage of patients who did not return increased to 70.7%.

It may be concluded that compliance with the STG improved as a result of the face to face education intervention. Moreover, it was found that cost efficiency improved in parallel and the cure rate seemed to be positively affected by the intervention.

Opsomming

Titel: 'n Opvoedkundige intervensie op voorskryfgewoontes van geneesmiddels vir suurverwante siektetoestande in 'n kliniek omgewing: 'n gevallestudie

Sleutel terme: *Rasionele geneesmiddel gebruik; standaard behandelings riglyne; essensiële geneesmiddel lys; suurverwante siektetoestande; peptiese ulkus; intervensie, effektiewe behandeling.*

Die Suid Afrikaanse nasionale medisyne beleid is in 1994 geïmplementeer om te verseker dat essensiële geneesmiddels beskikbaar en toeganklik is vir die hele bevolking, sowel as om die veiligheid, effektiwiteit en kwaliteit van geneesmiddels te verseker, en om die konsepte van individuele verantwoordelikheid vir gesondheid, voorkomende sorg en ingeligte besluitneming te bevorder. Studies oor die gebruik van geneesmiddels het na die implementering van die nasionale medisyne beleid egter getoon dat die Suid-Afrikaanse farmaseutiese sektor deur blindelingse en irrasionele geneesmiddelgebruik, hoë geneesmiddelpryse en veelvoudige medisynegebruik gekenmerk word.

'n Terugwerkende studie wat in 2001 afgelê is in die klinieke wat deur Evander Hospitaal voorsien is, het getoon dat slegs 11.9% van die voorskrifte vir dispepsie volgens die standaard behandelingsriglyne was. Dit het duidelik geblyk dat 'n intervensie nodig sou wees.

Die doel van die studie was om te bepaal of die voorskryfgewoontes in die behandeling van suurverwante siektetoestande by die Govan Mbeki munisipale klinieke wat deur Evander Hospitaal voorsien word, aangepas of verander sou word nadat die voorskrywers deur genoemde intervensie, wat in 2003 plaasgevind het, ingelig en opgelei is.

'n Empiriese voor-intervensie en na-intervensie studie is gedoen, met die gebruik van primêre data wat van pasiëntlêers in die klinieke verkry is. 'n Kwatitatiewe opname is gemaak van die gebruik van die studiemiddels

(magnesium trisilikaat suspensie, aluminium hidroksied/magnesium trisilikaat kombinasie tablette, simetidien, en omeprazool).
Om 'n basislyn te bepaal is al die pasiëntbesoeke vanaf 1 Julie 2001 tot 31 Desember 2001, waar die bogenoemde geneesmiddels voorgeskryf is, versamel. Vir die tydperk 1 Januarie 2002 tot 31 Desember 2002 is al die pasiëntbesoeke waar die studie geneesmiddels voorgeskryf is, geëvalueer. Addisionele data is versamel vir die tydperk 1 Januarie 2003 tot 30 Junie 2003 om die resultaat van behandeling te bepaal.

Alhoewel die pfi-waarde telkens op geen statistiese betekenisvolle korrelasie dui nie, was dit tog moontlik om belangrike tendense uit die data af te lei.

Slegs 8% van die voorskrifte het voor die intervensie aan die behandelingsbeleid voldoen. In die eerste ses maande ná die intervensie het die persentasie voorskrifte wat aan die beleid voldoen tot 15.2% gestyg. Dit het gedaal na 14.1% in die daaropvolgende ses maande.

Die aanname is gemaak dat pasiënte genees is indien hulle vir ses maande ná die laaste behandeling nie weer met dieselfde klagte teruggekeer het nie. Volgens hierdie aanname is daar afgelei dat 50.2% van die pasiënte voor die intervensie as genees beskou kon word. In die eerste ses maande ná die intervensie het die syfer tot 60.6% verbeter en in die daaropvolgende ses maande het dit verder verbeter tot 70.7%.

Dit kan dus afgelei word dat as gevolg van die intervensie, daar 'n verbetering in die persentasie voorskrifte wat aan die behandelingsbeleid voldoen het. Die koste effektiewiteit sowel as die genesings persentaise is albei positief beïnvloed deur die intervensie.

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CHAPTER 1: INTRODUCTION

Dyspepsia, in its many forms, has been mankind's companion since the advent of bad cooking, overindulgence and anxiety (Brunton, 1996:901).

1.1 Introduction

In 1994 the South African health department implemented a national drug policy. This policy had the following objectives:

- To ensure the availability and accessibility of essential drugs to all citizens.
- To ensure the safety, efficacy and quality of drugs.
- To ensure good dispensing and prescribing practices.
- To promote the rational use of drugs by prescribers, dispensers and patients through provision of the necessary training, education and information.
- To promote the concept of individual responsibility for health, preventative care and informed decision making (South Africa, 1994:4).

However drug utilisation studies performed after the implementation of the national drug policy showed that South Africa's pharmaceutical sector was characterised by, *inter alia*, the following:

- Indiscriminate and irrational drug use.
- Poly-pharmacy.
- High drug prices.
- Poor financial and physical controls in the public sector.
- High level of illegal drug trading (Summers & Suleman, 1996:1).

During 2000 South Africa spent about R8.25-billion on drugs (International Marketing Council of S.A., 2007:1). It has become increasingly important that studies be performed regularly to determine how effective these drugs are being used.

With an estimated 2% to 6% of patients consulting family physicians with dyspepsia as their presenting complaint (Vakil & Vairà, 2002:1) and mortality data estimates for 2000 in WHO regions showing that 0.4% (N = 6 045 172) of deaths were caused by peptic ulcer disease (PUD) (WHO, 2001:148) it became clear that acid-related disorders need to be taken into account.

In the United States, annual health care costs of peptic ulcer disease have been estimated at nearly $6 billion: $3 billion in hospitalisation costs, $2 billion in physician office visits, and $1 billion in decreased productivity and days lost from work (CDC, 1998:1).

From April 2001 to March 2002, R28 169.32 (0.71% of total pharmaceutical expenditure) was spent on antacids, proton pump inhibitors and H_2 receptor antagonists in the Govan Mbeki Municipal area (PDSX, 2003a:1; PDSX 2003b:1; PDSX, 2003c:1; PDSX, 2003d:1).

A retrospective study done in 2001 in the clinics supplied by Evander Hospital (Municipal and State clinics) showed that only 11.9% of prescriptions for acid-related disorders complied with the standard treatment guidelines (STG) and essential drugs list (EDL) (Botha *et al.*, 2001:1). It became evident that there was need for an intervention.

1.2 Background

The study focused on the rational treatment of acid-related disorders.

1.2.1 Rational Drug Use

The rational use of drugs can be described as a process whereby prescribers ensure that the indication, drug, patient, information given and monitoring of effects are appropriate (DSPRUD, 2006:1). The medicine should be prescribed in the correct dosage over the appropriate period. The patient must know why and how the medicine must be taken and the side effects that can influence him/her. It is also important that the medicine should be of good

quality and available in the appropriate quantity (Durban–Westville & Cape Town Universities, 1997:1).

1.2.2 Principles of effective prescribing

Dr. N.C. Dlamini Zuma (South Africa, 1998b: iii), stated that the EDL and STG are enabling and facilitative. The EDL and STG set a firm basis towards the attainment of equity in health care, developing rational use by all prescribers and patients, cultivating all-inclusive accountability and cost consciousness. It can therefore be deduced that by adhering to the EDL and the STG, pharmaceutical expenditure can be rationalised.

1.2.3 Previous studies

A retrospective study done in March 1999 in the Govan Mbeki municipal area reflected a shortfall in terms of the use of drugs from the essential drugs list as well as compliance to standard treatment guidelines (Botha, 2000:50). From this study it also became clear that the district was lacking as far as meeting the criteria set by the literature and provincial policy documents was concerned. Shortfalls were detected with regard to the use of drugs from the essential drugs list, compliance by the prescribers to the standard treatment guidelines, non-drug treatment, conforming of prescriptions to legal requirements and referral patterns (Botha, 2000: 50).

This was followed by the retrospective study conducted in 2001 in the clinics supplied by Evander Hospital (Municipal and State clinics) mentioned in 1.1 (Botha *et al.*, 2001:1). This study did not investigate the clinical outcomes of the prescriptions. The 2001 retrospective study identified the need for an intervention and in January 2002 a face to face education intervention was launched at the Govan Mbeki municipal clinics supplied by Evander Hospital.

1.2.4 Face to face intervention

Various intervention programmes were investigated (refer to paragraph 3.4.). It was decided that the face to face intervention would best suit the needs and

available resources at Evander Hospital and its clinics. In the face to face intervention educational information or materials were introduced to prescribers in individual or small groups (Le Grand *et al.*, 1999:94).

1.3 Problem statement

This study followed in the wake of the face to face education intervention mentioned above as it was deemed appropriate. This was done to evaluate and monitor the effect or impact of the intervention (Laing *et al.,* 1997:465). The research focused on the prescribing practices and therapeutic outcomes in the treatment of acid-related disorders at the Govan Mbeki municipal clinics supplied by Evander Hospital. Data was gathered accordingly.

In Mpumalanga the Department of Health's facilities were divided into three districts. Each district was subdivided according to the hospitals. Each hospital was the referral point for the primary health care clinics within a demarcated geographical area surrounding the hospital. This would include municipal clinics, state clinics and community health centres. These primary health care clinics would receive all their medication from the hospital's pharmacy. Drugs that were listed on the primary health care EDL were directly supplied to the clinics, and drugs that appeared on the hospital level EDL would be issued per patient on a doctor's prescription.

One of the questions that could be expected to arise would be the question regarding the possible effect that the face to face education intervention could have or actually did have on adherence to the STG by the prescribers and what effect any changes to prescribing practices could or did have on the therapeutic outcomes. Therefore a study on the prescribing habits for the treatment of acid-related disorders in the Govan Mbeki municipal clinics supplied by Evander hospital was considered. The conditions that were included in the study were peptic ulcer, heartburn, gastritis and indigestion. The focus was on the treatment prescribed for acid-related disorders, whether this treatment adhered to the STG, and what the therapeutic outcome of the treatment was.

In the forthcoming chapters the following will be discussed:

- The etiology and treatment of acid-related disorders and related diseases.
- Standard treatment guidelines for acid-related disorders.
- The history of the essential drugs concept.
- The South African perspective on the essential drugs concept.
- The principles of the essential drugs programme.
- Rational drug use and standard treatment guidelines with a brief definition of these concepts.
- Pharmacoeconomic relevance.
- Rational use by means of intervention strategies with particular emphasis on face to face intervention.
- Methodology and drug use indicators for this study.
- Results and discussion on the data gathered from the survey.
- Conclusion and recommendations as perceived from the results.

1.4 Framework for the study

The framework for this study will be described.

1.4.1 Research question

The research question can be divided into two parts:

- What effect the intervention had on adherence to the STG by the prescribers.
- What effect any changes to prescribing practices had on the therapeutic outcome.

1.4.2 Research objectives

The research objectives can be divided into general objectives and specific objectives.

1.4.2.1 General Objectives

To determine the effect of a face to face education intervention on the prescribing patterns of drugs for acid-related disorders at the Govan Mbeki municipal clinics supplied by Evander Hospital.

1.4.2.2 Specific Objectives

- To conduct a literature study on acid-related disorders with the focus being on the following points:
  - The pathology of acid-related disorders.
  - Proposed treatment of acid-related disorders as suggested in reference books and medical journals.
  - National treatment guidelines for acid-related disorders.
- To conduct a literature study on drugs for acid-related disorders with particular emphasis on the following:
  - Drugs listed on the EDL available at study clinics.
  - Mechanism of action of drugs for acid-related disorders.
- To conduct a literature study on rational drug use and possible intervention methods.
- To determine prescribing practices of drugs for acid-related disorders before the introduction of the intervention.
- To determine prescribing practices of drugs for acid-related disorders after the introduction of the intervention.
- To investigate the therapeutic outcome of drugs for acid-related disorders before the introduction of the intervention.
- To investigate the therapeutic outcome of drugs for acid-related disorders after the introduction of the intervention.

1.4.3 Research design

The research design is the plan of how the researcher intends to conduct the research (Mouton, 2001: 55). The research design was specified prior to data collection.

An in-depth literature study was conducted on acid-related disorders.

An empirical time series study with multiple observations (Kanavos *et al.*, 2007:102) was done on pre-intervention and post-intervention practices by making use of primary retrospective data obtained from patient files at the Govan Mbeki municipal clinics served by Evander Hospital. Quantitative data analysis techniques were applied.

1.4.4 Research method

The research process may be summarised as follows:

- A literature review to establish a background for the empirical study.
- A preliminary study to field-test data collection instruments.
- Fieldwork and data collection of pre-intervention data and post-intervention data.
- Quantitative and qualitative analyses of data.
- A report compiled listing results of literature and empirical studies.

1.4.5 Literature study

The in–depth literature study focused on the following:

- Pathology of acid-related disorders.
- Literature review during which emphasis was placed on the possible causes of acid-related disorders. The signs and symptoms used in the diagnosis of acid-related disorders were also explored.
- Proposed treatment of acid-related disorders.
- Various treatment methods for acid-related disorders listed in medical reference books and research reports were given.
- National treatment guidelines for acid-related disorders.
- The treatment guidelines for acid-related disorders as published by the National Department of Health were described in detail.
- The principles of rational drug use and various intervention methods were investigated.

1.4.6 Empirical study

All prescriptions at the selected Govan Mbeki municipal clinics supplied by Evander Hospital recorded during the period 1 July 2001 to 31 December 2001 where cimetidine, omeprazole, aluminium hydroxide/magnesium trisilicate tablets and magnesium trisilicate suspension were prescribed were studied to measure the prescribing habits. Clinics that were included were: Secunda Clinic, Evander Clinic, Kinross Clinic and Trichardt Clinic. All data was collected retrospectively.

An intervention in the form of face to face education took place during January 2002. All the prescriptions that were recorded during the period 1 January 2002 to 31 December 2002 where cimetidine, omeprazole, aluminium hydroxide/magnesium trisilicate tablets and magnesium trisilicate suspension were prescribed were analysed to measure the post–intervention prescribing habits. This was investigated to determine the impact of the intervention on the prescribing habits. All data was collected retrospectively.

In order to determine the outcome of the treatment that had been prescribed, all files of the patients who received treatment at any time during the period 1 July 2001 to 31 December 2002 were monitored for 6 months after the last treatment given. This required that those patients who received treatment in the period 1 July 2002 to 31 December 2002 were monitored until 30 June 2003.

A structured survey form was used to collect quantitative data from the Govan Mbeki municipal clinics supplied by Evander Hospital.

1.4.7 Division of chapters

Chapter 1: Introduction
Chapter 2: Literature review on etiology and treatment of acid related disorders
Chapter 3: Literature review on the essential drugs list, rational drug use and interventions

Chapter 4: Research Methodology
Chapter 5: Results and Discussion
Chapter 6: Conclusions and Recommendations

1.5 Chapter Summary

In chapter one the problem setting was given. The background for the study was established and previous studies were discussed. The framework of the study was described.

The focus of the study was on the effect that the face to face intervention had on the treatment prescribed for acid-related disorders, whether this treatment adhered to the STG, and what the therapeutic outcome of the treatment was. In order to determine the effect of the intervention an empirical pre-intervention and post-intervention study was done, using primary data obtained from patient files at the selected clinics.

Chapter 2 refers to a literature review that was done and presents descriptions of the etiology and treatment of acid-related disorders.

CHAPTER 2: ACID-RELATED DISORDERS: ETIOLOGY AND TREATMENT

In this chapter the physiology of the gastric processes as well as the etiology and treatment of dyspepsia, gastro-oesophageal reflux disease, gastritis, helicobacteriosis and peptic ulcers will be explored.

2.1 Anatomy of the gastrointestinal tract

The gastrointestinal tract (as shown in illustration 2.1) consists of the mouth, throat, oesophagus, stomach, small intestine, colon, rectum and the anus. The pancreas, liver and gall-bladder also play a role in the digestive processes (Merck, 2003a:1).

The oesophagus enters the stomach through the oesophageal sphincter. This circular muscle (indicated in illustration 2.2) prevents the stomach contents from flowing back into the oesophagus or throat (Merck, 2003b:3). Certain foods, (such as chocolate and peppermint) and smoking decrease the sphincter tone making reflux more likely.

The stomach consists of three regions: the cardia, fundus and antrum. Food is stored in the cardia and the fundus while the antrum contracts rhythmically, mixing the food with stomach acids and enzymes and grinding the food down to smaller pieces to aid digestion. The cells lining the stomach secrete three important substances: mucus (which coats the cells of the stomach lining to protect them from being damaged by acid and enzymes), hydrochloric acid (providing the highly acidic environment needed for pepsin to break down proteins) and the precursor of pepsin (an enzyme that breaks down collagen) (Merck, 2003a:9).

Illustration 2.1: The digestive system (Merck, 2003a: 1)

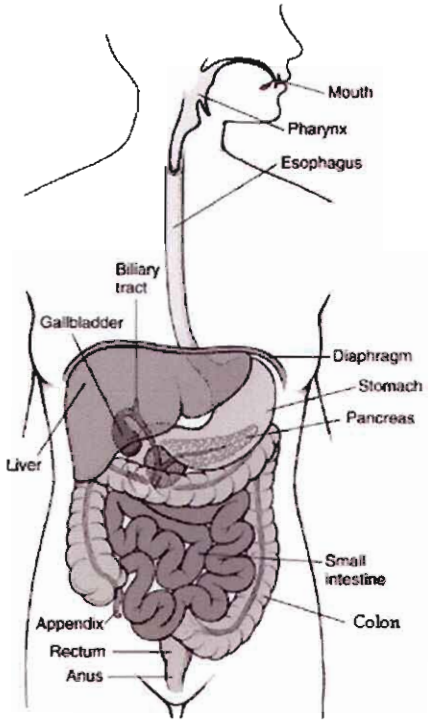
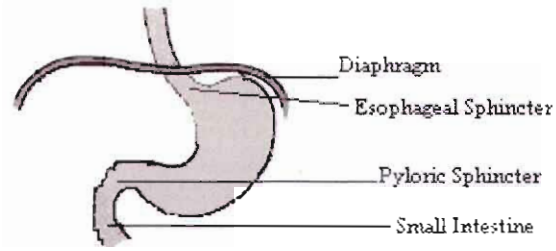


Illustration 2.2: The oesophageal and pyloric sphincters
(adapted from Merck, 2003a: 1)



The small intestine consists of three regions: the duodenum, jejunum and ileum. The stomach enters the duodenum through the pyloric sphincter. The stomach contents are released into the duodenum in small amounts to allow for absorption. Pancreatic enzymes (secreted by the pancreas) and bile (released by the liver and gall-bladder) enter the duodenum through the sphincter of Oddi. These enzymes and bile salts, as well as peristalsis in the duodenum, aid in digestion and absorption. The enzymes and bile salts also help reduce the acidity of the food that was released from the stomach. The

first part of the duodenal lining is smooth, but the rest of the lining has folds and small projections (villi and microvilli). These increase the surface area for absorption of nutrients. The intestine wall secretes mucus, water and small amounts of enzymes. (Merck, 2003a: 8)

2.2 Physiology of the gastric process

The gastrointestinal tract serves several functions: digestive, excretory, endocrine and exocrine (Katzung & Trevor, 1995:405). For the purpose of this study, the focus will be on the exocrine function of the gastrointestinal tract.

Dyspepsia may occur when an imbalance exists between the protective and aggressive factors responsible for the digestive process. The main protective factors are the mucosal prostaglandins as well as mucus and bicarbonate secreted from the surface epithelium (Corken & Herbst, 1993:205).

Gastric mucus is a thick secretion composed of water, electrolytes and a mixture of several mucopolysaccharides. It has the following protective properties:

- Mucus has adherent properties – it forms a thin film over food particles.
- It coats the wall of the gut and prevents food particles from making contact with the gut mucosa.
- Mucus is resistant to digestion by gastrointestinal enzymes.
- The mucopolysaccharides have amphoteric properties which are capable of buffering small amounts of acids or alkalis.
- It contains moderate quantities of bicarbonate ions (Corken & Herbst, 1993:206).

The surface epithelial cells secrete bicarbonate into the mucus. Cholinergic drugs stimulate bicarbonate secretion (Corken & Herbst, 1993: 206). Prostaglandins also stimulate the secretion of mucus and bicarbonate by adjacent superficial epithelial cells, contributing to the cytoprotective effects of endogenous prostaglandins. Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis, thereby blocking the cytoprotection offered by prostaglandins. The result is ulcer formation (Brunton, 1996:903).

The aggressive factors are those responsible for the digestive process. These are pepsinogen secretion and hydrochloric acid.

Pepsinogens are inactive pro-enzymes secreted by the gastroduodenal mucosa. Pepsinogen splits into pepsins in an acid environment. Pepsinogen secretion is increased by the following:

- Vagal stimulation;
- Cholinergic drugs;
- Acidification of the gastric mucosa and
- Histamine and gastrin (moderately) (Corken & Herbst, 1993:207).

Three major pathways regulate acid secretion:

- Neural stimulation via the vagus nerve.
- Endocrine stimulation via gastrin released from antral G cells.
- Paracrine stimulation by local release of histamine from enterochromaffin-like (ECL) cells (Brunton, 1996:902).

The paracrine enterochromaffin-like cells release histamine upon stimulation from the vagus nerve. Gastrin also stimulates the release of histamine. The histamine then activates H_2 receptors (linked to the stimulation of adenylyl cyclase), causing activation of the cyclic AMP pathway (Brunton, 1996:902). Activation of either the cyclic AMP - or Ca^{2+} - dependent pathway stimulates activation of H^+, K^+ - ATPase on parietal cells, with its insertion into the apical membrane and leading to the formation of secretory canaliculi, with a consequent secretion of H^+. This results in the accumulation of H^+ in the gastric lumen. An increase in the permeability of the apical membrane to K^+ and Cl^- accompanies activation of the proton pump (Brunton, 1996:903).

Prostaglandins, by inhibiting histamine-stimulated adenylyl cyclase activity in the parietal cell, reduce activity through the histamine-evoked cyclic AMP - dependent pathway and thereby reduce acid secretion (Brunton, 1996:903).

2.3 Etiology

Dyspepsia is defined as pain or discomfort in the upper abdomen (Vakil & Vaira, 2002:1). Dyspepsia (as well as heartburn, indigestion and abdominal pain) often presents with non-specific abdominal discomfort and is not associated with any of the following:

- Post-prandial discomfort.
- Anorexia.
- Minimal change in bowel habits.
- Melaena.
- Stress or psychogenic conditions (South Africa, 1998a: 54).

Intermittent dyspepsia may be associated with spicy food, alcohol, carbonated drinks, excessive smoking and use of non-steroid anti-inflammatory drugs such as ibuprofen and aspirin (South Africa, 1998a: 55).

NSAID-induced dyspepsia occurs as a result of the inhibition of prostaglandin synthesis, thereby blocking the cytoprotection offered by prostaglandins. The result is ulcer formation (Brunton, 1996:903).

Gastro oesophageal reflux (GORD) occurs when the lower oesophageal sphincter does not contract effectively, allowing gastric content to be pushed back up the oesophagus. The oesophagus does not have the protective mucus lining of the stomach and is susceptible to the hydrochloric acid of the stomach contents (Merck, 2003b:3). The severity of GORD is dependent on how weakened the lower oesophageal sphincter is, and the amount and duration of acid refluxed into the oesophagus. It is also common to find a hiatus hernia complicating GORD (West Shore endoscopy centre, 2002:1).

The most common symptom of GORD is heartburn, as well as any of the following symptoms:

- Sour or bitter taste.
- Hoarseness.
- Difficulty swallowing.
- Wheezing or coughing at night.
- Worsening of symptoms after eating, or when bending or lying down.

Constant irritation of the oesophagus by gastric acid can lead to inflammation, ulcers and bleeding. Scarring and narrowing of the oesophagus can also occur over time. Some patients can develop Barrett's oesophagus, which is a serious change in the cells lining the oesophagus. Barrett's oesophagus can be a precursor of oesophageal cancer (West Shore Endoscopy Centre, 2002:1).

Gastritis can be aggravated by various drugs. Tricyclic antidepressants, for example, have strong antimuscarinic effects, and can cause epigastric distress (Baldessarini, 1996:442). The following drugs can delay gastric emptying and decrease lower oesophageal sphincter tone (Brunton, 1996:903):

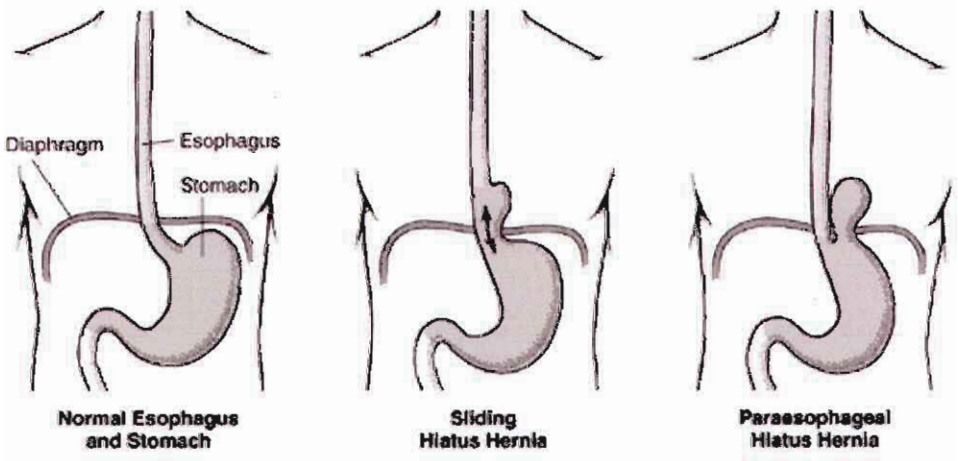
- Classic anticholinergic agents.
- Theophylline.
- Progesterone.

Diagnosis of GORD is usually made by obtaining a complete history. It can be confirmed by means of barium contrast x-ray. This will also assist in the diagnosis of hiatus hernia. Endoscopy can also prove very helpful in assessing the severity of the disease as well as determining the presence of complications (West Shore Endoscopy Centre, 2002:1). Oesophageal pH tests can be used to identify the relationship between symptoms and reflux and is usually used if patients are considered for surgical intervention (Merck, 2003b:3).

Hiatus hernia, shown in illustration 2.3., is a protrusion of a portion of the stomach from its normal position in the abdomen through the diaphragm. In a

sliding hiatus hernia, the junction between the oesophagus and the stomach as well as a portion of the stomach itself, all of which are normally below the diaphragm, protrude above it. In a paraoesophageal hiatus hernia, the junction between the oesophagus and stomach is in its normal place below the diaphragm, but a portion of the stomach is pushed above the diaphragm and lies beside the oesophagus. The symptoms are usually minor and are related to gastrooesophageal reflux. A paraoesophageal hiatus hernia may become strangulated and will require immediate surgery (Merck, 2003c:3).

Illustration 2.3: Hiatus hernia (Merck, 2003c:3)



Gastritis usually causes no symptoms. When symptoms do occur, they vary depending on the cause and may include pain and discomfort or nausea and vomiting. Various forms of gastritis have been documented.

MacSween and Whaley (1992: 692) referred to two forms of gastritis: acute gastritis and chronic gastritis.

Acute Gastritis refers to acute gastric symptoms that may arise following dietary indiscretion or stress, or the ingestion of agents such as alcohol, acids or alkalis. There is acute superficial inflammation without glandular loss or atrophy (MacSween & Whaley, 1992:692).

Chronic Gastritis can be classified into two types.
Autoimmune-associated gastritis (Type A) predominantly affects the fundus of the stomach and results in severe mucosal atrophy. Initially the mucosa is infiltrated in the foveolar area by plasma cells and lymphocytes. There is a gradual loss of the specialised cells in the glandular zone which becomes thinner. Eventually complete gastric atrophy occurs. The specialised glands are replaced by mucin secreting glands or intestinal ephithelium. These alterations result in progressive reduction in the secretion of acid, pepsin and intrinsic factor, eventually resulting in complete achlorhydria. The condition seldom causes recognisable gastric symptoms, but does lead to Vitamin B12 malabsorption (MacSween & Whaley, 1992:693).

Vitamin B12 absorption is mediated by receptor sites in the ileum that require it to be bound by a highly specific glycoprotein, intrinsic factor (Murray *et al.*, 1993:582). Vitamin B12 deficiency leads to impairment of the methionine synthase reaction (Murray *et al.*, 1993:583), which is required for the synthesis of DNA. Vitamin B12 deficiency results in impaired cell division, which then leads to the development of pernicious anaemia because the erythroblasts in the bone marrow can not divide (Robinson *et al.*, 1993:204). The neurologic disorder associated with Vitamin B12 deficiency may be secondary to a relative deficiency of methionine reaction (Murray *et al.*, 1993:583). Psychiatric manifestation such as impaired mentation and depression may be present.

The mucosal changes in Type A chronic gastritis are mediated by autoimmune mechanisms. In 90% of cases antibodies to parietal cells and in 50% of cases antibodies to intrinsic factor are present in the serum. The antibodies to intrinsic factor may also be present in the gastric juice and may often block the vitamin B12 binding site. Type A chronic gastritis is sometimes associated with other autoimmune diseases such as chronic thyroiditis and diabetes mellitus. It is also associated with an increased risk of gastric carcinoma (MacSween & Whaley, 1992:694). Eosinophilic gastritis can also be triggered by an allergic reaction to an infestation with roundworms (Merck, 2003b: 2).

Helicobacter associated gastritis (Type B chronic gastritis) is the most common type of gastritis. The lesions are usually more pronounced in the antrum or junctional zone. There is an intense plasma cell infiltration of the foveolar zone of the mucosa with variable involvement of the glandular zone. Some glandular atrophy and intestinal metaplasia may be observed on occasion and there may be hypochlorhydria of variable degree. Neutrophils are present in the *lamina propria* or superficial epithelium (MacSween & Whaley, 1992:694). In most cases minute curved bacillary organisms can be found in close apposition to the surface epithelium. The pathogenic role organisms (*Helicobacter Pylori*) play is becoming increasingly more accepted (MacSween & Whaley, 1992:694).

In **Mènètrier's disease** the stomach lining develops thick, large folds, enlarged glands and fluid-filled cysts. It may be due to an abnormal immune reaction as a result of *H. pylori* infection (Merck, 2003a:8).

The Merck manual home edition (Merck, 2003b:2) also documented other forms of gastritis:

- **Acute stress gastritis** (a form of erosive gastritis) is caused by a sudden illness or injury, for example, extensive skin burns and injuries involving major bleeding. The cause for this is not known.
- **Radiation gastritis** occurs when radiation is delivered to the lower left side of the chest or upper abdomen, where it can irritate the stomach lining.
- **Post gastrectomy gastritis** occur in patients who have undergone a partial gastrectomy where the surgery impaired blood flow to the lining or the lining had been exposed to excessive amounts of bile.

Helicobacteriosis refers to infection of the gastrointestinal tract with the bacteria *Helicobacter pylori. H. pylorus* was first documented to cause injury to the stomach in 1983 and has since been shown to be the main cause of peptic ulcer disease (Kaminstein, 2002:1).

