Prescribing patterns of benzodiazepines: A comparative study between two provinces in South Africa

C.D. VISSER

20029357

Dissertation submitted in partial fulfillment of the requirements for the degree *Magister Pharmaciae* at the Potchefstroom campus of the North-West University

Supervisor: Mrs. M.J. Basson

Co-supervisor: Prof. Dr. M.S Lubbe

Co-supervisor: Mrs. J.R. Burger

November 2010

ACKNOWLEDGEMENTS

I would like to express my appreciation and gratitude to the following people for their contribution to the successful completion of this dissertation:

- My supervisor: Mrs M.J. Basson in her capacity as supervisor for this study for her guidance and assistance.
- My co-supervisor: Prof. Dr. M.S Lubbe in her capacity as co-supervisor for this study as well as for her assistance with the database.
- My co-supervisor: Mrs J.R Burger in her capacity as co-supervisor for this study for her guidance and assistance.
- To the pharmacy benefit management company for providing the data for this dissertation.
- Me. A. Bekker, for her assistance with the analysis of the data.
- Mrs. M. Terblanche for assisting in the language editing of this dissertation.
- Mrs. H. Hoffman for assisting in the language and bibliography editing of this dissertation.
- Prof. Dr. J.J. Gerber for assisting in the language editing of the abstract.
- To all the personnel of the subject group of Pharmacy Practice and my fellow M-students for their support and advice.
- To Jacques (Trekker), Juan, Jeanine, Nicolene and Ruan, for all their friendship, support and love.
- To Marelise, her parents and brother, for their support, love and encouragement.
- To all my hostel and other friends, for all their friendship and support.
- To my parents, brother and sister, for their love, encouragement and support.

My gratitude is extended to the most important One, Jesus Christ and Lord, for giving me strength, courage and perseverance during this dissertation.

"Even youths grow tired and weary, and young men stumble and fall; but those who hope in the LORD will renew their strength. They will soar on wings like eagles; they will run and not grow weary, they will walk and not be faint". *Isaiah 40:30-31*

TABLE OF CONTENTS

CHAPTER 2: LITERATURE OVERVIEW

CHAPTER 3: RESEARCH METHODOLOGY

CHAPTER 4: RESULTS AND DISCUSSION

CHAPTER 5: CONCLUSION AND RECOMMENDATION

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Title: Prescribing patterns of benzodiazepines: A comparative study between two provinces in South Africa.

Keywords: Benzodiazepine, urbanisation, crime, insomnia, anxiety, age, sex, Gauteng, Northern Cape, days between refill, drug utilisation review.

Background: In 2007 the population density for the Gauteng Province was 614 persons per km^2 and in the Northern Cape Province it was 2.9 persons per km^2 . High population density leads to an increase in crime. This was evident in the percentage distribution of total crime reported from 2000 to 2003 of 27.4% in Gauteng Province, while the percentage distribution of total crime reported in the Northern Cape for the same period of time was 2,8%. Stress and insomnia can be caused by crime which is influenced by population density. Crime and high population density, may cause stress and fear, which may lead to insomnia and anxiety, which in turn may lead to an increase in benzodiazepine usage.

Objective: The general objective of this study was to investigate the benzodiazepine usage in the private health care sector in South Africa based on age, sex, geographical areas, prescriber type and days between refills.

Methods: The data were obtained from a medicine claims database of a pharmacy benefit management company covering the periods from 1 January 2006 to 31 December 2006 and 1 January 2008 to 31 December 2008. The statistical analysis was performed by making use of the Statistical Analysis System®. A drug utilisation review was performed.

Results: Patients claiming benzodiazepines represented about 7.25% of all patients in total database in 2006 and 7.97% in 2008. Female patients claimed more benzodiazepines than male patients in both Gauteng (67.24% in 2006 & 67.36% in 2008 respectively) and Northern Cape Province (67.77% in 2006 & 67.70% in 2008 respectively). Patients aged 40 years to 65 years claimed the highest number of benzodiazepine items, while patients younger than 12 years claimed the lowest number of benzodiazepine items.

The number of patients that claimed benzodiazepines in the Northern Cape was lower than those in Gauteng. The percentage of patients that claimed benzodiazepines in 2006 was 7.91% in Gauteng versus 8.96% in Northern Cape. In 2008 the percentage of patients that claimed benzodiazepines was 8.47% in Gauteng versus 9.51% in Northern Cape. The

percentage of benzodiazepine prescriptions claimed in Gauteng was 4.79% in 2006 and 5.10% in 2008. In the Northern Cape the percentages of benzodiazepine prescriptions claimed in 2006 and 2008 were 4.62% and 4.30% respectively.

General medical practitioners prescribed most of the benzodiazepine prescriptions in both Northern Cape and Gauteng Province. Trade name products that were mostly prescribed in the Gauteng was Adco-Alzam® 0.5 mg and in the Northern Cape it was Brazepam® 3 mg for both 2006 and 2008.

Conclusion: The difference in the prescribing patterns of benzodiazepines in Gauteng and the Northern Cape was not statistically significant. Recommendations for future research were made.

OPSOMMING

Titel: Voorskryfpatrone van bensodiasepiene: 'n Vergelykende studie tussen twee provinsies in Suid-Afrika.

Sleutelwoorde: Bensodiasepiene, verstedeliking, misdaad, slapeloosheid, angstigheid, ouderdom, geslag, Gauteng, Noord-Kaap, dae tussen herhaling van voorskrif, medisyneverbruiksevaluering.

Agtergrond: In 2007 was die bevolkingsdigtheid in Gauteng 614 persone per km^2 en in die Noord-Kaap slegs 2.9 persone per km^2. 'n Hoë bevolkingsdigtheid kan aanleiding gee tot 'n toename in misdaad. Dit het ook geblyk uit die persentasie verspreiding van die totale aangemelde misdaad in Suid-Afrika waarvan Gauteng 27.4% en Noord-Kaap 2.8% uitgemaak het vir die tydperk 2000 tot 2003. Misdaad en 'n hoë bevolkingsdigtheid, kan lei tot spanning en vrees, wat op hulle beurt weer aanleiding gee tot angs en slapeloosheid. Hierdie toestande kan aanleiding gee tot 'n toename in die gebruik van bensodiasepiene.

Doel: Die algemene doel van die studie was om die voorskrifpatrone van bensodiasepiene te ondersoek volgens verskillende ouderdomme, geslagte, geografiese gebiede, voorskrywers en dae tussen die hernuwing van voorskrifte in die private gesondheidsorgsektor van Suid-Afrika.

Metode: Die data is verkry vanaf 'n medisyne-eis databasis vir die tydperk 1 Januarie 2006 tot 31 Desember 2006 en 1 Januarie 2008 tot 31 Desember 2008. Die statistiese verwerking is gedoen met Statistical Analysis System ®. Die studie het 'n medisyneverbruiksevaluering behels.

Resultate: Die aantal pasiënte vir wie bensodiasepiene geëis was, het 7.25% in 2006 en 7.97% in 2008 van die totale databasis beslaan. Vroulike pasiënte het die meeste bensodiasepiene geëis in beide Gauteng (67.24% in 2006 & 67.36% in 2008) en die Noord-Kaap Provinsie (67.77% in 2006 & 67.70% in 2008) gebruik. Pasiënte tussen die ouderdom van 40 tot 65 jaar het die meeste bensodiasepiene gebruik. Pasiënte jonger as 12 jaar het die minste bensodiasepiene tydens die studietydperk gebruik. Die totale aantal pasiënte wat bensodiasepiene gebruik het, was minder in die Noord-Kaap as in Gauteng. Daar was 'n klein verskil tussen die persentasie pasiënte wat bensodiasepiene gebruik het in Gauteng (7.91%) en Noord-Kaap (8.96%) in 2006. In 2008 het die resultate relatief dieselfde gelyk vir Gauteng (8.47%) en Noord-Kaap (9.51%). Die persentasie bensodiasepien voorskrifte wat geëis is in

Gauteng was 4.79% vir 2006 en 5.10% vir 2008. Die Noord-Kaap se persentasie benzodiasepien voorskrifte wat geëis is, was vir 2006 en 2008, 4.62% en 4.30%.

Algemene praktisyns het die meeste bensodiasepien voorskrifte gegenereer in beide Noord-Kaap en Gauteng. Adco-Alzam® 0.5 mg was die handelsnaam wat die meeste voorgeskryf was in Gauteng en Brazepam® 3 mg was die handelsnaam wat die meeste voorgeskryf was in die Noord-Kaap, vir beide studie jare.

Gevolgtrekking: Die verskil tussen die Gauteng en Noord-Kaap se voorskryfpatrone was nie van statisties betekenisvol nie. In die studie is daar aanbevelings gemaak ten opsigte van moontlike toekomstig navorsing op die gebied.

CHAPTER 1

INTRODUCTION AND PROBLEM STATEMENT

1.1 INTRODUCTION

This chapter is an introduction to the rest of the dissertation and includes the problem statement, research objectives, research method and division of chapters.

1.2 PROBLEM STATEMENT

Urbanisation is part of modern societies and as such it affects people's lives worldwide. According to Howley (2009:792) urbanisation is a policy implemented by advanced capitalist societies to facilitate more sustainable development patterns. Apart from these considerations urbanisation also exercises an impact on the physical and psychological well-being of people, as can be seen in a quotation such as: "The answer is that place does indeed matter in case of the use of benzodiazepines" (Groenewegen *et al.,* 1999:1709).

In South Africa urbanisation is taking place constantly and often quite rapidly. South Africa exists mostly out of urban areas (60.2%) (United Nations, 2007:69). The Gauteng Province had the highest percentage of people living in an urban area with 96.3% in 2001, in comparison with the Northern Cape Province that had 80.7% people living in urban areas (Statistics South Africa, 2006:23).

One of the negative aspects associated with urbanisation is the extent of crime in urban areas (Howley, 2009:794). Very often people in urban areas complain about the restricted space, crime, cost of living, traffic, noise and pollution (Howley, 2009:794). Du Plessis and Louw (2005:4) added that the urbanisation rate is one of the factors associated with high levels of crime.

Crime may also be influenced by population density. Naude *et al.* (2009:322) claimed that this can be seen when examining crime statistics in South Africa. There is a correlation between population density and crime rates. The following table (Table 1.1) illustrates the correlation between population density and crime.

Table 1.1: Homicide rate of different places according to a certain time period (Burger, 2009:5; Population Reference Bureau, 2009; Statistics South Africa, 1999:51; Statistics South Africa, 2006; WHO, 1993).

Place	Year	Population density per square kilometre	Homicide rate per 100 000 people
Global	2008		7.6
United States	2008	32	5.8
United Kingdom	2008	255	2.3
Australia	1991	3	2.0
Brazil	2008	22	25.7
South Africa	2009	42	37.3
Venezuala	2009	31	48
Trinidad and Tobago	2008	260	37.3
Sierra Leone	2008	79	50
Gauteng	2003	519.5	27.4
Northern Cape Province	2003	2.3	2.8

From the Table 1.1 it is visible that there is a correlation between density and homicide rate, but the correlation was not applicable to all countries.

In the year 2007, one out of every five persons in South Africa had had an experience with crime, whether it happened to the person himself or herself or to someone he/she knows (Pharoah, 2009:1). From the year 1994 to 2007 in South Africa, nearly 310 000 murder cases have been reported, 711 000 rape cases and over 6.6 million incidences of assault, not even mentioning the number of burglaries (Altbeker, 2007:38).

The percentage of individuals who experienced at least one incident of crime in 1997 in South Africa was 14.6%. The percentage of individuals who had experienced at least one incident of crime in 1997 in Gauteng was 14.9% and in the Northern Cape Province the percentage was 13.0% (Statistics South Africa, 1999).

Crime and population density, may, in turn, cause stress, fear, insomnia and anxiety (Demombynes & Ozler, 2005:1; Krakow *et al.* 2001:2046).

Anxiety, insomnia, fear and stress are all linked together and interactive (Craig *et al*., 1995:1325; Tierney *et al.,* 2005:1012). Stress and fear caused by crime may therefore causes anxiety and insomnia.

The percentage of adolescents that have anxiety in Australia is 13.2%, compared to 5.8% in China, 13% in Hong Kong, 3.8% in Italy and 25% in Canada (Boyd *et al*., 2000:488). In a study done in America, 12.3% of the people had anxiety disorder (Kroenke *et al*., 2009:166). According to Stein and co-workers (2008:112), the prevalence of anxiety disorders in South Africa was 15.8%. The Gauteng and Northern Cape Province in South Africa had a lifetime prevalence percentage for anxiety disorder of 15.7% and 15% respectively in the year 2009 (Herman *et al*., 2009:341).

Insomnia affects almost 10% to 15% of people world wide (Richards, 2005:612). According to Richards (2005:612) almost 70% of Americans complain of insomnia regularly. In the United Kingdom almost five million people had experienced insomnia in the year 2005 (Richards, 2005:612). The percentage of people who uses prescription medicine for insomnia in Germany was 2.4%, compared to 5% in the United States, 9.8% in France and 11% in Canada (Morin *et al*., 2006:124).

Anxiety and insomnia are usually treated with benzodiazepines (Trevor & Way, 2009:371). The benzodiazepines are of the pharmacology class of sedative-hypnotic and anxiolytic drugs (Trevor & Way, 2009:371).

Benzodiazepines are relatively safe drugs, because an overdose of benzodiazepines will not be fatal to a patient (Trevor & Way, 2009:371). Patients that use benzodiazepines for longer than a year would have a relatively high probability (40% to 50% likelihood) to develop benzodiazepine dependence (Rossiter, 2010:475). Benzodiazepines can only be dispensed by means of a prescription by an authorised prescriber (South Africa, 2003:7). Benzodiazepines were claimed most frequently by females and elderly patients (Kairuz & Truter, 2007:305). The prevalence of benzodiazepine use in an adult population varies between 2% to 10% globally.

From the previous paragraphs it is evident that urbanisation, crime and stress may cause insomnia and anxiety and both these conditions are usually treated with benzodiazepines. Urbanisation in turn is linked to specific geographical areas. Therefore, this study intends to investigate whether there is a link between the prescribing patterns of benzodiazepines and geographical areas, specifically the Northern Cape and the Gauteng Province.

According to Judd *et al.* (2002:111) limited data to support the high prevalence of mental disorders in urban residents were available. Also, Tu *et al.* (2001:1344) stated that in future studies the identification of regions of prescribers would improve the prescribing of

benzodiazepines. In this study such limitations and recommendations of the other two studies will be investigated.

1.3 RESEARCH OBJECTIVE

The research objective consists of general objectives and specific objectives.

1.3.1 General objective

The general research objective of this study was to investigate the prescribing patterns of benzodiazepines in the Gauteng and Northern Cape Provinces.

1.3.2 Specific objectives

The specific research objectives were grouped into those with regard to the literature review and those pertaining to the empirical investigation.

1.3.2.1 Phase one: Literature review

Below specific objectives related to the literature review are listed.

- To describe and define the terms: urbanisation, crime, insomnia and anxiety.
- To establish from the literature the relationship between the geographical area, crime and urbanisation globally.
- To determine from the literature the relationship between geographical areas, crime and urbanisation, as applicable to South Africa.
- To depict from the literature the relationship between crime, urbanisation and anxiety and insomnia.
- To describe and define benzodiazepines.
- To investigate the prescribing patterns of benzodiazepines globally as well as in South Africa and to do so with regard to gender, age and active ingredients.

1.3.2.2 Phase two: Empirical investigation

The aims of the empirical investigation are describe according to the total data set and the benzodiazepine data. The following specific objectives could be formulated with regard to the data of the total data set.

- To determine and tabulate the age and gender of patients.
- To conduct research on the prescribing patterns in the different provinces in South Africa.
- To investigate prescribing patterns in the Gauteng Province and Northern Cape Province with regard to the gender and age.

The data of the benzodiazepine set were analysed according to the following objectives:

- To determine the prescribing patterns of benzodiazepine pertaining the Gauteng Province and Northern Cape Province.
- To determine the age of the patients to whom benzodiazepines had been prescribed.
- To investigate the prescribing patterns of benzodiazepines as applicable to the different genders groups.
- To establish the number of days between refills of the benzodiazepine prescriptions.
- To investigate and compare the prescribing patterns of benzodiazepines by the general medical practitioners, specialists and other practitioners.

1.4 RESEARCH METHODOLOGY

The research method included a literature review phase and the empirical investigation phase.

1.4.1 Phase one: Literature study

The literature (reported in chapter 2) review commenced with an overview of urbanisation, population density and crime and the impact that these aspects have on the prescribing of benzodiazepines. Benzodiazepines were defined, described and classified. The different prescribing patterns of benzodiazepines were determined.

1.4.2 Phase two: Empirical investigation

The empirical investigation consisted of various aspects that were discussed in-depth in Chapter 3. The study population contained all the patients on the medicine claims database as well as specifically all the patients who had received benzodiazepines for the two study periods (1 January 2006 to 31 December 2006 and 1 January 2008 to 31 December 2008). This study was carried out in the private health care sector of South Africa. A retrospective drug utilisation review was conducted, using secondary data that were obtained from the medicine claims database.