H. pylorus is a gram negative, spiral shaped organism, that contains flagella and produces the enzyme, urease, to protect it from gastric acid. It is the

production of this enzyme that is now utilised in diagnostic tests. Infection with *H. pylori* causes a form of chronic inflammation. In about 15% of infected persons, ulcer disease develops either in the stomach or duodenum (Kaminstein, 2002:1).

It is suspected that *H. pylori* infection is spread by feacal-oral or oral-oral routes. Possible environmental reservoirs include contaminated water sources (USA Dept of health and human services, 2003: 3). Infection is often initially asymptomatic, but some patients develop abdominal pain and nausea soon after infection (Kaminstein, 2002:1). *H. pylori* also produce VacA, a cytotoxin, and a protein called CagA (Kaminstein, 2002:1). In a study done by Figura *et al.* (1999:1) it was found that *H. pylori* (CagA-positive) infection increased the risk of autoimmune thyroid disorders.

Acute gastric erosion is an ulcerative lesion which remains confined to the mucosa and does not transgress the *lamina muscularis* (MacSween & Whaley, 1992:692). These lesions are a manifestation of acute mucosal damage and may produce gastric haemorrhage. There are often multiple lesions that are widely distributed throughout the stomach. Drug (such as aspirin) or alcohol induced lesions are often situated proximally in the body or the fundus of the stomach. Erosions caused by infection are often situated in the distal stomach or antrum (MacSween & Whaley, 1992:693).

Peptic ulcer is a distinctive form of ulceration which develops in sites exposed to the action of gastric secretions (MacSween & Whaley, 1992:695). The acute peptic ulcer penetrates the *lamina muscularis* mucosae but does not extend more deeply than the submucosa. Analgesic drugs such as aspirin may be implicated in some cases. Gastric haemorrhage is the usual form of clinical presentation and may be severe if a large submucosal artery becomes eroded. There are usually multiple lesions, which are 1 - 2 cm in diameter, located in the stomach or the first part of the duodenum. The healed lesions seldom leave scars (MacSween & Whaley, 1992:696).

Most chronic peptic ulcers are located at the zone of the junction between the antrum and the body on the lesser curvature. There is usually one lesion, but

very seldom more than two. The chronic ulcer usually has a diameter of between 1 and 3 cm, but some are much larger and are circular or oval.

Gastric ulcers are more common in older age groups especially in females, whereas duodenal ulcers mostly affect males. Post-prandial epigastric pain (dyspepsia) is the usual presenting symptom of peptic ulcer disease in uncomplicated cases (MacSween & Whaley, 1992:696). Healing of a chronic peptic ulcer will restore mucosal continuity but some scarring of the underlying submucosa and *muscularis* mucosa invariably persists.

Pyloric stenosis may follow ulceration in the duodenal bulb or the prepyloric area and may provoke recurrent vomiting with dehydration and chloride depletion, increased plasma bicarbonate and extracellular potassium loss leading to hypokalaemic alkalosis (MacSween & Whaley, 1992:697). Haemorrhage can occur when blood vessels are eroded. In cases where a major artery becomes eroded, surgery is often the only solution. Perforation of the affected viscus with escape of the gut contents into the peritoneal cavity can also occur. The material entering the peritoneal cavity is usually acidic and acts as a peritoneal irritant evoking severe abdominal pain. Because it is also infective it results in acute peritonitis (MacSween & Whaley, 1992:698).

Chronic peptic ulcers represent a disturbance of the normal balance between the potentially erosive effect of gastric acid and the resistance of the mucosal surface to this effect. In gastric ulceration, gastric acid production is usually normal and may even be reduced, and impaired mucosal resistance would appear to be the main problem. In duodenal ulcers, however, persistently high gastric acid levels, especially during the night, may be a major factor. In both cases *H. pylori* infection (present in 70% of gastric ulcer cases and 90% of duodenal ulcers) may be the cause. Cigarette smoking, analgesics and genetic factors are also widely regarded as causative factors in chronic peptic ulcers (MacSween & Whaley, 1992:699).

Chronic gastritis (Type A and Type B) may increase the risk of developing **gastric carcinoma**. Chronic gastritis is often associated with the appearance of intestinal metaplasia. Incomplete forms of this metaplasia could be

associated with the development of carcinoma. Unfortunately the prognosis for gastric carcinoma is very poor (MacSween & Whaley, 1992:700).

Oesophageal cancer appears as a stricture of the oesophagus, a lump, an abnormal plaque, or an abnormal connection between the oesophagus and the airways that supply the lungs. Risk factors include infection (*H. pylori*), impairment of the immune system and exposure to radiation. Endoscopy is the best diagnostic procedure if oesophageal cancer is suspected (Merck, 2003b:3).

Stomach cancer often begins at a site where the stomach lining is inflamed. *H. pylorus* has also been implicated in the development of stomach cancer (Merck, 2003b:3). Reynolds (1993:875) reports that misdiagnosis and inappropriate cimetidine treatment may occur when the initial symptoms of cancers of the gastrointestinal tract resemble benign gastrointestinal disorders. Therefore, peptic ulcer symptoms that do not resolve with treatment may indicate stomach cancer. Fewer than 20% of people with adenocarcinoma of the stomach survive longer than 5 years (Merck, 2003b:3). This indicates the importance of endoscopy in cases where peptic ulcer is suspected to rule out stomach cancer.

2.4 Treatment

The aim of treatment in acid-related disorders is to balance aggressive factors (gastric acid secretion, pepsin, *Helicobacter pylori* infection) against the cytoprotective factors (bicarbonate secretion, mucus secretion, prostaglandin production). Therapy is taken to relieve pain, promote healing and prevent recurrence (Brunton, 1996:901).

Dyspepsia

The South African Medicines Formulary (SAMF) (Gibbon, 2005:40) advises the use of antacids to treat dyspepsia. Five milliliters of the average antacid mixture should be sufficient to neutralise the normal fasting volume of gastric acid in the intact stomach. The doses required to relieve dyspeptic symptoms

are not associated with unacceptable side effects. The antacids are best taken an hour before meals, and again at bedtime.

Gastro oesophageal reflux disease (GORD)

The Canadian *Helicobacter pylori* Consensus Conference (Hunt & Thompson, 1998:35) stated that patients who have predominant symptoms that are characteristic of gastro-oesophageal reflux (heartburn) should not be tested for *H. pylori* as there is no correlation between *H. pylori* infection and GORD.

Non-drug treatment (Merck, 2003b:3)

- Raising the head of the bed 6 inches can prevent reflux during sleep.
- Avoid specific foods (e.g. fats, chocolate, coffee and alcohol).
- Stop smoking.
- Certain drugs namely, NSAID's, anthicholinergics, tricyclic antidepressants, calcium channel blockers and nitrates) should also be avoided where possible.

Drug treatment (Merck, 2003b:3)

- Healing requires acid reducing drugs over a 4- to 12-week period.
- Antacids taken at bedtime are often useful.
- Proton pump inhibitors have also proven very effective.

Hiatus hernia

Elevating the head of the bed while sleeping can prevent symptoms. Antacids and other drugs that prevent acid secretion can also relieve symptoms. A paraoesophageal hiatus hernia may be corrected surgically to prevent strangulation, but surgery is rarely needed (Merck, 2003c:3).

Peptic Ulcers

Before the discovery of *H. pylori* the majority of patients were given medication, such as H_2 blockers and proton-pump inhibitors, over a long term with no hope for a permanent cure. These medications relieve ulcer-related symptoms, heal gastric mucosal inflammation, and may heal the ulcer, but they do not treat the infection (USA Dept of health and human services, 2003:1). The likelihood that a peptic ulcer will recur within 1 year ranges from

60% to 80% in patients not treated with antibiotics. Patients that receive antibiotics as part of the treatment for peptic ulcers have only a 20% chance that the peptic ulcers will recur in the next year (Merck, 2003b: 2).

Vakil and Vaira (2002:1) found that non-invasive testing for *Helicobacter pylori*, followed by antibiotic treatment of those patients who tested positive, is effective in alleviating symptoms, reducing the need for endoscopic investigations, and decreasing the overall cost of managing dyspepsia.

H. pylori infection can be diagnosed by serological tests that measure specific *H. pylori* IgG antibodies, by a breath test using 13C- or 14C-labelled urea, a stool antigen test or by endoscopic biopsy (Vakil *et al,* 2000:1691; USA Dept of health and human services, 2003:1). Laine *et al* (1999: 3464) found that the whole-blood *H. pylori* IgG antibody tests (rapid test strips) achieved a sensitivity and specificity similar or better than those of widely used quantitative laboratory serological tests. As antibody testing is the recommended method to screen for *H. pylori* infection, Laine *et al* (1999:3464) stated that these rapid test strips may be used as the initial screening tests of choice for *H. pylori.* The cost for these rapid tests ranges between R13.84 and R74.13 (Cliawaived, 2007:1). Vakil *et al.* (2000:1691) found that the stool antigen test (at an average cost of between R889.56 and R896.62 per accurate diagnosis) was the most cost effective.

Therapy prescribed for *H. pylorus* infection consists of 10 - 14 days of one or two antibiotics, plus either ranitidine, bismuth subsalicylate, or a proton pump inhibitor. Acid suppression by the H_2 blocker or proton pump inhibitor in conjunction with the antibiotics helps alleviate ulcer-related symptoms, helps heal mucosal inflammation, and may enhance efficacy of the antibiotics against *H. pylori* at the gastric mucosal surface. Antibiotic resistance and patient non-compliance are the two major reasons for treatment failure. Triple treatment regimens have shown better eradication rates than dual treatment regimens. Longer length of treatment (14 days) results in better eradication rates. The American Food and Drug Administration (FDA) approved 8 treatment regimes as shown in Table 2.1 (USA Dept of health and human services, 2003:2).

Table 2.1: FDA approved treatment regimes

	Suppression of gastric acid secretion	Antibiotic 1	Antibiotic 2	Additional
1	Omeprazole 40mg QID x 4 weeks	Clarithromycin 500mg TID x 2 weeks		
2	Ranitidine bismutrex** 400mg BD x 4 weeks	Clarithromycin 500mg TID x 2 weeks		
3 *	H_2 receptor antagonist as directed x 4 weeks	Metrondidazole 250mg QID x 2 weeks	Tetracycline 500mg QID x 2 weeks	Bismuth subsalicylate 525mg QID x 2 weeks
* Although not FDA approved, amoxicillin has been substituted for tetracycline for patients for whom tetracycline is not recommended. **Ranitidine bismutrex is a combination of ranitidine and bismuth citrate (Reynolds, 1993:902)				
4	Lansoprazole 30mg BD x 10 days	Amoxycyllin 1gram BD x 10 days	Clarithromycin 500mg TID x 10 days	
5 ***	Lansoprazole 30mg BD x 14 days	Amoxycyllin 1gram TID x 14 days		
*** Amoxycyllin is indicated for patients who are either allergic or intolerant to clarithromycin or for infections with known or suspected resistance to clarithromycin				
6	Ranitidine bismutrex** 400mg BD x 4 weeks	Clarithromycin 500mg BD x 2 weeks		
7	Omeprazole 20mg BID x 10 days	Clarithromycin 500mg BD x 10 days	Amoxycyllin 1gram BD x 10 days	

2.5 Standard treatment guidelines

The standard treatment guidelines and essential drugs list for primary health care (South Africa, 1998a: 54) give the following management guidelines for the treatment of abdominal pain/dyspepsia/heartburn/indigestion:

Non-drug treatment

- Patient to stop smoking.
- Patient to limit alcohol intake.
- Patient to eat small frequent meals.
- Check haemoglobin.
- Check for a drug cause likely to be associated with dyspeptic symptoms.
- Educate patients on normal bowel functions and frequency.

Drug treatment

- Initiate drug therapy only after full assessment.
- Aluminium hydroxide 250mg/ magnesium trisilicate 500mg 2 - 4 tablets chewed or sucked when necessary (maximum of 16 tablets daily or continuous treatment for 7 days).

Referral criteria

- Abdominal pain at specific sites:
  - Right iliac fossa;
  - Lower abdomen and
  - Epigastric.
- Failure of treatment.
- Uncertain diagnosis.
- Blood in the stools.
- Abdominal mass.
- Signs of peritonitis.

The standard treatment guidelines and essential drugs list for hospital level care (South Africa, 1998b: 19) give the following management guidelines for the treatment of peptic ulcer:

Non-drug treatment

- Advise patient to avoid ulcerogenic medications (such as NSAID's).
- Advise patient to stop drinking alcohol and smoking.
- Health education.
- Lifestyle modification.

Drug treatment

- No risk factors and diagnosis unconfirmed

  Magnesium trisilicate 500mg/aluminium hydroxide 250mg, oral 1-2 tablets to be chewed 1 hour before and 3 hours after meals and at night for 4 weeks.

  OR

  Cimetidine, oral, 800mg at night for 4 weeks.

The following drug treatment may be prescribed by a gastroenterologist only:

- Endoscopy confirmed, *H. pylori* associated, duodenal ulceration

  Proton pump inhibitor in the morning for 7 days only, e.g.
  omeprazole, oral, 20mg daily.

  Plus

  Amoxicillin, oral, 1g twice daily.

  Plus

  Metronidazole, oral, 400mg twice daily, for one week.

- Gastric ulcer

  Proton pump inhibitor for 4 weeks, otherwise as above for duodenal ulcer, repeat endoscopy at 4 weeks.

- Endoscopically confirmed, *H. pylori* non-associated

  Cimetidine, oral, 800mg at night for 4 weeks.

The standard treatment guidelines and essential drugs list for hospital level care (South Africa, 1998b: 21) give the following management guidelines for the treatment of reflux oesophagitis:

Non-drug treatment

- Eliminate food and agents that reduce lower oesophageal sphincter function, such as fatty, grilled and/or spicy foods, chocolate, alcohol, tea and coffee, smoking, medicines such as NSAID's, anticholinergics, antidepressants, and smooth muscle relaxants.
- Weight reduction where necessary.
- Elevate the head end of the bed 10 - 15cm.
- Avoid supine position 3 - 4 hours after a meal.
- Surgical treatment is indicated when pharmacological treatment and other measures have failed.

Drug treatment

- First line:
  Magnesium trisilicate 500mg/aluminium hydroxide 250mg, oral 1-2 tablets to be chewed 1 hour before and 3 hours after meals and at night for 4 weeks.
- Second line:
  (Should only be used when proper antacid therapy and proper non-pharmacological treatment fail and only after endoscopic confirmation).
  H_2- antagonists, e.g.
  Cimetidine, oral 200-400mg twice daily
  and/or
  Proton pump inhibitors (only a gastroenterologist may prescribe) eg.
  Omeprazole, oral, 20mg daily.

The standard treatment guidelines and essential drugs list for hospital level care (South Africa, 1998b: 21) give the following management guidelines for the treatment of bile reflux:
Sucralfate, oral, 1g 4 times daily, 1 hour before each meal and at bedtime.

2.6 Drugs used for acid-related disorders

The various drugs that are used in the treatment of acid-related disorders will be discussed. Each of the chemical groups will be individually described, focusing on their indications, mechanism of action, adverse effects, contra-indications and dosages as they relate to acid-related disorders.

2.6.1 Antacids

Indications:
Dyspepsia, ulcer healing, gastro-oesophageal reflux, and reflux associated with documented oesophagitis are listed as indications for antacids (Gibbon, 2005:40).

Examples:

Magnesium compounds

Magnesium hydroxide (Gibbon, 2005:40)

Magnesium trisilicate (Gibbon, 2005:40)

Aluminium compounds

Aluminium hydroxide (Reynolds, 1993:869)

Algeldrate (Gibbon, 2005:41)

Calcium compounds

Calcium carbonate (Reynolds, 1993:873)

Combinations of aluminium, magnesium and calcium

Aluminium/magnesium (Gibbon, 2005:41)

Aluminium/magnesium/local anaesthetic (Gibbon, 2005:41)

Calcium/magnesium (Gibbon, 2005:41)

Antacids with antiflatulents

Dimethicone (Gibbon, 2005:41)

Simethicone (Gibbon, 2005:41)

Antacids with antispasmodics

Dicyclomine (Gibbon, 2005:42)

Mechanism of action:

The function of antacids is to neutralise the hydrochloric acid (HCl) secreted by gastric parietal cells. The antacids react with HCl to form chlorides, water, and carbon dioxide thereby neutralising the HCl. The chemical reactions are as follows (Brunton, 1996:910):

$$Mg(OH)_2 + 2HCl \xrightarrow{\text{slow /moderate}} MgCl_2 + 2H_2O$$

$$Al(OH)_3 + 3HCl \xrightarrow{\text{slow}} AlCl_3 + 3H_2O$$

$$CaCO_3 + 2HCl \xrightarrow{\text{fast}} CaCl_2 + H_2O + CO_2$$

$$NaHCO_3 + HCl \xrightarrow{\text{fast}} NaCl + H_2O + CO_2$$

The usefulness of antacids is influenced by their rates of dissolution and reactivity, physiologic effects of the cation, water solubility, and the presence of food in the stomach (Brunton, 1996:910). Because food increases the pH of the stomach, it can prolong the antacid's neutralising effect for up to 2 hours (Brunton, 1996:911). The very water-soluble $NaHCO_3$ is rapidly cleared from

the stomach and presents both an alkali and a sodium load. $CaCO_3$ can neutralise the HCl rapidly and effectively, however, Ca^{2+} may adversely activate the Ca^{2+} - dependent processes, leading to secretion of gastrin and HCl. Both carbonates liberate CO_2, which can cause abdominal distention and belching with acid reflux (Brunton, 1996:910).
The hydroxides of aluminium and magnesium are relatively insoluble and do not cause OH^- to accumulate to corrosive levels. $Mg(OH)_2$ reacts quickly while $Al(OH)_3$ reacts slowly. Combinations of these two antacids give a fast and sustained neutralising capacity (Brunton, 1996:911).

Dimethicone and Simethicone are surfactants and are often combined with antacids because they may reduce foaming and acid reflux (Brunton, 1996:910).

Adverse effects:
The adverse effects are dependent on which antacid is being used.

Magnesium compounds can cause fluid and electrolyte imbalances as they have a laxative effect if used alone. Hypermagnesaemia may cause nausea, vomiting, ECG changes, respiratory and mental depression and coma (Gibbon, 2005:41).

The aluminium compounds have the tendency to cause constipation when used alone. This could lead to haemorrhoids, fissures and faecal impaction. Hypophosphataemia may occur when high doses are used for long periods (Reynolds, 1993: 869).

Calcium-containing antacids have been associated with rebound acid hypersecretion, hypercalcaemia, and the milk-alkali syndrome and therefore high doses should be avoided (Gibbon, 2005:41; Reynolds, 1993:873). The milk-alkali syndrome results from ingestion of large quantities of calcium and absorbable alkali. The effects of this syndrome consist of hypercalcemia, reduced secretion of parathyroid hormone, phosphate retention, precipitation of calcium salts in the kidney, and renal insufficiency (Brunton, 1996:912).

Contra-indications:

The antacids should be used with caution in patients with renal failure (Gibbon, 2005:40).

Dosage:

The adult dosage for magnesium trisilicate suspension is 5 – 10ml taken orally as required (Gibbon, 2005:40). One to two magnesium trisilicate 500mg/aluminium hydroxide 250mg tablets can be sucked or chewed by adults 4 – 8 times daily. The daily dose of the magnesium trisilicate 500mg/aluminium hydroxide 250mg tablets must not exceed 16 tablets per 24 hours (Gibbon, 2005:40).

2.6.2 Proton pump inhibitors

Indications:

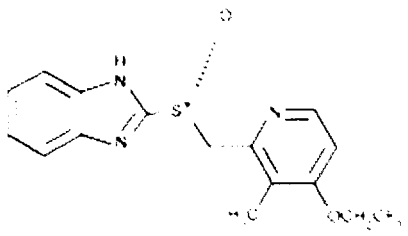
The proton pump inhibitors are indicated in the management of gastric and duodenal ulcers, reflux oesophagitis and Zollinger-Ellison syndrome. It is also used in conjunction with appropriate antibiotics in the eradication of *Helicobacter pylori* (Gibbon, 2005:42). Functional dyspepsia and treatment of non-steroid anti-inflammatory drug (NSAID) - associated gastritis/erosions are also given as indications (Snyman, 2006:246).

Examples:

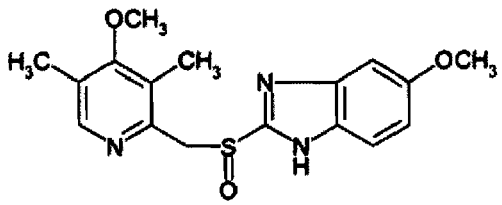
Omeprazole (Gibbon, 2005:42)
Esomeprazole (Gibbon, 2005:43)
Lansoprazole (Reynolds, 1993:887)
Pantoprazole (Gibbon, 2005:43)
Rabeprazole (Gibbon, 2005:43)

The chemical structures of omeprazole and lansoprazole (Answers, 2007:1) are given in Illustration 2.4.

Illustration 2.4: The chemical structures of lansoprazole and omeprazole



Lansoprazole



Omeprazole

Mechanism of action:

These drugs inhibit the H+, K+ - ATPase (proton pump) of the apical membrane of the parietal cell. At a neutral pH, omeprazole and lansoprazole are chemically stable, lipid soluble, weak bases that are devoid of inhibitory activity. They are pro-drugs that need to be activated in acidic conditions to be effective. These neutral weak bases reach parietal cells from the blood and diffuse into the secretory canaliculi, where the drugs become protonated and thereby trapped. The protonated agent rearranges to form a sulfenic acid and a sulfonamide. The sulfonamide interacts covalently with the sulfhydryl groups at the critical sites in the extracellular domain of the membrane–spanning H^+, K^+- ATPase. Full inhibition occurs with two molecules of inhibitor bound per molecule of enzyme. Omeprazole permanently inhibits enzyme activity in vivo; secretion of gastric acid resumes only after insertion of new molecules of H^+, K^+ - ATPase into the luminal membrane (Brunton, 1996:907).

These agents produce only small and inconsistent changes in the volume of gastric juice and in the secretion of pepsin and do not affect gastric motility (Brunton, 1996:908). Lind *et al.* (quoted by Brunton, 1996:908) found that omeprazole produces a dose-related inhibition of gastric acid secretion that persists after the drug has disappeared from the plasma. When given in appropriate dosages, omeprazole can reduce daily production of acid by more than 95% (Brunton, 1996:908).

Adverse effects:

These drugs are generally well tolerated. Some patients experience skin rashes, nausea, diarrhoea, dry mouth, constipation, flatulence and abdominal

colic. Headache, dizziness, somnolence, insomnia and pruritus have also been reported. Other effects include urticaria, myalgia and arthralgia (Brunton, 1996:908; Gibbon, 2005:42; Reynolds, 1993:896).

Contra-indications:

Gibbon (2005:42) warns that malignancy must first be excluded and that the proton-pump inhibitors must be used with caution in severe liver disease.

Dosage:

Dosages for omeprazole, as recommended in the South African Medicines Formulary (SAMF), (Gibbon, 2005:43) are given in Table 2.2.

Table 2.2: Dosages for omeprazole as per indication

Indication	**Adult dose**	**Paediatric dose**
Duodenal ulcer	Oral, 20mg daily for 2 - 4 weeks. Prevention of relapse, 10mg once daily, increased if necessary	
Gastric ulcer or reflux oesophagitis	Oral, 20mg daily for 2 - 4 weeks. Severe cases may require 40mg/day. Long-term management of reflux oesophagitis, 10mg daily	
NSAID-associated erosions	Oral 20mg daily for 4 - 8 weeks. Prevention 20mg daily	
Eradication of *H.pylori*	Oral, 20mg daily for 7 days in combination with appropriate antibiotics	
Zollinger-Ellison syndrome	Oral, initially 60mg once daily; dosage range 20 - 120mg/day, with doses over 80mg given in 2 divided doses. IV infusion, 40mg for up to 5 days	
Severe ulcerative reflux oesophagitis		Child's weight=10 - 20kg: Oral 10mg once daily, increase to 20mg daily if necessary; >20kg, 20mg once daily, increase to 40mg daily if necessary.

2.6.3 H_2-receptor antagonists

Until the mid-1970s no really effective medical treatment existed for duodenal ulcer, which remained a chronic, relapsing, often disabling and occasionally fatal disease. The outlook changed in November 1976 with the release in the UK of cimetidine, the first histamine two (H_2) receptor antagonist, which dramatically transformed management, resulting in swift symptom relief, ulcer healing and, on maintenance therapy, a marked reduction in relapse (Bardhan *et al.*, 2003:529).

Indications:

The H_2-receptor antagonists are indicated for the treatment of peptic ulcer, reflux oesophagitis, Zollinger-Ellison syndrome and prevention of stress ulcers in critically ill patients (Gibbon, 2005:44). The MIMS (Snyman, 2006:243) also lists duodenal ulcer, recurrent ulceration and erosive gastro-oesophageal reflux disorder as indications for H_2-receptor antagonists.

Examples:

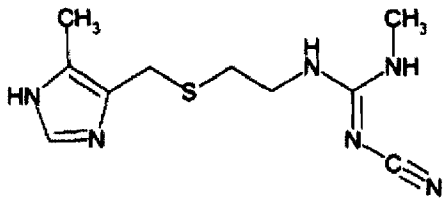
Cimetidine (Gibbon, 2005:44; Reynolds, 1993:874)

Ranitidine (Gibbon, 2005:45)

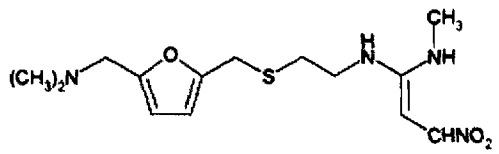
Nizatidine (Gibbon, 2005:45)

The chemical structures (Answers, 2007:1) are given in Illustration 2.5.

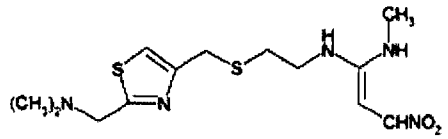
Illustration 2.5: The chemical structures of cimetidine, ranitidine and nizatidine



Cimetidine



Ranitidine



Nizatidine

Mechanism of action:

The H_2-receptor antagonists competitively inhibit the interaction of histamine with H_2-receptors in the parietal cells in the stomach (Gibbon, 2005:44). They are highly selective and have little or no effect on H_1-receptors. Although H_2-receptors are present in numerous tissues, including vascular and bronchial smooth muscle, these drugs interfere remarkably with physiological functions other than gastric secretion (Brunton, 1996:904).

H_2-receptor antagonists inhibit gastric acid secretion elicited by histamine and other H_2-receptor agonists in a dose-dependant, competitive manner (Brunton, 1996:904). The H_2-receptor antagonists inhibit basal and nocturnal acid secretion and this contributes in a major way to their clinical efficacy. They also reduce acid secretion stimulated by food, sham feeding, fundic distention and various pharmacological agents. The H_2-receptor antagonists reduce both the volume of gastric juice secreted and its H^+ concentration (Brunton, 1996: 905).

Use of the H_2-receptor antagonists should be tempered by awareness of their potential to produce adverse effects, potential drug-drug interactions, high

cost, and the fact that other agents have been shown to be effective in ulcer healing (Gibbon, 2005:44).

Adverse effects:

Headache, dizziness, nausea, diarrhoea, skin rashes and pruritis have been reported. Central nervous system (CNS) disturbances occur most frequently in the elderly and in impaired renal or hepatic function (Gibbon, 2005:44). Anti-androgenic activity may cause a loss of libido, gynaecomastia and impotence (Reynolds, 1993:874). Raised prolactin levels and galactorrhoea have been associated with intravenous (IV) or prolonged oral therapy (Gibbon, 2005:44).

Contra-indications:

Relative – impaired renal function (Gibbon, 2005:44).

Dosage:

The dosages reflected in the SAMF (Gibbon, 2005:44) are given in Table 2.3.

Table 2.3: Recommended dosage of cimetidine per indication

Adult dose	**Paediatric dose**
Peptic ulcer disease and reflux oesophagitis: Oral 200mg tds and 400mg at bedtime or 400mg bd or 800mg noctè. Maintenance 400mg noctè	Oral or IV, 20 - 40mg/kg/day (neonates 10 - 20mg/kg/day) in 4 divided doses
Zollinger-Ellison syndrome: Up to 2.4g/day in 4 divided doses	
IV 200mg 4-6 hourly by slow injection or infusion if cardiovascular impairment or higher dose needed.	

2.6.4 Prostaglandins

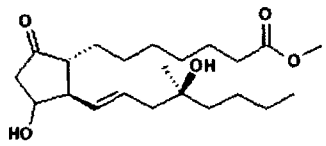
Indications:

The prostaglandin analogues are indicated for the protection against NSAID-associated gastric ulceration (Gibbon, 2005:45)

Examples:

Misoprostol (Gibbon, 2005:45)

Illustration 2.6: The chemical structure of misoprostol (Answers, 2007:1).



Mechanism of action:

Prostaglandins E_2 and I_2, the predominant prostaglandins synthesised by the gastric mucosa, inhibit the secretion of acid and stimulate the secretion of mucus and bicarbonate (Brunton, 1996:914). Misoprostol is a synthetic prostaglandin E_1 analogue (Gibbon, 2005: 45). The dose required to inhibit gastric acid secretion is higher than the dose needed to produce cytoprotective effects (enhanced secretion of mucous and HCO_3^-). The prostaglandin analogues are only moderately effective in the treatment of duodenal and gastric ulcers, but are particularly valuable as cytoprotective agents in patients who require NSAID (Brunton, 1996:914).

Adverse effects:

Diarrhoea occurs in about 30% of patients. Abdominal cramping can also occur (Brunton, 1996:914). Less frequent adverse effects are headache, constipation, nausea and vomiting (Gibbon, 2005:45).

Contra-indications:

The prostaglandin analogues are contra-indicated in pregnancy as they are potential abortifacients (Brunton, 1996:914). It is not recommended for use in children (Gibbon, 2005: 45).

Dosage:

The adult dose is one tablet (200µg) twice daily taken with food. It may be increased to 1 tablet 3 times per day. The maximum dose is 1 tablet 4 times per day. The misoprostol must be initiated concurrently with the NSAID and, where possible, the NSAID must be taken at the same time as the misoprostol (Gibbon, 2005:45; Snyman, 2006:248).

2.6.5 Cytoprotective agents

Indications:

Cytoprotective agents are indicated for peptic ulcer and gastro-oesophageal reflux disease (Gibbon, 2005:45).

Examples:

Sucrulfate (Gibbon, 2005:46; Snyman 2006:249)
Bismuth subcitrate (Gibbon, 2005:46)
Alginic acid (Gibbon, 2005:46)

Mechanism of action:

Sucralfate is a viscous, water-insoluble gel-like substance that has a weak buffering effect. The sucralfate adheres to epithelial cells and adheres very strongly to the base of ulcer craters, so avidly that it is difficult to wash the gel from the crater. The gel continues to adhere to ulcerated epithelium for longer than 6 hours. Antacids and food do not appear to affect the integrity of the adherent gel; proteins in foodstuffs adsorb to its surface, and thus add an additional cytoprotective layer. It also binds bile salts, which are implicated in the pathogenesis of gastric ulcers, thus providing another means by which sucralfate may achieve therapeutic utility.