The statistical analysis was carried out with the help of the Stastistical Analysis System® SAS 9.1® (SAS Institute Inc., 2007).

1.5 TERMS AND DEFINITIONS

The following terms were used throughout this study and would need to be defined:

- Active ingredient: This refers to the ingredient that produces the intended activity of a medicinal product. Such an ingredient can be administered on its own or in combination with one or more other ingredients.

- Medicine: Medicine is a substance or mixture of substances to be administered or applied for the prevention, treatment or healing of an illness. Medical science has to accept such a substance or mixture as ethical and it must be registered with the South African Medicines Control Council (MCC, 2010).

- Number of prescriptions: This refers to a written list of medicine items, as prescribed to a patient by any legal or authorised prescriber. For this study only prescriptions for the years 2006 and 2008 were taken into consideration.

- Number of items: The number of items refers to the total number of items claimed through the database during a specific time period.

- Patient: A patient is a person who receives medical treatment, care or medication on prescription by a legal prescriber or another medical professional (OED, 2010c).

- Prescriber: According to the Medicines and Related Substances Control Act (act 101 of 1965) a prescriber means “a medical practitioner, dentist, veterinarian, practitioner, nurse or other person registered under the Health Professions Act 1974” (South Africa, 1997).

- Psychiatrist: A psychiatrist is a medical practitioner that specialises in psychiatry after postgraduate training and must be appropriately qualified person registered with the Health Professions Council of South Africa (HPCSA, 2010; OED, 2010e).

- Total database: The total database includes all the medication or products claimed by the patients from their medical aid scheme according to this Pharmaceutical Benefit Management company during the study period.

1.6 ABBREVIATIONS

The following abbreviations and acronyms were used in this study:

- avg - average
- CNS - Central nervous system
- DUR - Drug utilisation review
- GABA - Gamma-aminobutyric acid
- GMP - General medical practitioner
- GMS - General Medical Services
- GP - Gauteng province
- HPCSA - Health Professions Council of South Africa
- HR - Homicide rate
- MIMS - Monthly Index of Medical Specialities
- NAPPI - National Approved Product Pricing Index
- NC - Northern Cape Province
- n_{GP} - number of patients, prescriptions or items in Gauteng Province
- n_{nc} - number of patients, prescriptions or items in Northern Cape Province
- NREM - non-rapid eye movement
- OCD - Obsessive-compulsive disorder
- PBM - Pharmaceutical Benefit Management company
- REM - Rapid eye movement
- SA - South Africa
- SAS - Statistical Analysis System®
- UK - United Kingdom
- WHO - World Health Organization

1.7 DIVISION OF CHAPTERS:

This study was divided into the following five chapters plus the list of references:

Chapter 1: Introduction and problem statement

Chapter 2: Literature review

Chapter 3: Empirical investigation

Chapter 4: Results and discussion

Chapter 5: Conclusions and recommendations

Chapter 6: Bibliography

1.8 CHAPTER SUMMARY

In this chapter the introduction, problem statement, research objectives, research methods, terms and definitions, abbreviations and the division of chapters have been discussed. The following chapter will focus on the literature review.

CHAPTER 2

LITERATURE OVERVIEW

2.1 INTRODUCTION

This chapter focuses on the definition of terms applicable to this study. The terms are urbanisation, crime, anxiety, insomnia and the class of drugs called benzodiazepines. This chapter provides an overview of the possible relation between urbanisation, crime, anxiety, insomnia and the use of benzodiazepines.

2.2 BACKGROUND

Louw and Bekker (1996:10) claimed that people in Africa had been living for almost all their lives in large open spaces until a few decades ago. Urbanisation caused diverse cultures to collide. The space in cities is usually finite and constrained, which is the opposite of what most of the cultures in Africa are accustomed to, and the resolution of conflict must take forms other than the break-up of groups, which is what they usually do. High density and lack of space cause friction that leads to conflict and violence (Louw & Bekker, 1996:10).

Although population density and agglomeration have a beneficial effect on business, it increases criminal activity (Naude *et al*., 2009:332). There is a positive correlation between population density and crime rates in South Africa (Naudé *et al*., 2009:319). In South Africa, the Gauteng Province had the highest population density and experienced the biggest portion of crime *versus* the Northern Cape Province that had the lowest population density and experienced the smallest portion of crime (Statistics South Africa, 2006:6). There are also a number of other factors that have an impact on crime in urban areas. These factors are the social, economic and demographic compositions of an urban area with its unique composition of industry and population groups (Naudé *et al*., 2009:319). Two factors that cause an increase in crime are population density and lack of space (cities) (Louw & Bekker, 1996:10; Naudé *et al*., 2009:319; Van Jaarsveld, 1985:146).

Straker *et al*. (1996:53) reported that nearly 74% of youths that reside in townships in South Africa have witnessed an assault, and 67% have witnessed a murder. More than 20% of those who had witnessed an assault or a murder had post-traumatic stress (Straker *et al*., 1996:51). Muris *et al*. (2008:1513) claimed that of all the fears that white children in South Africa can have, crime was feared third most by them with 47%.

Stress and fear are related to anxiety through either emotional states or mood states. Both stress and anxiety are part of an emotional state (Craig *et al*., 1995:1332; Stahl, 2010:1). Fear and anxiety are both mood states and are related to one other (Craig *et al*., 1995:1325; Stahl, 2010:1).

Krakow *et al.* (2001:2046) also indicated that stress and insomnia can be caused by crime which is influenced by population density, it can therefore be assumed that stress and fear caused by crime leads to anxiety and insomnia. Anxiety and insomnia are usually treated with benzodiazepines. The benzodiazepines are pharmacologically classified as sedative-hypnotic and anxiolytic drugs (Trevor & Way, 2009:371).

Diagram 2.1 shows the proposed relationships between the before-mentioned factors. The geographical area in which a person resides, presents a proposition of crime to which the person is related, which leads to insomnia and anxiety, which is treated with benzodiazepines.

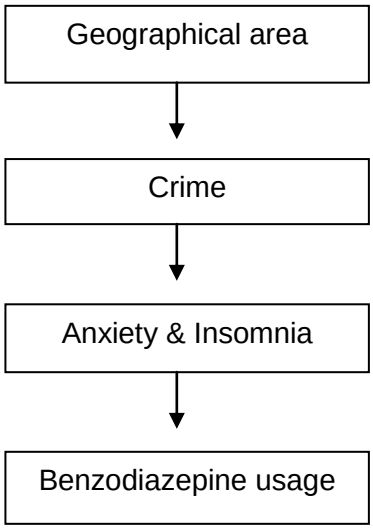


Figure 2.1: The correlation between geographical area, crime, anxiety, insomnia and benzodiazepine

2.3 URBANISATION

In the following paragraphs urbanisation is discussed, i.e. worldwide as well as in South Africa.

2.3.1 Background of urbanisation

The Oxford English Dictionary (2010f) defines urbanisation as “the process of investing with an urban character; the condition of being urbanized”. Urbanisation is therefore the making of an urban character (i.e., to convert or transform a town into a city). Urbanisation is also the

process of relocating the population from the rural areas towards the urban areas (Van Jaarsveld, 1985:5).

In the United States of America, urban areas are defined as a densely settled territory that meets the minimum population density requirements (i.e., an area that encompasses a population of at least 2 500 people) (United Nations, 2007:31). In England, urban areas are defined as localities with at least 1 500 people, and in Wales urban areas are defined as localities with at least 1 000 people (United Nations, 2007:31).

An urban area in South Africa is based on a classification of the dominant settlement type and the land use. Cities, towns, townships and suburbs are typical urban settlements. Hostels, institutions, recreational areas and smallholdings within or adjacent to any formal urban settlements are also classified as urban (Statistics South Africa, 1999). Non-urban areas in South Africa signify all areas not classified as urban (Statistics South Africa, 1999).

2.3.2 Urbanisation patterns

The first real waves of urbanisation started in North America and Europe in 1750 and it lasted until the 1950s (United Nations Population Fund, 2007:7). Urban growth increased from 10% to 52% and the number of urban areas increased from 15 million to 423 million globally during this time. The second wave of urbanisation was estimated to be from 1950 till 2030 (United Nations Population Fund, 2007:7).

The following figure illustrates the world population growth in urban areas and the decline in population in rural areas and the estimates of what the population in both rural and urban areas will be in 2050.

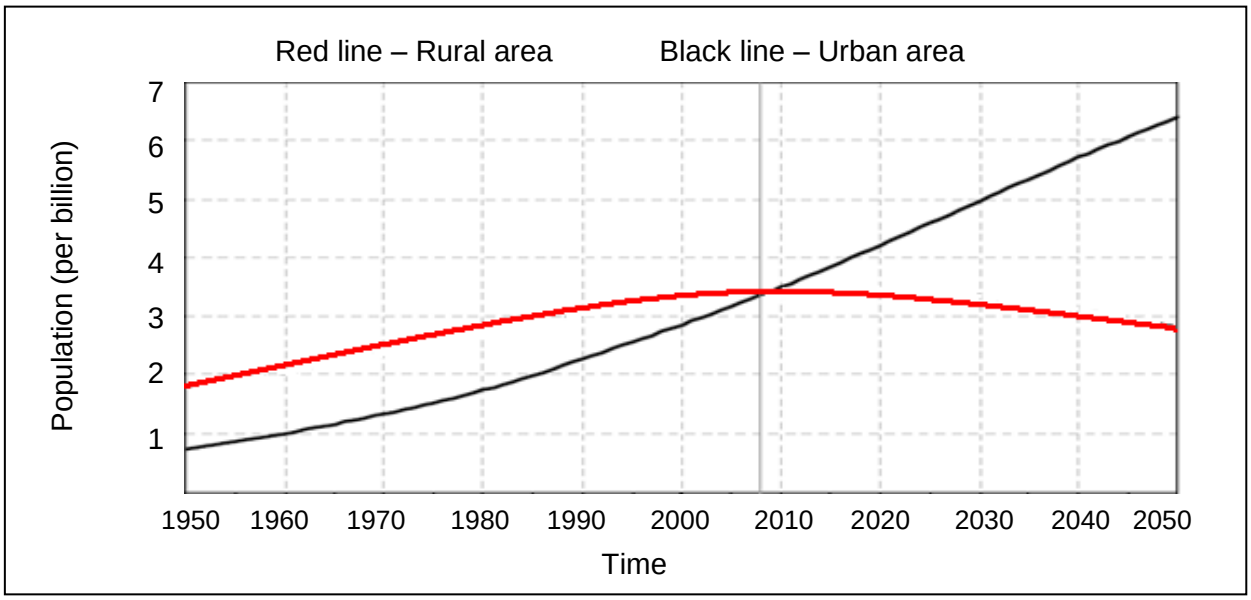


Figure 2.2: A graphical illustration of urban and rural populations of the world, 1950-2050 (United Nations, 2007:2)

The process of people migrating from non-urban areas to urban areas is a global tendency. The world population was 6.7 billion people in 2007. The United Nations expects the world population to grow to 9.2 billion by 2050. About 3.3 billion of the world population resided in urban areas in 2007 and is expected to grow with 51.6% to 6.4 billion people in 2050 (depicted in Figure 2.2). This escalation will cause the urban areas to absorb more people, and will cause a decline in population in rural areas. As a result of this increase in the number of people in urban areas, the population in rural areas is estimated to decrease by 0.6 billion people by 2050 (United Nations, 2007:1). According to the United Nations the proportion of the world's population living in urban areas was 50% in 2008 (Figure 2.2).

Urbanisation is expected to influence both urban and rural areas. Urban areas are expected to grow with 86% *versus* the rural areas that will decrease with 67% (United Nations, 2007:2). Table 2.1 (United Nations, 2007:69-70) illustrates the percentage of population of each country that resided in rural or urban areas in 2007.

Table 2.1: Comparison between different nations with regard to their urban and rural populations in 2007 (United Nations, 2007:69-72)

Country	Population in urban areas (in millions)	Population in rural area (in millions)	Total Population (in millions)	Percentage urban (%)
United Kingdom	54, 620	6, 149	60, 769	89.9
Mexico	81, 951	24, 584	106, 535	76.9
Australia	18, 373	2, 370	20, 743	88.6
New Zealand	3, 611	0, 567	4, 179	86.4
Brazil	163, 462	28, 329	191, 791	65.2
South Africa	29, 266	19, 310	48, 577	60.2

Some continents are still largely rural, like Africa and Asia where nearly six out of ten persons are still residing in rural areas (United Nations, 2007:1). Northern America was the most urbanised area in 2007 with 81.3%; followed by Latin America with 78.3% in second place and Europe with 72.2% in third place. Africa and Asia were the least urbanised areas in 2007 with Africa only 38.7% and Asia with 40.8% (United Nations, 2007:5). The United Kingdom had the highest percentage of urbanisation compared to South Africa that had the lowest percentage of urbanisation (refer to Table 2.1).

In 1970, 69% of the population of the United States lived in what the government statisticians called “metropolitan statistical areas*”. This increased to 75% in 1980, 77% in 1990 and 81.4% 2007 (Mieszkowski & Mills, 1993:135; United Nation, 2007:72). .

In conclusion, there are visible trends that more people are shifting towards the urban areas around the world. From Table 2.1, it is, however, evident that South Africa still has a relatively high number of people residing in rural areas, compared to other countries.

2.3.3 Urbanisation in South Africa

The migration from non-urban to urban areas in South Africa is visible from statistics dating back to 1911. For example, in 1911, 76% of the population in South Africa lived in non-urban areas. This decreased to 52% in 1970, and 46.8% in 1980 (Van Jaarsveld, 1985:15). In 2005, 40.3% of the South African population stayed in non-urban areas and in 2007, only 39.8% people were staying in non-urban areas in South Africa (United Nations, 2007:69). Accordingly, there were 60.2% of people living in urban areas in South Africa. Most of the people in South Africa thus reside in cities (United Nations, 2007:69).

In the community survey of 2007, conducted in South Africa (Statistics South Africa, 2007), it was found that a total of 991 919 people lived in Northern Cape Province in 2001 compared to 1 058 060 in 2007. The population density in this province in 2001 was 2.3 people per km^2 and in 2007 it increased to 2.9 people per km^2; this was subsequently the smallest ratio of all the provinces in SA. The Northern Cape had the biggest geographical area size among all the provinces, namely 361 830 km^2 (Statistics South Africa, 2007).

Gauteng on the other hand had the second biggest population in both the censuses of 2001 and 2007 (KwaZulu-Natal had the biggest population). The population in the Gauteng Province was 9 178 873 in 2001, compared to 10 451 713 in 2007 (Statistics South Africa, 2007). The population density of Gauteng was 519.5 people per km^2 in 2001 and increased to 614 people per km^2 of 2007. This was subsequently also the biggest ratio of all the provinces in South Africa (Statistics South Africa, 2006; Statistics South Africa, 2007:14). Gauteng therefore had the highest percentage of people residing in an urban area, 96.3%; compared to 3.7% residing in non-urban areas in the year 2001. In comparison, the Northern Cape Province had 80.7% people residing in urban areas and 19.3% people residing in non-urban areas (Statistics South Africa, 2006:23).

* A metropolitan area is the upmost form of urbanisation (OED, 2010d)

According to Beauregard (2009:580) a new phenomenon has started in the United States, and is spreading throughout the world; namely that people are moving from cities towards non-urban areas (Beauregard, 2009:580; Dillman, 1979:960; Mieszkowski & Mills, 1993:135). This phenomenon is also occurring in the Western countries of the world (Leetmaa & Tammaru, 2007:127). Some factors causing the phenomenon are: increased fear of crime, schooling considerations and concerns about urban congestion and pollution. This phenomenon has not been reported in South Africa (Dillman, 1979:960; Mieszkowski & Mills, 1993:135).

The following section provides an overview of crime and how it relates to urbanisation.

2.4 CRIME

This section provides a discussion on the causes of crime and the influence that crime has on people.

2.4.1 Definition

In a western society, crime is defined strictly as behaviour that breaks the law and is liable to public prosecution and punishment (Kennedy, 1990:1). According to the OED (2010a) crime is an evil or injurious act, or in other words, an offence. Violence is defined as the unlawful exercise of physical force, usually causing or intending to cause injury, which is by itself a crime (Brennan-Galvin, 2002:126). Violence has to be evident and conflictual, otherwise it is not really violence (Louw & Bekker, 1996:81). For the purpose of this study violence is applicable to humans only. In this study the terms violence and crime are used interchangeably.

2.4.2 Background of crime

Louw and Bekker (1996:80) claim that urban landscapes do not themselves generate violence but everything depends on how people, who reside there, mentally represent themselves. The problem with urban violence is furthermore complex and involves issues relating to the landscape, social differentiation and urban planning (Louw & Bekker, 1996:16).

In South Africa there are only a few people who have not yet been a victim of a crime (Pharoah, 2009:1). In some cultures in South Africa, it has become acceptable to commit crime in order to achieve something, for example, to obtain political dominance through a strike (Nomoyi, 2000:67).

Crime, *per se*, carries a high burden in terms of cost. For example, crime causes the nation to spend money on protection (fences, walls, and alarms). Crime furthermore has a stressful effect on people which causes higher health care costs and also affects their productivity at the workplace (Demombynes & Ozler, 2002:2).