A variety of mechanisms have been proposed to account for the cytoprotective and healing effects of sucralfate, including stimulation of prostaglandin synthesis, adsorption of pepsin, and stimulation of local production of epidermal growth factor (Brunton, 1996:913).

Bismuth compounds enhance secretion of mucous and bicarbonate. They also inhibit pepsin activity and bismuth subcitrate accumulates in the craters of gastric ulcers. These cytoprotective effects may be secondary to the antibacterial effect of bismuth compounds against *Helicobacter pylori* in the gastroduodenal mucosa (Brunton, 1996:910).

Alginates are extracted from algae and, used in combination with antacids, help to prevent reflux oesophagitis (Gibbon, 2005: 45).

Adverse effects:

Constipation (Snyman, 2006:249), and dry mouth and abdominal discomfort (Brunton, 1996:914), vertigo, drowsiness, skin rashes, pruritis and back pain (Reynolds,1993:905) occur occasionally with the use of sucralfate.

Bismuth reacts with bacterial H_2S which results in discolouration (black colour) of the oral cavity and the faeces (Brunton, 1996:910).

Dosage:

One gram of Sucralfate should be taken 4 times per day, 1 hour before meals and at bedtime for the treatment of gastric and duodenal ulcers (Gibbon, 2005:46).

2.6.6 *Helicobacter pylori* eradication

Double or triple antimicrobial therapies, in combination with antisecretory drugs, are being used successfully to treat peptic ulcers that are due at least in part to *Helicobacter pylori* infection (Brunton, 1996:909).

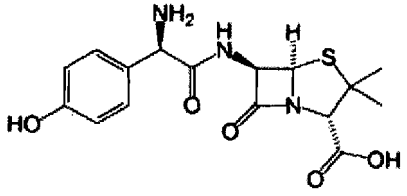
As discussed in 2.4. various antimicrobial agents, in differing combinations, are indicated for the eradication of *Helicobacter pylori*. The following antibiotics are listed in 2.4: amoxicillin, clarithromycin, metronidazole and tetracycline, and will be described below.

2.6.6.1 Amoxicillin

Amoxicillin is a β-lactam antibiotic (penicillin) (Mandell & Petri, 1996:1073).

Illustration 2.7: The chemical structure of amoxicillin

(Answers, 2007:1).



Indications:

Amoxicillin has a broad-spectrum activity against several Gram-positive organisms, Gram-negative cocci and some bacilli (Gibbon, 2005:260). It is indicated for the treatment of bacterial infections caused by susceptible organisms, prophylaxis of endocarditis and in combination therapy in *H. pylori* infection (Snyman, 2006:309).

Mechanism of action:

Amoxicillin inhibits the last step in cell wall synthesis (Katzung & Trevor, 1995:300). This occurs when the transpeptidase enzyme responsible for this final step is acylated by the penicillin (Mandell & Petri, 1996:1075). The peptidoglycan is a heteropolymeric component of the cell wall that provides rigid mechanical stability by virtue of its highly cross-linked latticework structure (Mandell & Petri, 1996:1074). Although inhibition of the peptidoglycan synthesis is demonstrably important, there are additional, related targets for the actions of penicillins; these are collectively termed penicillin-binding proteins (PBP). The interaction between the penicillins and the PBPs eventually become covalent.

The lysis of bacteria that usually follows their exposure to β-lactam antibiotics is ultimately dependent on the activity of cell-wall autolytic enzymes – autolysins or murein hydrolases. The relationship between inhibition of PBP activity and activation of autolysins is unclear. Interference of peptidoglycan assembly in the face of ongoing autolysin activity might lead to cell lysis, but the mechanism appears to be more complex (Mandell & Petri, 1996:1075).

Adverse effects:

Hypersensitivity occurs in up to 10% of patients. The Jarisch-Herxheimer reaction may occur when endotoxins are released by organisms killed by the antibiotic (Gibbon, 2005:258). Other adverse effects include skin rash, urticaria, gastro-intestinal disturbances and superinfections (Snyman, 2006:309).

Contra-indications:

Hypersensitivity to penicillins and infectious mononucleosis are contra-indications for the use of amoxicillin (Snyman, 2006:309; Gibbon, 2005:258).

Dosage:

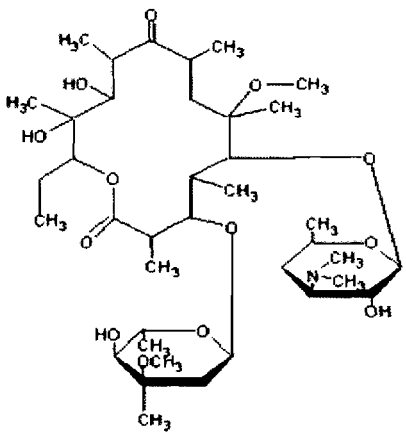
The dosage for *H. pylori* infections associated with duodenal ulceration is 750mg – 1gram twice daily in combination with other agents for 7 days (Snyman, 2006:309).

2.6.6.2 Clarithromycin

Clarithromycin is a macrolide antibiotic (Kapusnik-Uner *et al.*, 1996:1135).

The structure of clarithromycin is given in Illustration 2.8 (Answers, 2007:1).

Illustration 2.8: The Chemical structure of clarithromycin



Indications:

Clarithromycin is registered for use, in combination with a proton pump inhibitor, in the eradication of *H. pylori* to decrease recurrence of duodenal ulcer (Gibbon, 2005:269). It may also be used in the treatment of rickettsial infections, upper and lower respiratory tract infections, *Mycobacterium avium* or *Mycobacterium intracellulare* infections in HIV-positive patients in conjunction with other antimycobacterials (Snyman, 2005:271; Gibbon, 2005:269).

Mechanism of action:

Macrolide antibiotics are bacteriostatic or bacteriocidal agents that inhibit protein synthesis by binding reversibly to 50 S ribosomal subunits of sensitive microorganisms (Kapusnik-Uner *et al.*, 1996:1136; Katzung & Trevor, 1995:339). They appear to inhibit the translocation step wherein the nascent pepferase reaction fails to move to the P, or donor, site. Alternatively, macrolides may bind and cause a conformational change that terminates protein synthesis by indirectly interfering with transpeptidation and translocation (Kapusnik-Uner *et al.*, 1996:1137).

Adverse effects:

Gastro-intestinal disturbances, skin rashes, eosinophilia (Katzung & Trevor, 1995:339), reversible discolouration of the tongue with concomitant omeprazole, hepatic dysfunction, hypoglycaemia, leukopenia and thrombocytopenia have been reported. Allergic reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis. Transient CNS effects including convulsions and psychosis and hearing loss that is reversible on withdrawal of treatment can occur. Rarely QT prolongation, ventricular tachycardia and torsades de pointes also occur (Snyman, 2006:327).

Contra-indications:

Clarithromycin is contra-indicated in concomitant use of terfenadine, cisapride, pimozide and ritonavir (where doses are greater than 1g/day). Safety in pregnancy and breast-feeding has not been established (Snyman, 2006:327).

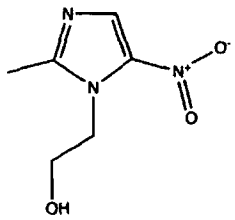
Dosage:

In *H. pylori* eradication the adult dosage is 500mg twice daily in combination with amoxicillin and omeprazole (Snyman, 2006:327).

2.6.6.3 Metronidazole

The structure of metronidazole (Answers, 2007:1) is given in illustration 2.9.

Illustration 2.9: The chemical structure of metronidazole



Indications:

Metronidazole is indicated for anaerobic infections (excluding actinomycosis), amoebic dysentery, amoebic liver abscess, trichomoniasis, giardiasis and acute necrotising ulcerative gingivitis. It is also included in regimens for eradication of *H. pylori* in peptic ulcer disease (Gibbon, 2005:463).

Mechanism of action:

Metronidazole is bactericidal; it inhibits nucleic acid synthesis by interacting with intracellular macromolecules (Gibbon, 2005; 643). Metronidazole can be considered a prodrug in the sense that it requires metabolic activation by sensitive organisms. Metronidazole inhibits DNA synthesis in *T. vaginalis* and *Clostridium bifermentans* and causes degradation of existing DNA in the latter microorganism. The activated metronidazole causes a loss of the helical structure of DNA, strand breakage, and impairment of DNA function (Tracy & Webster, 1996:996; Katzung & Trevor, 1995:340).

Adverse effects:

Nausea, anorexia, headache and a metallic taste in the mouth are frequently experienced. Other adverse effects include: reversible neutropenia, CNS effects (dizziness, vertigo, confusion, peripheral neuropathy, seizures, encephalopathy and cerebellar dysfunction with prolonged treatment) pseudomembranous colitis, hypersensitivity skin reactions, pancreatitis, flushing, fleeting joint pains and gynaecomastia. Candida overgrowth causing stomatitis and glossitis can occur (Gibbon, 2005:463).

Contra-indications:

Safety in pregnancy and lactation has not been established (Snyman, 2006:359). Relative contra-indications include epilepsy and other CNS disease. Other contra-indications are impaired hepatic function and a history of haematological disorders.

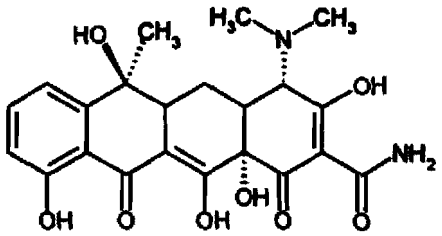
Dosage:

For the treatment of *H. pylori*-associated gastritis and duodenal ulceration the MIMS (Snyman, 2006:359) recommends 250mg metronidazole given 4 – 5 times daily for 14 days in conjunction with bismuth subcitrate and tetracycline.

2.6.6.4 Tetracycline

The structure of tetracycline (Answers, 2007:1)) is given in Illustration 2.10.

Illustration 2.10: The chemical structure of tetracycline



Indications:

Tetracycline is indicated for susceptible upper and lower respiratory tract infections, ophthalmic, intestinal infections, acne, Rickettsia, brucellosis, actinomycosis, Lyme disease, and eradication of *H. pylori* (USA Dept of health and human services, 2003:2; Snyman, 2006:333).

Mechanism of action:

Tetracyclines are thought to inhibit bacterial protein synthesis by binding to the 30 S bacterial ribosome and preventing access of aminoacyl tRNA to the acceptor (A) site on the mRNA-ribosome complex (Kapusnik-Uner *et al.*, 1996:1124).

Adverse effects:

Adverse effects listed in the MIMS (Snyman, 2006:333) are: Photosensitivity, raised intracranial pressure, gastro-intestinal disturbances, secondary fungal or bacterial overgrowth, superinfections, dermatitis, bladder dyscrasias, vaginitis, pseudomembrane colitis, allergic reactions, pericarditis, Henoch-Schönlein *purpura*, angioneurotic oedema, anaphylaxis, nail discolouration, bone growth interference, tooth discolouration and negative N_2 balance in elderly.

Contra-indications:

Renal impairment, pregnancy, lactation, children under 12 years and concomitant hepatotoxic medicines are listed as contra-indications (Snyman, 2006:333).

Dosage:

For peptic ulcer, the FDA suggests 500mg tetracycline given 4 times per day for 2 weeks in combination with a H_2 receptor antagonist, metronidazole and bismuth subsalicylate (USA Dept of health and human services, 2003:2; Snyman, 2006:359).

2.7 Chapter Summary

In chapter two a literature study was done, describing the anatomy and physiology of the gastrointestinal processes. The etiology of acid-related disorders was also described. The treatment of acid-related disorders as well as the standard treatment guidelines was listed. The drugs used for the treatment of acid-related disorders were investigated.

Chapter three provides an account of the background for the intervention. A literature review was done, describing the essential drug concept, rational drug use. Various intervention methods were also investigated.

CHAPTER 3: ESSENTIAL DRUGS, RATIONAL USE AND DRUG USE INTERVENTIONS

3.1 The essential drugs concept

The history and the principles of the essential drugs concept that led to the essential drugs list will be discussed.

3.1.1 The history of the essential drugs concept

The discovery of penicillin in 1928 by Alexander Flemming (History learning site, 2003:1) changed the medical world dramatically. Penicillin was first clinically used in 1941, followed shortly by chloroquine (1943) and streptomycin (1944). Vaccines for diptheria and tetanus toxoid were used on large military populations during World War II. Tetracycline, chloramphenicol, isoniazid, erythromycin, chorpromazine, the sulphonylureas, nystatin, and oral contraceptives (Dukes & O'Connor, 1997:18) came next. In a matter of 14 years medical practitioners and the public had access to drug compounds that could cure previously untreatable illnesses. The practitioners and public were willing to pay for the powerful products they were demanding. But by the 70s the difference between affluent and disadvantaged countries had become apparent. Affluent countries had every drug imaginable, while the poorer countries had limited access to drugs. Even within nations this contrast was apparent between urban and rural areas (Dukes & O'Connor, 1997:18). Something had to be done.

This imbalance gave rise to the Essential drugs concept. The idea was simple – concentrate on a basic list of reliable drugs to meet the most vital needs. It soon became apparent that an essential drugs list would resolve the problem created by limited financial resources. In fact, countries that had recently become independent saw an essential drugs programme (EDP) as a means of providing universal health care, in spite of the obstacles which were being encountered (Dukes & O'Connor 1997:19).

The South African perspective

Before South Africa became a democracy the pharmaceutical sector was characterised by an imbalance with regard to access to essential drugs. This impacted on the quality of care. With the aim of providing equitable health care to all its citizens, the Government of South Africa decided to approach the problem through the development of a national drug policy (NDP) (South Africa, 1994:3). The NDP that was consequently set up stipulated the development of an essential drugs programme which would include an EDL and standard treatment guidelines (STG) (South Africa, 1994:10).

In the foreword to the 1996 edition of the STG and EDL (South Africa, 1996:i) the Minister of Health stated that the EDL laid the foundation for ensuring the availability of essential medicines to all citizens. The Health Minister also stated that the STG virtually ensured the objectives of rational prescribing and optimal therapeutic outcome.

3.1.2 Principles of the essential drugs concept

The World Health Organisation defined essential drugs as *indispensable and necessary for the health needs of the population. They should be available at all times, in the proper dosage form, to all segments of society* (Dukes & Quick, 1997:8). They are those drugs that satisfy the priority health care needs of the population (WHO, 2006:1).

Dukes and Quick (1997:8) listed the following guiding principles embraced by the essential drugs concept:

- The vast majority of health problems for most members of the population can be treated with a small, carefully selected number of drugs.
- In practice, most doctors and other health professionals routinely use fewer than 200 drugs. Training and clinical experience should focus on the proper use of these few drugs.

- Procurement, distribution, and other supply activities can be carried out most economically and most efficiently for a limited number of pharmaceutical products.
- Patients can be better informed about the effective use of drugs when the number of drugs they are confronted with is limited.

A national drug policy is a commitment to a goal and a guide to action. When developing a drug policy it is important that all stakeholders in the pharmaceutical sector discuss and agree on common goals, and define priorities for action. The national drug policy document should be endorsed by the Minister of Health and be widely disseminated (WHO, 2003: 1).

3.2 Rational drug use

The definition of rational drug use is subjective. What could be considered as rational will be influenced by many factors and settings. The Concise Oxford dictionary (Allen, 1991:741) defines the word rational as: *of or based on reasoning or reason*. Should the purpose of dispensing be to earn enough income to survive, it would seem rational for a pharmacist to sell an antibiotic without a prescription. Should the aim be to prevent drug resistance, selling antibiotics over–the–counter would be irrational. Therefore, in defining the term rational drug use, one must first list criteria appropriate to the specific context. Laing and Santoso (1997:422) listed the following criteria in order to use the term 'rational drug use' in a biomedical context:

- Correct drug.
- Appropriate indication – the reason to prescribe is based on sound medical considerations.
- Appropriate drug, considering efficacy, safety, suitability for the patient, and cost.
- Appropriate dosage, administration, and duration of treatment.
- Appropriate patient – no contra–indication exists, and the likelihood of adverse reactions is minimal.
- Correct dispensing, including appropriate information for patients about the prescribed medicines.
- Patient adherence to the treatment.

Laing and Santoso (1997:422) quoted the definition for 'rational use of drugs' that was described by the Conference of Experts on the Rational Use of Drugs, (convened by the World Health Organisation) as follows:
The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.

For the purpose of this study the above definition will be adopted.

Irrational drug use can have a dramatic impact on the general health of the population. This impact can be seen in the following ways:

- Reduction in the quality of drug therapy leading to increased morbidity and mortality.
- Waste of resources leading to reduced availability of other vital drugs and increased costs.
- Increased risk of unwanted effects such as adverse drug reactions and the emergence of drug resistance, for example multiple drug resistant tuberculosis.
- Psychosocial impacts such as when patients come to believe that there is "a pill for every ill." This may cause increased demand for drugs (Laing & Santoso, 1997:422).

3.2.1 Standard treatment guidelines

The first edition of the essential drugs list (EDL) was published in 1996 and in the foreword the Minister of Health stated that the Department of Health was committed to ensuring that the medicines on the EDL would be available in all its primary health care facilities (South Africa, 1996:i).

The problem of equitable access to drugs was being addressed. The EDL was published with the standard treatment guidelines (STG). The STG was the first step in ensuring the proper use of the drugs that were now being made available.

In the national drug policy specific objectives were listed, including the following:

- To ensure good dispensing and prescribing practices.
- To promote the rational use of drugs by prescribers, dispensers and patients through provision of the necessary training, education and information (South Africa, 1994:4).

However, promoting rational drug use remains a challenge. Internationally the medical profession has generally resented any suggestion that it might be acting irrationally as a group or that it might be in need of guidance or control.

During a study performed in 2000 within the Govan Mbeki municipal clinics supplied by Evander Hospital (previously known as the Highveld Ridge Health district) it was found that 22% of all drugs prescribed did not adhere to the STG (Botha, 2000:50).
The study included prescriptions from doctors, district surgeons as well as nurses.

The World Health Organisation (WHO) suggested that drugs selected for the EDL have sound and adequate data on their efficacy and safety available from clinical studies (Hogerzeil, 1997:123). The national drug policy (NDP) followed the guidelines suggested by the WHO and listed as one of the drug selection criteria that there should be sufficient proven scientific data available regarding the effectiveness of the product (South Africa, 1994:10).

The EDP and STG underlying philosophy is evidence–based medicine, i.e. sound and adequate data exists to support the adherence to the STG. The question is: "Why would prescribers deviate from the STG?"

Laing and Santoso (1997:425) suggest the following possible reasons why prescribers do not adhere to the STG:

- Inadequate training.
- Out–dated prescribing practices due to lack of continued professional development.
- Role models that prescribe irrationally.

- Heavy patient load.
- Profit where income is dependent on drug sales.
- Pressure from the patient.
- Unreliable drug supply.

In the introduction of the 1998 edition of the Primary Health Care EDL and STG (South Africa, 1998a:ii) Professor Mokhobo stated that evidence–based data regarding efficacy, safety, risk–benefit ration, and acceptable quality had been used. One would expect with the transparency of the selection process, that the medical profession would show confidence in the EDL and STG. The abovementioned studies, however, show that the necessary confidence was not instilled. In a report that appeared in the newspaper "Beeld" in August 1995 (Marais, 1995:3) the national health care plan was strongly criticised. The greatest concern was about the financing, and Dr Rapiti was quoted as saying that there was little transparency and concurrence in the NDP. He went on to say that the proposal that PHC nurses be the first to treat patients was dangerous and very expensive. The Pharmaceutical Society expressed concern that the EDL would not save the state any money as distribution of medicines would be problematic. Marais (1995:3) also stated that various medical groups were increasingly concerned that their criticisms of the NDP were being ignored and that their commentary was not being considered in the creation of the policy document.

In order to truly understand the reason why the medical profession lacked confidence in the EDP (essential drug programme) one would have to investigate the steps that were followed during the creation of the EDL. It would seem that the medical societies felt excluded from the process, whereas the Department of Health stated that experts had been consulted during the process (South Africa, 1996: ii). For the purpose of this study we will, however, not take an in-depth look at the reason for this distrust of the EDL.

3.2.2 Diagnosis

Dukes and Quick (1997:14) state that drug use includes diagnosing, prescribing, dispensing and proper consumption by the patient. The first step

to rationally select the treatment regime that will give the patient the best possible outcome is the diagnosis. The correct treatment cannot be prescribed if the diagnosis made was not correct. The standard treatment guidelines (STG) and essential drugs list for primary health care included a description of the signs and symptoms (South Africa, 1998a:v) to aid in the process of making a diagnosis.

3.3 Pharmacoeconomics

Pharmacoeconomics evaluates and compares the costs and outcomes associated with drug therapy. It is motivated by the basic principle that financial resources are limited and that the organisational needs generally exceed available resources (McCloskey, 2001:143). Pharmacoeconomics is a tool of management which should be applied to strategic and operational decisions about pharmaceutical development, production or consumption (University of Dundee, 2007:4). It is the management of drug consumption that this study will be focused on.

3.3.1 Principles

Pharmacoeconomic studies helped to provide data on making critical decisions, such as determining which drugs should be on the organisation's formulary, defining the best organisational strategy for managing a particular disease state, and selecting the most appropriate agent to treat a patient's medical condition (McCloskey, 2001:143).

3.3.2 Pharmacoeconomic evaluation

Four methods of pharmacoeconomic evaluation are distinguished:

- Cost-minimisation analysis: Calculating the cost of two or more alternatives that have the same outcome to identify the lowest-cost option. For example, in the event of two different drugs being equally effective, the least expensive can be selected.

- Cost-effectiveness analysis: measuring both costs and benefits of alternatives to find the strategy with the best ratio of benefits, measured in therapeutic or programme effects, per money unit. For example, two antibiotics are compared on the cost per child cured taking into account the difference in efficacy.
- Cost-utility analysis: same as cost-effectiveness analysis, except that benefits are measured in "utility" units, for example, the cost per quality of life year saved of treating childhood pneumonia with drug A versus treating tuberculosis with short-course chemotherapy.
- Cost-benefit analysis: comparison of the costs and benefits of an intervention by translating the health benefits into a money value, so that both costs and benefits are measured in the same unit. For example, what is the cost-benefit ratio (value of costs per value of life saved) for treating childhood pneumonia versus the cost-benefit ratio for saving lives through improved road lighting (Hansen *et al*, 1997:34)?

For the purpose of this study a cost-effective analysis will be done. This will be done to ensure that no unintended effect on total cost would occur. Drug use interventions could have unintended effects, such as increases in hospitalisation as illustrated in a study done by Soumerai *et al.* (quoted by Laing *et al.*, 1997: 478).

3.3.3 Cost of treatment of acid-related disorders

Various factors need to be considered when calculating the actual cost of treating a disease state. In addition to the actual medical cost of administering the treatment, loss in productivity and sick leave can also have an impact on the economy of a country. Intangible costs pertaining to quality of life are more difficult to measure than the direct medical and indirect costs (McCloskey, 2001:144).

All possible costs need to be taken into account when considering which treatment would best suit the particular patient in that clinic setting.

The costs involved in medical treatment that can be measured are shown in Table 3.1.

Table 3.1: Costs involved in medical treatment (McCloskey, 2001:144–145)

Direct Costs	Medical	Acquisition costs Monitoring costs Preparation costs Professional fees of physicians, pharmacists Administrating the treatment e.g. IV admin sets Treatment of adverse drug reactions
	Non–Medical	Transport Ancillary support e.g. Home care services
Indirect costs	Related to morbidity and mortality	Loss of productivity
Intangible costs	Difficult to assign monetary value	Pain and suffering

In South Africa about 80% of the population have limited access to pharmaceutical services and are only consuming about 20% of the pharmaceutical budget, and Dr. M. Tshabalala–Msimang, in her message to the PSSA conference (Tshabalala–Msimang, 2001:9) stated that Government had an obligation to take active steps to intervene and regulate in such a way that this scenario improves.

In the South African Medical Journal editorial, Walters and Valodia (2004:173) stated that the depth of clinical and actuarial resources in our country must be utilised to balance costs with access to, and quality of, patient care.

3.4 Rational use interventions

There are various intervention methods that can be used to encourage the rational use of drugs. Great care needs to be taken when deciding which intervention or combination of interventions would be best suited to a specific environment and drug use problem.

3.4.1 Introduction

In order to optimise drug use in an organisation the following activities must continuously take place:

- Assessing current patterns of drug use.
- Defining standards of appropriate practice patterns and identifying problems and their causes.
- Carrying out interventions to improve specific problems.
- Evaluating improvements and monitoring subsequent practices (Ross–Degnan, 1997:431).

Interventions are most effective when they target specific problem behaviours, for example, a training programme discouraging polypharmacy in general will likely have less impact than training targeted at:

- Specific commonly overused drugs or
- Specific health problems in which polypharmacy is common (Laing *et al.*, 1997:465).

Once drug use patterns have been assessed and evaluated, the problems and their causes can be identified. The next step would be to identify which method of intervention would be appropriate to address the identified drug use problem. The interventions should be carefully selected with regard to efficacy, feasibility for implementation in the existing system, and cost (Laing *et al.*, 1997:465).

Drug use intervention strategies can be classified into three main categories:

- Educational:

  By providing information the prescribers are persuaded to change inappropriate prescribing habits, for example:

  - Training of prescribers;
  - Printed materials and
  - Approaches based on face to face contact.
- Managerial: The prescribers are guided in the decision–making process for example:
  - Limiting selection, procurement and distribution and
  - Prescribing and dispensing approaches such as standard treatment guidelines and course of therapy packaging.
- Regulatory: Prescribers are forced to restrict the decision–making process in prescribing for example:
  - Drug registration;
  - Limited drug lists;
  - Prescribing restrictions and
  - Dispensing restrictions (Laing et al., 1997:466).

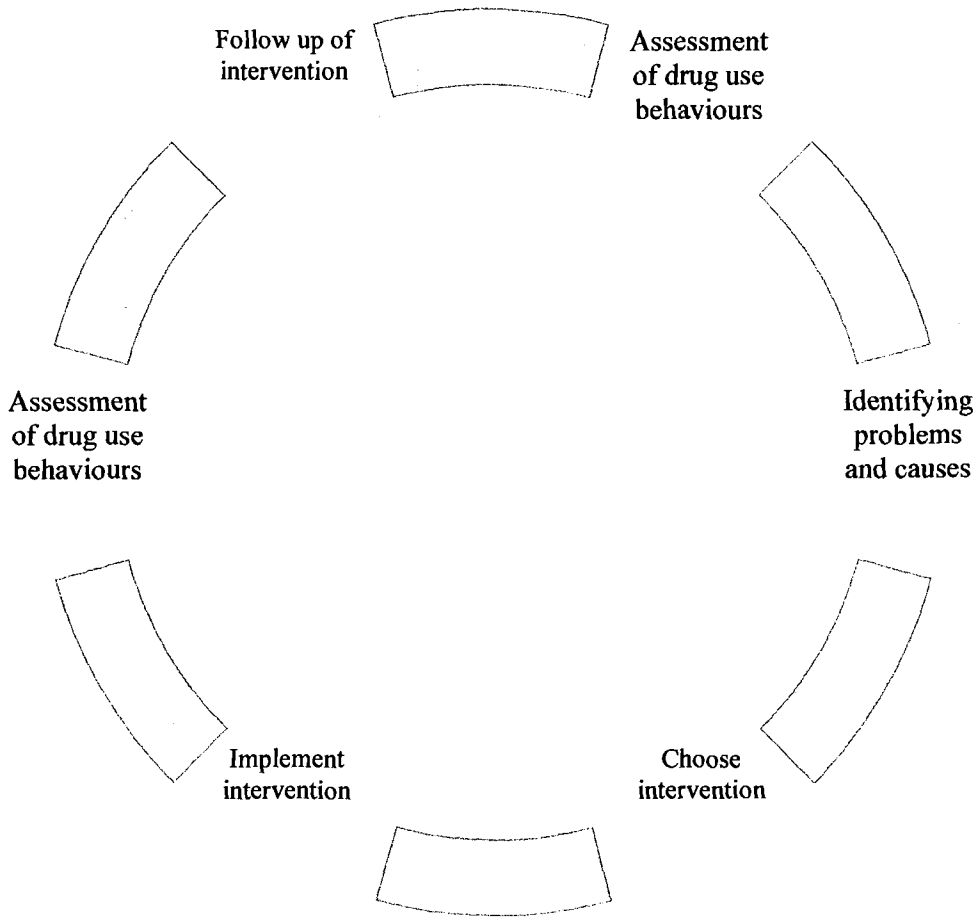
An intervention can only be effective if it is focused on achieving a specific goal and targeted at those prescribers who have a particular prescribing problem (Laing *et al.*, 1997:467). When interventions of different types are combined, the impact is likely to be synergistically increased (Laing *et al.*, 1997:466).

It is also very important that all interventions are followed up, as most interventions have a limited impact over time. Although there may be an initial improvement, prescribers tend to revert to their previous behaviour (Laing *et al.*, 1997:467).

The keys to successful intervention can be summarised in Illustration 3.1.

Illustration 3.1: Successful intervention

(Adapted from Laing *et al.*, 1997:467)



3.4.2 Face to face interventions

The most effective means of changing behaviour has consistently been face to face contact (Laing *et al.*, 1997:471).

Face to face education has many unique advantages. It is a flexible strategy and not limited to a specific place or setting (MEDUNSA, 2001:4). There is no need for large, often costly, venues. The effect on work flow is also reduced as only one health worker is occupied while his/her colleagues can continue to consult patients. Face to face education allows for two–way communication (MEDUNSA, 2001:4). Interaction between the educator and the prescriber allows the reasons for irrational prescribing to be identified and addressed. This is vital if the prescriber's behaviour is to be changed.

For face to face educational approaches to be effective the following principles need to be adopted:

- Established credibility of educator (MEDUNSA, 2001:3).
- Focusing on specific problems and targeting the audience of prescribers (Laing *et al.*, 1997:471).
- Relevant to actual therapeutic decisions (MEDUNSA, 2001:3).
- Understanding (MEDUNSA, 2001:3) and addressing the underlying causes of the prescribing problems (Laing *et al.*, 1997:471).
- Allowing an interactive discussion and involving the targeted audience (Laing *et al.*, 1997:471).
- Using concise and authoritative materials based on credible scientific information (Laing *et al.*, 1997:471).
- Giving sufficient attention to solving practical problems encountered by prescribers in real settings (Laing *et al.*, 1997:471).
- Using simplicity of language and common dialects (MEDUNSA, 2001:3).
- Repeating key messages (MEDUNSA, 2001:3).

The intervention process used in this study will be discussed in 4.5.

3.5 Measuring outcomes of interventions

When evaluating the effect of an intervention it is important to measure possible outcomes.

3.5.1 Outcomes

An outcome is a consequence of drug therapy intervention and includes the following:

- Clinical outcomes which evaluate the favourable and unfavourable results of treatment.
- Humanistic outcomes which evaluate the effect on the patient's quality of life.

- Economic outcomes which evaluate all the costs associated with the drug and medical care (McCloskey, 2001:144).

3.5.2 The rationale behind outcome measurement

In order to maximise the net health benefit derived from the use of health care resources, the focus has moved to the evaluation of the end results of medical systems and interventions (Brown *et al.*, 2005:17). Efficiency implications arise with the choice of drug and length of course of therapy. Efficiency can be defined as getting the most output for a given quantity of resources (Hansen *et al.*, 1997:33).

Public health is concerned with using available resources to achieve maximum health improvements for the population (Dukes & Quick, 1997:8). Inappropriate prescribing impacts on both financial (overuse of pharmaceuticals) as well as human resources. Underuse of drugs, for example, may produce excess cost by increasing the probability of prolonged disease and eventual hospitalisation (Laing & Santoso, 1997:424).

One of the reasons why public health services are in a distressed position is the huge shortage of nurses (Anon, 1990: 10). In most of the hospitals there simply are not enough staff members to deal with the influx of patients (Swanepoel & Van der Spuy, 1997:16). Unfortunately the situation has not improved in recent years. Health Minister Manto Tshabalala-Msimang announced in 2004 that medical assistants would be trained to alleviate the shortage of doctors, particularly in rural areas (SAPA, 2004:1). Because of this shortage of personnel in state medical facilities, minimising the time per patient without affecting the clinical care has become a priority.

When interventions in drug prescribing are done, unintended effects can occur. For example, Soumerai *et al.* (as quoted in Laing *et al.*, 1997:478) found that in New Hampshire (USA) unintended increases in nursing home admissions occurred when restrictions were placed on the number of drugs that could be prescribed to outpatients. Although small savings were made on drug costs, the cost of extra admissions outweighed these savings. Another

possible unintended effect can occur when patients are forced to visit health centres more frequently as a result of limitations that were placed on the length of treatment (Laing *et al.*, 1997:479). It is therefore important to monitor for such unintended effects when assessing the outcome of an intervention.

3.5.3 Relevance to this study

In this study the intervention strategy was educational. Prescribers were persuaded to change inappropriate prescribing habits by encouraging them in face to face contact to adhere to the standard treatment guidelines. The goal of the intervention strategy was to reduce treatment costs by, *inter alia*, the following:

- Decrease in prescribing of secondary level drugs
  Secondary (or hospital) level drugs are not kept at primary health care facilities. These drugs may only be prescribed by a medical doctor. Prescriptions for these drugs are sent to the referral hospital for dispensing. The dispensed drugs are then sent back to the primary health care facility, where the patient then collects the medication. This causes a delay in treatment, an increase in administration and transport costs as well as an increase in human resource requirements.
- Decrease in duration of treatment
  The longer the duration of treatment, the more drugs need to be dispensed.
- Decrease in number of visits by the patient
  The more visits by the patient, the greater the burden on human resources.

Veldhuyzen Van Zanton (2002:23) noted that the lack of validated outcome measures in the study of dyspepsia treatment resulted in a lack of consensus amongst researchers on how best to measure outcomes in functional dyspepsia trials. When conducting a randomised clinical trial to evaluate a therapy, the primary outcome measure must match the anticipated treatment effect (Rabeneck *et al.*, 2001:760). Therefore the measurement instrument

must be carefully researched and planned. Various instruments have been developed and will be discussed further on.

The outcome measurement tools used in this study will be discussed in 4.6.1.

3.5.4 Severity of dyspepsia assessment (SODA)

SODA is a multidimensional measure intended for use as primary outcome measure in randomised clinical trials. It consists of scales that measure pain intensity, non-pain symptoms and satisfaction scales (Rabeneck *et al.*, 2001:760).

SODA is a self-administered questionnaire and asks patients to provide responses pertaining to the previous 7 days. The SODA pain intensity scale is a multi-item measure and provides a more reliable measure than a single-item scale. The SODA scale does not, however, discriminate well among patients with low levels of satisfaction (Rabeneck *et al.*, 2001:760). Wristers *et al.* (2002: 32) found that SODA was a reliable, valid instrument for use as a measure of dyspepsia tolerability in future clinical trials.

3.6 Chapter Summary

In chapter three the history and principles of the essential drugs concept was described. Rational drug use was defined and the process of establishing standard treatment guidelines as well as the challenges in encouraging adherence was discussed. Drug use interventions, the measurement of the effects of these interventions and their relevance to this study were explained. Although it could not be utilised in this study the SODA measurement tool was briefly described.
Chapter 4 contains a detailed description of the research methodology.

CHAPTER 4: RESEARCH METHODOLOGY

In this chapter the methodology of the study will be discussed.

4.1 General methodology

The nature of the research was the following:

- A survey form
- An empirical quantitative time series study that included multiple observations of the study population before and after the intervention.

Primary data obtained from patient files at the clinics was used.

The timeline for progress of the research is shown in Appendix F.

4.2 Research instruments

The data was collected by means of a survey questionnaire. See Appendix A for an example of the survey questionnaire. The abbreviations used to describe the various drug use indicators included on the survey questionnaire are defined in Appendix B. A pilot test was done in July 2003 by testing the abovementioned survey questionnaire on a random sample of 50 prescriptions that had been written at Secunda Clinic. Various shortcomings were identified and the survey questionnaire was adjusted accordingly. One example is that in the initial survey questionnaire no allowance was made for those prescriptions that did not have the diagnosis specified. The Health Problem Description was then altered to include 3.a. Not specified. This made completing the survey questionnaire more efficient. Similarly the NSAID's, and amitriptyline were added to the list of drugs. As stated in 4.6.3.7 and 4.6.3.8 these drugs may aggravate the symptoms of acid-related disorders.

Description of data analysis software

The Epi Info™ software was used for data analysis. It is based on Microsoft Access™ and consists of various components. The first of these components used in the data analysis is 'Make View'. The database is designed in 'Make

View'. For this study two data entry forms (called "views") were designed for the capturing of data. The first data entry form shown in Appendix C, was used for capturing patient information. For example, the patient's age, gender and smoking habits were included in this questionnaire. The second data entry form, shown in Appendix D, was used for capturing prescription information for example, treatment prescribed, duration of treatment and diagnosis.

The second component of Epi Info™ is 'Enter Data'. The data collected on the survey questionnaire was then entered into the two relevant data entry forms. The prescription data entry form was designed so that certain data captured on a prescription data entry form would automatically repeat on the next data entry form. For instance, for a patient receiving chronic medication, once this information had been entered into the data entry form, the next form for a prescription for that patient would automatically contain the same data. It would not be necessary to recapture the data each time. If the patient's treatment did change, however, the new prescription details could be entered and this new information was automatically repeated. This expedited the capturing of data.

Each data entry form is used to create a table in a Microsoft Access™ database. These tables could be linked by defining the relationship between them. A unique key (data entry field) was given to each patient. In the patient information data entry form the data entry field "Patient ID" formed the unique key. Once the information had been entered into the patient details data entry form, the linked data entry form (in this case the prescription information data entry form) could be accessed. For each patient more than one prescription could be entered on this linked data entry form. Epi Info™ automatically repeated the unique key of the patient detail data entry form onto each prescription information data entry form for a particular patient. It was therefore not necessary to enter the patient ID data on the prescription information data entry form. The unique key (Patient ID) allowed Epi Info™ to link up each patient's prescription information data entry form to his/her patient information data entry form.

The number of patients included in this study amounted to 632 patients, with a total of 994 prescriptions. An additional 52 prescriptions written between 1 January 2003 and 30 June 2003 were also captured on Epi Info™ to enable the researcher to determine the outcome of treatment. These 1046 prescriptions were then linked to the 632 patient profiles.

The final component used in this study was 'Analysis'. 'Analysis' is the programme in Epi Info™ used for analysing data (CDC, 2005). The data from the data base was imported into 'Analysis' and statistically analysed.

During the analysis of the data the two data entry forms (questionnaires) were merged. Because of the merger, the data could be exported to Excel where further adjustments could be made to the spreadsheet. For instance, another column was added, and all the patients who had received one of the antidiabetic drugs available in the State could be identified as being diabetic (see 4.6.2.12). The same could be done for other conditions or drug use indicators. The frequency of patients treated at each facility could also be determined using the same procedure. Because the data entry forms were merged, the details of patients who moved between health facilities, for instance, could be entered on the patient data entry form. The data from the prescriptions from the different facilities could then also be entered on the merged data entry forms without affecting the statistics. Although the data entry forms were designed to allow for roaming patients, none of the patients included in the study moved between the study facilities.

In October 2003 a pilot test was performed on the Epi Info™ data entry forms to ensure that the data collected could be quickly and accurately captured. This was done by entering 20 prescriptions into Epi Info™. The tab order for the capturing of data was then changed to speed up the data capturing. Pilot tests were done in October 2003 on the analysis of data to ensure that all the variables were correctly described for efficient and accurate analysis.

An overview of Epi Info™ 2002 and a brief description on how Epi Info™ can be utilised are given in Appendices G and H respectively.

4.3 Research design

The research design can be described as "an evaluation research: experimental outcome study" as its aim was to answer the question whether an intervention (in this case the face to face education intervention) had been successful or 'effective' (Mouton, 2001:160). The research was done to determine what intended and unintended outcomes materialised after the intervention.

4.4 Obtaining data

Ross-Degnan (1997:438) suggested that useful information can be obtained from case records and that the audit process can start with a drug after the criteria has been defined for correct or incorrect use of a drug. The case records of the patients who received the drug(s) are identified and reviewed, and the treatment of the disease is recorded and classified as correct or incorrect. Capellà (1992:71) stated that, by using data on prescriptions, it is possible to relate prescribing patterns to many other aspects, including the following:

- Study the relationship between the prescribed medicine and the apparent indication.
- Identify illnesses most frequently treated.
- Identify and study prescription determinants, such as the influence of particular information or publicity campaigns on prescribing.

A quantitative survey on the usage of magnesium trisilicate suspension, aluminium hydroxide/magnesium trisilicate tablets (combination), cimetidine or omeprazole use was conducted. These drugs are only indicated for acid-related conditions (Snyman, 2006:243). These are also the only drugs, used at the study facilities, indicated in the EDL for use in acid-related disorders (South Africa, 1998a:207; South Africa, 1998b:303).

To determine a baseline, all prescriptions where magnesium trisilicate suspension, aluminium hydroxide/magnesium trisilicate tablets, cimetidine or omeprazole had been prescribed from 1 July 2001 to 31 December 2001 were collected. For the period 1 January 2002 to 31 December 2002 retrospective data was collected in the form of all the prescriptions where

magnesium trisilicate suspension, aluminium hydroxide/magnesium trisilicate tablets (combination), cimetidine or omeprazole had been prescribed. Thereafter retrospective data was collected for the period 1 January 2003 to 30 June 2003 to determine the outcome of treatment given to patients in the period 1 July 2002 to 31 December 2002.

The data was collected from patient treatment files that are kept at the clinics. Prescriptions and stock cards were used to select patients. The patient details were included on the prescriptions and stock cards. These allowed the researcher to consult the files and obtain a complete consultation and treatment history of the patient. All the data collected was retrospective.

Sampling

The population for this study consisted of all the patients to whom magnesium trisilicate suspension, aluminium hydroxide/magnesium trisilicate tablets (combination), cimetidine or omeprazole had been prescribed at the Govan Mbeki municipal clinics supplied by Evander Hospital during the period 1 July 2001 to 31 December 2002. Two hundred and ninety one (291) patients were enrolled into the study from July 2001 to December 2001. A further 341 patients were enrolled into the study during 2002.

The population size was limited (N = 632), therefore all prescriptions that were eligible for the study were included. Random sampling was not used.

4.5 Intervention

Following the retrospective study on the treatment of acid-related disorders in 2001 at the Govan Mbeki Municipal clinics supplied by Evander Hospital (Botha *et al.*, 2001:1) it was decided that an intervention was needed. A workshop was held in Pretoria during September 2001 to plan the format for the intervention. This workshop was attended by the pharmacists at Evander Hospital and facilitated by the Medical University of South Africa's School of Pharmacy.

For the intervention to be effective it needs to be focused to achieve a specific goal (Laing *et al.,* 1997:465). The first step was to determine the objectives of the intervention. These were listed as follows:

- An increase in the percentage of prescriptions that adhere to the STG.
- A reduction in total cost to the pharmaceutical budget.
- A decrease in morbidity rates.

Once the objectives had been determined, the particular prescribers that needed to be targeted by the intervention had to be identified (Laing *et al.,* 1997:465). It was decided that all prescribing categories would be targeted.

Various interventions were investigated before deciding which method would be utilised. The advantages and disadvantages of each of the methods relative to the Evander hospital setting were listed (as below):

Training of prescribers (Educational) (Laing *et al.*, 1997:466)

Advantages:

- Creates a change mindset of prescribers.
- It has long term effects.
- The effect can spill over to other ailments – for example improvement in STG compliance for other illnesses.
- Face to face education is possible in small groups.
  - The staff requirements in hospital and clinics remained constant so the trainers could not extract all the doctors for a session together. The same situation existed with nurses.
  - The face to face education is more interactive – the trainers would be able to address individual questions and concerns.

Disadvantages:

- Cross contamination could occur as the prescribers rotated between health facilities.

Implement motivation system (Regulatory) (Laing *et al.*, 1997:466)

Advantages:

- The effect would be immediate.

Disadvantages:

- The duration of the effect would be short.
- It could lead to escape behaviour (prescribers could begin prescribing other inappropriate drugs).
- It is a high maintenance intervention.

After considering the abovementioned advantages and disadvantages it was decided that the face to face education intervention would be implemented. The plan was to invite the prescribers to join the pharmacy personnel for coffee in the pharmacy office. This was done because the doctors at Evander hospital did not have a designated coffee room and seldom had chance to drink coffee while working.

The implementation of the intervention was delayed until January 2002, as some of the pharmacists were delegated by the Provincial administration to be trained as assessors of pharmacist assistants and could not give the necessary attention to the preparation for the face to face sessions. It was also decided that the education could be preventative if the community service doctors were trained from the outset to prescribe the drugs optimally and rationally before they enter the clinics (Truter, 2001:17).

Two pharmacists had been trained on rational drug use, as well as the face to face training method, and were delegated to address the prescribers. If the work load permitted, the other pharmacists would assist in the discussion. The two delegated pharmacists were fluent in English and Afrikaans. The discussion was therefore held in whichever one of the aforementioned languages the prescriber felt most comfortable with. Unfortunately the discussions could not be held in the first language of all the prescribers. For example, three of the medical officers at Evander hospital were Cuban and there were no pharmacists that could speak Spanish. But all the prescribers were comfortable with either English or Afrikaans.

In January 2002 the invitations were extended to the prescribers. The invitations were verbally delivered on a one-to-one basis. The invitations were also repeated at the Pharmaceutical and Therapeutics Committee meetings.

The doctors in particular were keen to accept the invitation. The PHC nurses often visited the hospital when they accompanied patients to the hospital, delivered medicine orders, referral prescriptions or laboratory samples or came to see the hospital management. The nurses were invited for coffee during these visits to the hospital.

It was during these coffee breaks, that the pharmacists addressed the problems of EDL adherence. The relaxed atmosphere allowed for open discussion, allowing the prescribers an opportunity to express their views and list the problems they were experiencing while visiting the outlying clinics. The pharmacy also had medical reference books and these were made available to the prescribers. The prescribers were encouraged to approach the pharmacy personnel with medicinal queries, i.e. personally or by telephonic communication.

The following key points were addressed during the face to face discussion:

- The prescriber was introduced to the pharmacy personnel.
- An open invitation for discussion between prescribers and pharmacy personnel was extended.
- The prescriber was introduced to the pharmacy procedures regarding issuing of stock to clinics.
- The trainer ensured that each prescriber had his/her own copy of the STG and EDL (primary level, hospital level and paediatric).
- The trainer ensured that the prescriber understood the format of the STG and EDL.
- Rational drug use and effective prescribing were broadly explained.
- The prescriber was informed of pharmaceutical budget restrictions.
- The impact of out-of-stock situations and the motivation-order system was discussed.
- The results of pre-intervention pilot study were shared.
- The STG for the treatment of acid-related disorders were reviewed.
- Possible reasons for non-adherence, e.g. patient expectations, heavy workload were discussed.
- Solutions for non-adherence were formatted.
- The prescriber was encouraged to adhere to the EDL.

The face to face intervention sessions varied in length because some of the prescribers had more questions and concerns than others. The PHC nurses, for instance, were more familiar with the EDL and STG and did not require detailed explanations of the format of these books.

Principles of face to face education

As discussed in 3.4.2. various principles need to be considered when implementing face to face education. These principles were each included in the planning of the intervention as illustrated in Table 4.1.

Table 4.1: Principles of face to face education implemented.

Principle of face to face education	**Plan for implementation**
Established credibility of educator (MEDUNSA, 2001:3).	Introduce prescriber to pharmacy personnel, explain how STG and EDL were set up.
Focusing on specific problems and targeting the audience of prescribers (Laing *et al.*, 1997:471).	Focus on acid-related disorders, target prescribers working at clinics.
Understanding (MEDUNSA, 2001:3) and addressing the underlying causes of the prescribing problems (Laing *et al.*, 1997:471).	Encourage discussion of possible reasons for non-adherence to STG.
Allowing an interactive discussion and involving the targeted audience (Laing *et al.*, 1997:471).	Create relaxed atmosphere and open discussion, giving the prescribers chance to express their views and list the problems they are experiencing at clinics.
Using concise and authoritative materials based on credible scientific information (Laing *et al.*, 1997:471).	Share results of pre-intervention study and review STG for the treatment of acid-related disorders with prescriber.
Giving sufficient attention to solving practical problems encountered by prescribers in real settings (Laing *et al.*, 1997:471).	Invite prescriber to suggest solutions for non-adherence.
Using simplicity of language and common dialects (MEDUNSA, 2001:3).	Try to speak in a language they are comfortable with – first language preferable.
Repeating key messages (MEDUNSA, 2001:3).	At end of discussion encourage prescriber again to adhere to EDL.

4.6 Analysis

Qualitative (nominal) and quantitative (both discrete and continuous) data (Waning & Montagne, 2001:79; Carrol & Carrol, 2002:5) was gathered during the empirical study. The data was captured and statistically analysed using Epi Info™, (Version 3.2.2. 2005 release) (CDC, 2005). The data was also exported to Microsoft® Office Excel to allow for certain statistical calculations. For instance the filter function was employed in Microsoft™ Office Excel spreadsheet to expedite the classification of the STG adherence of the prescriptions. This spreadsheet was then analysed using Epi Info™ and contingency tables were drawn up. Various descriptive statistical calculations were used depending on the data type.

The total number of cases involved in the study will be indicated by the symbol 'N' (De Wet *et al.*, 2003: 63).

In 4.6. below the term "patient" refers only to those patients who were included in the study. The term "prescription" refers to those prescriptions that were included in the study.

Decimals were rounded off to two.

Classification Variable

A classification variable is one that takes on only a few different numerical values or it is a variable indicating categories. A frequency table shows how many times a certain value or category occurred in the data array at hand (De Wet *et al.*, 2003: 60).

Arithmetic mean (Steyn *et al.*, 1999:99)

The arithmetic mean (or average) of a set of observations x1, x2,....xn is defined by:

$$\bar{x} = \frac{x1 + x2 + \ldots\ldots + xn}{n}$$

$$= \frac{\sum x}{n}$$

Median

The median of n observations is defined as the

$$\frac{(n+1)^{th}}{2}$$

value in the data array (Steyn *et al.*, 1999: 103).

Mode

The mode is the value most often occurring in the data set (Steyn *et al.*, 1999:104).

Standard deviation

The standard deviation (Steyn *et al.*, 1999:130) of x1, x2,....xn is defined by

$$s = \frac{\sqrt{\sum (x - x)^2}}{n - 1}$$

Percentile

If $1 \leq i\ (N = 1) \leq n$, the ith percentile can be determined as the

$$\frac{i\ (n + 1)\ th}{100}$$

value in the data array (Steyn *et al.*, 1999:106).

Contingency table

Contingency tables are commonly used to describe the co-variation of two classification variables. This is done by showing the frequencies of the two classification variables across different categories. Advantages of contingency tables are the ease of construction and the ease of interpretation (De Wet *et al.*, 2003: 135).

For each of the contingency tables the row percentage and the column percentage were calculated. The row percentage was calculated by first totaling each row. The value of each square in that row was then divided by that row's total and multiplied by 100. This was done for each row in the contingency table. To determine the column percentage, each column was individually totaled. The value of each square in that column was then divided by that column's total and multiplied by 100. This was done for each column in the contingency table. Therefore, the total of the column percentages for all the squares in a column will be 100%. Likewise, the total of the row % in a row will be 100%. An example is given in Table 4.2.

Table 4.2: Example of contingency table

	Column 1	Column 2	Column 3	Column 4	Total
Row A	**A1**	**A2**	**A3**	**A4**	**A1+A2+A3+A4**
Row %	A1/(A1+A2+A3+ A4) X 100	A2/(A1+A2+A3+ A4) X 100	A3/(A1+A2+A3+ A4) X 100	A4/(A1+A2+A3+ A4) X 100	100%
Column %	A1/(A1+B1+C1+ D1) X 100	A2/(A2+B2+C2+ D2) X 100	A3/(A3+B3+C3+ D3) X 100	A4/(A4+B4+C4+ D4)X 100	A1+A2+A3+A4/ (A5+B5+C5+D5) X 100
Row B	**B1**	**B2**	**B3**	**B4**	**B1+B2+B3+B4**
Row %	B1/(B1+B2+B3+ B4) X 100	B2/(B1+B2+B3+ B4) X 100	B3/(B1+B2+B3+ B4) X 100	B4/(B1+B2+B3+ B4) X 100	100%
Column %	B1/(A1+B1+C1+ D1) X 100	B2/(A2+B2+C2+ D2) X 100	B3/(A3+B3+C3+ D3) X 100	B4/ (A4+B4+C4+D4) X 100	B1+B2+B3+B4/ (A5+B5+C5+D5) X 100
Row C	**C1**	**C2**	**C3**	**C4**	**C1+C2+C3+C4**
Row %	C1/(C1+C2+C3+ C4) X 100	C2/(C1+C2+C3+ C4) X 100	C3/(C1+C2+C3+ C4) X 100	C4/(C1+C2+C3+ C4) X 100	100%
Column %	C1/(A1+B1+C1+ D1) X 100	C2/(A2+B2+C2+ D2) X 100	C3/(A3+B3+C3+ D3) X 100	C4/ (A4+B4+C4+D4) X 100	C1+C2+C3+C4/ (A5+B5+C5+D5) X 100
Row D	**D1**	**D2**	**D3**	**D4**	**D1+D2+D3+D4**
Row %	D1/(D1+D2+D3+ D4) X 100	D2/(D1+D2+D3+ D4) X 100	D3/(D1+D2+D3+ D4) X 100	D4/(D1+D2+D3+ D4) X 100	100%
Column %	D1/(A1+B1+C1+ D1) X 100	D2/(A2+B2+C2+ D2) X 100	D3/(A3+B3+C3+ D3) X 100	D4/ (A4+B4+C4+D4) X 100	D1+D2+D3+D4/ (A5+B5+C5+D5) X 100
Total	**A1+B1+C1+D1**	**A2+B2+C2+D2**	**A3+B3+C3+D3**	**A4+B4+C4+D4**	**E1+E2+E3+E4**
Row %	A1+B1+C1+D1/ (D1+D2+D3+D4) X 100	A2+B2+C2+D2/ (D1+D2+D3+D4) X 100	A3+B1+C1+D1/ (D1+D2+D3+D4) X 100	A4+B4+C4+D4/ (D1+D2+D3+D4) X 100	100%
Column %	100%	100%	100%	100%	100%

Therefore, the row percentage uses a total row count as the basis for computing a percentage. It is the percentage of the observations within a particular row category that are in a specified category of the column variable (Utts & Heckard, 2007:197).

In the same way, the column percentage can be defined as the percentage of the observations within a particular column that are in a specified category of

the row variable, and a total column count is used as the basis for computing the percentage (Utts & Heckard, 2007:197).

Phi Coefficient

The Phi coefficient (φ) is a measure of association derived from the Pearson chi-square statistic. It has the range $-1 \leq 0 \leq 1$ for 2 x 2 tables (SAS, 2006:1). The φ coefficient can be used to represent the degree and direction of dependence between the two characteristics A and B (Steyn *et al.*, 1999:556).

The φ coefficient for two variables (x,y) is also defined (Anon, 2006:1) as:

$$\varphi = \frac{a(d) - b(c)}{\sqrt{(a+b)(c+d)(a+c)(b+d)}}$$

For the 2 x 2 table:

		y	
x		a	b
		c	d

The above formula was used in Chapter 5 to determine the φ coefficient for the 2 x 2 tables.

For tables larger than 2 x 2, a measure called "Cramer's phi" is derived by the following formula (where N= the total number of observations, and k= the smaller of the number of rows and columns):

$$\text{Cramer's phi} = \sqrt{\frac{\text{Chi - square}}{N(k-1)}}$$

Interpretation of the correlation coefficient (φ)

The correlation coefficient measures the strength of a linear relationship between two variables. The value always falls between -1 and 1. The closer the correlation is to -1 or to 1, the closer the relationship is to being perfectly linear (Childrens Mercy, 2006:2).

Cohen (as quoted in Steyn, 2005: 22) proposes the following criteria for use in determining the strength of the relationship between two variables.

- φ =0.1 Small effect
- φ = 0.3 Medium effect
- φ = 0.5 Large effect

For the purposes of this study the above criteria will be used.

4.6.1 Measuring outcomes

The SODA (Severity of dyspepsia assessment) questionnaire (mentioned in 3.5.4.) could not be used in this study because the researcher did not have access to patients during treatment. Providing patients with the SODA questionnaire would have relied on a patient's ability to recall symptom relief within the 7-day period after receiving treatment. As some prescriptions had been issued up to 2 years before the study, this would not have been feasible. Therefore, another measurement tool had to be developed to determine the outcome of treatment.

Santos (2000:312) based the measurement of success of treatment on the assumption that the patient did not return for a repeat visit for the same gastrointestinal disorder. Santos also noted that this assumption did not take into account that the patient may have consulted medical help elsewhere or may not have been able to afford to return to the private clinic.

For the purpose of this study the following assumptions have been made:

Once a patient had received treatment one of the following outcomes could occur:

- Cure
- No relief from symptoms
- Relief or suppression of symptoms

In order to measure the above possible outcomes, further assumptions were made, namely:

- If the illness is cured, the patient will not return for treatment of the same complaint.
- If there is no relief of symptoms the patient will return before the end of duration of treatment and the treatment will be changed.
- If the treatment successfully suppresses the symptoms the patient will continue returning to the health facility for continuation of the same treatment.

Measurement of the above outcomes may be influenced by the following possible events:

- Patient remains with the same health facility.
- Patient changes health facility.
- Patient passes away from related or unrelated cause.

The difficulty arises then in classifying the outcome in cases where the patient did not return to the health facility. The patient may have been cured, may have passed away or may have changed health facility. Change of health facility can occur for various reasons: change of residential address, dissatisfaction with service or the patient might not be able to afford the health facility fee.

The health facilities that were included in the study are all state run, and only non-medical aid patients attend these clinics. It is unlikely that the patients would seek medical attention from private institutions as they did not have medical aid. The patients do not have to pay for treatment received at the

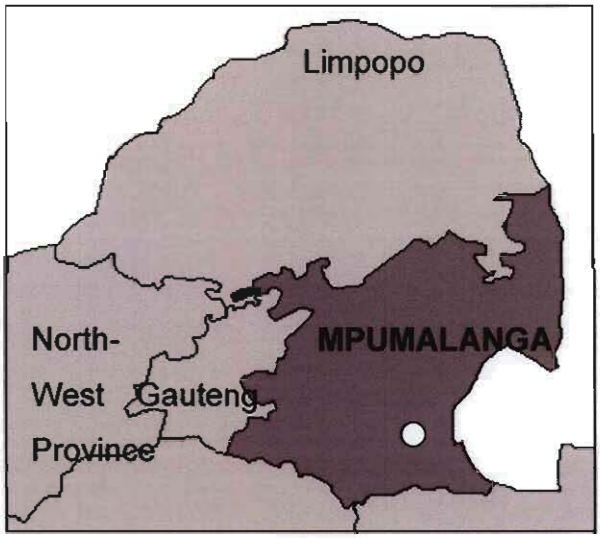
facilities included in the study. The patients are also restricted to attend the health facility closest to their residence so random changes in health facility are unlikely. This was taken into account in the study design. Deaths, if known, are recorded in health facility patient files.

Therefore, the assumption was made, that if a patient did not return with the same complaint, that the patient had been cured.

4.6.2 Demographics

The study took place in parts of the Govan Mbeki Municipal area. This area is located in the south-eastern region of Mpumalanga. Illustration 4.1 shows the geographical location of Mpumalanga. The Govan Mbeki municipal area is indicated by the circle.

Illustration 4.1: Northern Provinces of South Africa



The following facilities are included in this area:

- One Provincial Hospital
  Evander hospital was the first point of referral from the primary health care facilities, mobile clinics and community health centres.
- Two community health centres (CHC) (managed by Department of Health)
- Four primary health care (PHC) clinics (managed by municipality)
- One primary health care (PHC) clinic (managed by Department of Health)
- Two mobile clinics (managed by Department of Health)

Only the four municipal primary health care (PHC) clinics supplied by Evander hospital were included in the study population – although the medical officers and community service doctors as well as the central pharmaceutical services were shared by all these facilities. The professional nurses were not rotated among the facilities.
Records of the general patient and facility demographics were not kept by the facilities. Comparisons could therefore not be made between those patients included in the study and the general population treated by the facilities.

The following patient and facility demographics will be quantitatively investigated:

4.6.2.1 Enrolment demographics

The date of the first prescription per patient was investigated in order to determine when the patient was enrolled into the study. The frequency for each year and the percentage of the total number of patients were calculated. This was done to determine how many patients who were enrolled in 2001 still formed part of the study in 2002 and how many new patients were enrolled in 2002.

The frequency of patients who were included in the study for each year was also calculated. The percentage of the total number of patients was calculated.

4.6.2.2 Age demographics of the study population

The frequency of patients treated in each age group was used to determine the percentage of patients treated in a specific age group.

The patient's age was recorded at the time of the first prescription written during the study period.

The patients' ages were divided into three categories:

- Under 19 years (0 < 19)
- 19 to under 46 years (19 < 46)
- 46 years and older (46 ≤)

Age is a factor to be taken into consideration because increasing age decreases the tension of the upper oesophageal sphincter and the stomach lining's capacity to resist damage decreases, which can increase the chances for dyspeptic symptoms (Merck, 2003d:1).

4.6.2.3 Gender demographics of study population

The frequency of patients treated in each gender group was used to calculate the percentage of patients treated in each of the gender groups.

A 2 x 2 contingency table was drawn up, comparing the gender demographics of this study to those of the study done by Botha in 2000.

During the study done by Botha (2000:48) it was found that all service providers in the district treat more female than male patients. The gender demographics of this study will be compared to the results of Botha's study. This would show whether there were specific gender patterns to acid-related disorders.

4.6.2.4 Race demographics

To determine the percentage of patients treated in each of the race groups, the number of patients treated in each race group was calculated.

4.6.2.5 Prescriber demographics

To determine the percentage of prescriptions for the treatment of acid-related disorders written by each prescriber qualification group, the number of prescriptions written by each prescriber qualification group was calculated.