2.4.3 Factors affecting crime

There are several factors that increase the chance of a person being a victim of crime in South Africa (Pharoah, 2009:1). These factors include, *inter alia*, the following:

- Race
  In case of housebreaking, coloured people were the most likely to be the victims. In the case of property theft and robbery African people were the most likely to be victims, whilst white people were more likely to be victims of assault (Pharoah, 2009:2).
- Gender
  Men were more likely to be the victim of property theft, robbery and assaults than women (Pharoah, 2009:2).
- Age
  According to Nomoyi (2000:69) criminals globally, are between the age of 15 and 35 years. Because this group of people is relatively strong and mobile, they can commit a crime and escape more easily (Buvinic & Morrison, 2000:61). This age group is responsible for committing more crimes than other age groups (Nomoyi, 2000:69; Parry *et al*., 2004:168). Violence and property crime were most likely to occur to victims between the age of 16 and 25 years. The older a person gets, the higher are the chances of getting robbed (Pharoah, 2009:2).
- Citizenship
  People, who were born in a different country than South Africa were more likely to experience housebreakings, but were less likely to experience property theft (Pharoah, 2009:2).
- Location
  People residing in urban areas near a rural area, were more likely to be a victim of crime. People residing in more dense areas were also more likely to experience crime (Pharoah, 2009:2). Countries with a high rate of urbanisation tend to have higher crime levels (Nomoyi, 2000:68; Parry *et al*., 2004:168). People residing in rural areas in South Africa, are more likely to be a victim of assault, compared to people in urban areas that were more likely to be a victim of property theft, robbery and housebreakings (ISS, 2005).
- Education
  Low levels of education are global and may be the reason for high levels of crime in South Africa (Nomoyi, 2000:68).
- Lifestyle factors
  People who go out at night were more likely to be a victim of crime (Pharoah, 2009:2).

Based on findings from the Institute for Security Studies people in Gauteng Province were more likely to experience housebreakings, property theft and robbery than people in the Northern

Cape Province during 2005 (ISS, 2005). The Northern Cape Province had the highest assault rate per person (ISS, 2005; Pharoah, 2009:2).

2.4.4 Prevalence of crime

The global homicide rate (HR)* was 7.6 in 2009 (Burger, 2009:5). The United States had a homicide rate of 5.8 and the United Kingdom had a homicide rate of 2.3 in 2008 (Burger, 2009:5). Based on the 1991 homicide rates, Australia had an HR of 2.0, this homicide rate is positioned between Iceland with an HR of 1.9 and Canada with an HR of 2.1 (WHO, 1993). In 2008, Venezuela experienced a homicide rate of 48, Trinidad and Tobago a HR of 37.3, Brazil a homicide rate of 25.7 and Mexico an HR of 10 (Burger, 2009:6). The HR of South Africa was 37.3 in 2009 after a sharp decrease from 67.9 in 1996 (Burger, 2009:5).

The province with the highest crime rate in South Africa is Gauteng. The percentage distribution of the total crime reported from 2000 to 2003 was 27.4% in all years. The province with the lowest percentage distribution of crime reported in South Africa was the Northern Cape Province with 2.8% from 2000 to 2003 (Statistics South Africa, 1999:51).

The crimes that occurred the most frequently in South Africa in 2009 were house robberies, business robberies and car hijackings. These three crimes are called the trio crimes and their level was 249.3 per 100 000 people in South Africa in 2009 (Burger, 2009:7). These trio crimes occurring in the Gauteng and Northern Cape Province are illustrated in Table 2.2.

Table 2.2: Trio crimes in Gauteng and Northern Cape Province (Burger, 2009:8)

Province and trio crimes	**Incidence occurrences**
Gauteng:	
• House robbery	8 122
• Business robbery	6 216
• Car hijacking	7 626
Northern Cape:	
• House robbery	12
• Business robbery	54
• Car hijacking	5

* The homicide rates are calculated by the number of homicide cases per 100 000 population (Burger, 2009:5)

The numbers of incidences for trio crimes in the Gauteng Province are perceived to be much higher than in the Northern Cape Province. This can be due to the fact that the Northern Cape Province has a smaller population than the Gauteng Province (Statistics South Africa, 2007).

Crime that is usually found in urban areas are theft and burglary, with increases in prevalence ascribed to urbanisation (Van Jaarsveld, 1985:147).

According to Burger (2009:3) there have been claims that some of the police stations in South Africa did not record all the incidences of crime correctly or that some of the crime statistics ha been manipulated. Although this can be true, the number of police stations that were accused accounted for only one per cent of all the police stations. This will have nearly no impact on the national statistics (Burger, 2009:4). Crime statistics moreover have a shortcoming in the sense that not all victims report the crime to the police and thus the statistics cannot always be regarded as fully accurate (Van Jaarsveld, 1985:146).

The following section is an overview with regard to anxiety. The influence of crime on anxiety is also discussed.

2.5 ANXIETY

In this section the causes of anxiety, the different types of anxiety and the treatment of anxiety will be discussed.

2.5.1 Definition of anxiety

Anxiety is a normal emotion experienced at some time or another by virtually all humans (Norman *et al.,* 1997:490). According to Porter and Beers (2006:1672) anxiety is a distressing, unpleasant emotional state of nervousness and uneasiness. Janeway (2009:37) states that anxiety is the fear of danger or a state of mood. This fear of danger can be described as the "freeze, take flight, or fight" reaction that occurs when a human experiences fear (Stahl, 2010:1). Anxiety is sometimes seen as a mood state or mood disorder. When anxiety is a mood state it refers to the different experiences felt when having anxiety (Craig *et al*., 1995:1325).

2.5.2 Background of anxiety

Anxiety sometimes has a greater purpose than merely distressing people. When people find themselves in a dangerous situation, anxiety helps to prepare the body and mind for what is coming. When anxiety reaches a certain level, it no longer exerts a positive feeling but causes a dysfunction and distress. If anxiety reaches this stage, it is considered a disorder. Anxiety can change relatively quickly from being calm to a severe anxiety attack (Porter & Beers, 2006:1672).

Every person experiences anxiety differently. The onset of anxiety can differ from sudden onset to a few days (Porter & Beers, 2006:1672). Table 2.3 provides a summary of the different types of anxiety.

Table 2.3: Description of the different anxiety disorders

Generalised Anxiety Disorder	• It is an excessive feeling of anxiety and worrying, occurring most days for more than six months (Tierney *et al*., 2005:1013). • The anxiety disorder that occurs most general among people is the generalised anxiety disorder (Tierney *et al*., 2005:1013). • It usually appears at the age of 20 to 35 years as a diagnosable disorder and occurs more in women than in men (Tierney *et al*., 2005:1013). • The symptoms that occur are apprehension, worry, irritability, insomnia, somatic, cardiac, gastrointestinal and neurological symptoms (Moch, 2009:22). • The lifetime prevalence of generalised anxiety disorder in South Africa for all ages was 2.7% in 2006 (Stein *et al.,* 2008:112).
Panic disorder	• Panic disorder is characterised by short-lived, recurrent, unpredictable episodes of intense anxiety accompanied by marked physiological manifestations (Tierney *et al*., 2005:1013). • The symptoms that occur are agoraphobia, dyspnoea, tachycardia, palpitations, headaches, dizziness, choking, smothering feelings, nausea, sleep attacks and anticipation (Moch, 2009:22). • Panic disorder has a propensity to be more familiar than the other disorders and appears in people younger than the age of 25 years. The female-to-male ratio is 2:1 (Tierney *et al*., 2005:1013). In 2006 the lifetime prevalence of panic disorder in South Africa was 1.2% (Stein *et al.,* 2008:112). • Patients with this disorder have a tendency to become demoralised, hypochondriacal, agoraphobic and depressed. One in every four patients who have panic disorder also have obsessive-compulsive disorder (Tierney *et al*., 2005:1013).

Table 2.3: Description of the different anxiety disorders (continued)

Obsessive-compulsive disorder (OCD)	• People suffering from this disorder seem weird and absurd to the public, but to them the only method to relief the anxiety is to do the ritual performance. Patients that have compulsive disorder usually show the following symptoms: predictability, orderly, conscientious, intelligent, food binging, purging, compulsive running, tics, trichotillomania, onychophagia, hypochondriasis, Tourette's syndrome and eating disorders (Tierney *et al*., 2005:1013). • Globally the incidence of OCD was 2 – 3% in the year 2005. The ratio between male and female is almost the same, but with a higher incidence in young, divorced, separated and unemployed people (Tierney *et al*., 2005:1013).
Phobic disorder	• Phobic disorder is the unrealistic and intense anxiety relating to certain fears. An example of a phobia is agoraphobia, social phobia, and specific phobia (Tierney *et al*., 2005:1013). • Agoraphobia is the fear of public places. It develops early in adult life (Tierney *et al*., 2005:1013). Places that agoraphobia people will try to avoid are crowds, stores, bridges, tunnels, travelling, theatres and small rooms (Moch, 2009:22). The lifetime prevalence of agoraphobia in South Africa was 9.8% for all people in South Africa for 2006 (Stein *et al.,* 2008:112). • Social phobia is extreme and persistent anxiety about certain social situations for example public speaking or writing, eating and drinking in public, initiating or maintaining conversations (Moch, 2009:22). The lifetime prevalence of social phobia in South Africa was 2.8% in 2006 (Stein *et al.,* 2008:112). • Specific phobia is the fear of the anticipation of a specific object or situation, for instance the fear of flying, heights, storms, animals, receiving an injection and blood (Moch, 2009:22).

Table 2.3: Description of the different anxiety disorders (continued)

Dissociative disorder	• Dissociation is when people are doing something and then forgetting why they are doing it. Dissociative disorder makes people forget a whole series of events, this can be for only a few seconds up to hours. This disorder is usually triggered by stress or trauma (Porter & Beers, 2006:1678). • The symptoms that occur are fatigue, amnesia, somnambulism, dissociative identity disorder and depersonalisation (Tierney *et al*., 2005:1013).

Although not all the causes of anxiety disorders are known, anxiety may be caused *inter alia* by mental and physical factors. A mental factor can be a response to environmental stressors, for example the ending of a significant relationship or exposure to a life-threatening disaster (Stein *et al.,* 2008:112). Table 2.4 illustrates all the different causes of anxiety.

Table 2.4: The different causes of anxiety

Causes of anxiety	**Example**
Environmental	• Poverty • Job strain • Gender, women experience anxiety more easily • Urbanisation • Stress and trauma (Craig *et al*., 1995:1334; Janeway, 2009:37; Judd *et al.,* 2002:104; Stahl, 2010:31)
Medical illnesses	• Endocrine and metabolic disorders: Hyperthyroidism, hypoglycaemia, pheochromocytoma, anaemia and porphyria. • Neurologic diseases: Epilepsy, migraine, Parkinson's disease and tremor. • Psychiatric diseases: Depression, mania, schizophrenia, delirium, dementia and eating disorders. • Cardiovascular diseases: Angina, congestive heart failure, arrhythmias, myocardial infarction and hypertension. • Gastrointestinal diseases: peptic ulcer and irritable bowel syndrome. • Respiratory diseases: asthma, chronic obstructive pulmonary disease, pneumonia and pulmonary oedema. • Other diseases: Human immunodeficiency virus (HIV) and lupus erythematosus (Moch, 2009:21; Porter & Beers, 2006:1672)
Other physical causes	• Use of drugs like corticosteroids, cocaine, amphetamines and caffeine (Moch, 2009:21; Porter & Beers, 2006:1672). • Withdrawal from alcohol, sedatives and illicit drugs can also cause anxiety (Moch, 2009:21; Porter & Beers, 2006:1672).

Fatigue and sleep disturbances are common symptoms of anxiety. Sympathomimetic symptoms of anxiety are further both a response to a central nervous system state and a reinforcement of further anxiety. Anxiety can be like a spiral, it can become self-generating through the symptoms that reinforce the reaction (Tierney *et al*., 2005:1012).

Anxiety, fear and stress are all linked together and interactive (Craig *et al*., 1995:1325; Tierney *et al.,* 2005:1012). Anxiety exists out of two important components namely psychologic and

somatic. The psychological components refer to tension, fears and apprehension and the somatic components which refer to the tachycardia, hyperventilation, palpitations, tremor and sweating (Tierney *et al.,* 2005:1012). Table 2.5 illustrates the different fears among different South African cultures' children.

Table 2.5: The prevalence of fears among South African children (Muris *et al*., 2008:1513)

Race of the child	**Fear**
Black children	1. Snakes 2. Crocodiles 3. Death 4. Predators 5. Spiders
White children	1. Death 2. Crime 3. Gangs 4. Snakes 5. Spiders
Coloured children	1. Death 2. Snakes 3. Crocodiles 4. Crime 5. Weapons

Muris *et al.* (2008:1513) conducted a study on the fears of fourteen-year-old children in South Africa. Data from this study (depicted in Table 2.5) indicate that crime fills white and coloured children with fear.

2.5.3 Prevalence of anxiety

The percentage of adolescents that have anxiety in Australia was 13.2%, compared to 5.8% in China, 13% in Hong Kong, 3.8% in Italy and 25% in Canada (Boyd *et al*., 2000:488). In a study done in America with 198,678 respondents, 12.3% had a lifetime diagnosis of anxiety disorder (Kroenke *et al*., 2009:166). According to Stein and co-workers (2008:112), the prevalence of anxiety disorders in South Africa was 15.8%. The Gauteng Province had a lifetime prevalence percentage for anxiety disorder of 15.7% and Northern Cape Province had percentage of 15% in the year 2009 (Herman *et al*., 2009:341). The province with the highest lifetime prevalence percentage for anxiety was the Free State with 21.5% (Herman *et al*., 2009:341).

The lifetime prevalence of anxiety in South Africa is more present in the age group 35 to 49 years, in the high income group and in divorced or separated people (Stein *et al.,* 2008:112).

Anxiety, fear and stress are all linked together as mentioned in section 2.5.2. Stress and urbanisation are also causes of insomnia (Harvey & David, 2009:2). The following section provides an overview of insomnia.

2.6 INSOMNIA

Humans spend a third of their lives sleeping. Sleeping is necessary for humans' health and general well-being (Richards, 2005:611). The sleep requirements of persons differ. The average sleeping hours a person needs, would be between seven to nine hours every night (Richards, 2005:611).

There are three major sleep disorders namely dyssomnias (insomnia), hypersomnias (disorders of excessive sleepiness) and parasomnias (abnormal behaviours during sleep). For the purpose of this study, only insomnia will be discussed in full because only insomnia is treated with benzodiazepines (Tierney *et al*., 2005:1048).

Hypersomnias are disorders of excessive sleepiness such as sleep apnoea, narcolepsy, Kleine-Levin syndrome and nocturnal myoclonus. Hypersomnias are more severe than insomnia (Tierney *et al*., 2005:1049).

Parasomnia manifests as abnormal behaviours during sleep such as sleep terror, nightmares, sleepwaking and enuresis. Parasomnia occurs more frequently in children and less in adults (Tierney *et al*., 2005:1050).

2.6.1 Definition of insomnia

The word insomnia is derived from the Latin word for "no sleep" (Harvey & David, 2009:1). Insomnia is when a person finds it difficult to fall asleep or stay asleep, intermittent wakefulness during night or waking up too early (Harvey & David, 2009:1; Moch, 2010:18; Tierney *et al*., 2005:1048).

There are two types of insomnia, namely primary and secondary insomnia (Harvey & David, 2009:1; Moch, 2010:18):

- Primary insomnia is insomnia that is not caused by any environmental or health problems.
- Secondary insomnia is insomnia that is caused by environmental or health problems.

Insomnia is further classified into three groups based on the duration of the insomnia (Harvey & David, 2009:1; Moch, 2010:18; Wilson & Nutt, 2008:31):

- Transient insomnia is usually for a few days only (less than a week). It is mostly caused by stress, change of job, or examinations.
- Short-term insomnia usually lasts between one week to a month. It usually occurs with continuous stress, such as the death of a loved one.
- Chronic insomnia emerges when insomnia continues for longer than a month.

2.6.2 Background of sleep disorders

Sleep can be divided into two states, namely REM (rapid eye movement) sleep and NREM (non-rapid eye movement) sleep. REM sleep is also known as dream sleep, D state sleep or paradoxical sleep. REM can be separated into stages 1, 2, 3 and 4. Stages 3 and 4 are called delta sleep. The second state is NREM sleep which is also called S stage sleep. Dreaming usually occurs in the REM and not to the same extent in the NREM state (Harvey & David, 2009:2; Tierney *et al*., 2005:1048).

Sleep happens in cycles. There are nearly four to five REM cycles per night, it accounts for almost one-fourth of the total night's sleep. The first REM period occurs about 80 to 120 minutes after onset of sleep and lasts approximately 10 minutes (Tierney *et al*., 2005:1048). The other REM periods are longer. As people age, the REM stays the same but stages 3 and 4 changes (delta sleep) and these changes can cause insomnia in the elderly (Tierney *et al*., 2005:1048).