The results before the intervention and after the intervention were calculated separately.

Three prescriber categories were investigated in this study, the first being the primary health care nurse. These are professional nurses registered with the South African Nursing Council. They would consult patients and prescribe medication on the primary health care EDL where indicated. The PHC nurse would dispense his/her own prescriptions only.

The second category was the community service doctor. These doctors had recently completed their medical internship and were doing their compulsory one year community service. These doctors had all been trained at a South African university.

The third category was the medical officer. These doctors had been employed by the state on a permanent basis. At the time of the study only one of these doctors had been trained in South Africa. The other medical officers had been trained in foreign countries, such as Cuba. Most of these medical officers that trained in countries other than South Africa had specialised during their training.

4.6.2.6 Percentage pregnant patients in the study population

To determine the percentage of female patients who were pregnant and were treated for acid-related disorders, the number of pregnant female patients was calculated.

4.6.2.7 Percentage of patients who received a gastroscopy

The number of patients who had received a gastroscopy was determined and used to calculate the percentage of patients included in the study that received a gastroscopy.

4.6.2.8 Facility demographics

To determine the percentage of patients who were treated for acid-related disorders at each facility, the number of patients treated for acid-related disorders at each facility was calculated. This was done for each facility. The results were graphically represented.

4.6.2.9 Employment demographics

To determine the percentage of patients who were employed, the frequency of patients who were employed was used.

This was repeated for the patients who were unemployed.

4.6.2.10 Marital status demographics

To determine the percentage of patients who were married, the number of patients who were married was determined. This was repeated for the divorced, single and widowed patients.

As discussed in 4.8.3 patients living alone tend to show poorer compliance to treatment regimes and this could have an influence on the therapeutic outcomes of treatment.

4.6.2.11 Percentage of patients who smoke

To determine the percentage of patients who smoke, the frequency of patients who were smoking at the time of the study was calculated.

The number of patients who were questioned about their smoking habits by the prescriber was calculated and stratified by prescriber category. The percentage of the total number of patients was also determined.

Smoking can decrease the tone of the oesophageal sphincter, making reflux more likely (Merck, 2003b:3).

4.6.2.12 Percentage of patients who are diabetic

To determine the percentage of patients being treated for insulin dependent diabetes, the number of patients being treated with insulin was calculated. This was repeated for those patients with non insulin-dependent diabetes.

Diabetes can cause delayed emptying of the stomach which can worsen gastro-oesophageal reflux (MacSween & Whaley, 1992:694).

4.6.3 Drug use indicators

The following quantitative drug use indicators were used for the purpose of this study:

4.6.3.1 Average number of visits per patient

To determine the average number of visits per patient, the number of times each patient was treated at one of the study facilities during the study period was calculated and divided by the total number of patients included in the study.

4.6.3.2 Percentage of different diagnoses made

To determine the percentage of different diagnoses that were made, the number of prescriptions where a specific diagnosis was made was used. This was done for each diagnosis. The percentage of prescriptions where no diagnosis was specified was also investigated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

The results were represented in a contingency table and Cramer's phi was calculated.

Laing and Santoso (1997: 422) stated that in order to conform to the criteria of rational drug use, prescribers should follow a standard process of prescribing. This process should start with a diagnosis to define the problem that requires intervention.

In the professional guidelines set out by the HPCSA (2006:7) prescribers were advised to apply their minds when making diagnoses and considering appropriate treatment. Prescribers were also advised to keep accurate and up-to-date patient records (HPCSA, 2006:10). Regulation 2418 of the Nursing Act (South Africa, 1978:50) also stipulates that prescribers must record the diagnosis made on the patient's file or treatment record.

In some of the patient files the symptom complex was recorded. Symptoms were listed as heartburn, epigastric pain, or indigestion. Where these symptoms were listed but no diagnosis such as gastritis, dyspepsia, or peptic ulcer was recorded the patient was classified as suffering from dyspepsia/heartburn/indigestion/abdominal pain as per the standard treatment guideline diagnosis (South Africa, 1998a: 54). For those prescriptions where no symptoms or diagnosis were recorded, the diagnosis was classified as diagnosis not specified.

4.6.3.3 Percentage of different drug treatments

To determine the percentage of different drug treatments that were prescribed, the number of prescriptions where a specific drug treatment was prescribed was calculated. This was done for each drug treatment.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

4.6.3.4 Percentage of different dosage regimes for cimetidine

To determine the percentage of different dosage regimes for cimetidine that were prescribed, the number of cimetidine prescriptions where a specific dosage regime was prescribed was compared to the total number of cimetidine prescriptions. This was done for each dosage regime.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

A contingency table was drawn up comparing the frequencies of different combinations of dosages and duration of treatment before and after the intervention and Cramer's phi was calculated.

4.6.3.5 Different treatment regimes and diagnoses

The different treatment regimes and the different diagnoses were compared. The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

4.6.3.6 Percentage of prescriptions containing propulsives

To determine the percentage of prescriptions containing propulsives, the frequency of prescriptions containing propulsives was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

In the study facilities only those drugs that are listed on the essential drugs list were available. Two propulsives were being used at the time of the study: metoclopramide and cisapride (South Africa, 1998b:303). Cisapride was a tertiary level drug and prescribers had to complete a motivation form when prescribing cisapride.

4.6.3.7 Percentage of prescriptions containing non-steroid anti-inflammatory drugs

The frequency of prescriptions containing NSAID's was calculated in order to determine the percentage of prescriptions containing NSAID's.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

Chronic use of NSAID's increases the relative risk for serious adverse gastrointestinal events three-fold (Insel, 1996:622). As discussed in 2.5 patients should be advised to avoid ulcerogenic medications (such as NSAID's).

4.6.3.8 Percentage of prescriptions containing tricyclic and other antidepressants

To determine the percentage of prescriptions containing antidepressants, the number of prescriptions containing antidepressants was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

Tricyclic antidepressants have strong antimuscarinic effects, and can cause epigastric distress (Baldessarini, 1996:442).

Psychological factors greatly influence contractions of the intestine, secretion of digestive enzymes, and other functions of the digestive system (Merck, 2003a:2).

In the study facilities only those drugs that are listed on the essential drugs list were available. Two tricyclic antidepressants were being used at the time of the study: amitriptyline and imipramine. In addition to the above tricyclic antidepressants fluoxetine was also used (South Africa, 1998:102).

4.6.3.9 Percentage of prescriptions containing thyroxin sodium

To determine the percentage of prescriptions containing thyroxin sodium, the number of prescriptions containing thyroxin sodium was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

In a study done by Figura *et al.* (1999:1) it was found that *H. pylori* (CagA-positive) infection increased the risk of auto-immune thyroid disorders.

4.6.3.10 Percentage of prescriptions containing theophylline

To determine the percentage of prescriptions containing theophylline, the number of prescriptions containing theophylline was used.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

Theophylline should be avoided (Brunton, 1996:903) in patients receiving treatment for dyspepsia as it can cause gastrointestinal distress (Katzung & Trevor, 1995:154).

4.6.3.11 Percentage of prescriptions containing progesterone (Prempak™)

To determine the percentage of prescriptions containing progesterone (Prempak™), the frequency of prescriptions containing progesterone was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

Brunton (1996:903) stated that progesterone decreases lower oesophageal sphincter tone and can delay gastric emptying.

4.6.3.12 Percentage of prescriptions containing calcium channel blockers

The number of prescriptions containing calcium channel blockers was determined so that the percentage of prescriptions containing calcium channel blockers could be calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. These results were tabulated in a 2 x 2 contingency table in order to calculate the phi coefficient.

Certain drugs such as calcium channel blockers can decrease the tone of the lower oesophageal sphincter (Merck, 2003b:3).

In the study facilities only those drugs that are listed on the essential drugs list were available. Three calcium channel blockers were being used at the time of the study: nifedipine (South Africa, 1998a:10), verapamil and diltiazem (South Africa, 1998b: 62).

4.6.3.13 Percentage of prescriptions that complied with STG

To determine the number of prescriptions that complied with the standard treatment guidelines the number of prescriptions that complied with STG was compared to the total number of prescriptions.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. Results for the first 6 months after the intervention and those for the second 6 months were also compared to determine the maintenance of the intervention's effect.

A 2 x 2 contingency table was drawn up comparing the prescriptions before the intervention with those after the intervention according to their adherence to the STG. The phi coefficient was then calculated to determine whether there was a statistical relationship between the intervention and the STG adherence.

In order to determine the compliance to the standard treatment guidelines (STG), each prescription was evaluated on three points:

- Was there a diagnosis indicated?
- Did the type of treatment comply with the STG for the diagnosis indicated?
- Did the duration of treatment comply with the STG for the diagnosis indicated?

If any one or more of the questions were answered with a "no" it would mean that the prescription did not adhere to the STG.

In 1.2.1 the definition for rational drug use was discussed. The Durban-Westville and Cape Town universities (1997:1) suggest that the treatment is rational when a diagnosis is made, and the medicine is prescribed in the correct dosage over the appropriate period. Dr N.C. Dlamini-Zuma (South Africa, 1998b:iii) stated that the STG set a firm basis towards developing rational drug use.

If all three the abovementioned points were answered in the affirmative, it was accepted that the treatment complied with the standard treatment guidelines. In cases where there was no diagnosis specified, it was determined that the treatment did not comply with the standard treatment guidelines.

The relevant data was both qualitative and quantitative. Although criteria were set to evaluate whether a prescription adhered to the standard treatment guidelines, the researcher had to use some discretion when determining the adherence. The adherence was then given the value of "yes" or "no" which was then quantitatively analysed.

For example: A patient was diagnosed with peptic ulcer and was prescribed cimetidine 400mg twice daily for 6 months. No gastroscopy was done. The prescription was written by a community service doctor. Using the three criteria listed above the prescription can be evaluated as follows:

- Was there a diagnosis indicated?
  Yes.
- Did the type of treatment comply with the STG for the diagnosis indicated?
  No – the correct treatment would have been magnesium trisilicate 500mg/aluminium hydroxide 250mg, oral 1 - 2 tablets to be chewed 1 hour before and 3 hours after meals and at night for 4 weeks or cimetidine, oral, 800mg at night for 4 weeks.
- Did the duration of treatment comply with the STG for the diagnosis indicated?
  No – the correct treatment should only have been prescribed for 4 weeks.

As two of the questions were answered with a "no" the prescription did not adhere to the STG.

4.6.3.14 Contingency table of prescriptions that complied with STG and prescriber qualification category

Compliance to STG guidelines was determined by comparing each prescription to the STG for the relevant diagnosis (as given in 4.6.3.13).
A contingency table was drawn up comparing the STG compliance and the prescriber qualification category. Percentages of column and row totals were determined.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention. The results were also graphically represented.

4.6.3.15 Percentage of different treatment outcomes

To determine the percentage of treatment outcomes, the number of prescriptions that resulted in each of the possible treatment outcomes was calculated. These results were tabulated in a 2 x 2 contingency table and the phi coefficient was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.
Results for the first 6 months after the intervention and those for the second 6 months were also compared to determine the maintenance of the intervention's effect.

4.6.3.16 Contingency table of treatment outcomes and STG compliance

A contingency table was drawn up comparing the different treatment outcomes and the STG compliance (as given in 4.6.3.13). Percentages of column and row totals were determined.
This was done for each treatment regime and for each diagnosis.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.
Results for the first 6 months after the intervention and those for the second 6 months were also compared to determine the maintenance of the intervention's effect.
A further table was drawn up comparing the treatment outcomes with the STG compliance for all the prescriptions written during the study period and the phi coefficient was calculated.

4.6.3.17 Contingency table of treatment outcomes and diagnoses

A contingency table was drawn up comparing the different treatment outcomes and the different diagnoses. Percentages of column and row totals were determined.

This was done for each treatment regime and for each diagnosis and the phi coefficient was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

4.6.3.18 Contingency table of treatment outcomes and treatment regime

A contingency table was drawn up comparing the different treatment outcomes and the different treatment regimes. Percentages of column and row totals were determined.
This was done for each treatment regime and for each treatment outcome.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

4.6.3.19 Contingency table of prescriptions that complied with STG and diagnoses

A contingency table was drawn up comparing the different diagnoses and the STG compliance (as given in 4.6.3.13). Percentages of column and row totals were determined and the phi coefficient was calculated.

The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

4.6.3.20 Percentage of prescriptions that had a diagnosis specified

A 2 x 2 contingency table was drawn up comparing the prescriptions before the intervention with those after the intervention according to the recording of a diagnosis. The phi coefficient was then calculated.

4.6.3.21 Cost of treatment before and after the intervention

A contingency table was drawn up comparing the cost of treatment per STG compliance. The results before the intervention and after the intervention were calculated separately in order to determine the effect of the intervention.

The arithmetic mean, variance, standard deviation, minimum and maximum values, median, mode, 25th percentile and 75th percentile were determined.

The cost of the treatment was calculated by determining the number of tablets (or as in the case of the magnesium trisilicate suspension, the number of 200ml bottles) that would be issued to the patient for the duration of the treatment. The cost of each tablet and bottle was obtained from the pharmaceutical distribution system computer software (PDSX) that was used in the hospital pharmacy at the time of the study. Reports were drawn showing the value of the relevant medication received by the pharmacy. The cost per tablet (or 200ml bottle magnesium trisilicate suspension) was then multiplied by the total number of tablets (or 200ml bottles magnesium trisilicate suspension) that would be required. In Table 4.3 the cost of treatment for different dosage regimes of the drugs that were prescribed during the study was given. These costs are calculated for a four-week treatment period.

Table 4.3: Cost of Treatment per month

Treatment	Cost per month
Omeprazole 20mg tablets daily (PDSX, 2003a:1)	R 77.20
Cimetidine 200mg tablets daily (PDSX, 2003b:1)	R 6.32
Cimetidine 200mg tablets bd (PDSX, 2003b:1)	R 12.64
Cimetidine 200mg tablets tds (PDSX, 2003b:1)	R 18.96
Cimetidine 200mg tablets qid (PDSX, 2003b:1)	R 25.27
Cimetidine 400mg tablets daily (PDSX, 2003b:1)	R 4.03
Cimetidine 400mg tablets bd (PDSX, 2003b:1)	R 8.05
Magnesium trisilicate co suspension 200ml (PDSX, 2003c:1)	R 2.94
Aluminium hydroxide 250mg/magnesium trisilicate 500mg tablet 20 tablets (PDSX, 2003d:1)	R 5.20

4.7 Validity and reliability

Validity is the degree to which a study instrument actually measures what it is meant to measure (Waning & Montagne, 2001:123).

In this study the instrument used was a survey questionnaire that was completed by the researcher, based on information found in prescription registers and patient files kept at the clinics. The survey questionnaire was designed to obtain all the relevant information that would be needed to determine any changes in the prescribing pattern and possible outcomes. The data was then captured on an Epi Info™ database and statistically analysed.

In order for the instrument to be valid it should be able to measure any changes that occurred in the prescribing pattern after the intervention had been done. As the survey questionnaire collects all data regarding diagnosis, diagnostic investigations and medication prescribed, it gives sufficient data to allow the researcher to monitor any changes in the prescribing patterns and changes in the possible outcomes.

Reliability is the degree of stability exhibited when a measurement is repeated under identical conditions (Waning & Montagne, 2001:123).

In this study the survey questionnaire was objective and relied solely on written information. It did not rely on a patient's perception of, for example, pain which could be influenced by many other factors. The data collector could also not influence the data due to her own perceptions. Reliability of the instrument could, however, have been compromised by poor record keeping at the clinics.

At the Govan Mbeki municipal clinics included in the study, annual external audits were done and complete stock records were kept at the clinics.

Poor history taking could also affect the reliability of the instrument. Because the survey questionnaire was completed retrospectively, cases where the diagnosis was not specified could not be fully studied. For instance, it was difficult to determine whether the antacid or cimetidine had been prescribed to treat active dyspeptic symptoms or to prevent dyspeptic complications in cases where patients were also receiving NSAID. If the survey questionnaire had been completed at the time of prescribing, the researcher could have inquired about the reason for the prescription while the consultation was still fresh in the prescriber's memory.

As mentioned in 3.2 Laing and Santoso (1997:422) suggested that one of the criteria for rational drug use is appropriate indication (the reason to prescribe is based on sound medical considerations). This would imply that if a drug is to be prescribed rationally, the prescriber should not only base the decision to prescribe on sound medical considerations but should also indicate those considerations in the patient file. Simply put, the prescriber should keep record of all diagnoses made.

The degree of completeness or incompleteness to which record keeping or history taking had been executed, was therefore included in the study and formed part of the instrument. For example, provision was made for recording smoking habits, history of peptic ulcer disease and previous gastroscopies.

Regulation 2418 of the Nursing Act (50/1978) stipulates that prescribers must record the diagnosis made on the patient's file or treatment record (South Africa, 1978:50). The prescription is then regarded as valid and adhering to legal requirements.

Confounding variables

A confounding variable influences the relationship between an independent variable (face to face education – intervention) and a dependent variable (prescribing pattern – compliance with STG), altering the true relationship between them (Waning & Montagne, 2001: 124).

Possible confounding variables that may have influenced the statistical relationship between the intervention and the outcome are, *inter alia*, the following:

- Patient factors
  - A change in the disease state.
    For this reason the diagnosis was measured each time a prescription was written – the assumption was made that the diagnosis was not static.
  - Relocation of the patient (Discussed in 4.6.1).
  - Poor patient compliance (Discussed in 4.8.3).

- Medication factors
  - Out of stock situations (when the prescribed drug was unavailable and could have been substituted by another treatment) (Discussed in 4.8.6).
  - Side effects of medication resulting in change of treatment prescribed and non-compliance to STG.
  - Patients that were not subjected to prescribed medication but were (only advised on lifestyle modification.) (Discussed in 4.8.1).

- Educational factors
  - Prescribers could have attended other courses during study period, e.g. Promoting rational drug use course (PRDU).

    During the study period the PRDU was not presented in the Govan Mbeki municipal area, but prescribers could have attended CPD courses held at other facilities.
  - Peer review, mentoring.

    Other medical professionals could have influenced the prescribing patterns.

    The doctors met once a week and the professional nurses met on Friday mornings. This allowed opportunities for case studies to be discussed.
- Pharmaceutical manufacturer
  - Promotional training.

    Manufacturers could have offered training encouraging the use of their product. To the researcher's knowledge, the only training sponsored by pharmaceutical manufacturers during the study period was training on hypertension (specifically ACE-inhibitors) and diabetes.

- Personnel factors
  - Staff rotation between clinics.
  - Resignations of trained personnel and appointment of new personnel (Discussed in 4.8.5).

4.8 Bias and limitations

Various forms of possible bias have been identified.

4.8.1 Selection bias

Because only those patients who received specific treatments (aluminium hydroxide/magnesium trisilicate tablets, magnesium hydroxide suspension, cimetidine tablets, or omeprazole tablets) were included in the study, selection bias could have occurred.

Patients that could have been erroneously excluded could, *inter alia*, have been the following:

- Those patients where the complaint of an acid-related disorder was ignored by medical personnel.
- Those who were advised on lifestyle modification with no treatment given.
- Those who received a prescription that was dispensed at another facility or retail pharmacy (Discussed in 4.6.1).
- Those who received other treatment, i.e. hyoscine butyl bromide.
- Those patients who were referred to another facility with no prescription given.
- Those patients who received treatment for an acid-related disorder but without any record being kept of the consultation and treatment.

Record was kept of all stock that was issued for auditing purposes. It is unlikely that a patient would receive treatment with no record being kept. Botha (2000:31) found that in the clinics supplied by Evander hospital only 5.76% (N = 382) of patients were treated without medication being dispensed.

The population (prescriptions for antacids, H_2-receptor antagonists and proton-pump inhibitors at clinics) was of such a nature that all the patients receiving the relevant treatment during the study period (population) could be included in the study. This decreased the possibility of selection bias.

4.8.2 Recall bias

The ability of the study subjects to remember previous events or exposures (Waning & Montagne, 2001:124) could influence the study results as well as interviewer bias. These did, however, not pose a problem in this study as study subjects were not interviewed during this study.

4.8.3 Patient compliance

The assumption was made that the patients took the treatment exactly as it had been prescribed. The treatment regime could, however, have been compromised by poor patient compliance.

Kass *et al.* (quoted by Benet, 1996: 1704) stated that 49% of patients made minor mistakes in the timing of doses; 40% of patients made major omissions in dosing; 10% of patients frequently overdosed; and only 1% of patients made no mistakes.

Patient factors that may have influenced the compliance of patients included in the study could, *inter alia*, have been the following:

- Age:
  Elderly patients present problems related to self-neglect or lapses in memory (Benet, 1996:1704).

- Living alone (Marital status):
  Poor compliance occurs more often in patients who live alone (Benet, 1996:1704).

- Dosage regime (Dosing interval):
  When a medication is prescribed more frequently than twice a day, it is less likely to be taken as prescribed (Benet, 1996:1704).

The abovementioned factors were therefore recorded.

4.8.4 Other interventions

In September 2000, the department of Health in Mpumalanga implemented a motivational system for the prescribing of lansoprazole and omeprazole. For the pharmacy to order any of these two drugs the prescribing doctor had to complete a two page form. This form had to be included in the order to the provincial medicine depot. This was an example of a regulatory intervention (Laing *et al.*, 1997:466). Although the effect of this intervention was not

studied, it could have had an influence on the effects of the educational intervention that was implemented 16 months later in Evander.

4.8.5 Prescriber turnover

Staff resignations, transfers and appointment of new staff could have affected the outcome of the intervention. Staff that had attended the face to face education sessions could have left and been replaced by staff that had not attended the education sessions.

With the appointment of new staff, one of four possibilities could have occurred:

- The old staff could have passed the information they received in the face to face education sessions on to the new staff, and the new staff could have adhered to the STG.
- The old staff could have passed the information they received in the face to face education sessions on to the new staff, and the new staff could have decided not to adhere to the STG.
- The new staff did not receive any of the information given in the face to face education sessions, but still adhered to the STG.
- The new staff did not receive any of the information given in the face to face education sessions, and did not adhere to the STG.

The interaction between old and new prescribers was not measured, so the effect that any possible interactions may have had could not be determined.

The staff turnover at the study facilities during the study period is given in Table 4.4.

Table 4.4: Prescriber turnover at study facilities

	PHC	MO	CSD
At start of study period	8	3	3
Resigned during pre-intervention phase			
Appointed during pre-intervention phase			
Resigned at onset of intervention			3
Appointed at onset of intervention		1	3
Resigned during 1st six months post intervention			1
Appointed during 1st six months post intervention			1
Resigned during 2nd six months post intervention	1		
Appointed during 2nd six months post intervention			
Total number that attended intervention still working December 2002	7	4	2

One primary health care nurse resigned during the last 6 months of the study period. A replacement nurse was only appointed after the study period had ended. During June 2002 one of the community service doctors was transferred and another CSD (that had completed the first 6 months of her community service at another facility in the province) was appointed.

All the primary healthcare nurses and medical officers that prescribed during pre-intervention phase attended the intervention and continued to prescribe for six months following the intervention. Two of the CSD-'s that prescribed during the pre-intervention phase left, one stayed on as a medical officer and attended the intervention.

4.8.6 Out of stock situations

During the study period various out of stock situations occurred with the two antacid medications kept at the study facilities. The cimetidine that was supplied per prescription from Evander hospital was in stock for the full study period. The out of stock situations of the two antacids are represented in Table 4.5.

Table 4.5: Out of stock situations at facilities.

	Aluminium hydroxide/magnesium trisilicate tabs	Magnesium trisilicate suspension	Both antacids out of stock simultaneously
Dates out of stock	10 July 2001 to 26 February 2002	1 July 2001 to 26 July 2002	10 July 2001 to 26 July 2001
Number of working days that the clinic was out of stock	166	19	12
Dates out of stock	22 March 2002 to 28 March 2002	7 February 2002 to 27 March 2002	22 March 2002 to 27 March 2002
Number of working days that the clinic was out of stock	5	34	5
Total number of working days that the clinic was out of stock	**171**	**53**	**17**

There were two periods during the study when there were no antacids available at the facilities. These two periods amounted to a total of 17 working days where no antacids were available at the facilities. During the remainder of the study period at least one of the two antacid medications was always available. As discussed in 2.5 the standard treatment guideline suggests use of either one of the two antacids. Therefore, if one was out of stock, it would still be within the STG if the prescriber substituted the one antacid for another.

4.9 Ethical issues

The Department of Health in Mpumalanga has an Ethics Committee. Before any research can be conducted within the Health Department of Mpumalanga permission must first be obtained from this committee. Permission was obtained from the Ethics Committee in Nelspruit (Mokoena, 2003:1), the Govan Mbeki municipal manager, the Sister-in-charge of the Govan Mbeki municipal clinics supplied by Evander Hospital, and the Hospital Superintendent at Evander Hospital for the study to be done.

The ethics committee of the Department of Health requires that the researcher(s) completes an application form. This application form must be submitted along with a complete research proposal, verification from the relevant university department that the researcher is enrolled as a student at that university. The researcher must first obtain permission from the heads of the facilities that will form part of the research, and this must be indicated on the application form.

Such information as had been gained about patients was treated as confidential. Prescriber details and the details of the patient were not included in the data reporting.

Only drugs registered for the use of acid-related disorders were investigated. No patient received a placebo or an experimental treatment.

4.10 Chapter summary

In Chapter four the research methodology and the research design were clarified. The research instruments that were used and the process by which the data was obtained were described. The validity and reliability of the data instruments, as well as possible bias were discussed. The analysis of the data was illustrated. Limitations and bias that could have had an influence on the results of the study were investigated. Ethical issues of the study were discussed.
The results of the study and a brief discussion on the results will be given in chapter five.

CHAPTER 5: RESULTS AND DISCUSSION

In this chapter the data collected will be statistically presented.

5.1 Demographics (patient and facility)

5.1.1 Enrolment demographics

Table 5.1: The percentage of patients enrolled per year

Year enrolled	Frequency	Percent
2001	291	46.00%
2002	341	54.00%
Total	632	100.00%

N = 632

Table 5.2: The percentage patients included in the study per year

No of patients in study	Frequency	Percent
Only received treatment during 2001	117	18.50%
Received treatment during 2001 as well as 2002	174	27.50%
Only received treatment during 2002	341	54.00%
Total	632	100.00%

N = 632

Discussion of results:

In the period 1 July 2001 to 31 December 2001, 291 (46%) patients were treated with one of the study drugs. Of those patients 174 received one of the study drugs during 2002 as well. Between January 2002 and December 2002 a further 341 (54%) patients were treated with one of the study drugs.

5.1.2 Age demographics of the study population

Table 5.3: The percentage of patients treated per age group

Age group	Frequency	Percent
0 < 19 years	4	0.63%
19 < 46 years	100	15.82%
46 ≤ years	154	24.37%
Unknown	374	59.18%
Total	632	100.00%

N = 632

Discussion of results:

The ages of 59.18% of the patients had not been recorded on the patient files. The ages of patients had been recorded in 258 cases. Of these (N = 258) 59.69% were older than 46 years.

5.1.3 Gender demographics of study population

Table 5.4: The percentage patients treated per gender group

Gender	Frequency	Percent
Male	105	16.60%
Female	257	40.70%
Unknown	270	42.70%
Total	632	100.00%

N = 632

Discussion of results:

The majority (42,70%) of patient included in the study did not have their gender recorded on the patient file. Of the total number of patients treated at the facilities for dyspeptic symptoms that had their gender recorded 70.99%

were female and 29.01% were male (N = 362). In the study done by Botha (2000: 46) it was found that 62.57% of the patients treated at the health facility were female.

Table 5.5.: Gender for Botha study vs. Gender for acid-related disorders study

	Female	Male
Acid-related disorders study (N = 362)	70.99	29.01
Botha study (N = 382)	62.57	37.43

Table 5.5 compares the prevalence of gender for all visits to the health facilities (Botha, 2000:46) to the prevalence of gender (for those that were recorded) for acid-related disorders. The phi coefficient for Table 5.5 is 0.09, which indicates that there is no relationship between gender and the prevalence of acid-related disorders.

5.1.4 Race demographics

Table 5.6: The percentage patients treated per race group

Race	Frequency	Percent
Coloured	17	2.70%
Indian	19	3.00%
Caucasian	291	46.00%
African	305	48.30%
Total	632	100.00%

N = 632

Discussion of results:

Of the patients who were treated 48.3% were African and 46% of the patients were Caucasian. The Indian and Coloured patients were 3% and 2.7% respectively.

5.1.5 Prescriber demographics

Table 5.7: The percentage of prescriptions per prescriber qualification ***before*** the intervention

Prescriber qualification	Frequency	Percent
Medical officer	1	0.30%
Community service doctor	153	37.30%
Primary health care nurse	256	62.40%
Total	410	100.00%

N= 410

Table 5.8: The percentage of prescriptions per prescriber qualification ***after*** the intervention

Prescriber qualification	Frequency	Percent
Medical officer	7	1.20%
Community service doctor	204	34.90%
Primary health care nurse	373	63.90%
Total	584	100.00%

N = 584

Table 5.9: The percentage of prescriptions written in 2003 per prescriber qualification

Prescriber	Frequency	Percent
Medical officer	1	1.90%
Community service doctor	28	53.80%
Primary healh care nurse	23	44.20%
Total	52	100.00%

N = 52

Discussion of results:

After the intervention, the percentage patients seen by a primary health care nurse increased by 1.5%, and those seen by the medical officers increased from 0.3% to 1.2%. The community service doctors consulted 2.4% fewer patients after the intervention. There was an increase in the percentage of prescriptions written by the community service doctors and a decrease in the percentage of prescriptions written by the primary health care nurses in 2003.

5.1.6 Percentage pregnant patients in study population

Table 5.10: The percentage female patients treated per pregnancy status

Pregnancy status	Frequency	Percent
Pregnant	3	1.20%
Unknown	81	31.50%
Not pregnant	173	67.30%
Total	257	100.00%

N = 257

Discussion of results:

Only three of the files of the female patients who were treated indicated that the patients were pregnant. The files of 31.5% of the female patients who were treated did not indicate whether or not the patient was pregnant.

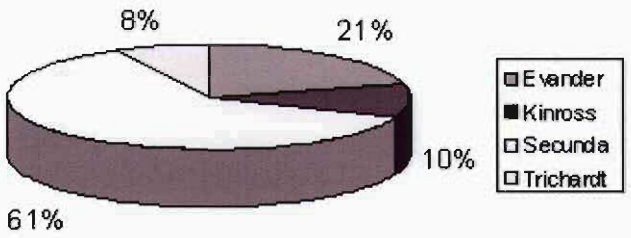
5.1.7 Percentage of patients who received a gastroscopy

Only one patient file (0.16%) recorded that the patient had undergone a gastroscopy (N = 632).

5.1.8 Facility demographics

The results of the percentage patients treated per facility are graphically represented in Figure 5.1.

Figure 5.1: The percentage patients treated per facility



Discussion of results:

Of the clinics surveyed, Secunda clinic saw the highest number of patients with a complaint of dyspeptic symptoms (61.23%). Evander Clinic treated 20.7% of the patients, Kinross treated 10.44% and Trichardt clinic treated 7.59% of the patients.

5.1.9 Employment demographics

Table 5.11: The percentage patients treated per employment status

Employment status	Frequency	Percentage of total
Employed	31	4.90%
Unemployed	132	20.90%
Unknown	469	74.20%
Total	632	100.00%

N = 632

Discussion of results:

Only 25.8% of the patients' employment status was known. Of those patients, 19% were employed and 81% were unemployed (N=163).

5.1.10 Marital status demographics

Table 5.12: The percentage patients treated per marital status

Marital Status	Frequency	Percent
Divorced	26	4.10%
Widowed	27	4.30%
Single	52	8.20%
Married	109	17.20%
Unknown	418	66.10%
Total	632	100.00%

N = 632

Discussion of results:

Only 33.9% of the patients' marital status was known. Of those patients, 50.9% were married, 12.6% were widowed, 12.1% were divorced and 24.3% were single (N = 214).

5.1.11 Percentage of patients who smoke

Table 5.13: The percentage patients treated per smoking habits

Smoker?	Frequency	Percent
Smoker	22	3.50%
Non smoker	46	7.30%
Unknown	564	89.20%
Total	632	100.00%

N = 632

Discussion of results:

Only 10.8% of the patients treated for acid-related disorders were questioned by the prescriber about their smoking habits and had the smoking habits recorded in their files. Of those that were questioned by the prescriber, 33.3% were smokers (N = 66).

Table 5.14: Questioning of patients smoking habits per prescriber

Questioned about smoking habits	Community service doctor	Primary health care nurse	Medical officer	TOTAL
Smoker	20	2	0	22
Row %	90.91	9.09	0.00	100.00
Col %	11.43	0.44	0.00	3.48
Non-smoker	0	5	2	7
Row %	0.00	71.43	28.57	100.00
Col %	0.00	1.11	33.33	1.11
Not asked	155.00	444.00	4	603
Row %	25.70	73.63	0.66	100.00
Col %	88.57	98.45	66.67	95.41
Total	175	451	6	632
Row %	27.69	71.36	0.95	100.00
Col %	100.00	100.00	100.00	100.00

N = 632

Of the patients who consulted a community service doctor 11.43% were asked about their smoking habits by the prescriber. Only 1.55% (0.44% smokers + 1.11% non-smokers) of the patients who consulted a primary healthcare nurse and 33.33% of the patients who consulted a medical officer were questioned about their smoking habits by the prescriber.

5.1.12 Percentage of patients who are diabetic

Table 5.15: The percentage patients treated per insulin dependent diabetes

	Frequency	Percent
Insulin dependent diabetic	3	0.50%
Not insulin dependent diabetic	629	99.50%
Total	632	100.00%

N= 632

Table 5.16: The percentage patients treated per non-insulin dependent diabetes

	Frequency	Percent
Non insulin-dependent diabetic	8	1.30%
Not non insulin-dependent diabetic	624	98.70%
Total	632	100.00%

N = 632

Discussion of results:

Of the patients treated for acid-related disorders 1.3% of the patients were non insulin-dependent and 0.5% of the patients were insulin-dependent diabetics.

5.2 Drug Use indicators

The following drug use indicators were used for the purpose of this study:

5.2.1 Average number of visits per patient

Table 5.17: Frequency of number of visits to facilities

Number of visits	Frequency	Percentage
1	423	66.9%
2	102	16.1%
3	53	8.4%
4	25	4.0%
5	18	2.8%
6	6	0.9%
7	1	0.2%
8	2	0.3%
9	1	0.2%
21	1	0.2%
Total	632	100.0%

N = 632

Discussion of results:

Of the patients who attended the health facilities 66.9% of the patients only attended the health facilities once and 16.1% attended the facilities twice. There was one patient who received treatment 21 times during the study period. The average number of visits per patient was 1.7.

5.2.2 Percentage of different diagnoses made

Table 5.18: The percentage of prescriptions written per diagnosis ***before and after*** the intervention

Diagnosis	Before intervention	After intervention	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	30	84	114
Row %	26.3	73.7	100
Col %	7.3	14.4	11.5
Gastritis	13	15	28
Row %	46.4	53.6	100
Col %	3.2	2.6	2.8
Not specified	357	445	802
Row %	44.5	55.5	100
Col %	87.1	76.2	80.7
Other	5	11	16
Row %	31.3	68.8	100
Col %	1.2	1.9	1.6
Peptic ulcer	5	29	34
Row %	14.7	85.3	100
Col %	1.2	5	3.4
TOTAL	410	584	994
Row %	41.2	58.8	100
Col %	100	100	100

N = 994

Phi coefficient = 0.01

Discussion of results:

After the intervention there was a decrease of 10.9% in the prescriptions where no diagnosis was specified. There was an increase of 7.1% in the percentage of prescriptions where the diagnosis was for dyspepsia. There was also 4.2 times increase in the percentage of prescriptions where the diagnosis was for peptic ulcer. The phi coefficient showed that there was no statistical relationship between the intervention and the frequencies of the diagnoses.

5.2.3 Percentage of different drug treatments

Table 5.19: The percentage of prescriptions written per drug or drug combination ***before and after*** the intervention

Drug treatment	Before intervention	After intervention	Total
Aluminium hydroxide/ magnesium trisilicate tablets + cimetidine	4	2	6
Row %	66.67	33.33	100.00
Column %	0.98	0.34	1.32
Aluminium hydroxide/ magnesium trisilicate tab	21	77	98
Row %	21.43	78.57	100.00
Column %	5.12	13.18	18.31
Cimetidine	104	92	196
Row %	53.06	46.94	100.00
Column %	25.37	15.75	41.12
Cimetidine + magnesium trisilicate suspension	18	45	63
Row %	28.57	71.43	100.00
Column %	4.39	7.71	12.10
Magnesium trisilicate suspension	262	368	630
Row %	41.59	58.41	100.00
Column %	63.90	63.01	126.92
Omeprazole	1	0	1
Row %	100.00	0.00	100.00
Column %	0.24	0.00	0.24
Total	410	584	994
Row %	41.25	58.75	100.00
Column %	100.00	100.00	

N = 994

Phi coefficient = 0.01

Discussion of results:

The percentage of prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine, the prescriptions for cimetidine, magnesium trisilicate suspension and omeprazole all decreased by 0.6%, 9.6%, 0.9% and 0.2% respectively after the intervention. The percentage of prescriptions for cimetidine with magnesium trisilicate suspension increased by 3.3% and those for aluminium hydroxide/magnesium trisilicate tablets increased by 8.1% after the intervention. The phi coefficient showed that there was no

statistical relationship between the intervention and the choice of drug treatment.

5.2.4 Percentage of different dosage regimes for cimetidine

Table 5.20: Dosage and duration of cimetidine prescriptions ***before and after*** the intervention

		Before or after intervention					
		Before	Col %	Row %	After	Col %	Row %
Dosage and duration	200mg dly 4 weeks	1	0.8	50	1	0.7	50
	200mg dly 3 months	8	6.4	88.9	1	0.7	11.1
	200mg dly 4 months	0	0	0	3	2.2	100
	200mg dly 6 months	5	4	35.7	9	6.5	64.3
	200mg bd 2 weeks	0	0	0	1	0.7	100
	200mg bd 4 weeks	2	1.6	33.3	4	2.9	66.7
	200mg bd 3 months	8	6.4	72.7	3	2.2	27.3
	200mg bd 4 months	5	4	55.6	4	2.9	44.4
	200mg bd 6 months	54	42.4	77.9	15	10.8	22.1
	200mg tds 1 week	0	0	0	1	0.7	100
	200mg tds 2 weeks	2	1.6	40	3	2.2	60
	200mg tds 3 weeks	0	0	0	1	0.7	100
	200mg tds 4 weeks	1	0.8	10	9	6.5	90
	200mg tds 2 months	0	0	0	1	0.7	100
	200mg tds 3 months	1	0.8	12.5	7	5	87.5
	200mg tds 4 months	2	1.6	50	2	1.4	50
	200mg tds 6 months	10	8	66.7	5	3.6	33.3
	200mg qid 6 months	2	1.6	100	0	0	0
	400mg dly 6 months	0	0	0	2	1.4	100
	400mg bd 1 week	0	0	0	4	2.9	100
	400mg bd 2 weeks	0	0	0	10	7.2	100
	400mg bd 4 weeks	3	2.4	21.4	11	7.9	78.6
	400mg bd 2 months	0	0	0	4	2.9	100
	400mg bd 3 months	2	1.6	25	6	4.3	75
	400mg bd 4 months	3	2.4	25	9	6.5	75
	400mg bd 5 months	1	0.8	100	0	0	0
	400mg bd 6 months	16	12.8	41	23	16.5	59
	TOTAL	126	100	47.3	139	100	52.7

N = 265

Phi coefficient = 0.01

Discussion of results:

After the intervention there was a decrease in the percentage of prescriptions for cimetidine where the dosage regime was 200mg daily (1.1%), 200mg bd (34.9%) and 200mg qid (1.6%). There was a decrease from 42.4% to 10.8% in the prescriptions for 200mg cimetidine twice daily for 6 months. There was an increase in the percentage of prescriptions for cimetidine where the dosage regime was 200mg tds (8.0%). This is a cause of concern as medication prescribed more frequently than twice a day is less likely to be taken as prescribed. The prescriptions written for 400mg cimetidine once daily increased by 1.4%, and those for 400mg twice daily increased by 28.2%. The percentage of prescriptions where the total daily dose of cimetidine was 800mg increased from 21.7% to 48.2%.

There was an increase in the percentage of prescriptions that were for 2 months or less (7.2% to 36%), as well as for those prescriptions which were made repeatable for 4 months (8.0 % to 12.9%). The percentage of those prescriptions that were for 3 months (15.2% to 12.2%), 5 months (0.8% to 0%) and 6 months (68.8% to 38.8%) all decreased after the intervention. The phi coefficient showed that there was no statistical relationship between the intervention and the dosage of cimetidine.

5.2.5 Different treatment regimes and diagnosis

Prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine ***before*** the intervention

Before the intervention there were only four prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine. There was one prescription where the diagnosis was for dyspepsia. This prescription was written for 6 months. There were two prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine where the diagnosis was gastritis. One prescription was for 4 weeks and the other was for 6 months. There was one prescription written for 6 months where the diagnosis was not specified. These results were not tabulated.

Prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine ***after*** the intervention

After the intervention there were only 2 prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine. Both prescriptions were for 4 weeks, the first being for dyspepsia and the second prescription for a peptic ulcer. These results were not tabulated.

Discussion of results:

After the intervention, the prescriptions that contained cimetidine with aluminium hydroxide/magnesium trisilicate tablets were only for 4 weeks. Before the intervention three of the four prescriptions had been for 6 months. The diagnosis had been specified on each of the post-intervention prescriptions.

Table 5.21: The percentage of prescriptions for aluminium hydroxide/ magnesium trisilicate tablets per diagnosis according to the duration of treatment ***before*** the intervention

	DURATION OF TREATMENT (DAYS)					
Diagnosis	**1 week**	**2 weeks**	**4 weeks**	**4 months**	**6 months**	**TOTAL**
Dyspepsia/heartburn/ indigestion/abdominal pain	1	1	3	0	1	6
Row %	16.7	16.7	50	0	16.7	100
Col %	25	50	23.1	0	100	28.6
Diagnosis not specified	3	1	9	1	0	14
Row %	21.4	7.1	64.3	7.1	0	100
Col %	75	50	69.2	100	0	66.7
Other	0	0	1	0	0	1
Row %	0	0	100	0	0	100
Col %	0	0	7.7	0	0	4.8
TOTAL	4	2	13	1	1	21
Row %	19	9.5	61.9	4.8	4.8	100
Col %	100	100	100	100	100	100

N = 21

Table 5.22: The percentage of prescriptions for aluminium hydroxide/ magnesium trisilicate tablets per diagnosis according to the duration of treatment ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	1 week	2 weeks	4 weeks	2 months	3 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	23	1	3	0	0	0	27
Row %	85.2	3.7	11.1	0	0	0	100
Col %	79.3	100	7.7	0	0	0	35.1
Diagnosis not specified	6	0	36	4	1	3	50
Row %	12	0	72	8	2	6	100
Col %	20.7	0	92.3	100	100	100	64.9
TOTAL	29	1	39	4	1	3	77
Row %	37.7	1.3	50.6	5.2	1.3	3.9	100
Col %	100	100	100	100	100	100	100

N = 77

Discussion of results:

The prescriptions for aluminium hydroxide/magnesium trisilicate tablets increased slightly in duration of treatment after the intervention. Before the intervention 90.4% of the prescriptions were for 4 weeks or less which decreased to 89.6% after the intervention. Those for 2 months or longer increased from 9.6% to 10.4%. The prescriptions with a diagnosis for dyspepsia increased from 28.6% to 35.1%, and those with no diagnosis specified decreased from 66.7% to 64.9% after the intervention.

Table 5.23: The percentage of prescriptions for magnesium trisilicate suspension with cimetidine per diagnosis according to the duration of treatment ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	**2 weeks**	**4 weeks**	**3 months**	**6 months**	**TOTAL**
Dyspepsia/heartburn/ indigestion/abdominal pain	1	0	0	3	4
Row %	25	0	0	75	100
Col %	50	0	0	33.3	22.2
Diagnosis not specified	1	3	4	6	14
Row %	7.1	21.4	28.6	42.9	100
Col %	50	100	100	66.7	77.8
TOTAL	2	3	4	9	18
Row %	11.1	16.7	22.2	50	100
Col %	100	100	100	100	100

N = 18

Table 5.24: The percentage of prescriptions for magnesium trisilicate suspension with cimetidine per diagnosis according to the duration of treatment ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	1 week	2 weeks	3 weeks	4 weeks	2 months	3 months	4 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	0	1	1	2	1	0	0	6	11
Row %	0	9.1	9.1	18.2	9.1	0	0	54.5	100
Col %	0	14.3	100	33.3	50	0	0	35.3	24.4
Gastritis	0	4	0	0	1	0	1	1	7
Row %	0	57.1	0	0	14.3	0	14.3	14.3	100
Col %	0	57.1	0	0	50	0	16.7	5.9	15.6
Diagnosis not specified	1	2	0	4	0	2	3	6	18
Row %	5.6	11.1	0	22.2	0	11.1	16.7	33.3	100
Col %	100	28.6	0	66.7	0	40	50	35.3	40
Peptic ulcer	0	0	0	0	0	3	2	4	9
Row %	0	0	0	0	0	33.3	22.2	44.4	100
Col %	0	0	0	0	0	60	33.3	23.5	20
TOTAL	1	7	1	6	2	5	6	17	45
Row %	2.2	15.6	2.2	13.3	4.4	11.1	13.3	37.8	100
Col %	100	100	100	100	100	100	100	100	100

N = 45

Discussion of results:

Before the intervention, 50% of the prescriptions for cimetidine with magnesium trisilicate suspension were for 6 months and the other 50% were for 2 weeks, 4 weeks and 3 months. After the intervention the duration of treatment differed more, and only 37.8% of the prescriptions were for 6 months. The number of prescriptions where no diagnosis was specified decreased by 37.8% and those where the diagnoses were for dyspepsia, gastritis or peptic ulcer all increased by 2.2%, 15.6% and 20% respectively.

Table 5.25: The percentage of prescriptions for cimetidine per diagnosis according to the duration of treatment ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	4 weeks	3 months	4 months	5 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	1	4	1	0	4	10
Row %	10	40	10	0	40	100
Col %	33.3	26.7	11.1	0	5.4	9.8
Gastritis	1	4	2	0	1	8
Row %	12.5	50	25	0	12.5	100
Col %	33.3	26.7	22.2	0	1.4	7.8
Diagnosis not specified	1	7	5	1	65	79
Row %	1.3	9.1	6.3	1.3	82.3	100
Col %	33.3	46.7	50.0	100	86.7	76.0
Other	0	0	0	0	2	2
Row %	0	0	0	0	100	100
Col %	0	0	0	0	2.7	2
Peptic ulcer	0	0	2	0	3	5
Row %	0	0	40	0	60	100
Col %	0	0	22.2	0	4.1	4.9
TOTAL	3	15	10	1	75	104
Row %	2.9	14.4	9.6	1	72.1	100
Col %	100	100	100	100	100	100

N = 104

Table 5.26: The percentage of prescriptions for cimetidine per diagnosis according to the duration of treatment ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	1 week	2 weeks	4 weeks	2 months	3 months	4 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	0	1	4	2	2	0	3	12
Row %	0	8.3	33.3	16.7	16.7	0	25	100
Col %	0	14.3	23.5	66.7	16.7	0	8.1	13
Gastritis	0	0	1	0	2	1	0	4
Row %	0	0	25	0	50	25	0	100
Col %	0	0	5.9	0	16.7	8.3	0	4.3
Diagnosis not specified	3	4	8	1	5	7	27	55
Row %	5.5	7.3	14.5	1.8	9.1	12.7	49.1	100
Col %	75	57.1	47.1	33.3	41.7	58.3	73	59.8
Other	0	0	3	0	0	1	1	5
Row %	0	0	60	0	0	20	20	100
Col %	0	0	17.6	0	0	8.3	2.7	5.4
Peptic ulcer	1	2	1	0	3	3	6	16
Row %	6.3	12.5	6.3	0	18.8	18.8	37.5	100
Col %	25	28.6	5.9	0	25	25	16.2	17.4
TOTAL	4	7	17	3	12	12	37	92
Row %	4.3	7.6	18.5	3.3	13	13	40.2	100
Col %	100	100	100	100	100	100	100	100

N = 92

Discussion of results:

After the intervention the prescriptions where cimetidine was prescribed for 6 months decreased by 31.9%. Those for 4 weeks or less increased from 2.9% to 30.4%. The prescriptions where no diagnosis was specified decreased by 16.2%. Those prescriptions where the diagnoses were for peptic ulcer increased from 4.9% to 17.4%.

The prescription for magnesium trisilicate suspension with omeprazole ***before and after*** the intervention

Before the intervention there was only one prescription for omeprazole for 3 months where the diagnosis was not specified. After the intervention there were no prescriptions for omeprazole. These results were not tabulated.

Table 5.27: The percentage of prescriptions for magnesium trisilicate suspension per diagnosis according to the duration of treatment ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	1 week	2 weeks	4 weeks	2 months	3 months	4 months	5 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	3	3	3	0	0	0	0	0	9
Row %	33.3	33.3	33.3	0	0	0	0	0	100
Col %	6	10.7	1.9	0	0	0	0	0	3.4
Gastritis	0	2	1	0	0	0	0	0	3
Row %	0	66.7	33.3	0	0	0	0	0	100
Col %	0	7.1	0.6	0	0	0	0	0	1.1
Diagnosis not specified	47	23	153	5	10	2	1	7	248
Row %	19	9.3	61.7	2	4	0.8	0.4	2.8	100
Col %	94	82.1	96.2	100	100	100	100	100	94.7
Other	0	0	2	0	0	0	0	0	2
Row %	0	0	100	0	0	0	0	0	100
Col %	0	0	1.3	0	0	0	0	0	0.8
Peptic ulcer	0	0	0	0	0	0	0	0	0
Row %	0	0	0	0	0	0	0	0	
Col %	0	0	0	0	0	0	0	0	0
TOTAL	50	28	159	5	10	2	1	7	262
Row %	19.1	10.7	60.7	1.9	3.8	0.8	0.4	2.7	100
Col %	100	100	100	100	100	100	100	100	100

N = 262

Table 5.28: The percentage of prescriptions for magnesium trisilicate suspension per diagnosis according to the duration of treatment ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Diagnosis	1 week	2 weeks	4 weeks	2 months	3 months	4 months	5 months	6 months	TOTAL
Dyspepsia/heartburn/ indigestion/abdominal pain	4	0	20	0	2	0	0	7	33
Row %	12.1	0	60.6	0	6.1	0	0	21.2	100
Col %	6.1	0	9.2	0	12.5	0	0	21.2	9.1
Gastritis	2	1	0	0	0	0	0	1	4
Row %	50	25	0	0	0	0	0	25	100
Col %	3	6.3	0	0	0	0	0	3	1.1
Diagnosis not specified	59	13	203	11	13	1	1	21	322
Row %	18.3	4.0	63.0	3.4	4.0	0.3	0.3	6.5	100
Col %	89.4	81.3	90.6	100	81.3	100	100	63.6	87.5
Other	0	2	1	0	1	0	0	2	6
Row %	0	33.3	16.7	0	16.7	0	0	33.3	100
Col %	0	12.5	0.5	0	6.3	0	0	6.1	1.6
Peptic ulcer	1	0	0	0	0	0	0	2	3
Row %	33.3	0	0	0	0	0	0	66.7	100
Col %	1.5	0	0	0	0	0	0	6.1	0.8
TOTAL	66	16	224	11	16	1	1	33	368
Row %	17.9	4.3	60.9	3.0	4.3	0.3	0.3	9.0	100
Col %	100	100	100	100	100	100	100	100	100

N = 368

Discussion of results:

Before the intervention 94.7% of the prescriptions for magnesium trisilicate suspension did not have the diagnosis specified. This decreased to 87.5% after the intervention. The percentage of prescriptions that were for 6 months increased from 2.7% to 9.0%.

5.2.6 Percentage of prescriptions containing propulsives

Table 5.29: 2 x 2 table of the percentage of prescriptions written containing propulsives ***before and after*** the intervention.

	No propulsives prescribed	**Propulsives prescribed**	**TOTAL**
Before intervention	403	7	410
Row %	98.3	1.7	100
Col %	41.6	28	41.2
After intervention	566	18	584
Row %	96.9	3.1	100
Col %	58.4	72	58.8
TOTAL	969	25	994
Row %	97.5	2.5	100
Col %	100	100	100

N=994

Phi coefficient = 0.04

Discussion of results:

The percentage of prescriptions containing propulsives increased from 1.7% to 3.1% after the intervention. The phi coefficient showed that there was no statistical relationship between the prescribing of propulsives and the intervention.

5.2.7 Percentage of prescriptions containing non-steroid anti-inflammatory drugs

Table 5.30: 2 x 2 table of the percentage of prescriptions written containing NSAID's ***before and after*** the intervention

	NSAID's prescribed	No NSAID's prescribed	TOTAL
Before intervention	42	368	410
Row %	10.2	89.8	100
Col %	42.4	41.1	41.2
After intervention	57	527	584
Row %	9.8	90.2	100
Col %	57.6	58.9	58.8
TOTAL	99	895	994
Row %	10	90	100
Col %	100	100	100

N = 994

Phi coefficient = 0.01

Discussion of results:

The percentage of prescriptions that contained NSAID's decreased by 0.4% (10.2% - 9.8%) after the intervention. The phi coefficient showed that there was no statistical relationship between the prescribing of NSAID's and the intervention.

5.2.8 Percentage of prescriptions containing tricyclic and other antidepressants

Before the intervention there were twenty prescriptions for amitriptyline and seven prescriptions for fluoxetine.

After the intervention there were fifteen prescriptions for amitriptyline and three prescriptions for fluoxetine.

Table 5.31: 2 x 2 table of the percentage of prescriptions written containing antidepressants ***before and after*** the intervention

	Antidepressants prescribed	**No Antidepressants prescribed**	**TOTAL**
Before intervention	27	383	410
Row %	6.6	93.4	100.0
Col %	3.0	386.9	41.2
After intervention	18	566	584
Row %	3.1	96.9	100.0
Col %	2.0	571.7	58.8
TOTAL	45	949	994
Row %	4.5	95.5	100.0
Col %	5.0	958.6	100.0

N = 994

Phi coefficient = 0.08

Discussion of results:

The percentage patients who received antidepressant treatment decreased from 6.6% to 3.1% after the intervention. The phi coefficient showed that there was no statistical relationship between the intervention and the number of prescriptions for antidepressants.

5.2.9 Percentage of prescriptions containing thyroxin sodium

Table 5.32: 2 x 2 table of the percentage of prescriptions written containing thyroxin sodium ***before and after*** the intervention

	Thyroxin sodium prescribed	No thyroxin sodium prescribed	TOTAL
Before intervention	9	401	410
Row %	2.2	97.8	100.0
Col %	1.0	405.1	41.2
After intervention	7	577	584
Row %	1.2	98.8	105.8
Col %	0.8	582.8	58.8
TOTAL	16	978	994
Row %	1.6	98.4	100.0
Col %	1.8	987.9	100.0

N = 994

Phi coefficient = 0.04

Discussion of results:

The percentage of prescriptions that included thyroxin decreased by 1.0% (2.2% - 1.2%) after the intervention. The phi coefficient showed that there was no statistical relationship between the intervention and the number of prescriptions for thyroxin sodium.

5.2.10 Percentage of prescriptions containing theophylline

Table 5.33: 2 x 2 table of the percentage of prescriptions written containing theophylline ***before and after*** the intervention

	Theophylline prescribed	**No theophylline prescribed**	**TOTAL**
Before intervention	10	400	410
Row %	2.4	97.6	100.0
Col %	1.1	404.0	41.2
After intervention	8	576	584
Row %	1.4	98.6	100.0
Col %	0.9	581.8	58.8
TOTAL	18	976	994
Row %	1.8	98.2	100.0
Col %	2.0	985.9	100.0

N = 994

Phi coefficient = 0.04

Discussion of results:

The percentage patients who received theophylline decreased from 2.4% to 1.4% after the intervention. The phi coefficient showed there was no statistical relationship between the intervention and the number of prescriptions for theophylline.

5.2.11 Percentage of prescriptions containing progesterone (Prempak™)

Table 5.34: 2 x 2 table of the percentage of prescriptions written containing progesterone ***before and after*** the intervention

	Progesterone prescribed	No progesterone prescribed	TOTAL
Before intervention	17	393	410
Row %	4.1	95.9	100.0
Col %	1.9	397.0	41.2
After intervention	8	576	584
Row %	1.4	98.6	100.0
Col %	0.9	581.8	58.8
TOTAL	25	969	994
Row %	2.5	97.5	100.0
Col %	2.8	978.8	100.0

N = 994

Phi coefficient = 0.09

Discussion of results:

The percentage patients who received progesterone decreased from 4.1% to 1.4% after the intervention. There was no statistical relationship between the intervention and the number of prescriptions for progesterone.

5.2.12 Percentage of prescriptions containing calcium channel blockers

Table 5.35: 2 x 2 table of the percentage of prescriptions written containing calcium channel blockers ***before and after*** the intervention

	Calcium channel blockers prescribed	No calcium channel blockers prescribed	TOTAL
Before intervention	17	393	410
Row %	4.1	95.9	100.0
Col %	1.9	397.0	41.2
After intervention	18	566	584
Row %	3.1	96.9	100.0
Col %	2.0	571.7	58.8
TOTAL	35	959	994
Row %	3.5	96.5	100.0
Col %	3.9	968.7	100.0

N = 994

Phi coefficient = 0.03

Discussion of results:

The percentage of patients who received calcium channel blockers decreased from 4.1% to 3.1% after the intervention. The phi coefficient showed no statistical relationship between the intervention and the number of prescriptions for calcium channel blockers.

5.2.13 Percentage of prescriptions that complied with STG

Table 5.36: The percentage of prescriptions written that adhered to the standard treatment guidelines ***before*** the intervention

	Frequency	Percent
Did not comply with STG	377	92.00%
Complied with STG	33	8.00%
Total	410	100.00%

N = 410

Table 5.37: The percentage of prescriptions written that adhered to the standard treatment guidelines ***0 < 6 months after*** the intervention

	Frequency	Percent
Did not comply with STG	284	84.80%
Complied with STG	51	15.20%
Total	335	100.00%

N = 335

Table 5.38: The percentage of prescriptions written that adhered to the standard treatment guidelines ***6 ≤ 12 months after*** the intervention

	Frequency	Percent
Did not comply with STG	214	85.90%
Complied with STG	35	14.10%
Total	249	100.00%

N = 249

Discussion of results:

During the 6 months following the intervention the STG compliance improved by 7.2% (8% to 15.2%). In the second 6 months following the intervention there was a slight decrease in the compliance from 15.2% to 14.1%.

Table 5.39: 2 x 2 table of the percentage STG compliance ***before and after*** the intervention

	STG compliance		
	Complied with STG	**Did not comply with STG**	**TOTAL**
Before intervention	33	377	410
Row %	8.0	92.0	100.0
Col %	27.73	43.09	41.2
After intervention	86	498	584
Row %	14.7	85.3	100.0
Col %	72.27	56.91	58.8
TOTAL	119	875	994
Row %	12.0	88.0	100.0
Col %	100	100	100.0

N = 994

Phi coefficient = 0.03

The phi coefficient showed that there was no statistical relationship between the intervention and the STG compliance.

5.2.14 Contingency table of prescriptions that complied with STG and prescriber qualification category

Table 5.40: The percentage of prescriptions written that adhered to the standard treatment guidelines ***before*** the intervention per prescriber category

	PRESCRIBER			
	Community service doctor	**Medical officer)**	**Primary health care nurse**	**TOTAL**
Did not comply with STG	133	1	243	377
Row %	35.3	0.3	64.5	100.0
Col %	86.9	100.0	95.3	92.0
Complied with STG	20	0	13	33
Row %	63.6	0.0	36.4	100.0
Col %	13.6	0.0	4.7	8.0
TOTAL	153	1.0	256	410
Row %	37.6	0.2	62.2	100.0
Col %	100.0	100.0	100.0	100.0

N = 410

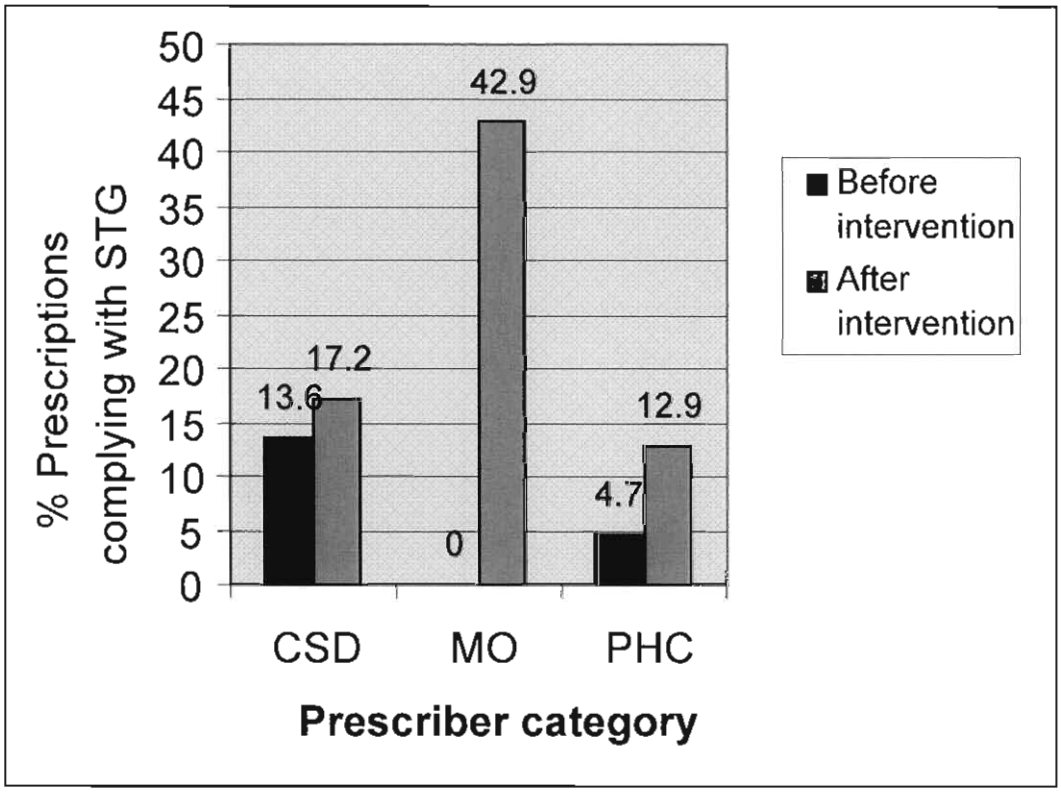
Table 5.41: The percentage of prescriptions written that adhered to the standard treatment guidelines ***after*** the intervention per prescriber category

	PRESCRIBER			
	Community service doctor	**Medical officer)**	**Primary health care nurse**	**TOTAL**
Did not comply with STG	169.0	4.0	325.0	498.0
Row %	33.9	0.8	65.3	100.0
Col %	82.8	57.1	87.1	85.3
Complied with STG	35.0	3.0	48.0	86.0
Row %	40.7	3.5	55.8	100.0
Col %	17.2	42.9	12.9	14.7
TOTAL	204.0	7.0	373.0	584.0
Row %	34.9	1.2	63.9	100.0
Col %	100.0	100.0	100.0	100.0

N =584

The results shown in Table 5.40 and Table 5.41 were graphically represented in Figure 5.2.