The following aspects can change stage 3 and 4 of REM sleep, which will lead to insomnia (Harvey & David, 2009:2; Kamel & Gammack, 2006:465; Moch, 2010:19; Ohayon, 2002:105). The aspects are for example:

- Life style – Environmental factors (urbanisation), stress and shift working.
- Use, abuse or withdrawal of psychoactive substances – alcohol, caffeine, cocaine, amphetamines, opioid and hypnotics.
- Mental disorders – bipolar disorder, depressive disorders, psychotic disorders and eating disorder.
- Medical condition – heart disease, arthritis, gastric ulcer, epilepsy, Huntington's disease, Parkinson's disease, migraine, headache, allergy and menopause.
- Breathing disorder – sleep apnoea, hypoventilation and asthma.

Psychiatric disorders and insomnia are in many cases related. For example, persons that experience depression also experience insomnia. Depression influences sleep in that it decreases the total sleep time and causes the REM to have an earlier onset (Tierney *et al*., 2005:1048).

Alcohol abuse can cause sleep disturbances (Harvey & David, 2009:3). In the case of little alcohol intake (one to two glasses), the alcohol can reduce stress and help the onset of sleep, but in the case of excessive alcohol intake it disrupts the normal sleep cycle. Acute alcohol intake can cause reduced REM sleep during the first half of the night. Vivid dreams and frequent awakenings are common. Chronic alcohol abuse increase stage 1 and decreases REM sleep (Harvey & David, 2009:3; Tierney *et al*., 2005:1048).

Heavy smoking (more than a pack a day) causes difficulty to fall asleep. Excess intake near bedtime of caffeine, cocaine and other stimulants causes decreased total sleep time (Harvey & David, 2009:3).

2.6.3 The treatment of insomnia

The treatment for insomnia can be psychological or medical (Harvey & David, 2009:4; Kamel & Gammack, 2006:466; Tierney *et al*., 2005:1048).

The lifestyle changes that can help with the treatment of insomnia include the following (Harvey & David, 2009:4; Kamel & Gammack, 2006:466; Tierney *et al*., 2005:1048):

- Going to bed every day at the same time.
- Going to bed when sleepy.
- The usage of the bed is only for sleep and sex.
- Do not use caffeine and nicotine before bedtime.
- Take a hot bath about two hours before sleep, exercise daily and spend some time in the sun.
- Avoid excessive alcohol, large meals and limit fluids in the evening.

The medical treatment includes the following drugs (Harvey & David, 2009:4; Kamel & Gammack, 2006:466; Tierney *et al*., 2005:1048):

- Benzodiazepines
- Other sedative hypnotics (e.g., zolpidem)
- Antihistamines
- Antidepressants

The benzodiazepines and the other sedative hypnotics are the drugs of choice for treating insomnia (Tierney *et al*., 2005:1049). Antihistamines are used for over the counter treatment of insomnia. In secondary insomnia that is caused by depression, the antidepressants are the drugs of choice (Harvey & David, 2009:7; Wilson & Nutt, 2008:33)

Findings from a study done on the effect of benzodiazepine on insomnia, showed that the average time of sleep of patients who used benzodiazepines was 61.8 minutes longer, compared to those who used placebo. In patients who used benzodiazepines, the average time to fall asleep was 14.3 minutes shorter than in patients who received placebo (Gray, 2005:32).

2.6.4 Prevalence of insomnia

Insomnia affects almost 10% to 15% of people worldwide (Harvey & David, 2009:3; Richards, 2005:612). Globally, approximately one out three elderly persons experience insomnia (Richards, 2005:612; Wilson, 2008:132). According to Richards (2005:612) and Moch (2010:18), almost 75% of adults in America complain about transient insomnia regularly. The prevalence of transient insomnia in America was 50% in the year 2005 and in the year 2009 it was between 30 to 40% (Harvey & David, 2009:3; Richards, 2005:612). The number of Americans who had chronic insomnia in the year 2009 was between 10% to 15% (Harvey & David, 2009:3). In the United Kingdom almost five million people experienced a sleep disorder in the year 2004 (Richards, 2005:612). The percentage of people who used prescription medicine for insomnia in Germany was 2.4%, 5% in United States, 9.8% in France and 11% in Canada for the year 2002 (Morin *et al*., 2006:124).

Insomnia is generally more common among females than males (Moch, 2010:18). The reason why females are more likely to develop insomnia is because of their hormones. The hormone levels fluctuate during menstruation, pregnancy and menopause which may lead to insomnia (Harvey & David, 2009:3). The age group which is more likely to experience insomnia is the elderly (Moch, 2010:18). The elderly have a greater chance than younger people to develop medical conditions, that may lead to insomnia (Harvey & David, 2009:3).

2.6.5 Benzodiazepines, insomnia and anxiety: common ground

Based on the foregoing discussions, it can be concluded that insomnia and anxiety can be caused by stress and fear. Stress and fear are caused, *inter alia*, by crime. There is also a correlation between geographical areas and the incidence of crime.

The following section provides a discussion on benzodiazepines and their use in the treatment of anxiety and insomnia.

2.7 BENZODIAZEPINES

This section focuses on the background, mechanism of action, indications, pharmacokinetics, contra-indications, drug interactions, dependence, withdrawal, legislation, prevalence and prescribing patterns of benzodiazepines.

2.7.1 Background

According to Longo and Johnson (2000), benzodiazepine was developed because of the toxicity of barbiturates that developed during the long-term usage for insomnia and anxiety. The first benzodiazepine, chlordiazepoxide, was introduced in 1961 (Perez & Tudor, 1993:175). Because chlorpromazine was classified as a tranquilliser at that stage, benzodiazepines are still sometimes called 'minor tranquillisers' (Rogers *et al*., 2007). It has been nearly 25 years since the last benzodiazepines were introduced on the pharmaceutical market (Costa, 1999:391). The benzodiazepine that was the most recently synthesised and released for clinical practice is midazolam (Borchardt, 1999:65). Figure 2.3 illustrates the basic chemical structure for a benzodiazepine (adapted from Sweetman, 2010).

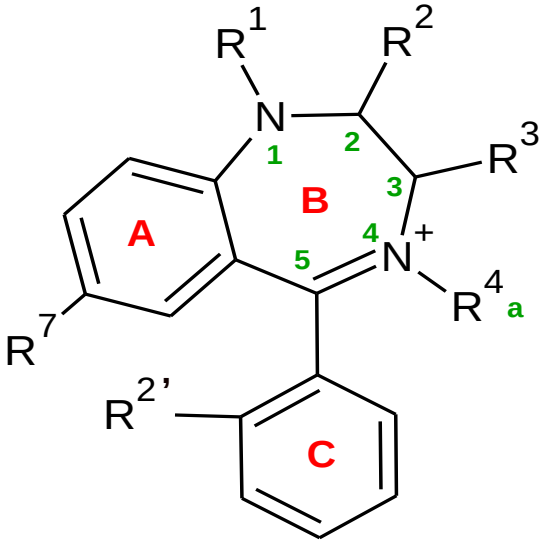


Figure 2.3: Schematic illustration of benzodiazepine (adapted from Sweetman, 2010)

Various benzodiazepines have been released for clinical practice. Their structures are more or less the same, however, the benzodiazepines do differ at the positions where there are R's (i.e., methyl, oxygen, or nitrogen compounds) in Figure 2.3. If the positions of the R's are changed, the property of the benzodiazepine also changes for example from a short-acting benzodiazepine to a long-acting benzodiazepine (Charney *et al*., 2006).

Benzodiazepines have been classified in various ways. According to The Monthly Index of Medical Specialities (MIMS), benzodiazepines are being classified under central nervous system drugs as a sedative hypnotic and an anxiolytic (Snyman, 2009:13a). Charney *et al.* (2006) classified benzodiazepine under central nervous system drugs as a hypnotic and sedative. Benzodiazepine is also classified as a sedative-hypnotic drug (Trevor & Way, 2009:271).

For a drug to be an effective anxiolytic it must reduce the anxiety and bring a calming effect to the patient. The same goes for a hypnotic drug, for it to be effective it must cause drowsiness and maintain a state of sleep (Trevor & Way, 2009:371).

The effectiveness of the therapeutic drug class of benzodiazepine is important because when sleep does not occur immediately the patient can take an overdose. Barbiturates are fatal in an overdose. Barbiturates cause general anaesthesia when the intake exceeds the limited dose and in an overdose it depresses the respiratory system and the vasomotor centres in the medulla, leading to a coma and ultimately death (Trevor & Way, 2009:371). In contrast, benzodiazepine is relatively safe in high doses or overdose. After a certain dose it reaches a plateau, after which it does not cause depression of the respiratory system and further no depression of the vasomotor centres (Trevor & Way, 2009:371). Benzodiazepines can be fatal when they are combined with alcohol or opiates and are thus safe when they are taken as a single regime (Trevor & Way, 2009:371).

Figure 2.4 provides an illustration of the different effects that benzodiazepines and barbiturates have on the central nervous system (CNS) at different doses. (Longo & Johnson, 2000:2123; Trevor & Way, 2009:371).

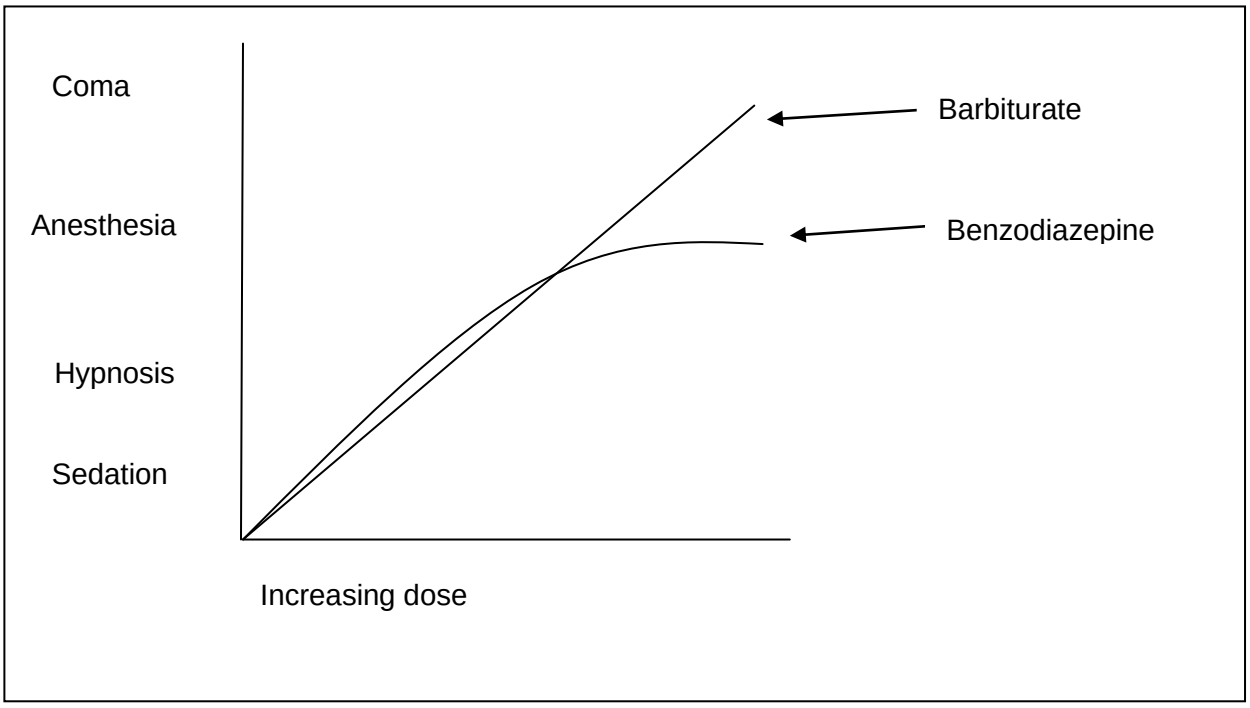


Figure 2.4: CNS effects of barbiturates and benzodiazepines (Adapted from Longo & Johnson, 2000:2123; Trevor & Way, 2009:371)

2.7.2 Mechanism of action

The effects that benzodiazepines exhibit on the human body are due to the action they have on the central nervous system. The brain is one of the components of the central nervous system

and is important in the action of work of benzodiazepines (Borchardt, 1999:66; Rossiter, 2010:474). Benzodiazepines' mechanism of action is mediated by enhancement of the activity of gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter in the brain (Rossiter, 2010:474; Stahl, 2010:102). Benzodiazepines bind to the $GABA_A$ receptor that increases affinity of the receptor, causing the receptor to open and increase the release of chloride (Longo & Johnson, 2000:2122; Stahl, 2010:102). The $GABA_A$ receptor has five subtypes, α_1, α_2, α_3, α_4 and α_5. The subtype α_1 has mainly sedative properties, whereas the α_2, α_3, α_4, and α_5 subtypes have anxiolytic activity. The subtypes α_2 and α_3 are situated in the amygdale and cortical areas of the brain, and the α_5 is located in the hippocampus region of the brain. Both of these regions are responsible for anxiolytic effects (McKernan *et al*., 2000:590).

2.7.3 Indications

Benzodiazepines are primarily indicated for the treatment of insomnia and anxiety states (Trevor & Way, 2009:381). Table 2.6 illustrates the different benzodiazepines according to their indications and trade names in South Africa.

Table 2.6: Classification of benzodiazepines (Snyman, 2009:3; Trevor & Way, 2009:381)

Sedative hypnotics		**Anxiolytics**	
Active ingredient	**Trade name**	**Active ingredient**	**Trade name**
Brotizolam	• Lendormin®	Alprazolam	• Adco-Alzam® • Azor® • Merck Alprazolam® • Xanor® • Zopax®
Diazepam	• Aspen Diazepam®	Bromazepam	• Brazepam® • Bromaze® • Lexotan® • Sandaoz Bromazepam®
Flurazepam	• Dalmadorm® • Hypnor® • Ryhypnol® • Sandoz Flunitrazepam®	Chlorazepate	• Tranxene®
		Chlordiazepoxide	• Librium®
Loprazolam	• Dormonoct®	Clobazam	• Urbanol®
Lormetazepam	• Loramet® • Noctamid®	Diazepam	• Betapam® • Pax® • Sandoz Diazepam® • Tranject® • Valium®
Midazolam	• Dormicum® • Midacum® • Midanium®	Ketazolam	• Solatran®
Nitrazepam	• Arem® • Mogadon® • Sandoz Nitrazepam®	Lorazepam	• Ativan® • Tranqipam®
		Prazepam	• Demetrin®
Temazepam	• Normison®	Oxazepam	• Purata® • Sandoz Oxazepam® • Serepax®
Triazolam	• Halcion®		

Benzodiazepines can also be used for treatment of various other ailments and conditions, e.g.:

- Conversion disorders.
- Convulsions.
- Management of alcohol withdrawal.

- Muscle spasm.
- Pre-anaesthetic.
- Chest pain

(Sweetman, 2010; Rossiter, 2010:474)

A conversion disorder refers to a physical illness that occurs in the absence of physical pathology. Conversion disorders can also be called hysteria. This disorder can be treated with diazepam or alprazolam (Sweetman, 2010).

Epilepsy is a chronic neurological condition in other words it is a chronic disorder of the brain that affects people. Benzodiazepines can be used in the management of *status epilepticus*, febrile convulsions and convulsions with fever. In the case of chronic epileptic states, the use of benzodiazepines is limited due to their development of dependence and problems with tolerance (Rossiter, 2010:474; Sweetman, 2010; Trevor & Way, 2009:379). There are currently almost fifty million people with epilepsy worldwide. The proportion of the general population with active epilepsy is estimated to be nearly 4 to 10 per 1,000 people at a certain time (WHO, 2009). In South Africa, about one person in every hundred has epilepsy (Epilepsy South Africa, 2008).

The first symptom of alcohol withdrawal syndrome presents itself as a hyper adrenergic state with the following symptoms: tremor, tachycardia, sweating, and hypertension (Rossiter, 2010:474; Sweetman, 2010). Other symptoms that can occur with initial symptoms are: disorientation, anxiety, impaired concentration, depression, agitation, gastro-intestinal symptoms, insomnia, nightmares and hallucinations (Rossiter, 2010:474; Sweetman, 2010). The condition can progress towards a potentially fatal delirium tremens. Benzodiazepines are mostly used to relieve the symptoms of the alcohol withdrawal syndrome and if they are used correctly, it can prevent delirium tremens (Rossiter, 2010:474; Sweetman, 2010).

The benzodiazepines exert inhibitory effects on the polysynaptic reflexes and internuncial transmission and at high doses they may also depress transmission at the skeletal neuromuscular junction (Trevor & Way, 2009:379). Benzodiazepines can be used in relieving joint inflammation or trauma or spasm resulting from spasticity, dystonia, stiff-man syndrome, cerebral palsy, poisoning or tetanus (Rossiter, 2010:474; Sweetman, 2010; Trevor & Way, 2009:379).