Figure 5.2: % Prescriptions that are STG compliant per prescriber category



CSD	Community service doctor
MO	Medical officer
PHC	Primary healthcare nurse

Discussion of results:

After the intervention there was an improvement in STG compliance in all three categories of prescribers. The community service doctors improved by 3.6%, the medical officers from 0% to 42.9% and the primary health care nurses by 8.2%.

5.2.15 Percentage of different treatment outcomes

Table 5.42: The percentage treatment outcomes ***before*** the intervention

Outcome	Frequency	Percent
Changed prescription immediately	37	9.00%
Changed prescription later	34	8.30%
Did not return	206	50.20%
Repeated same prescription immediately	73	17.80%
Repeated same prescription later	60	14.60%
Total	410	100.00%

N = 410

Table 5.43: The percentage treatment outcomes the ***0 < 6 months after*** the intervention

Outcome	Frequency	Percent
Changed prescription immediately	26	7.80%
Changed prescription later	13	3.90%
Did not return	203	60.60%
Repeated same prescription immediately	50	14.90%
Repeated same prescription later	43	12.80%
Total	335	100.00%

N = 335

Table 5.44: The percentage treatment outcomes ***6 ≤ 12 months after*** the intervention

Outcome	Frequency	Percent
Changed prescription immediately	15	6.00%
Changed prescription later	3	1.20%
Did not return	176	70.70%
Referred to next level	1	0.40%
Repeated same prescription immediately	39	15.80%
Repeated same prescription later	15	6.00%
Total	249	100.00%

N = 249

Discussion of results:

As discussed in 3.5.3 one of the goals of the intervention was to decrease the duration of treatment required to cure a patient. In 4.6.1 the possible outcomes of treatment were described. For the intervention to have a beneficial impact on the treatment outcomes, the percentage of patients who did not return for treatment would need to decrease.

In the first 6 months following the intervention there was an increase of 10.4% in the percentage of patients who did not return for treatment. In the next 6 - month period this increased by a further 10.1%.

The percentages of prescriptions where the treatment was repeated (from 32.4% to 27.7%) or changed (from 17.3% to 11.7%) all decreased initially. Those where the prescription was changed immediately (from 14.9% to 15.8%) increased in the second 6 month period, but the percentages remained lower than before the intervention (17.8%).

Table 5.45: The percentage treatment outcomes ***before and after*** the intervention

Outcome	Before intervention	After intervention	Total
Changed prescription immediately	37	41	78
Row %	47.4	52.6	100
Col %	9	7	7.8
Changed prescription later	34	16	50
Row %	68	32	100
Col %	8.3	2.7	5
Did not return	206	379	585
Row %	35.2	64.8	100
Col %	50.2	64.9	58.9
Referred to next level	0	1	1
Row %	0	100	100
Col %	0	0.2	0.1
Repeated same prescription immediately	73	89	162
Row %	45.1	54.9	100
Col %	17.8	15.2	16.3
Repeated same prescription later	60	58	118
Row %	50.8	49.2	100
Col %	14.6	9.9	11.9
TOTAL	410	584	994
Row %	41.2	58.8	100
Col %	100	100	100

N = 994

Phi coefficient = 0.01

Discussion of results:

The percentage of prescriptions where the patient did not return with the same complaint increased from 50.2% to 64.9%. The phi coefficient showed no statistical relationship between the intervention and the outcome of prescriptions.

5.2.16 Contingency table of treatment outcomes and STG compliance

Table 5.46: The percentage treatment outcomes per STG compliance ***before*** the intervention

	OUTCOME					
	Changed prescription immediately	**Changed prescription later**	**Did not return**	**Repeated same prescription immediately**	**Repeated same prescription later**	**TOTAL**
Did not comply with STG	35	31	193	67	51	377
Row %	9.3	8.2	51.2	17.8	13.5	100
Col %	94.6	91.2	93.7	91.8	85	92
Did comply to STG	2	3	13	6	9	33
Row %	6.1	9.1	39.4	18.2	27.3	100
Col %	5.4	8.8	6.3	8.2	15	8
TOTAL	37	34	206	73	60	410
Row %	9	8.3	50.2	17.8	14.6	100
Col %	100	100	100	100	100	100

N = 410

Discussion of results:

Before the intervention 39.4% of the patients where the prescriptions complied with the STG did not return and 18.2% had the same prescription repeated.

Table 5.47: The percentage treatment outcomes per STG compliance

0 < 6 months after the intervention

	OUTCOME						
	Changed prescription immediately	Changed prescription later	Did not return	Referred to next level	Repeated same prescription immediately	Repeated same prescription later	TOTAL
Did not comply with STG	21	10	174	0	43	36	284
Row %	7.4	3.5	61.3	0	15.1	12.7	100
Col %	80.8	76.9	85.7	0	86	83.7	84.8
Did comply to STG	5	3	29	0	7	7	51
Row %	9.8	5.9	56.9	0	13.7	13.7	100
Col %	19.2	23.1	14.3	0	14	16.3	15.2
TOTAL	26	13	203	0	50	43	335
Row %	7.8	3.9	60.6	0	14.9	12.8	100
Col %	100	100	100	100	100	100	100

N = 335

Discussion of results:

In the first 6 months after the intervention 56.9% of the patients where the prescriptions complied with the STG did not return and 13.7% had the same treatment repeated immediately and 13.7% had the same treatment repeated later.

Table 5.48: The percentage treatment outcomes per STG compliance

6 ≤ 12 months after the intervention

	OUTCOME						
STG compliance	**Changed prescription immediately**	**Changed prescription later**	**Did not return**	**Referred to next level**	**Repeated same prescription immediately**	**Repeated same prescription later**	**TOTAL**
Did not comply with STG	12	3	151	0	36	12	214
Row %	5.6	1.4	70.6	0	16.8	5.6	100
Col %	80	100	85.8	0	92.3	80	85.9
Did comply to STG	3	0	25	1	3	3	35
Row %	8.6	0	71.4	2.9	8.6	8.6	100
Col %	20	0	14.2	100	7.7	20	14.1
TOTAL	15	3	176	1	39	15	249
Row %	6	1.2	70.7	0.4	15.7	6	100
Col %	100	100	100	100	100	100	100

N = 249

Discussion of results:

In the second 6 months following the intervention the percentage of patients who did not return where the prescriptions complied with the STG increased to 71.4%.

In the first six months of the study, of those patients who did not return, 6.3% of the patients had prescriptions that adhered to the STG. In the last six months of the study, a 7.9% higher percentage of those patients who did not return had prescriptions that did adhere to the STG.

Table 5.49: The percentage treatment outcomes per STG compliance for ***all*** prescriptions

	OUTCOME						
STG compliance	**Changed prescription immediately**	**Changed prescription later**	**Did not return**	**Referred to next level**	**Repeated same prescription immediately**	**Repeated same prescription later**	**TOTAL**
Did not comply with STG	68	44	518	0	146	99	875
Row %	7.8	5	59.2	0	16.7	11.3	100
Col %	87.2	88	88.5	0	90.1	83.9	88
Did comply to STG	10	6	67	1	16	19	119
Row %	8.4	5	56.3	0.8	13.4	16	100
Col %	12.8	12	11.5	100	9.9	16.1	12
TOTAL	78	50	585	1	162	118	994
Row %	7.8	5	58.9	0.1	16.3	11.9	100
Col %	100	100	100	100	100	100	100

N = 994

Phi coefficient = 0.003

The phi coefficient showed that there was no correlation between the adherence to the STG and the outcome of treatment.

5.2.17 Contingency table of treatment outcomes and diagnosis

Table 5.50: The percentage treatment outcomes per diagnosis ***before*** the intervention

	DIAGNOSIS					
Outcome	**Dyspepsia**	**Gastritis**	**Diagnosis not specified**	**Other**	**Peptic ulcer**	**TOTAL**
Changed prescription immediately	5	0	32	0	0	37
Row %	13.5	0.0	86.5	0.0	0.0	100.0
Col %	16.7	0.0	9.0	0.0	0.0	9.0
Changed prescription later	3	1	29	1	0	34
Row %	8.8	2.9	85.3	2.9	0.0	100.0
Col %	10.0	7.7	8.1	20.0	0.0	8.3
Did not return	12	4	183	3	4	206
Row %	5.8	1.9	88.8	1.5	1.9	100.0
Col %	40.0	30.8	51.3	60.0	80.0	50.2
Repeated same prescription immediately	5	4	62	0	1	73
Row %	6.8	5.5	86.3	0.0	1.4	100.0
Col %	16.7	30.8	17.6	0.0	20.0	17.8
Repeated same prescription later	5	4	50	1	0	60
Row %	8.3	6.7	83.3	1.7	0.0	100.0
Col %	16.7	30.8	14.0	20.0	0.0	14.6
TOTAL	30	13	357	5	5	410
Row %	7.3	3.2	87.1	1.2	1.2	100.0
Col %	100.0	100.0	100.0	100.0	100.0	100.0

N = 410

Phi coefficient = 0.01

Table 5.51: The percentage treatment outcomes per diagnosis ***after*** the intervention

	DIAGNOSIS					
Outcome	**Dyspepsia**	**Gastritis**	**Diagnosis not specified**	**Other**	**Peptic ulcer**	**TOTAL**
Changed prescription immediately	9	1	25	1	5	41
Row %	22	2.4	61	2.4	12.2	100
Col %	10.7	6.7	5.6	9.1	17.2	7
Changed prescription later	5	2	8	0	1	16
Row %	31.3	12.5	50	0	6.3	100
Col %	6	13.3	1.8	0	3.4	2.7
Did not return	51	8	298	8	14	379
Row %	13.5	2.1	78.6	2.1	3.7	100
Col %	60.7	53.3	67	72.7	48.3	64.9
Referred to next level	1	0	0	0	0	1
Row %	100	0	0	0	0	100
Col %	1.2	0	0	0	0	0.2
Repeated same prescription immediately	9	2	69	2	7	89
Row %	10.1	2.2	77.5	2.2	7.9	100
Col %	10.7	13.3	15.5	18.2	24.1	15.2
Repeated same prescription later	9	2	45	0	2	58
Row %	15.5	3.4	77.6	0	3.4	100
Col %	10.7	13.3	10.1	0	6.9	9.9
TOTAL	84	15	445	11	29	584
Row %	14.4	2.6	76.2	1.9	5	100
Col %	100	100	100	100	100	100

N = 584

Phi coefficient = 0.01

Discussion of results:

Following the intervention, the percentages of patients who did not return for treatment of an acid-related disorder increased where the diagnoses were dyspepsia (from 5.8% to 13.5%), gastritis (from 1.9% to 2.1%) and other (from 1.5% to 2.1%). But those prescriptions where the diagnoses indicated peptic ulcer showed an increase in changes to the treatment (0% to 20.6%). Those

prescriptions where the diagnoses had not been specified showed an increase (from 51.3% to 67.0%) in the percentage of patients who were cured. The phi coefficient of the prescriptions before the intervention showed that there was no statistical relationship between outcome and diagnosis. The phi coefficient of the prescriptions written after the intervention showed that there was no statistical relationship between outcome and diagnosis.

5.2.18 Treatment outcomes and treatment regime

Treatment outcomes of prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine ***before*** the intervention

Before the intervention there were only four prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine. One prescription (written for 6 months) was changed immediately. Two patients who had prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine (both written for 6 months) were cured. One prescription that had been written for 4 weeks was repeated immediately. These results were not tabulated.

Treatment outcomes of prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine ***after*** the intervention

After the intervention there were only 2 prescriptions for aluminium hydroxide/magnesium trisilicate tablets with cimetidine. One was for four weeks and the patient did not present with the same complaint. The other was written for four weeks and the prescription was repeated at a later date. These results were not tabulated.

Discussion of results:

Before the intervention two of the four patients who received aluminium hydroxide/magnesium trisilicate tablets with cimetidine did not present again with the same complaint. After the intervention 1 of the 2 patients who

received aluminium hydroxide/magnesium trisilicate tablets with cimetidine did not return. These results were not tabulated.

Table 5.52: The percentage treatment outcomes for aluminium hydroxide/magnesium trisilicate tablets ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	1 week	2 weeks	4 weeks	4 months	6 months	TOTAL
Changed prescription later	1	0	3	0	0	4
Row %	25	0	75	0	0	100
Col %	25	0	23.1	0	0	19
Did not return	2	0	7	1	0	10
Row %	20	0	70	10	0	100
Col %	50	0	53.8	100	0	47.6
Repeated same prescription immediately	0	1	2	0	0	3
Row %	0	33.3	66.7	0	0	100
Col %	0	50	15.4	0	0	14.3
Repeated same prescription later	1	1	1	0	1	4
Row %	25	25	25	0	25	100
Col %	25	50	7.7	0	100	19
TOTAL	4	2	13	1	1	21
Row %	19	9.5	61.9	4.8	4.8	100
Col %	100	100	100	100	100	100

N = 21

Table 5.53: The percentage treatment outcomes for aluminium hydroxide/magnesium trisilicate tablets ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	1 week	2 weeks	4 weeks	2 months	3 months	6 months	TOTAL
Changed prescription immediately	0	0	5	0	0	1	6
Row %	0	0	83.3	0	0	16.7	100
Col %	0	0	12.8	0	0	33.3	7.8
Changed prescription later	0	0	2	0	0	0	2
Row %	0	0	100	0	0	0	100
Col %	0	0	5.1	0	0	0	2.6
Did not return	23	1	25	3	0	2	54
Row %	42.6	1.9	46.3	5.6	0	3.7	100
Col %	79.3	100	64.1	75	0	66.7	70.1
Referred to next level	1	0	0	0	0	0	1
Row %	100	0	0	0	0	0	100
Col %	3.4	0	0	0	0	0	1.3
Repeated same prescription immediately	0	0	3	1	0	0	4
Row %	0	0	75	25	0	0	100
Col %	0	0	7.7	25	0	0	5.2
Repeated same prescription later	5	0	4	0	1	0	10
Row %	50	0	40	0	10	0	100
Col %	17.2	0	10.3	0	100	0	13
TOTAL	29	1	39	4	1	3	77
Row %	37.7	1.3	50.6	5.2	1.3	3.9	100
Col %	100	100	100	100	100	100	100

N = 77

Discussion of results:

Following the intervention the percentage of patients who had been prescribed aluminium hydroxide/magnesium trisilicate tablets and did not return with a similar complaint increased from 47.6% to 70.1%. Those who had their prescriptions changed immediately increased from 0% to 7.8%. There was one patient who was referred to the hospital for further treatment after the intervention.

Table 5.54: The percentage treatment outcomes for magnesium trisilicate suspension and cimetidine ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	2 weeks	4 weeks	2 months	3 months	6 months	TOTAL
Changed prescription immediately	0	0	0	0	3	3
Row %	0	0	0	0	100	100
Col %	0	0	0	0	33.3	16.7
Changed prescription later	1	0	0	2	2	5
Row %	20	0	0	40	40	100
Col %	50	0	0	50	22.2	27.8
Did not return	1	1	0	0	0	2
Row %	50	50	0	0	0	100
Col %	50	33.3	0	0	0	11.1
Repeated same prescription immediately	0	2	0	2	3	7
Row %	0	28.6	0	28.6	42.9	100
Col %	0	66.7	0	50	33.3	38.9
Repeated same prescription later	0	0	0	0	1	1
Row %	0	0	0	0	100	100
Col %	0	0	0	0	11.1	5.6
TOTAL	2	3	0	4	9	18
Row %	11.1	16.7	0	22.2	50	100
Col %	100	100	100	100	100	100

N = 18

Table 5.55: The percentage treatment outcomes for magnesium trisilicate suspension and cimetidine ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	1 week	2 weeks	3 weeks	4 weeks	2 months	3 months	4 months	6 months	TOTAL
Changed prescription immediately	0	0	0	0	0	1	2	6	9
Row %	0	0	0	0	0	11.1	22.2	66.7	100
Col %	0	0	0	0	0	20	33.3	35.3	20
Changed prescription later	0	1	0	1	0	0	0	0	2
Row %	0	50	0	50	0	0	0	0	100
Col %	0	14.3	0	16.7	0	0	0	0	4.4
Did not return	0	3	1	4	2	4	4	6	24
Row %	0	12.5	4.2	16.7	8.3	16.7	16.7	25	100
Col %	0	42.9	100	66.7	100	80	66.7	35.3	53.3
Repeated same prescription immediately	0	1	0	0	0	0	0	5	6
Row %	0	16.7	0	0	0	0	0	83.3	100
Col %	0	14.3	0	0	0	0	0	29.4	13.3
Repeated same prescription later	1	2	0	1	0	0	0	0	4
Row %	25	50	0	25	0	0	0	0	100
Col %	100	28.6	0	16.7	0	0	0	0	8.9
TOTAL	1	7	1	6	2	5	6	17	45
Row %	2.2	15.6	2.2	13.3	4.4	11.1	13.3	37.8	100
Col %	100	100	100	100	100	100	100	100	100

N = 45

Discussion of results:

After the intervention, the percentage of patients who had been prescribed magnesium trisilicate suspension with cimetidine and were cured increased by 42.2%. Those who had their prescription repeated immediately decreased

from 38.9% to 13.3%. There was a 3.3% increase in those patients who had the same prescription repeated later.

Table 5.56: The percentage treatment outcomes for cimetidine ***before*** the intervention

	DURATION OF TREATMENT (DAYS)						
Outcome	**4 weeks**	**2 months**	**3 months**	**4 months**	**5 months**	**6 months**	**TOTAL**
Changed prescription immediately	0	0	1	0	0	25	26
Row %	0	0	3.8	0	0	96.2	100
Col %	0	0	6.7	0	0	33.8	25.5
Changed prescription later	2	0	2	2	0	4	10
Row %	20	0	20	20	0	40	100
Col %	66.7	0	13.3	20.0	0	5.3	9.6
Did not return	0	0	5	4	0	27	36
Row %	0	0	13.9	11.1	0	75.0	100
Col %	0	0	33.3	40.0	0	36.0	34.6
Repeated same prescription immediately	0	0	6	4	1	15	26
Row %	0	0	24	15.4	3.8	57.7	100
Col %	0	0	40	40.0	100	20.3	25.0
Repeated same prescription later	1	0	1	0	0	4	6
Row %	16.7	0	16.7	0	0	66.7	100
Col %	33.3	0	6.7	0	0	5.3	5.8
TOTAL	3	0	15	10	1	75	104
Row %	2.9	0	14.7	9.6	1	72.1	100
Col %	100	100	100	100	100	100	100

N = 104

Table 5.57: The percentage treatment outcomes for cimetidine ***after*** the intervention

	DURATION OF TREATMENT (DAYS)							
Outcome	**1 week**	**2 weeks**	**4 weeks**	**2 months**	**3 months**	**4 months**	**6 months**	**TOTAL**
Changed prescription immediately	0	0	1	0	3	1	5	10
Row %	0	0	10	0	30	10	50	100
Col %	0	0	5.9	0	25	8.3	13.5	10.9
Changed prescription later	0	2	1	1	0	0	0	4
Row %	0	50	25	25	0	0	0	100
Col %	0	28.6	5.9	33.3	0	0	0	4.3
Did not return	3	4	14	2	4	7	13	47
Row %	6.4	8.5	29.8	4.3	8.5	14.9	27.7	100
Col %	75	57.1	82.4	66.7	33.3	58.3	35.1	51.1
Repeated same prescription immediately	0	0	1	0	3	4	19	27
Row %	0	0	3.7	0	11.1	14.8	70.4	100
Col %	0	0	5.9	0	25	33.3	51.4	29.3
Repeated same prescription later	1	1	0	0	2	0	0	4
Row %	25	25	0	0	50	0	0	100
Col %	25	14.3	0	0	16.7	0	0	4.3
TOTAL	4	7	17	3	12	12	37	92
Row %	4.3	7.6	18.5	3.3	13	13	40.2	100
Col %	100	100	100	100	100	100	100	100

N = 92

Discussion of results:

The percentage patients who did not return with the same complaint after receiving cimetidine increased from 34.6% before the intervention to 51.1% after the intervention. There was also an increase in the number of patients who had their prescriptions repeated immediately with 12.7% more prescriptions being repeated immediately for 6 months.

Table 5.58: The percentage treatment outcomes for magnesium trisilicate suspension ***before*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	1 week	2 weeks	4 weeks	2 months	3 months	4 months	5 months	6 months	TOTAL
Changed prescription immediately	1	1	2	0	3	0	0	0	7
Row %	14.3	14.3	28.6	0	42.9	0	0	0	100
Col %	2	3.6	1.3	0	30	0	0	0	2.7
Changed prescription later	1	1	12	0	0	0	1	0	15
Row %	6.7	6.7	80	0	0	0	6.7	0	100
Col %	2	3.6	7.5	0	0	0	100	0	5.7
Did not return	32	7	112	1	3	1	0	0	156
Row %	20.5	4.5	71.8	0.6	1.9	0.6	0	0	100
Col %	64	25	70.4	20	30	50	0	0	59.5
Repeated same prescription immediately	7	14	5	2	2	0	0	5	35
Row %	20	40	14.3	5.7	5.7	0	0	14.3	100
Col %	14	50	3.1	40	20	0	0	71.4	13.4
Repeated same prescription later	9	5	28	2	2	1	0	2	49
Row %	18.4	10.2	57.1	4.1	4.1	2	0	4.1	100
Col %	18	17.9	17.6	40	20	50	0	28.6	18.7
TOTAL	50	28	159	5	10	2	1	7	262
Row %	19.1	10.7	60.7	1.9	3.8	0.8	0.4	2.7	100
Col %	100	100	100	100	100	100	100	100	100

N = 262

Table 5.59: The percentage treatment outcomes for magnesium trisilicate suspension ***after*** the intervention

DURATION OF TREATMENT (DAYS)

Outcome	1 week	2 weeks	4 weeks	2 months	3 months	4 months	5 months	6 months	TOTAL
Changed prescription immediately	1	0	9	0	1	0	0	5	16
Row %	6.3	0	56.3	0	6.3	0	0	31.3	100
Col %	1.5	0	4	0	6.3	0	0	15.2	4.3
Changed prescription later	1	2	4	0	1	0	0	0	8
Row %	12.5	25	50	0	12.5	0	0	0	100
Col %	1.5	12.5	1.8	0	6.3	0	0	0	2.2
Did not return	50	4	167	7	10	1	1	13	253
Row %	19.8	1.6	66	2.8	4	0.4	0.4	5.1	100
Col %	75.8	25	74.6	63.6	62.5	100	100	39.4	68.8
Repeated same prescription immediately	7	9	15	2	4	0	0	15	52
Row %	13.7	17.6	28.8	3.9	7.8	0	0	29.4	100
Col %	10.6	56.3	6.7	18.2	25	0	0	45.5	14.1
Repeated same prescription later	7	1	29	2	0	0	0	0	39
Row %	17.9	2.6	74.4	5.1	0	0	0	0	100
Col %	10.6	6.3	12.9	18.2	0	0	0	0	10.6
TOTAL	66	16	223	11	16	1	1	33	368
Row %	17.9	4.3	60.9	3	4.3	0.3	0.3	9	100
Col %	100	100	100	100	100	100	100	100	100

N = 368

Discussion of results:

There was an increase of 9.3% in the percentage patients who were cured after receiving magnesium trisilicate suspension. There was an increase of 1.6% in the prescriptions for magnesium trisilicate suspension that were changed immediately.

Treatment outcome for the prescription for magnesium trisilicate suspension and omeprazole ***before and after*** the intervention

Only one patient received omeprazole with magnesium trisilicate suspension for 3 months ***before*** the intervention. There were no prescriptions for omeprazole with magnesium trisilicate suspension ***after*** the intervention. These results were not tabulated.

5.2.19 Contingency table of prescriptions that complied with STG and diagnosis

Table 5.60: The percentage of prescriptions written that adhered to the standard treatment guidelines ***before*** the intervention per diagnosis

Diagnosis	Not STG compliant	STG compliant	TOTAL
Dyspepsia/heartburn/indigestion/ abdominal pain	15	15	30
Row %	50	50	100
Col %	4	45.5	7.3
Gastritis	0	13	13
Row %	0	100	100
Col %	0	39.4	3.2
Not specified	357	0	357
Row %	100	0	100
Col %	94.7	0	87.1
Other	0	5	5
Row %	0	100	100
Col %	0	15.2	1.2
Peptic ulcer	5	0	5
Row %	100	0	100
Col %	1.3	0	1.2
TOTAL	377	33	410
Row %	92	8	100
Col %	100	100	100

N = 410

Phi coefficient = 0.04

Table 5.61: The percentage of prescriptions written that adhered to the standard treatment guidelines ***after*** the intervention per diagnosis

Diagnosis	Not STG compliant	STG compliant	TOTAL
Dyspepsia/heartburn/indigestion/ abdominal pain	24	60	84
Row %	28.6	71.4	100
Col %	4.8	69.8	14.4
Gastritis	0	15	15
Row %	0	100	100
Col %	0	17.4	2.6
Not specified	445	0	445
Row %	100	0	100
Col %	89.4	0	76.2
Other	0	11	11
Row %	0	100	100
Col %	0	12.8	1.9
Peptic ulcer	29	0	29
Row %	100	0	100
Col %	5.8	0	5
TOTAL	498	86	584
Row %	85.3	14.7	100
Col %	100	100	100

N = 584

Phi coefficient = 0.04

Discussion of results:

Before the intervention, only 50% of the prescriptions where the diagnosis was dyspepsia/heartburn/indigestion/abdominal pain complied with the STG. After the intervention, 71.4% of these prescriptions complied with the STG. The prescriptions where the diagnosis was gastritis or other complied with the STG, both before and after the intervention. None of the prescriptions where the diagnosis was peptic ulcer complied with the STG. The phi coefficient of the prescriptions before the intervention showed that there was no statistical

relationship between diagnosis and STG compliance. The phi coefficient of the prescriptions written after the intervention showed that there was no statistical relationship between diagnosis and STG compliance.

5.2.20 Percentage of prescriptions that had a diagnosis specified

Table 5.62: 2 x 2 table of the percentage of prescriptions per diagnosis specified ***before and after*** the intervention

	Diagnosis not specified	Diagnosis specified	TOTAL
Before intervention	357	53	410
Row %	87.1	12.9	100.0
Col %	44.5	27.6	41.2
After intervention	445	139	584
Row %	76.2	23.8	100.0
Col %	55.5	72.4	58.8
TOTAL	802	192	994
Row %	80.7	19.3	100.0
Col %	100.0	100.0	100.0

Phi coefficient = 0.14

Discussion of results:

Before the intervention 87.1% of the prescriptions did not have a diagnosis specified. After the intervention this decreased to 76.2%. The phi coefficient showed that there was a small positive statistical relationship between the intervention and the recording of a diagnosis.

5.2.21 Cost of treatment before intervention compared to cost of treatment after intervention

Various statistical markers were used to compare the cost of the treatment that was given before the intervention with that of the treatment given after the intervention.

These markers are represented in Table 5.63.

Table 5.63: Comparison of statistical markers for cost of treatment ***before and after*** the intervention

	Before intervention		After intervention	
STG compliance	No	Yes	No	Yes
No. of observations	377	33	498	86
Total cost of treatment	8,611.36	683.48	6,852.96	948.30
Mean	22.84	20.71	13.76	11.03
Variance	1,177.54	781.22	462.96	341.36
Std deviation	34.32	27.95	21.52	18.48
Minimum	2.02	2.94	2.02	2.94
25th percentile	2.94	2.94	2.94	2.94
Median	2.94	5.20	2.94	5.20
75th percentile	37.92	31.20	14.19	8.63
Maximum	240.42	107.04	131.40	131.40
Mode	2.94	2.94	2.94	2.94

N = 994

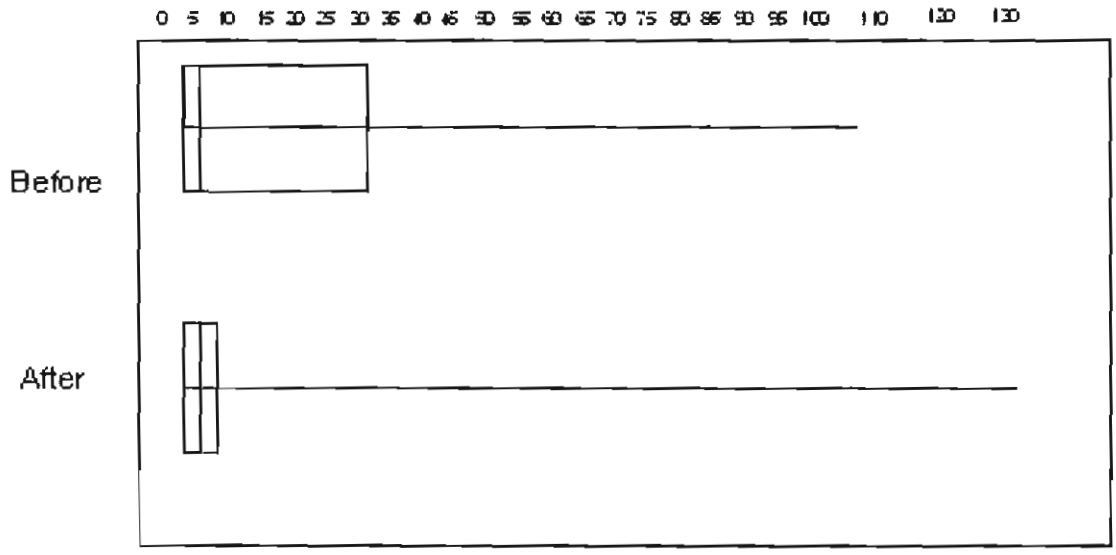
Discussion of results:

The average cost per prescription for the STG compliant prescriptions was lower than that for the prescriptions that did not comply with the STG. This was the case before the intervention (R20.71 vs. R22.84) as well as after the intervention (R11.03 vs. R13.76). The mode of the prescriptions, whether STG compliant or not, before or after the intervention remained 2.94. The prescriptions for 1 bottle magnesium trisilicate suspension cost 2.94 (PDSX, 2003c:1).