Benzodiazepines are furthermore regarded as suitable drugs for minor surgery because it has anxiolytic, sedative, amnesia, muscle relaxant and anticonvulsant properties. Benzodiazepines are not associated with emetic activities, which make it more suitable as anaesthetic premedication or as a sedative cover for varieties of minor surgeries, diagnostic procedures including dental procedures, bronchial or gastro-intestinal endoscopy, radiology, cardiac

catheterisation, and cardioversion. Benzodiazepines can also be used for terminally ill patients in the intensive care units. They are also suitable where conscious sedation is needed for example the reduction of abolition of physiological and psychological responses to the stress without loss of consciousness, co-operation or protective reflexes (Rossiter, 2010:474; Sweetman, 2010; Trevor & Way, 2009:379).

Benzodiazepines can be used for the treatment of ischemia and angina. The anxiolytic, neurological, anti-inflammatory and muscle relaxant properties of benzodiazepines allow for a reduction in ischemia and angina. A decrease in catecholamine production can be due to the anxiolytic effect of benzodiazepines (Huffman & Stern, 2003:430).

2.7.4 Pharmacokinetics

Benzodiazepines are metabolised by the liver into glucuronides that are then excreted into the urine. Benzodiazepines can be divided into four groups, based on the elimination half-life of the drugs. The elimination half-life is the time required for half of the amount of the substance to be eliminated from the body. The half-life of a drug plays an important role with regard to the pharmacokinetic properties of the drug (Norman *et al.,* 1997:493; Trevor & Way, 2009:374).

The four groups are (Longo & Johnson, 2000:2124; Norman *et al.,* 1997:493; Rossiter, 2010:474; Sweetman, 2010; Trevor & Way, 2009:374):

- Ultra short-acting

  The ultra short-acting benzodiazepine has a half-life of less than six hours. Benzodiazepines that are ultra short-acting are midazolam and triazolam.
- Short-acting

  The short-acting benzodiazepines have a half-life of between six hours and twelve hours. In general short-acting benzodiazepines cause dependence more easily than the rest of the benzodiazepines. Benzodiazepines that are short-acting are brotizolam, loprazolam, lormetazepam, oxazepam and temazepam.
- Intermediate-acting

  The intermediate-acting benzodiazepine has a half-life of between twelve and twenty-four hours. Benzodiazepines that are intermediate-acting are alprazolam, bromazepam and lorazepam.
- Long-acting

  The long-acting benzodiazepines have a half-life of longer than twenty-four hours. Benzodiazepines that are long-acting are chlordiazepoxide, clobazam, clonazepam, clorazepate, diazepam, flunitrazepam, flurazepam, ketazolam, nitrazepam and prazepam.

The elimination half-life can be influenced by a few factors such as age, liver disease, other drugs and plasma protein binding. In the case of elderly and patients with liver disease the elimination half-life is increased because the liver function to metabolise the benzodiazepine is impaired (Sweetman, 2010; Trevor & Way, 2009:376). Other drugs can cause the inhibition of the liver enzymes, resulting in an increase of elimination half-life of the benzodiazepines. The binding of benzodiazepines to plasma protein extends the time it takes the liver to metabolise them (Sweetman, 2010; Trevor & Way, 2009:376).

The elimination half-life is not the same as the duration of action. The duration of action is influenced by the absorption, distribution and excretion. The benzodiazepines can be presented in different pharmaceutical forms namely oral, rectal, intravenous and intranasal routes (York, 2002:1). The route of administering is influenced by various factors. It must be assessed how fast the onset of the drug action will occur and what pharmaceutical form would be appropriate for the patient to take. For example, the intravenous route or rectal route is the most suitable for a patient who has an epileptic attack but oral and nasal routes will be most suitable for children (York, 2002:3).

2.7.5 Contra-indications

Benzodiazepine has certain contra-indications. The first contra-indication is when a patient has myasthenia gravis. Benzodiazepines may cause the muscles to relax and would thus worsen the myasthenia gravis (Stahl; 2010:103). The second contra-indication is when a patient has respiratory disorders, such as chronic obstructive pulmonary disease and limited pulmonary reserves, that may be exacerbated by benzodiazepines (Norman *et al.,* 1997:493; Rossiter, 2010:475). The third contra-indication is that it crosses the placenta, which makes benzodiazepines class D teratogens (Stahl, 2010:103). Benzodiazepines are therefore not recommended during pregnancy or breast-feeding. Infants are vulnerable to the effects of benzodiazepines especially if the mother had used benzodiazepines during pregnancy. The withdrawal symptoms can then be seen in the infant for almost 2 to 3 weeks after birth (Longo & Johnson, 2000:2125; Norman *et al.,* 1997:493). The fourth and last contra-indication is linked to hepatic diseases because the drug can aggravate CNS dysfunction by enhancing GABA activity (Rossiter, 2010:475; Stahl, 2010:103).

2.7.6 Side-effects

The adverse effects of benzodiazepine can be divided into two groups, *i.e.* regular effects and irregular effects (Rossiter, 2010:476).

2.7.6.1 Frequently observed side-effects

The adverse effects that are due to the mechanism of action on the CNS include drowsiness, impaired judgement, diminished motor skill and confusion. The drowsiness and impaired judgement can cause severe job accidents when working with machinery. This effect can also cause impairment of the ability to drive any vehicle, thus caution should be taken when benzodiazepines are used (Rossiter, 2010:476; Sweetman, 2010; Trevor & Way, 2009:382). The drowsiness, impaired judgement and confusion can also cause older people to bump into objects and then stumble and fall which may cause hip fractures (Egan *et al*., 2000:1181). The amnesia effect can be accountable for the difficulty in learning new information (Sweetman, 2010).

The adverse effects that are caused due to the action of benzodiazepines on the autonomic nervous system are dry mouth, blurred vision, urinary retention and excessive perspiration. These effects usually occur at the onset of intake of benzodiazepines and the effects disappear after a few weeks (Norman *et al*., 1999:494).

2.7.6.2 Less frequently observed side-effects

The less frequently observed side-effects are depression, nausea, vomiting, constipation, skin rashes, weight gain, blurred vision, jaundice, hypotension and headache (Norman *et al*., 1999:494; Rossiter, 2010:476).

Reactions that appear and then suddenly disappear are hyper-excitability, aggression and rage (Rossiter, 2010:476).

Flunitrazepam, the so-called “date-rape” drug, is usually used for insomnia but is also used by criminals to sedate people and rape them (Trevor & Way, 2009:382).

2.7.7 Drug interactions

The drug interactions in Table 2.7 are drug interactions that will enhance the adverse effects of benzodiazepines. Occasionally drugs are given with benzodiazepines to enhance the sedative effect, usually for anaesthesia purposes (Trevor & Way, 2009:383).

Table 2.7: The clinical effect of drugs that interact with benzodiazepines (Norman *et al*., 1997:494; Rossiter, 2010:475)

Interacting drug	**Mechanism of interaction**	**Clinical effect**
Alcohol, anticonvulsants, neuroleptics, antidepressants and antihistamines.	Enhances the adverse effects of the central nervous system.	Increased sedation
Antacids and anticholinergics	Decreased absorption	Delayed onset of acute clinical effects of benzodiazepine
Cimetidine	Inhibition of metabolism	Increased toxic effects due to elevated plasma concentrations of diazepam
Digoxin	Protein binding of diazepam altered	Increased digoxin levels
Disulfiram	Decreased metabolism	Increased effects of benzodiazepine
Oral contraceptives, isoniazid	Reduction in metabolism	Prolongation of elimination half-life and effect of benzodiazepines
Rifampicin	Increased metabolism	Elimination half-life of benzodiazepine shortened

2.7.8 Dependence

Dependence is to rely or trust on something or someone (OED, 2010b). Dependence on benzodiazepines can occur due to a too high therapeutic dose, using short-acting benzodiazepines rather than long-acting benzodiazepines for long terms and when patients with a history of drug or alcohol dependence use benzodiazepines (Sweetman, 2010; Rossiter, 2010:475). In addition, patients may develop dependence by habit or addiction (De las Cuevas *et al*., 2003:301). There is still uncertainty how the dependence mechanism works but it is alleged that it reduces GABA activity at the GABA receptors (Sweetman, 2010).

There are two types of dependence, namely physiological and physical dependence. Physiological dependence is distinguished by the occurrence of tolerance. Physical

dependence is described by the presence of the withdrawal syndrome that follows the dose reduction or administration of an antagonist (De las Cuevas *et al*., 2003:301). Psychological and physiological dependence pose the main problem associated with benzodiazepines (Sweetman, 2010). The psychological components of dependence manifest in the same neurotic behaviours of cigarette smokers and coffee drinkers. The physiological component of dependence is a more serious complication (Trevor & Way, 2009:379). The physiological component can be described as a state where the patient needs continued drug administration to prevent a withdrawal syndrome (Sweetman, 2010). The physiological dependence can be characterised by increased anxiety, insomnia, and central nervous system excitability that may progress to convulsions.

The withdrawal syndrome of sedative-hypnotics shows the following signs that are similar to those of the more common anxiety states, *i.e*. anxiety, panic attacks, agoraphobia, insomnia, nightmares, depression, dysphoria, excitability, restlessness, poor memory and concentration, dizziness, light-headedness, weakness "jelly legs", tremor, muscle pain, stiffness, sweating, night sweats, palpitations and blurred or double vision (Sweetman, 2010).

Physical dependence with benzodiazepine users is reported to be 15% to 30% of total users in Sweden (Bendtsen *et al*., 1999:460). Rossiter (2010:475) claims that nearly 40% to 50% of users are dependent on benzodiazepines after a year of usage. In another study (De las Cuevas *et al*., 2003:300) it is stated that 47% of patients who took benzodiazepines for longer than a month developed dependence. The type of prescriber who prescribed the most of the prescriptions to patients who showed dependence was the psychiatrist with 60.4% and in the second place were the general practitioners with 36.8% (De las Cuevas *et al*., 2003:300).

2.7.9 Withdrawal

Withdrawal symptoms are caused when patients who used benzodiazepines for longer than several weeks, stop the treatment abruptly without dose titration (Norman *et al*., 1997:495). The symptoms can appear between a few hours and 10 days, depending on what type of benzodiazepine the patient had used. The short-acting benzodiazepines' withdrawal symptoms appear immediately, whereas medium-acting benzodiazepines' withdrawal symptoms appear within 48 hours and the long-acting benzodiazepines' withdrawal symptoms appear between 5 to 10 days. The symptoms usually disappear within a week but may persist to a month or even a year (Lader, 1999:403; Sweetman, 2010).

Symptoms of the withdrawal syndrome that are less common in anxiety states and relatively specific to benzodiazepine withdrawal include perceptual distortions, sense of movement, depersonalisation, derealisation, hallucinations, distortion of body image, tingling, numbness altered sensation, fornication, sensory hypersensitivity, muscle twitches, jerks, tinnitus,

psychotic symptoms, confusion, delirium, and convulsions (Ashton, 2005:251; Norman *et al*., 1997:495; Sweetman, 2010).

Patients treated with short-acting or medium-acting benzodiazepines should first replace treatment with long-acting agents (for example diazepam), before treatment cessation. If the patient is using a short-acting or medium-acting benzodiazepine and wants to stop treatment, the benzodiazepine should be replaced for diazepam. The short-acting or medium-acting benzodiazepine dose must first be tapered down before changing to the equivalent of diazepam 5mg. The diazepam dose should then be lowered by 10% of the daily dose every two weeks (Rossiter, 2010:475). If a patient has difficulty in the lowering of the dose every two weeks, the dose can be held at the same level for a few more weeks before reducing the dose again. The withdrawal from benzodiazepines can take some time and it may last between four weeks and a year. However, it is better for the patient to go too slow than too fast (Sweetman, 2010).

2.7.10 Legislation

According to the South African Medicine and Related Substances Act, (Act 101 of 1965 as amended 1997) benzodiazepines are classified as Schedule 5 drugs (South Africa, 2003:7). Only a pharmacist, a pharmacist intern, or pharmacist's assistant, acting under the personal supervision of a pharmacist, upon a written prescription issued by an authorised prescriber or on the verbal instructions of an authorised prescriber who is known to such pharmacist, may dispense a schedule 5 drug. The authorised prescriber who has given verbal instructions to a pharmacist to dispense a prescription shall within seven days after giving such instructions furnish such pharmacist with a prescription confirming such instructions. Benzodiazepines cannot be prescribed for longer than 6 months, because they are schedule 5 medicine items. Benzodiazepines can be prescribed for longer than 6 months only when the authorised prescriber has consulted a registered psychiatrist. When the patient is a psychiatrist, the patient must then see another psychiatrist, before issuing a new prescription. Flunitrazepam is the only benzodiazepine of all the benzodiazepines that is schedule 6. Schedule 6 medicine can only be repeated with a new prescription (South Africa, 2003:7).

2.7.11 Prescribing patterns of benzodiazepines

Findings from a study by Egan and co-workers (2000:1181) showed that the "type of physician, who prescribes benzodiazepines the most" is a male practitioner who graduated before the year 1980 (Egan *et al*., 2000:1181). The number of psychiatrist practitioners are relatively limited in underdeveloped countries, thus general practitioners have a relatively higher responsibility in the prescribing of benzodiazepines in underdeveloped countries (Srisurapanont *et al*., 2005:28). Female patients living in most-deprived areas are more likely to receive diazepam than those living in less-deprived areas. Female patients are furthermore slightly more likely to receive a

prescription for diazepam than male patients. The ratio between male and female patients using benzodiazepines in Canada was 1.7:1 and in South Africa it was 1.57:1 (Kairuz & Truter, 2007:305; Neutel, 2005:191). Prescribing rates show a gender difference which increases steadily from early adult life. Women of middle-age are the most common recipients of a diazepam prescriptions (Quigley *et al*., 2006:148).

According to Kairuz and Truter (2007:305) and Quigley *et al.* (2006:148) there is an increase in the number of prescriptions per patient with increasing age. Benzodiazepine prescribing has higher rates in middle-age categories (45-64 years) and in the more urbanised areas (Quigley *et al*., 2006:148).

2.7.12 Prevalence of benzodiazepines

The prevalence of benzodiazepine use in an adult population varies between 2% to 10%. Over 25 million prescriptions for benzodiazepines were written only in the United Kingdom (UK) (Robertson & Treasure, 1996). The United States prescriptions were almost three times more than the UK's prescriptions, with Valium® (diazepam) as the world's best-selling drug in the year 1996 (Robertson & Treasure, 1996). The prescribing of benzodiazepines in Ireland had increased from 87 defined daily doses (DDD's) in 1995, to 116 DDD's in 2000 (Department of Health and Children Dublin, 2002). A preliminary analysis by General Medical Services (GMS) of recent prescribing trends demonstrated that there has been a significant rise (from 469 to 571.9) in the rate of diazepam prescriptions per 1000 patients over the period 2000 to 2003 (Quigley, 2001:331).

During a study done in England it was revealed that the majority of patients who used benzodiazepine used it as a hypnotic (70%) (Heather *et al*., 2004:147). The patients who did not use the benzodiazepines, for hypnotic purposes, used it for anxiolytic (27%) purposes or for both anxiolytic and hypnotic purposes (3%). Seventy-nine per cent of patients reported that their benzodiazepine medication was for night use only. More than half of the patients (55%) were prescribed temazepam, 22% diazepam and 14% nitrazepam. The general practioners were responsible for most of the prescriptions for benzodiazepines in England, 88%, while 11% were prescribed by a hospital doctor (Heather *et al*., 2004:147).

During a study in Sweden, 6% of the study population received one or more prescriptions for benzodiazepines. The female patients accounted for 60% and a large percentage of the people were older than 60 years (40%). Diazepam was the benzodiazepine that was the most frequently prescribed with 23%, followed by oxazepam 19%, temazepam 14%, lorazepam 12% and nitrazepam 9%. Diazepam and oxazepam recipients tended to be younger than 60 years, whereas temazepam, lorazepam and nitrazepam were popular with people 60 years and older (Groenewegen *et al*., 1999:1706). In Canada, the benzodiazepine that was the most frequently

prescribed was lorazepam with 36%, followed by clonazepam with 10% and lastly diazepam with 5% (Neutel, 2005:193). In Canada, lorazepam was the benzodiazepine that was the most commonly used with 25% and in Australia it was diazepam that was most frequently used with 33% (Smith *et al.*, 2008:548).

Alprazolam, clonazepam, diazepam and lorazepam are listed among the top 100 most commonly prescribed medications in America (Longo & Johnson, 2000:2121). Diazepam and alprazolam were the two most frequently prescribed benzodiazepines in South Africa (Kairuz & Truter, 2007:305).

2.8 CONCLUSION

Living space is influenced by population density (refer to paragraph 2.2). If the living space is restricted, conflicts erupt and this leads to crime (refer to paragraph 2.2). Another factor that has an influence on the crime is demographic composition, thus the population density (refer to paragraph 2.2). In South Africa the Northern Cape Province and the Gauteng Province were the most contradictory in terms of crime and population density (refer to paragraph 2.3.3 & 2.4.4).

Crime, violence and population density can cause poor mental well-being in a neighbourhood (refer to paragraph 2.2). Poor mental health, in turn, can cause insomnia (refer to 2.6.2). A victim of crime can experience stress and fear, leading to insomnia and anxiety (refer to paragraph 2.4). Benzodiazepines are used for the treatment of insomnia and anxiety (refer to paragraph 2.5).

In South Africa, there is a shortage of recent geographical and criminal data because the national census was last done in 2001. The author could only find one published study about the usage of benzodiazepines in South Africa. The prevalence of insomnia in South Africa could also not be found.

The Gauteng Province had a higher population density and had in generally a higher crime rate than the Northern Cape Province (refer to paragraphs 2.3.3 & 2.4.4). However, the crime per capita was relatively similar for the two provinces. Because of this, anxiety and insomnia are supposed to be higher in the Gauteng Province than in the Northern Cape Province. From the literature it is proposed that Gauteng Province would have a higher benzodiazepines usage than the Northern Cape Province. The benzodiazepine usage per capita is proposed to be relatively similar.

2.9 CHAPTER SUMMARY

In this chapter urbanisation, crime, anxiety, insomnia and benzodiazepines were discussed. These terms were defined and the possible relationships between the different terms were highlighted. The discussion of these aspects correlate with the general and specific goals and aims of this study as presented in chapter 1.

Chapter 3 will provide a general layout of the research methodology of this study.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

In this chapter the research objectives, empirical methodology, data sources and database will be discussed.

3.2 GENERAL RESEARCH OBJECTIVE

The general research objective of this study was to investigate the prescribing patterns of benzodiazepines in the Gauteng and Northern Cape.

3.3 SPECIFIC RESEARCH OBJECTIVES

The specific research objectives were grouped into those with regard to the literature review and those pertaining to the empirical.

3.3.1 Literature review

The specific objectives of the literature review included the following:

- To describe and define the terms urbanisation, crime, insomnia and anxiety
- To establish from the literature the relationship between the geographical area, crime and urbanisation globally
- To determine from the literature the relationship between geographical areas, crime and urbanisation, as applicable to South Africa
- To depict from the literature the relationship between crime, urbanisation and anxiety and insomnia
- To describe and define benzodiazepines
- To describe the prescribing patterns of benzodiazepines, globally as well as in South Africa with regard to gender, age and active ingredients.

3.3.2 Empirical investigation

The following data were analysed with regard to the total set of data:

- The age and gender of patients
- The prescribing patterns in the different provinces in South Africa
- The prescribing patterns in the Gauteng Province and Northern Cape Province with regard to the gender and age.

The following data were analysed with regard to the benzodiazepine data on the total database:

- The prescribing patterns of benzodiazepine in the Gauteng and Northern Cape Provinces
- The age of the patients to whom benzodiazepines were prescribed
- The prescribing patterns of benzodiazepines amongst the different gender groups
- The days between refills of the benzodiazepine prescriptions
- The prescribing patterns of benzodiazepines by the general medical practitioner, specialists and other practitioners.

3.4 RESEARCH DESIGN

A research design specifies the methods and procedures for collecting and analysing the needed information (Zikmund *et al*., 2010:66). The data of this study had already been assembled, therefore the data obtained for analysis in this study were secondary data. The benefit of using secondary data was that availability was relatively fast and that it was less expensive than primary data.

3.4.1 Relevance

The data were collected from the private care sector by a South African PBM for the years of 2006 and 2008. The data were therefore relevant to the private health care sector in South Africa.

3.4.2 Quality

The quality of secondary data is always a concern, because the source may not always be trustworthy. The data were collected from the private health care sector by a PBM. The PBM is registered with the Council for Medical Schemes and is thus trustworthy.

3.4.3 Timeliness

The data were assembled during 2006 and 2008 and can be regarded as recent.

3.4.4 Completeness

This PBM represented 35.51% of all PBMs (Council for Medical Schemes, 2010). The people that claimed from this PBM formed 4.15% in 2006 and 2.65% in 2008 of all people in South Africa (Statistics South Africa, 2007).

3.4.5 Research Method

A retrospective drug utilisation review was conducted.

3.4.5.1 Drug utilisation review

Drug utilisation has been defined as "the prescribing, dispensing, administering, and ingesting of drugs" (Serradell, *et al*., 1987:994). The World Health Organization (WHO) went a step further with the defining of drug utilisation and included outcome variables. Drug utilisation is defined by the WHO as "the marketing, distribution, prescription and use of drugs in society, with special emphasis on the resulting medical, social and economic consequences" (WHO, 2003). Guo *et al.* (1995:1175) claim that DUR (Drug Utilisation Review) is "an authorised, structured and ongoing programme that reviews, analyses and interprets patterns of drug usage in a given health care delivery system against predetermined standards". A DUR is thus a programme that reviews the appropriateness and cost-effectives of prescribing patterns in medicine.

A drug utilisation review can be classified into quantitative and qualitative DURs (Sjöqvist & Birkett, 2003:80). Quantitative DUR is defined by Inesta (1992:353) as the study of trends and number of drugs used. Quantitative DUR is all about the gathering and collecting of data. From such data the present states and trends of prescribing patterns are described and observed (Sjöqvist & Birkett, 2003:80).

Inesta (1992:353) defines qualitative DUR as the process that analyses the appropriateness of drug use. The problem with this is that it can only be analysed if the diagnoses is known. The majority of prescriptions that reach the pharmacy do not have a diagnosis of the illness on it. This makes it difficult to give the appropriate treatment (Inesta, 1992:353).

The main use of DUR programmes is to manage the prescribing of drugs and the costs of drugs through DUR studies. The DUR studies can be divided into three types, namely prospective, concurrent and retrospective reviews (Guo *et al.,* 1995:1175).

- **Prospective reviews**

  A prospective review is the review is the nearest to the ideal. A prospective review begins before the patient receives the medicine. The data for the prospective review are obtained from the patient's medical history. The medical history can be obtained through interviews and historical records. For this type of review, a computer that is equipped with the

necessary software is needed (Guo *et al.,* 1995:1175; Truter, 1994:17). Prospective reviews help the pharmacists to find problems with the drug therapy before the medicine is dispensed (Soumerai & Lipton, 1995:1641).

Retrospective and prospective DUR can be used together. The retrospective DUR detects the problems and with the prospective DUR the problems can be prevented (Truter, 1994:18).

- **Concurrent reviews**

  Concurrent reviews are taking place during the dispensing process. When a problem is discovered, the dispensing is stopped until the patient's problem, such as incorrect dosage has been resolved (Truter, 1994:17).

  Concurrent reviews are more expansive and time consuming than retrospective studies, but can be used more efficiently in preventing problems. Concurrent reviews can cause a reducing in costs, if the process is done during dispensing and not after dispensing (Guo *et al.,* 1995:1175; Truter, 1994:17).

- **Retrospective studies**

  A retrospective drug utilisation study is an approved, systematic process that captures, reviews, analyses, and interprets aggregate medication use data within specific health care environments (Erwin, 1991:596). The data that are collected and analysed are data about drugs that have already been dispensed after a prescription was issued for the drugs, thus the use of the drugs has already commenced (Guo *et al.,* 1995:1176). A retrospective drug utilisation study does not have any impact on patients while busy using their drugs. But a retrospective drug utilisation study can prevent inappropriate prescribing and high drug costs in the future (Guo *et al.,* 1995:1176). Retrospective studies are relatively inexpensive, the data can be accessed without any difficulty and the study can easily be accomplished (Truter, 1994:17).

A retrospective study is used in this study. Because the data were secondary data (data that had previously been collected in a specific health care environment).

3.5 DATA SOURCE

Data were obtained from 1 January 2006 to 31 December 2006 and 1 January 2008 to 31 December 2008 from a medical aid claims database (a South African Pharmaceutical Benefit Management company).

The study population consisted out of all the prescriptions for benzodiazepine medicine items on the medical claims database for the two study periods. The study periods were from 1 January 2006 to 31 December 2006 and 1 January 2008 to 31 December 2008.

The fields that were used in this study included the following:

- Date of dispensing the prescription.
- Qauntity of medicine items dispensed.
- Sex of the patient.
- Date of birth of patient.
- The prescriber type.
- Days between refills.
- Geographical areas.
- Trade names.
- NAPPI codes.

3.6 DATA ANALYSIS

The statistical analysis was carried out with the help of the Statistical Analysis System® SAS 9.1.3® (SAS Institute Inc., 2010).

3.6.1 Classifications systems

The Monthly Index of Medical Specialities (MIMS) and the NAPPI (National Approved Product Pricing Index) codes were among of the different classification systems that were used to classify the medicine claimed through the database.

3.6.1.1 MIMS classification

The Monthly Index of Medical Specialities (MIMS) classification system classifies the medicine according to its pharmacological action. In this study benzodiazepines was classified under central nervous system drugs as sedative hypnotic and anxiolytic drugs. These benzodiazepines were then assembled according to the trade names that were allocated to them by the pharmaceutical companies (Snyman, 2009:11a).

3.6.1.2 The NAPPI code

Every one of the medications recovered from the database was recognised by the drug's unique NAPPI code. This NAPPI code is a nine-digit code and every product can be distinguished by the code. This code is usually used to identify the product name, strength and the manufacturer (Snyman, 2009:7a).

3.6.2 Statistical analysis

During the processing of the data various statistical methods were used to analyse the data, namely the arithmetic mean, standard deviation and effect sizes.

3.6.2.1 Arithmetic mean (average)

According to Banerjee (2003:3) the arithmetic mean is the sum of all values making up the set of observations divided by their number.

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

The following describes the equation's symbols (Bland, 2000:60):

$\bar{x}$ = arithmetic mean or average

$\sum x$ = the sum

n = number of observations

3.6.2.2 Standard deviation

According to Bland (2000:62) the standard deviation is the variance calculated from the squares of the observations. It is also a measure of the spread of data about their mean, weighting each item by its distance from the centre of the distribution (Banerjee, 2003:5)

$$s = \sqrt{\frac{\sum x - \overline{x}^{\,2}}{n-1}}$$

s = standard deviation

x = value in the data set

$\overline{x}$ = the arithmetic mean

n = number of observations

3.6.2.3 Effect sizes (*d*-values)

Cohen (1988:9) stated that effect size is the degree to which the phenomenon is present in the population.

Cohen's *d* (Steyn, 2009):

$$d = \frac{\mu_1 - \mu_2}{\sigma}$$

- d = effect size
- μ_1 = average of item 1
- μ_2 = average of item 2
- σ = the largest standard deviation between item 1 and item 2

Effect size indices can be used for comparing different groups. If the effect size is large enough, a difference is regarded as practically significant.

Effect size can be divided into three categories (Steyn, 2009):

- *d* = 0.2: small effect size

  This occurrence means that the effect size is relatively small to the error of variation.

- *d* = 0.5: Medium effect size

  This effect size is large enough to be identified.

- *d* = 0.8 Large effect size

  This effect size gives a significant difference

3.7 MEASUREMENTS

The following measurements were used in the analysis of the prescribing patterns of benzodiazepine medicine.

3.7.1 Prevalence

The National Cancer Institute (NCI) (2009) stated that prevalence is a statistic of primary interest in public health, because prevalence recognises the intensity of burden of disease or health-related events on the population and health care system (NCI, 2009). Prevalence indicates new and pre-existing incidence that are taken into account on a specific date (NCI, 2009). Prevalence is also a function for the incidence of the disease and survival (NCI, 2009). Prevalence is determined as follows (Waning & Montagne, 2001:108):

$$\text{Prevalence} = \frac{\text{Number of existing cases in a population at a particular point of time}}{\text{Total number of people in the population}}$$

Prevalence was used in this study to calculate the number of times a patient received a benzodiazepine prescription or benzodiazepine medicine item.

3.7.2 Age

According to Taketomo *et al.* (2000:15), children are classified as based on their date of birth. The PBM's data were dived into five different age groups, namely children, adolescents, young adults, older adults and elderly.

The different categories of each age group are as follows:

- Group 1: $0 < x \leq 12$ years (Children)
- Group 2: $12 < x \leq 18$ years (Adolescents)
- Group 3: $18 < x \leq 40$ years (Young adults)
- Group 4: $40 < x \leq 65$ years (Older patients)
- Group 5: $x \geq 65$ years (Elderly)

The age was calculated on the 1 January 2007 to be used as the age for the period 1 January 2006 to 31 December 2006, and 1 January 2009 to be used as the age for the period of 1 January 2008 to 31 December 2008. This was done to ensure that no patient would be counted more than once.

3.7.3 Gender

The term "sex" or gender refers to the uniqueness that defines men and women from each other. The characteristics that form this uniqueness is their biological and physiological characteristics, and their behaviours, activities and attributes in a given society (WHO, 2010). For the purpose of this study it will be assumed that gender and sex are synonyms.

The gender was discussed in 3 categories: female, male and unknown. The unknown category was used when the patient's gender was not indicated.

3.7.4 Prescriber type

The prescribers on the database were divided into the following groups:

- General medical practitioner: This group includes all the medical prescribers that are registered with the Health Professions Council of South Africa as general medical practitioner (HPCSA, 2010).
- Psychiatrist: This group includes all the psychiatrists registered with the Health Professions Council of South Africa (HPCSA, 2010).
- Other: This group consists of all the following prescribers (HPCSA, 2010):

Anaesthesiology, approved day clinics, cardiology, cardiology paediatrics, clinical haematology, community dentistry, community health, dermatology, diagnostic radiology, gastroenterology, general dental practice, group practices, group practices/hospitals, homeopaths, maxillor-facial & oral surgery, neurology, neurosurgery, nuclear medicine, obstetrics & gynaecology, oncology, ophthalmology, oral pathology, orthodontics, orthopaedics, otorhinolaryngology, paediatrics, pathology, periodontics, urology, surgery / paediatric surgery, radiothology / oncology, private hospital (A tariff), private hospital (B tariff), physician / immunologist / rheumatologist / nephrotologist / diabetologist / endocrinologist, physical medicine, plastic and reconstructive surgery, prosthodontics, provincial hospital, pulmonology, radiography, thoracic surgery, rheumatology, operating theatre / day.

3.7.5 Geographical area

For this study, the geographical area was allocated according to the postal codes of the physical address of the prescriber that had prescribed any medicine that was claimed by this medical aid scheme. This was done by utilising the postal address of every practitioner that the medical aid scheme provided. For the purpose of this study was the focus on the Gauteng and the Northern Cape Provinces.

3.7.6 Days between refills

The days between refills were defined as the time period that the medicine was dispended to the patient.

Days between refills = Date of the last prescription – Date of the first prescription

For the purpose of this study the time periods were divided as indicated below:

- Group 1: $0 < x \leq 30$ days
- Group 2: $30 < x \leq 60$ days
- Group 3: $60 < x \leq 90$ days
- Group 4: $90 < x \leq 120$ days
- Group 5: $120 < x \leq 150$ days
- Group 6: $x \geq 180$ days

3.8 ETHICAL ASPECTS

The name of the Pharmaceutical Benefit Management Company (PBM) from which this data were received is nowhere to be mentioned in this study for the sake of confidentiality. Also for the same reason the medical aid schemes contracted by this PBM were not indicated on the data. This research was ethical, according to the North-West University standards (NWU-0046-08-S5).

All the patients on the PBM were from the private health care sector. Every patient in a PBM has a member number, but for the sake of confidentiality, all patients were allocated a “dummy” member number by the PBM.

3.9 LIMITATIONS OF THIS STUDY

- It was difficult to pinpoint a geographical area to the precise location of the patient because only the physical address of the prescriber’s consultation room where the patients went for their prescriptions or medicine was available and also the pharmacy’s physical address where the prescription had been dispensed.
- This data of the medical claims could not prove whether the patients were taking their medicine or not.
- According to good practice every prescriber is required and supposed to write the ICD 10 code on each prescription, however, the ICD 10 codes had not yet been fully implemented on the database. Thus was it not possible to relate the prescription to a specific disease.
- This PBM did not have any data of patients who paid personally for the medication as it contained only data of the medical schemes that paid for the medication.

3.10 CHAPTER SUMMARY

This chapter focused on the research methodology. In this chapter the general research objective, specific research objectives, research design, data source, data analyses, measurements and ethical aspects were discussed. Measurements such as prevalence, age, gender, prescriber type and geographical were also discussed.

The results of this study will be discussed in chapter 4 and the conclusions and recommendation will be presented in chapter 5.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 INTRODUCTION

In this chapter the results obtained from the empirical analyses of the study are discussed. The data were extracted from a PBM database from 1 January 2006 to 31 December 2006 and 1 January 2008 to 31 December 2008.

The total database was examined with the focus on geographical area and prescribing patterns of benzodiazepines in the different provinces in South Africa. The Northern Cape Province and Gauteng Province were more thoroughly analysed than the other provinces. The benzodiazepines were analysed according to pharmacological groups of 1.2.1 and 1.3.1, based on the MIMS classification system for pharmacological therapeutics in South Africa (Snyman, 2009:3). The differences between prescribing patterns of the various age groups and genders were investigated. The number of days between refills was also investigated.

Figure 4.1 is an illustration of how the data were analysed.