There was a greater variance shown in prescriptions that did not adhere to the STG (R1774.54 before the intervention and R462.96 after the intervention) than those prescriptions that did adhere to the STG (R781.22 before the intervention and 341.36 after the intervention).

The statistical markers (25th percentile, Median, 75th percentile, minimum and maximum) for the cost of treatment of the STG compliant prescriptions are graphically represented in Figure 5.3.

Figure 5.3: Box and whisker graphs for STG compliant prescriptions ***before and after*** the intervention



The statistical markers represented in Figure 5.3 indicate that both the distribution of costs before the intervention and the distribution of costs after the intervention were positively skewed.

5.3 Limitations

Limitations and bias that could have had an influence on the results were discussed in 4.8. These limitations and sources of bias are listed as follows:

- Selection bias.
- Recall bias.
- Patient compliance.
    - Age.

      Of the patients included in the study, 24.4% were older than 46 years.
    - Living alone.

      Of the patients included in the study, 16.6% were not married.
    - Dosage regime.

      A percentage of 14.4% of the prescriptions for Cimetidine that were included in the study had 3 times or 4 times daily regimes.
- Other interventions.
- Prescriber turnover.
- Out of stock situations.

5.4 Chapter summary

In this chapter the data collected before and after the intervention was analysed. The data were tabulated using the Epi Info™ programme. The patient and facility demographics were determined. Various drug use indicators were applied to analyse the prescription data to determine the STG adherence and the outcome of the treatment. Prescriptions written before the intervention were compared to those written after the intervention.
Conclusions drawn from the results of the study as well as recommendations will be given in chapter six.

Chapter 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The following objectives were met.

6.1.1 The prescribing practices of drugs for acid-related disorders *before* presentation of the face to face education intervention.

Only 8% of the prescriptions adhered to the STG before the presentation of the face to face education intervention (Table 5.36). The community service doctors had an STG adherence rate of 13.6%, and the PHC nurses had an STG adherence rate of 4.7% (Table 5.40). There was only one prescription written by a medical officer. This prescription did not adhere to the STG. Unspecified diagnoses appeared in 87.1% of the prescriptions in the patient files and this affected the STG adherence rate (Table 5.62). Of those prescriptions that did have the diagnosis specified 62.3% (33 of 53 prescriptions) did comply with the STG (Table 5.60).

6.1.2 The prescribing practices of drugs for acid-related disorders *after* presentation of the face to face education intervention.

In the first six months following the intervention (January 2002 – June 2002), STG compliance increased from 8% to 15.2% (Table 5.37). In the following six-month period (July 2002 – December 2002), the STG compliance decreased to 14.1% (Table 5.38). After the intervention the community service doctors had an increase in the adherence rate from 13.6% to 17.2%, the rate for medical officers increased from 0% to 42.9% and the rate for PHC nurses increased from 4.7% to 12.9% (Table 5.41). There was a slight improvement in history taking of 10.9% as only 76.2% (Table 5.62) of the prescriptions did not have the diagnosis specified. Of those prescriptions that did have the diagnosis specified there was a 0.6% decrease to 61.9% (86 of 139 prescriptions) in STG compliance (Table 5.61). This decrease could be due to more prescriptions indicating a diagnosis for peptic ulcer, but none of these adhered to the STG.

6.1.3 The therapeutic outcome of drugs for acid-related disorders prescribed *before* presentation of the face to face education intervention

Before the intervention 50.2% of the patients did not return for further treatment. A further 9% had the treatment changed immediately, 8.3% had the treatment changed later, 17.8% had the same treatment repeated immediately and 14.6% had the same treatment repeated at a later date (Table 5.42).

Based on the postulation made in paragraph 4.6.1 that the patients who did not return for further treatment were cured, it may therefore be argued that a cure-rate of 50.2% may be assumed.

6.1.4 The therapeutic outcome of drugs for acid-related disorders prescribed *after* presentation of the face to face education intervention

As shown in Table 5.43, in the first six months after the intervention had taken place the percentage patients who did not return increased from 50.2% to 60.6%. There was a decrease in the patients who had their prescriptions changed as well as those who had their prescriptions repeated.

In the second six months after the intervention (Table 5.44) there was a further 10.1% increase in the percentage of patients who did not return. There was a further decrease in the percentage of patients who had their prescription changed immediately. The prescriptions that were changed later decreased to 1.2%. The percentage of prescriptions that were repeated immediately increased slightly, but remained lower than the percentage before the intervention. The percentage of prescriptions that were repeated later decreased further.

6.2 Effect of the face to face education intervention

The effect, if any, that the intervention had on the prescribing habits, was determined by comparing the percentage of prescriptions that adhered to the

STG before the presentation of the face to face education intervention with the percentage of prescriptions that adhered to the STG after the presentation of the intervention. The phi coefficients were calculated to determine the strength of the statistical correlation of the relationship. Although the phi coefficients that were calculated did not show a high statistical correlation, it was still possible to recognize important tendencies in the data.

Following the intervention, there was an overall improvement in the adherence to the standard treatment guidelines (STG) by all three prescriber categories (Table 5.37). Table 5.62 showed that there was an improvement in the history taking. The phi coefficient of 0.14 indicated that there was a small positive statistical relationship between the intervention and the recording of a diagnosis. In the next six month period there was a decrease in the STG adherence, although the overall adherence was still higher than that before the intervention (Table 5.38). This change seen in the adherence to the STG was expected. Laing *et al.* (1997:467) stated that after an initial improvement, prescribers tended to revert to their previous behaviour.

To determine the possible effect of the intervention on the cure rate, the percentage of patients who were treated before the intervention that did not return for treatment was compared to the percentage of patients who were treated after the intervention that did not return for treatment after the intervention.

There was an increase in the cure rate from 50.2% and to 60.6% in the first six months after the intervention (Table 5.42; Table 5.43). The cure rate continued to increase to 70.7% in the second six-month period (Table 5.44).

6.3 Personal observations

Various observations were made during data gathering and analyses.

6.3.1 The 2003 edition of the standard treatment guidelines

In the 2003 Edition of the STG, cimetidine was changed from a hospital level drug to a primary health care level drug. It was indicated for the treatment of abdominal pain, dyspepsia, heartburn or indigestion where no response had been obtained from aluminium hydroxide/magnesium trisilicate tablets. The prescribed dose for the cimetidine was 400mg daily for 14 days (South Africa, 2003:21).

Before the intervention there were no prescriptions for cimetidine 400mg daily. After the intervention there were two prescriptions for cimetidine 400mg daily. Both prescriptions were for 6 months (Table 5.20). If the new edition of the STG had been in place at the time of the study, none of the prescriptions for cimetidine would have adhered to the STG.

6.3.2 Record keeping and retrieval

Record keeping was generally satisfactory at the health facilities surveyed, although some patient files were difficult to trace. Exact records were kept of drug issues for audit purposes, but the information on stock cards was not always sufficient to trace the patient file.

6.3.3 History taking

Diagnoses, if made, were poorly recorded on the patient files. Patients' smoking habits were also seldom recorded. It is recommended that the health facilities educate health workers on the importance of proper diagnosis before treatment, as well as documenting all relevant signs and symptoms, the final diagnoses and all treatment steps taken. After the intervention there was an improvement of 10.9% in the recording of the diagnosis. In 76.2% of the prescriptions written after the intervention there was still no reference to the diagnosis made (Table 5.62).

6.3.4 Factors affecting patient compliance

After the intervention, there was an increase in those prescriptions where the dosage schedule was more than twice a day (Table 5.20). This could lead to a decrease in patient compliance, which in turn could affect the therapeutic outcome of the treatment.

6.3.5 Factors affecting treatment outcome

As discussed in 2.5 non-steroid anti-inflammatory drugs should be avoided in acid-related disorders. A percentage of 10% of the patients on treatment for acid-related disorders had also been receiving NSAID (Table 5.30).
The antidepressants, theophylline, thyroxin, progesterone or calcium channel blockers are given for chronic medical conditions. The frequency of prescribing for all five of the abovementioned drug groups decreased after the intervention (Tables 5.31, 5.33, 5.32, 5.34 and 5.35 respectively). There are two possible explanations for this trend. The first is that the patients who received treatment for acid-related disorders had been prescribed other medications for their chronic illnesses while the treatment for acid-related disorders remained the same. The second possible explanation is that those patients who received antidepressants, theophylline, thyroxin, progesterone and calcium channel blockers no longer required treatment for the dyspeptic symptoms. Since the prescribers were restricted to those drugs on the essential drugs list, the first option would seem unlikely.

As discussed in 2.4 the patients who were given long-term treatment with H_2 blockers had no hope of a permanent cure. Recurrence of peptic ulcers within the first year can be decreased up to four times by adding antibiotics to the treatment (Merck, 2003b: 2; USA Dept of health and human services, 2003:1).

6.3.6 STG compliance and maintenance of rational drug use

Although there was an improvement in STG compliance, there was no statistical relationship between STG compliance and the intervention

(Table 5.39). Further interventions and education will have to be launched to ensure further improvement in STG compliance.

6.3.7 Interpersonal interaction

The informal communication with the prescribers during the intervention improved the interpersonal interaction between the different disciplines within the Govan Mbeki municipal area. Improved patient education (by the prescribers) could also have led to the improvement in the adherence to the STG as well as the improved cure rate.

6.4 Recommendations

- Health facilities should educate health workers on the importance of thorough record keeping. Particular emphasis needs to be placed on the recording of the diagnosis.
- An intervention programme targeted at improving history taking needs to be implemented.
- Prescribers should receive training on factors that could affect patient compliance.
- The prescribing of NSAID's in patients where such treatment is contra-indicated needs to be addressed and further follow-up of the intervention is needed.
- The prescribers must be encouraged on a regular basis to use the triple therapy for those patients with a diagnosis of peptic ulcer as advised in the STG, instead of long-term prescriptions for cimetidine.
- At all times careful attention needs to be given to improving the interpersonal relationships between prescribers and dispensers as well as professionals from other disciplines. Dieticians, for instance, can prove to be valuable when educating patients on lifestyle modification.
- Further qualitative studies could be done to determine what effect interpersonal and cross-discipline relationships in the hospital environment could have on patient care.

- Further investigations could be done to see what effect, if any, the intervention had exercised on patterns with regard to other disease treatments.
- Attention needs to be given in the province to the treatment of peptic ulcers. Access to gastroscopies is limited, and the delays in the motivation system for the ordering of omeprazole could deter prescribers from prescribing the correct tests and treatment even in those cases that do require it.
- It is strongly recommended that the province should investigate the possible use of other non-invasive diagnostic methods for the detection of *H. pylori* infection in patients, as these are possibly more accessible and possibly more cost effective than gastroscopies.

6.5 Further studies

It is recommended that prospective follow-up studies be done. Measurement of the treatment outcomes can be changed. Use of the SODA measurement tool would prove to be useful in determining the success of treatment.

6.6 Chapter summary

In this chapter the objectives of the study were revisited to determine what effect the face to face intervention had had on the adherence to the STG and what changes may have occurred to the treatment outcomes. Based on the findings of the study, various recommendations were made.

There was an improvement in the adherence to the STG as well as in the treatment cure rate. Recommendations for further intervention and follow-up studies were made.

All the objectives of the study were met. This concludes the study.

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Appendix A: Detailed indicators prescription encounter form

Detailed Indicators Encounter Form

Facility: _____ 31

Data Collector: Jackie | Other

R 29 | P 30

Pregnant Y 9 | N 10

Race

Caucasian 24	
African 25	
Asian 26	
Coloured 27	
Other 28	

Encounter #

Pt survey #

# of visit

Investigations:

Gastroscopy	Y 22	
Other(specify)	Y 23	

Prescriber		
PHC Sr 6	M.O. 7	Com Ser Dr 8

Outcome	
Change Rx stat	
Changed Rx later	
No return	
Referral	
Repeat stat	
Repeat later	

DOB

Pt./Pres #	Date	Name	Age			Sex	
			0–18 1	19–45 2	46 –3	M 4	F 5

Smoker NO 58 | YES 55

How long smoking 57

When Quit 56

Cigarettes per day

Employed Y 33 | N 34

Married 35	Single 36	Widowed 37	Divorced 38

Health Problems	Health Problem Description.	Code	Yes
	1. Dyspepsia/heartburn/Indigestion/Abd. Pain.	11	
	2. Peptic Ulcer (Duodenal/Gastric)	12	
	3.a. Not specified	13	
	3.b.Other (specify)		

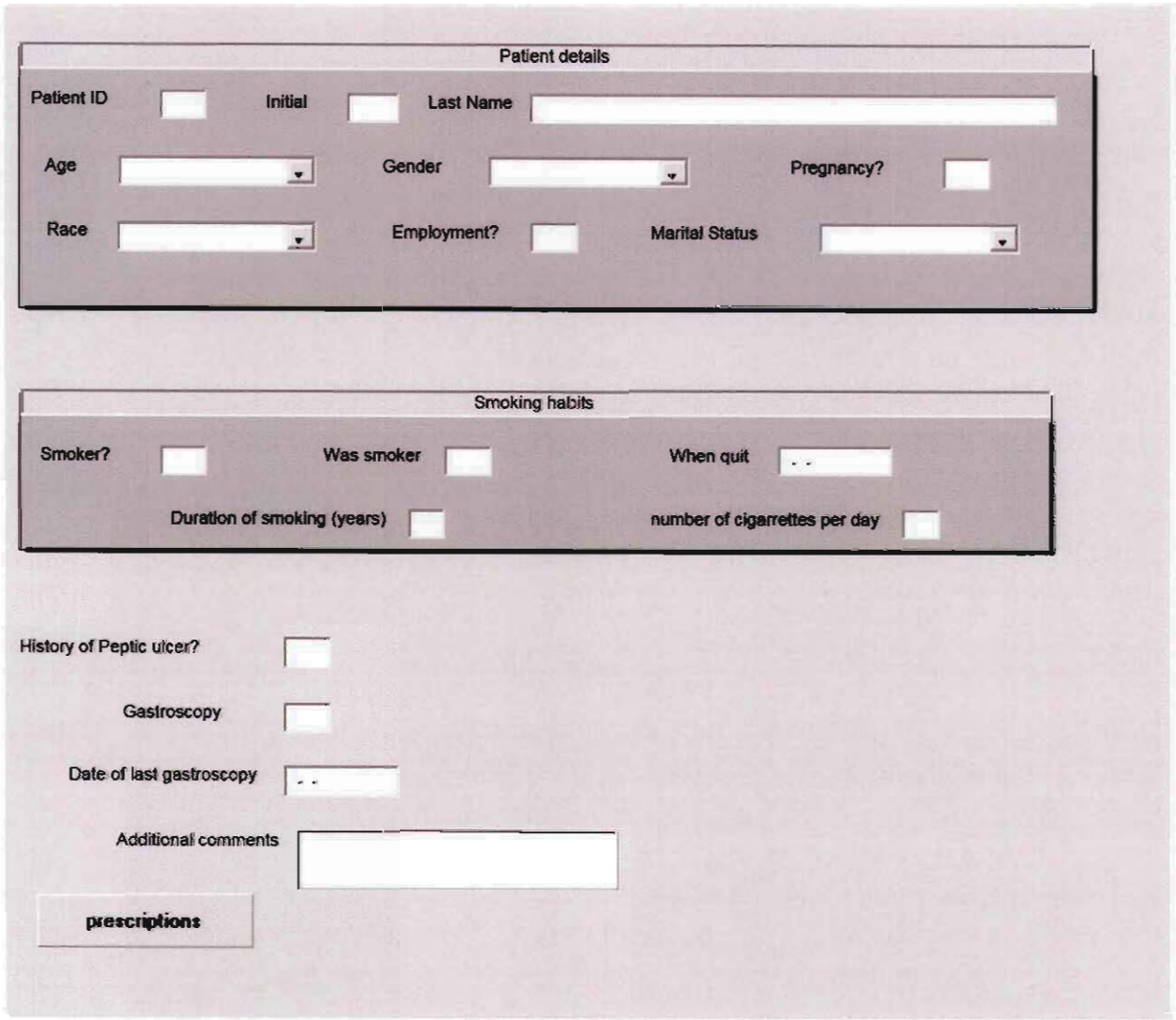
Drugs	Name and Strength	Code	Dose	Dosage interval					Duration Days	Quant	Unit	Cost/unit	Total cost	Adher STG	
				dly 39	bd 40	tds 41	qid 42	Other 43						Y 53	N 54
	1. Cimetidine 200mg/400mg tablet	14									1 tab				
	2. Omeprazole	15									1 tab				
	3. Al. Hyd./ Mg. Trisil. Tablet	16									1 tab				
	4. Mag. Trisilicate susp.	17									2 x 200ml				
	5. Amoxycillin 250mg	18													
	6. Metronidazole 200mg.	19													
	7. N.S.A.I.D. (specify)	20													
	8.a. Amitriptylline 10mg/25mg tab	21a													
	8.b Thyroxine sodium 0.05mg / 0.1mg tab	21b													
	8.c														
	8.d														
	8.e														
	8.f														

Additional comments on back

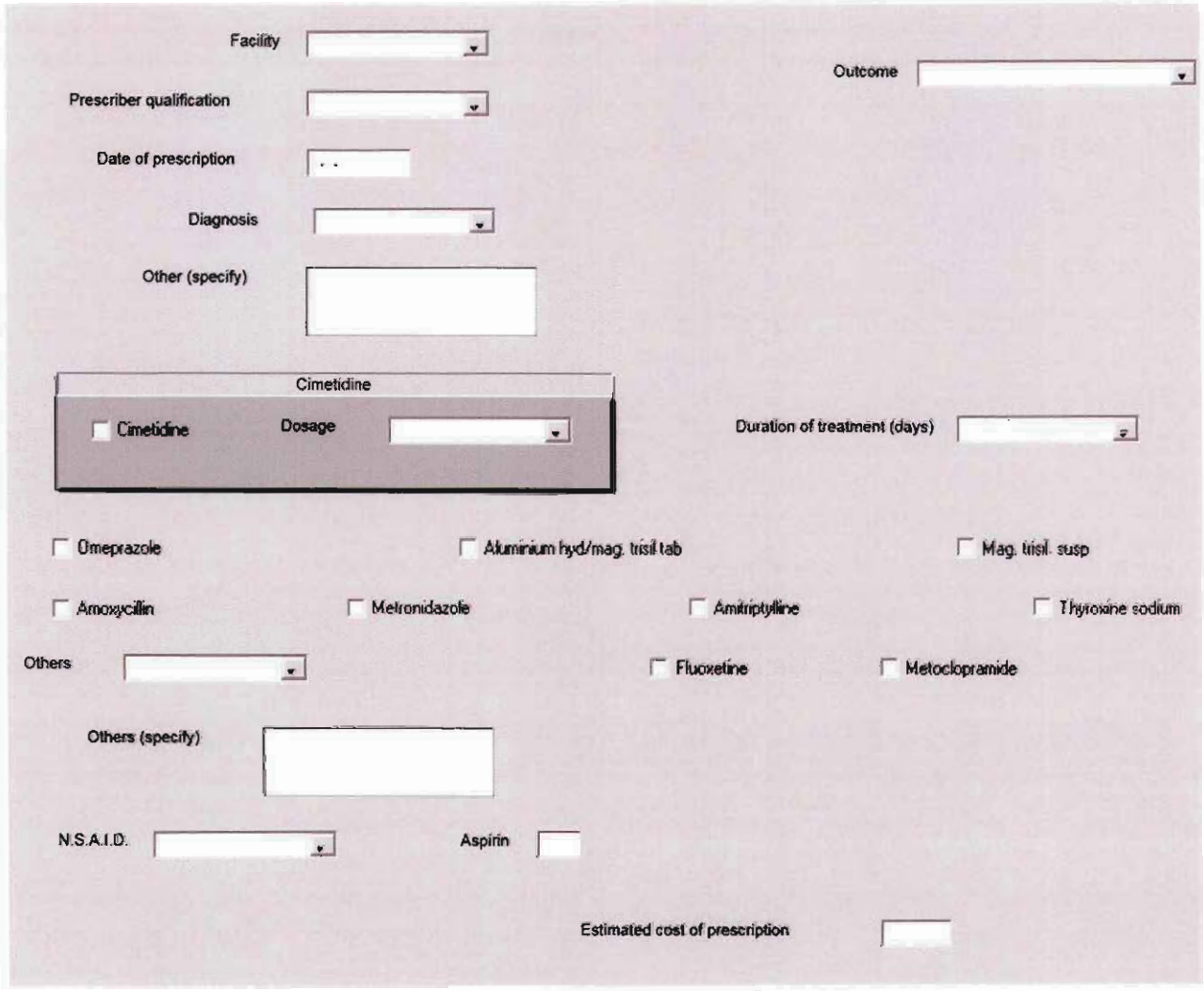
Appendix B: Indicators

Code	Indicator		Specifications
1	Age	0–18	Age Category of patients
2		19–45	Age Range
3		46–	
4	Sex	M	Gender of patient M = Male
5		F	F = Female
6	Prescriber	PHC Nurse	Primary health care prof. Nurse
7		M.O.	medical officer (doctor)
8		Com. Ser. Doc.	community service doctor
9	Pregnant	Y	Patient is pregnant
10		N	Patient is not pregnant
11	Diagnosis	Dyspepsia/heartburn/Indigestion/abd. P	(includes gastritis and oes. Reflux)
			Diagnosis as noted in file of
12		Peptic ulcer	patient by clinician.
59		Not specified	
13		Other	All other ailments incl. Unrelated illnesses
14	Treatment	Cimetidine	Treatment prescribed for patient
15		Omeprazole	
16		Al hyd/Mg. Tris. Tab	
17		Mg trisil suspension	
18		Amoxicillin	
19		Metronidazole	
20		NSAID	
21		Other	other medicines incl. Non–medicinal and referrals
21a		Amitryptylline 10mg/25mg tablet	
21b		Thyroxine Sodium 0.1mg/0.05mg tab	
22	Investigations	Gastroscopy	Pt referred for gastroscopy – include date
23		Other	Incl. Lab tests, X–rays and all other investigations
24	Race	Caucasian	White
25		African	Black
26		Asian	Indian
27		Coloured	
28		Other	Other races not in list.
29	Data Type	R	Retrospective data before 1 August 2001.
30		P	Prospective data
31	Facility 31a	Secunda	Institution where survey was done.
31b		Evander	
31c		Trichardt	
31d		Kinross	
33	Employment	Employed	Patient has employment
34	status	Unemployed	Patient currently unemployed
35	Marital status	Married	
36		Single	
37		Widowed	
38		Divorced	
39	Dosage	Dly	Once daily dose
40		Bd	Twice daily dose
41		Tds	Three times daily dose
42		Qid	Four times daily dose
43		Other	Specify
44	Duration	1/52	Treatment given for 1 week
45		2/52	Treatment given for 2 weeks
46		1/12	Treatment given for 1 month
47		2/12	
48		3/12	Treatment given for 3 months
49		4/12	
50		5/12	
51		6/12	Treatment given for 6 months
52		other	Treatment given for different length of time (days)
53	Adher. To STG	Y	Prescription adheres to STG as per diagnosis
54		N	Prescription does not adhere to STG
55	Smoker	Yes	
56		No	
57	Smoking habits	How long smoking	
58		when did he patient quit	
	Patient name		The patients name on file
	Pt # / pres #		Patients file number or number of the prescription
	Total Cost of Rx		Total value of prescription(all items given) in Rand
	Quantity Cimet		Quantity of cimetidine tablets issued
	Dose Cimetidine		Dose of cimetidine prescribed in mg.

Appendix C: Patient details data entry form



Appendix D: Prescription data entry form



Appendix E: Table of results of survey done in Govan Mbeki Municipal area during 2001

Highveld Ridge

Patient demographics	Male	Female	0–19 years	20–45 years	46< years	Caucasian	African	Asian	Coloured
Number of patients	40	172	0	65	148	172	32	9	0
% of patients treated	18.90%	81.10%	0%	30.50%	69.50%	80.70%	15%	4.30%	0%

Prescriber categories	M.O.	C.S.D.	Secunda	Evander	Trichardt	Lebohang	Embalenhle	Kinross
Number of patients	4	209	189	16	0	1	1	2
% of patients treated	1.90%	98.10%	90.40%	7.60%	0%	0.47%	0.47%	1%

Cost per perscription	STG	Reviewed
Peptic ulcer diagnosed	R18.619	R 24.21
Dyspepsia diagnosed	R6.58	R 25.46

Adherence to STG	M.O.	C.S.D.
	1	9
n=	4	209
	25%	4.31%

Key

Gender: Male
Female

Age: 0–19 years
20–45 years
Over 46 years

Race: Caucasian
African
Indian
Coloured

Prescriber M.O: Medical Officer
C.S.D: Community Service Doctor

Facility: Secunda TLC clinic
Evander TLC clinic
Trichardt TLC clinic
Lebohang Community health centre
Embalenhle Community health centre
Kinross TLC clinic

Appendix F: Progress timeline (Task schedule)

Task	Jan - Mar 03	April - June 03	Jul - Sep 03	Oct - Dec 03	Jan - Mar 04	April - June 04	Jul - Sep 04	Oct - Dec 04	Jan - Mar 05	April - June 05	Jul - Sep 05	Oct - Dec 05	Jan - Mar 06	April - June 06	July 06 – Dec 06	Jan 07 – May 07
Literature review: Research methodology	x															
Write research proposal	x															
Literature review: the essential drug concept		x														
Self-study Epi info™ statistical programme		x														
Permission for study from Ethics committee		x														
Literature review: treatment of dyspepsia			x													
Design data collection form			x													
Pilot test data collection form			x													
Design Epi info™ questionnaires				x												
Pilot test Epi info™ questionnaires				x												
Collect data from prescriptions					x	x										
Follow up on files of patients who received treatment							x	x								
Enter data in Epi info questionnaires									x	x	x					
Do data analysis												x				
Do follow up literature review													x	x		
Complete dissertation														x		
Submit dissertation for examination															x	
Revise dissertation																x

Appendix G: Overview of Epi Info™ 2002

Epi Info™ 2002 (Version 3.2.2. 2005 release) (CDC, 2005)

These programs are provided in the public domain to promote public health.

Epi Info is a series of programs for Microsoft Windows 95, 98, NT, and 2000 for use by public health professionals in conducting outbreak investigations, managing databases for public health surveillance and other tasks, and general database and statistics applications. With Epi Info and a personal computer, physicians, epidemiologists, and other public health and medical workers can rapidly develop a questionnaire or form, customise the data entry process, and enter and analyse data.

Epidemiologic statistics, graphs, and tables are produced with simple commands like READ, FREQ, LIST, TABLES, and GRAPH. A component called *Epi Map* displays geographic maps with data from Epi Info. Epi Info is in the public domain and can be downloaded from the Internet. CD-ROM copies and printed manuals are expected to be available from private vendors.

The first version of Epi Info was released in 1985. A study in 1997 documented 145,000 copies of the DOS versions of Epi Info and *Epi Map* in 117 countries. The DOS manual and/or programs have been translated into 13 non-English languages.

An internal review of server logs in 2001 documented over 250,000 downloads of Epi Info 2000 and Epi6 from over 130 countries.

Epi Info™ 2002 is written in Visual Basic, Version 6. It uses the Microsoft Access file format as a gateway to industry database standards. Although Epi Info™ 2002 data is stored in Microsoft Access files for maximum compatibility with other systems, many other file types can be analysed, imported, or exported.

Epi Info™ 2002 includes a Geographic Information System (GIS), called *Epi Map*, built around the MapObjects program from Environmental Systems Research, Inc. (ESRI), the producers of ArcView. *Epi Map* is compatible with GIS data from numerous Internet sites in the popular ESRI formats.

Epi Info™ 2002 retains many features of the familiar Epi Info for DOS, while offering Windows strengths like point-and-click ease of use, graphics, fonts, and painless printing. The programs, documentation, and teaching materials are in the public domain (although "Epi Info" is a CDC trademark), and may be freely copied, distributed, or translated

Using Epi Info™ 2002 (Version 3.2.2. 2005 release) (CDC, 2005)

Epi Info™ 2002 is a database and statistics program for public health professionals. Although it can be programmed to produce systems for repeated or permanent use, it can also be used interactively for rapid questionnaire design, data entry, and analysis during an investigation.

Setting up a new database in Epi Info™ 2002 is done in *MakeView*, the View or questionnaire designer. *MakeView* allows any number of fields or questions to be placed on successive pages of a questionnaire or form. Related Views (data entry forms) can also be constructed using buttons for point-and-click access. Legal values, automatic code fields, and more complex data-entry operations can be included in the data entry form at the time it is designed or later.

Once a data entry form is designed, it is saved automatically. A menu choice called ENTER DATA or simply running the *Enter* program with the new data entry form will automatically construct another table in the same database (MDB) for storing the data, and present the form ready for data entry.

During data entry, the special constraints selected during design become active, and the user can move from record to record in several ways, or search for records having particular values. Records are saved automatically whenever a new page or record is requested.

Access to data in Epi Info Views (data entry form) or data tables, or in a variety of other file formats including HTML and those with ODBC drivers, requires only the READ command in *Analysis*. Output in HTML format is produced by LIST, FREQuency, TABLES, and several other commands. Data cleaning can be performed with the aid of RECODE, IF, and SELECT statements. The MAP and GRAPH commands allow data to be linked to industry standard shapefiles for mapping and to be represented in a variety of graph types.

A special purpose program called *NutStat* compares data on height, weight, age, sex, and arm circumference with international reference standards for

assessment of nutritional status. *NutStat* can be linked to an Epi Info™ 2002 data entry form for data entry or used alone.

The *Epi Map* program allows a variety of maps to be constructed and linked to data in Epi Info or Access data tables. *Epi Map* offers a high degree of compatibility with the popular ArcView program of the Environmental Systems Research Institute, Inc. (ESRI).

Epi Info™ 2002 can be downloaded from the Internet or obtained on CD-ROM from a variety of sources. Using the programs requires that they be installed on a computer or network under Windows 95, 98, NT, or 2000 using the s*etup* program provided. Many of the features of Epi Info™ 2002 are different from those of Epi Info, Version 6, for DOS.

Appendix H: Glossary

BD	Dosage regime is twice daily
CSD	Community service doctor
Drug use indicator	Variable that measures the use of drugs
EDL	Essential drugs list
EDP	Essential drug programme
FDA	American food and drug administration
H. pylori	*Helicobacter pylori*
MO	Medical officer (doctor)
NDP	National drug policy
NOCTè	Dosage regime is at night only
NSAID	Non-steroid anti-inflammatory drugs
PHC	Primary health care
PSSA	Pharmaceutical society of South Africa
QID	Dosage regime is four times per day
Referral prescription:	Prescriptions written by a doctor visiting the clinic. The prescription was dispensed by the hospital pharmacy and issued to the patient by the clinic staff.

SAMF	South African medicines formulary
SODA	Severity of dyspepsia assessment
STG	Standard treatment guidelines
TDS	Dosage regime is three times per day