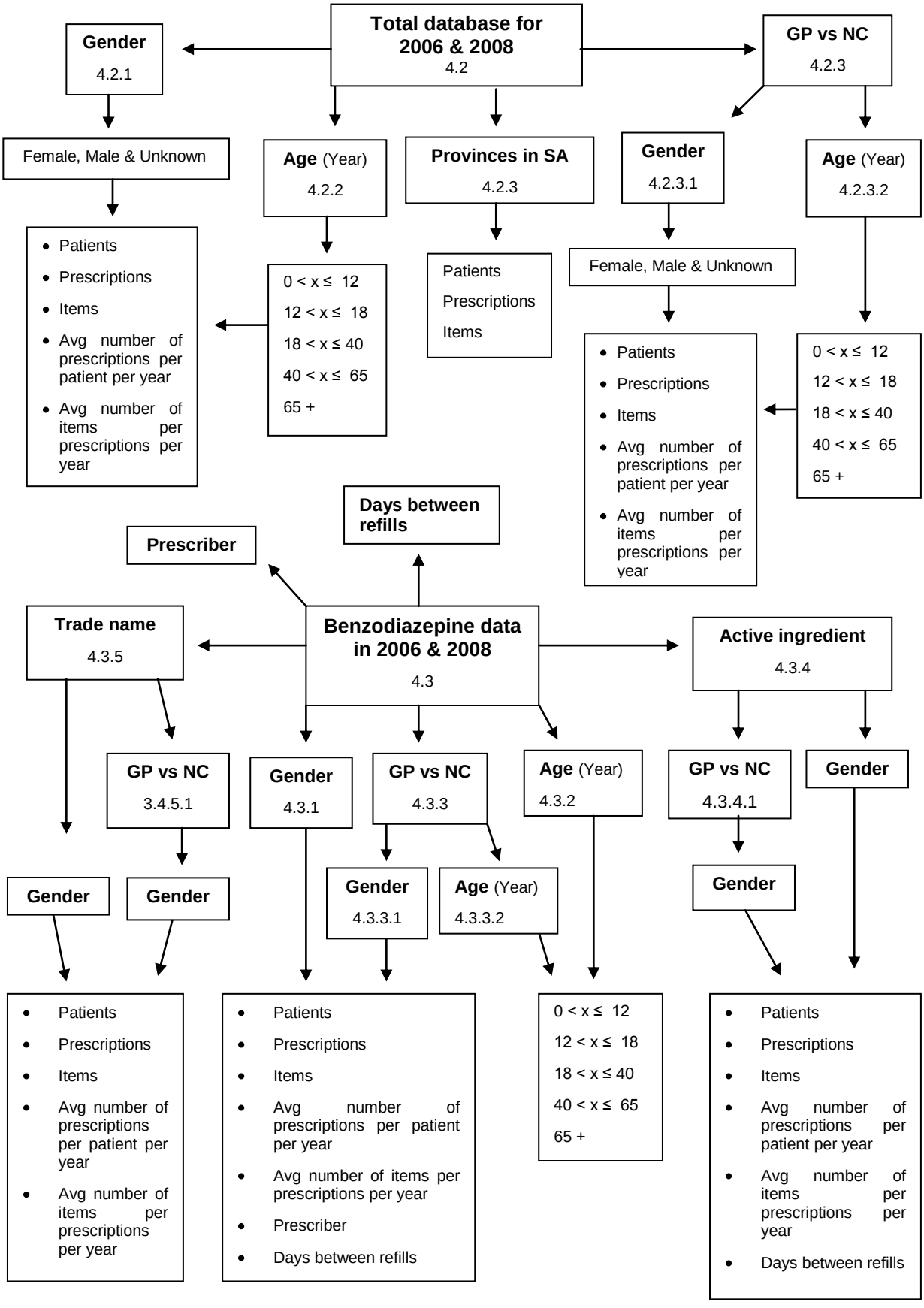


Figure 4.1: Schematic illustration of how the data were analysed

4.1.1 Annotations regarding the interpretation of the results

- The numerical values of the data were rounded off to two decimal places, this means that the percentages may not always add up to 100%.

- The number of patients and prescriptions can differ between the total data and the geographical data because some patients lived in one province and claimed their medicine in another province. Thus, some patients could have been counted in more than one province.

4.2 GENERAL ANALYSIS OF THE TOTAL DATABASE

Medical aid schemes administered by the PBM represented 35.51% of all registered medical schemes in South Africa (Council for Medical Schemes, 2010). The data used for this study represented a section of the private health care sector of South Africa.

Table 4.1 provides a general overview of the total database. This table refers to the complete data for the years of 2006 and 2008.

Table 4.1: Basic characteristics of the total database

	GENDER			AGE (YEARS)				
	Female	Male	Unknown	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
Number of patients								
N_{2006} = 1 964 381	1 113 427	849 635	1 319	282 549	138 935	581 406	740 455	221 036
N_{2008} = 1 290 017	728 051	561 966	-	150 400	92 923	340 115	533 493	173 086
Number of prescriptions								
N_{2006} = 9 223 281	5 543 056	3 675 209	4 965	797 704	371 247	1 986 049	3 933 168	1 818 180
N_{2008} = 7 120 035	4281971	2 838 064	-	439 598	259 859	1 276 037	3 172 467	1 627 912
Number of items								
N_{2006} = 21 113 422	12 699 707	8 403 158	10 557	2 005 107	882 991	4 449 232	9 197 629	4 578 463
N_{2008} = 16 439 253	9 893 928	6 545 325	-	1 085 511	602 822	2 855 035	7 658 730	4 237 155
Average number of prescriptions per patient								
2006 (4.70±6.15)	4.98±6.52	4.33±5.62	3.76±4.97	2.88±2.96	2.72±2.86	3.52±4.32	5.52±6.78	8.58±9.46
2008 (5.52±6.87)	5.88±7.27	5.05±6.27	-	3.01±3.13	2.88±3.12	3.92±4.67	6.29±7.18	9.89±10.03
Average number of items per prescriptions								
2006 (2.37±1.55)	2.29±1.52	2.29±1.46	2.13±1.37	2.47±1.34	2.34±1.33	2.18±1.31	2.25±1.47	2.41±1.80
2008 (2.43±1.64)	2.31±1.58	2.31±1.52	-	2.40±1.34	2.25±1.31	2.14±1.30	2.28±1.52	2.48±1.87

The 2006-database consisted of a total number of 1 964 381 patients compared to 1 290 017 patients during 2008, indicating a decrease of 34.33% (Table 4.1).

In 2006, a total number of 9 223 281 prescriptions were claimed (containing 21 113 422 medicine items) compared to 7 120 035 prescriptions and 16 439 253 claimed medicine items for 2008 (Table 4.1). The total cost for in 2006 (i.e., R1 959 738 734.09) decreased *in sync* with the total number of items and prescriptions to R1 785 871 013.85 during 2008 - a decrease in total cost of 8.87%.

The difference between the average number of prescriptions per patient in 2006 and 2008 was not practically significant (d = 0.12), and was thus irrelevant (refer to Tables A.1 & A.2, Appendix A). The difference in the average number of items per prescription per year 2006 and 2008 were also practically insignificant (d < 0.8) (refer to Tables A.1 & A.2, Appendix A).

There were a decrease in the number of people that claimed according to this database from the year 2006 to 2008.

4.2.1 Analysis based on patient's gender

The gender can be divided into three groups namely: female, male and unknown. The unknown category was used when the patient's gender was not indicated. Table 4.2 illustrated the percentage that each gender accounted for in the specific period. The prevalence for each gender was calculated from Table 4.1 by dividing the number of patients, prescriptions and items (n) by the total number of patients, prescriptions and items (N) for the study periods and then multiplied by 100.

Table 4.2: Gender distribution in the total database

		Percentage of gender in total database (%)	
Year		2006	2008
Patients	Female	56.68	56.44
	Male	43.25	43.56
	Unknown	0.07	-
Prescriptions	Female	60.1	60.14
	Male	39.85	39.86
	Unknown	0.05	-
Items	Female	60.15	60.18
	Male	39.80	39.82
	Unknown	0.08	-

4.2.1.1 Female patients

Female patients represented 56.68% (n = 1 113 427) of the total number of patients on the total database in 2006, and 56.44% (n = 728 051) in 2008. The gender that claimed the most prescriptions was the females with 60.1% (n = 5 543 056) in 2006 and 60.14% (n = 4 281 971) in 2008. The total number of items claimed by the female gender for 2006 was 60.15% (n = 12 699 707) and 60.18% (n = 9 893 928) in 2008 (Table 4.2).

The average number of prescriptions per female patient per year was 4.98±6.52 in 2006 and 5.88±7.27 in 2008. An average number of items per prescription claimed by females was 2.29±1.52 in 2006 and 2.31±1.58 in 2008. The difference between the two years was in both instances, i.e., (average number of prescriptions per patient and average number of items per prescription) not practically significant, with *d*-values smaller than 0.2 (refer to Tables A.1 & A.2, Appendix A).

4.2.1.2 Male patients

Males represented a smaller portion of the total number of patients on the total database, at 43.25 % (n = 849 635) in 2006 and 43.56% (n = 561 966) in 2008. In 2006, 39.85% (n = 3 675 209) of all prescriptions were claimed by males, and 39.86% (n = 6 545 325) in 2008. The number of items that were claimed by males represented 39.80% (n = 8 403 158) in 2006 and 39.82% (n **=** 6 545 325) in 2008.

The average number of prescriptions per male patient was 4.33±5.62 in 2006 compared to 5.05±6.27 in 2008. The average numbers of items per prescription claimed by the male gender were 2.29±1.46 in 2006 and 2.31±1.52 in 2008. Effect sizes for both the average number of prescriptions per patient and average number of items per prescription were below 0.2 (i.e., d = 0.12 and 0.01 respectively). The increase in the average number of prescriptions per patient and average number of items per prescription from 2006 to 2008 was thus practically insignificant (refer to Tables A.1 & A.2, Appendix A).

4.2.1.3 Unknown gender category

This category represented a small proportion of the total database. This category was only part of the database for 2006 and not for 2008, because all the claims had a reported gender status in 2008. This category represented only 0.07% (n = 1 319) of all the patients in 2006 and only 0.05% (n = 4 965) of this category had claimed prescriptions in 2006. The number of items claimed by the unknown category was 0.08% (n = 10 557) in 2006.

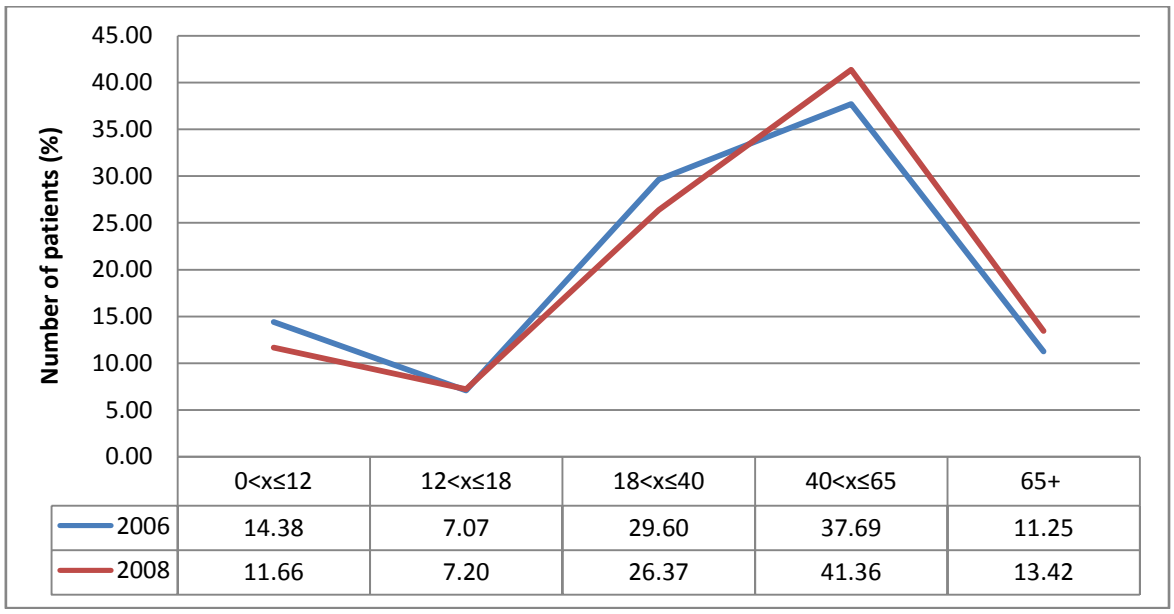
The average number of prescriptions per patient was 3.76±4.97 and the average number of items per prescription was 2.13±1.37.

4.2.2 Analyses based on the patients' age

The analyses were done based on different age groups of the patient. The age groups were as follows (amended in chapter 3.7.2):

- Age group 1 – Patients older than 0 years and patients younger than 12 years, 12 included ($0 < x \leq 12$).
- Age group 2 – Patients older than 12 years and patients younger than 18 years, 18 included ($12 < x \leq 18$).
- Age group 3 – Patients older than 18 years and patients younger than 40 years, 40 included ($18 < x \leq 40$).
- Age group 4 – Patients older than 40 years and patients younger than 65 years, 65 included ($40 < x \leq 65$).
- Age group 5 – Patients older than 65 years (65 +).

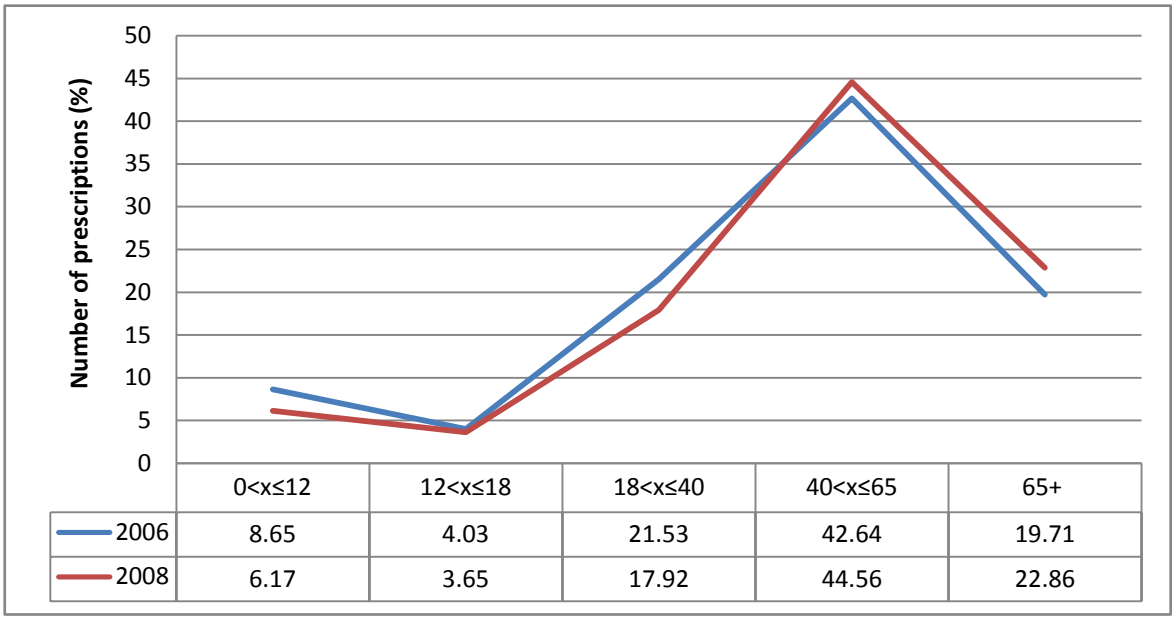
Figure 4.2 illustrates the percentage distribution of the age groups in the total database for the years 2006 and 2008. The prevalence for each age group was calculated from Table 4.1 by dividing the number of patients (n) by the total number of patients (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2006	14.38	7.07	29.60	37.69	11.25
2008	11.66	7.20	26.37	41.36	13.42

Figure 4.2: Prevalence distribution of the different age groups

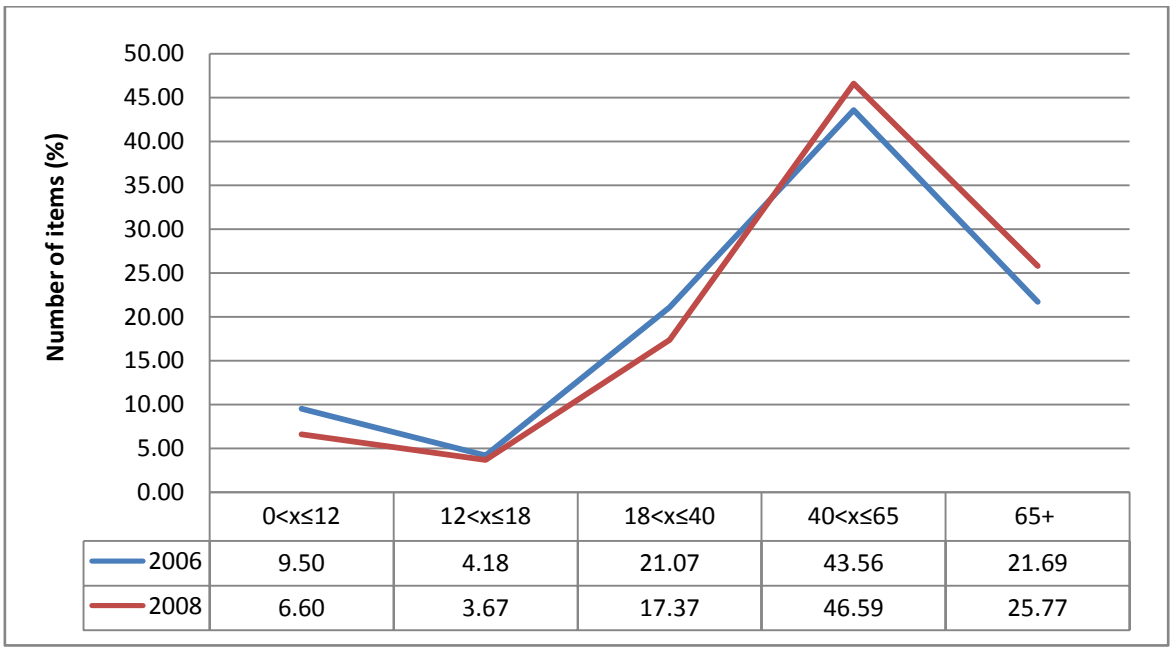
The following figure (4.3) illustrated the percentage of prescriptions that were claimed by each age group for the years 2006 and 2008. The prevalence for each age group was calculated from Table 4.1 by dividing the number of prescriptions (n) by the total number of prescriptions (N) for 2006 and 2008, then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2006	8.65	4.03	21.53	42.64	19.71
2008	6.17	3.65	17.92	44.56	22.86

Figure 4.3: Percentage of prescriptions claimed according to age groups

The following figure (4.4) illustrates the percentage of items that each age group claimed. The prevalence for each age group was calculated from Table 4.1 by dividing the number of items (n) by the total number of items (N) for 2006 and 2008, then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2006	9.50	4.18	21.07	43.56	21.69
2008	6.60	3.67	17.37	46.59	25.77

Figure 4.4: The percentage of items claimed by each age group.

Figures 4.2, 4.3 and 4.4 will be discussed in the following sections (4.2.2.1 to 4.2.2.5).

4.2.2.1 Age group 1

Patients from age group 1 represented 14.38% (n = 282 549) of all patients in 2006 and 11.66% (n = 150 400) in 2008 (Figure 4.2). The percentage of prescriptions that were claimed by this age group for 2006 was 8.65% (n = 797 704) and decreased to 6.17% (n = 439 598) in 2008 (Figure 4.3). The number of items represented 9.50% (n = 2 005 107) and 6.60% (n = 1 085 511) for 2006 and 2008 of the total number of items respectively (Figure 4.4).

The average number of prescriptions per patient per year between 0 to 12 years was 2.88±2.96 in 2006 and 3.01±3.13 in 2008. The difference between the calculated *d*-values for the two study periods was practically insignificant (refer to Table A.1, Appendix A). The average number of items per prescription was 2.47±1.34 in 2006 and 2.40±1.34 in 2008 for this group. The *d*-value for the difference in years for the average number of items per prescription was 0.05. This indicates a small effect that means the differences between in 2006 and 2008 were practically insignificant (refer to Table A.2, Appendix A).

4.2.2.2 Age group 2

According to Figure 4.2, only 7.07% (n = 138 935) and 7.20% (n = 92 923) patients were between the ages of 12 and 18 years in 2006 and 2008. The number of prescriptions that were claimed by this group, was 4.03% (n = 371 247) in 2006 and 3.65% (n = 259 859) in

2008 (Figure 4.3). The number of items was claimed by patients between 12 and 18 years, was 4.18% in 2006 and 3.67% in 2008 (Figure 4.4) of the total number of items claimed.

The average number of prescriptions per patient per year for this group was 2.72±2.86 in 2006 and 2.89±3.12 in 2008. The average number of items per prescription for patients between 18 and 40 years was 2.34±1.33 in 2006 and 2.25±1.31 in 2008. The *d*-values for the average number of prescriptions per patient and the average number of items per prescription were 0.06 and 0.07 respectively (refer to Tables A1 & A2, Appendix A). These values were smaller than 0.2, which means the difference was not practically significant.

4.2.2.3 Age group 3

The number of patients per year in age group 3 was 29.60% (n = 581 406) in 2006, this decreased to 26.37% (n = 340 115) in 2008 (Figure 4.2). The number of prescriptions claimed for patients between the years of 18 to 40, was 21.53% (n = 1 986 049) in 2006 and 17.92% (n = 1 276 037) in 2008 (Figure 4.3). The number of items represented 21.07% (n =4 449 232) and 17.37% (n = 2 855 035) for 2006 and 2008 (Figure 4.4).

The average number of prescriptions claimed per patient (between 18 to 40 years) was 3.52±4.32 and 3.92±4.67 for 2006 and 2008 respectively. The difference between the two years was not practically important (refer to Table A1, Appendix A). The average number of items per prescription for age group 3 was 2.18±1.31 and 2.14±1.30. The *d*-value (0.03) illustrated that the difference between 2006 and 2008 was practically insignificant (refer to Table A.2, Appendix A).

4.2.2.4 Age group 4

The number of patients between 40 and 65 years represented 37.69% (n = 740 455) of the number of patients in 2006 and 41.36% (n = 533493) in 2008 (Figure 4.2). The total number of prescriptions claimed by age group 4 was 42.64% (n = 3 933 168) in 2006 and 44.56% (n = 3 172 467) in 2008 (Figure 4.3). The total number of items in age group 4 represented 43.56% (n = 9 197 629) in 2006 and 46.59% (n = 7 658 730) in 2008 (Figure 4.4).

The average number of prescriptions per patient was 5.52±6.78 in 2006 and 6.29±7.18 in 2008. The difference between 2006 and 2008 provided a *d*-value of 0.11, indicating a practical insignificance (refer to Table A.1, Appendix A). In 2006 and 2008, the average numbers of items per prescription were 8.58±9.46 and 9.89±10.03 respectively. The *d*-value (0.02) for the dissimilarity between 2006 and 2008 was not practically significant (refer to Table A.2, Appendix A).

4.2.2.5 Age group 5

In 2006 and 2008, the number of patients in age group 5 indicated 11.25% (n = 221 036) and 13.42% (n = 173 086) (Figure 4.2). The number of prescriptions claimed by patients older than 65 years represented 19.17% (n = 1 818 180) in 2006 versus 22.86% (n = 1 627 912) in 2008 (Figure 4.3). The number of items for patients older than 65 years increased from 21.69% in 2006 (n = 4578463) to 25.77% in 2008 (n = 4237155) of the total number of items claimed in 2006 and 2008 respectively (Figure 4.4).

The average number of prescriptions per patient was 8.58±9.46 in 2006 and 9.89±10.03 in 2008. The dissimilarity between 2006 and 2008 provided a *d*-value of 0.13 which signified a small difference and thus the difference was not practically significant (refer to Table A1, Appendix A). The average number of items per prescription was 2.41±1.80 and 2.48±1.87. The *d*-value (0.04) for the difference between the two years was practically insignificant (refer to Table A.2, Appendix A).

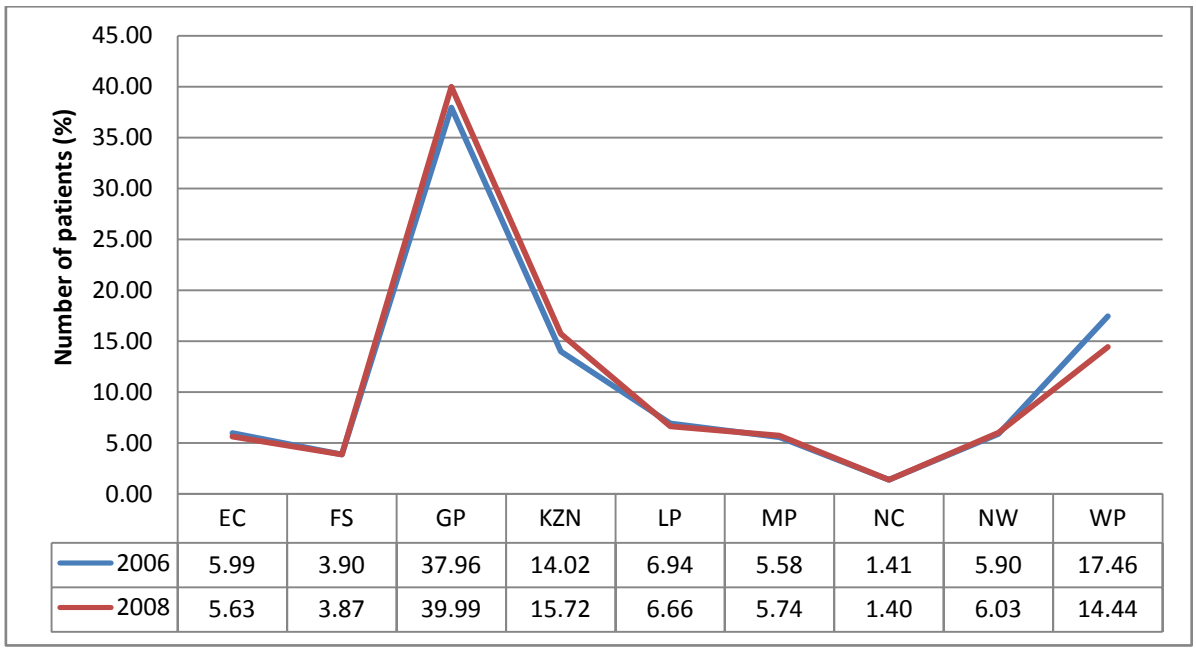
4.2.3 Analysis based on provinces

The following Table 4.3 illustrates the number of patients, prescription and items claimed per province for 2006 and 2008.

Table 4.3: Number of patients, prescriptions and items according to provinces

Provinces in South Africa	Years	Number of patients (n)	Number of prescriptions (n)	Number of items (n)
Eastern Cape (EC)	**2006**	117 560	669 844	1 516 411
	2008	72 605	525 080	1 198 226
Free State (FS)	**2006**	76 666	451 162	1 024 829
	2008	49 896	339 887	779 955
Gauteng (GP)	**2006**	745 573	3 630 346	8 545 665
	2008	515 825	2 848 499	6 700 970
Kwazulu-Natal (KZN)	**2006**	275 492	1 391 916	3 158 899
	2008	202 760	1 132 195	2 622 032
Limpopo (LP)	**2006**	136 338	547 051	1 337 434
	2008	85 908	359 702	869 606
Mpumalanga (MP)	**2006**	109 562	464 617	1 102 747
	2008	74 093	358 700	852 837
North West (NW)	**2006**	115 950	546 168	1 333 599
	2008	77 830	415 360	991 484
Northern Cape (NC)	**2006**	27 724	137 499	317 515
	2008	18 069	111 011	254 492
Western Cape (WC)	**2006**	342 878	1 353 953	2 703 483
	2008	186 237	1 015 137	2 138 087

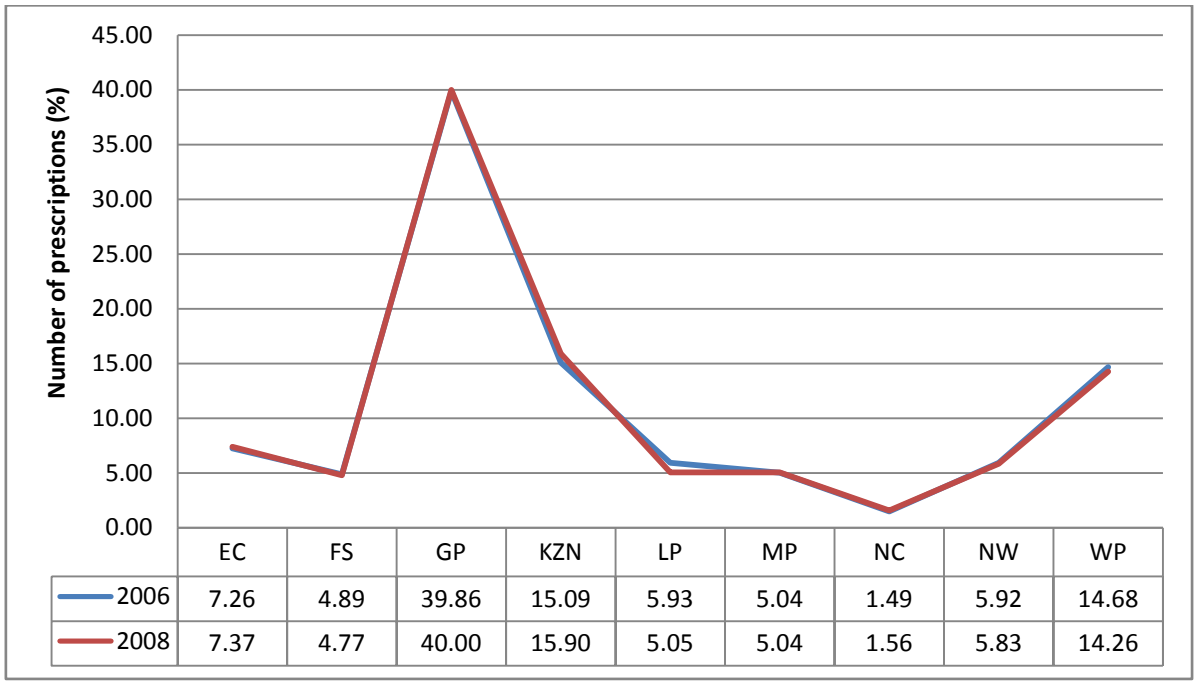
Figures 4.4, 4.5 and 4.6 will be discussed following figure 4.7. Figure 4.5 illustrates the percentage of patients that claimed from the total database in each province. The prevalence for each province was calculated from Tables 4.1 and 4.2 by dividing the number of patients (n) by the total number of patients (N) and then multiplying by 100.



	EC	FS	GP	KZN	LP	MP	NC	NW	WP
2006	5.99	3.90	37.96	14.02	6.94	5.58	1.41	5.90	17.46
2008	5.63	3.87	39.99	15.72	6.66	5.74	1.40	6.03	14.44

Figure 4.5: Percentage distribution of patients per province

Figure 4.6 exemplified the number of prescriptions claimed by each province from the total database. The prevalence for each province was calculated from Table 4.1 and 4.2 by dividing the number of prescriptions (n) by the total number of prescriptions (N) and then multiplying by 100.

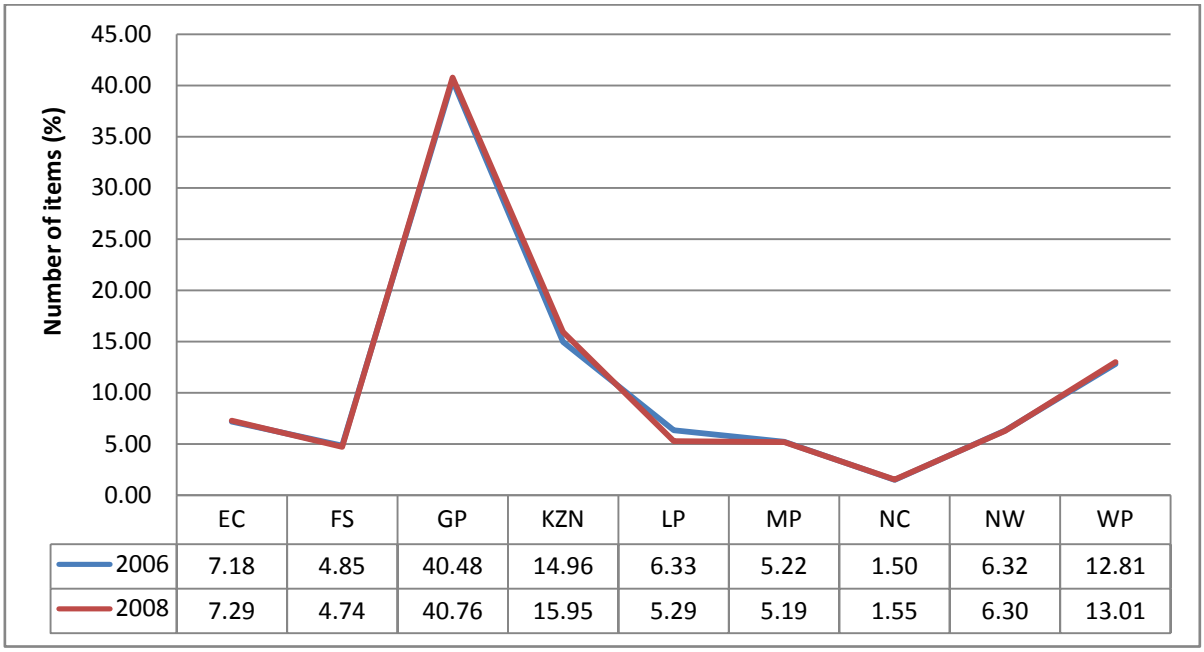


	EC	FS	GP	KZN	LP	MP	NC	NW	WP
2006	7.26	4.89	39.86	15.09	5.93	5.04	1.49	5.92	14.68
2008	7.37	4.77	40.00	15.90	5.05	5.04	1.56	5.83	14.26

Figure 4.6: Percentage distribution of prescriptions per province

The following Figure 4.7 demonstrated the number of items that were claimed in each province from the total data base. The prevalence for each province was calculated from

Tables 4.1 and 4.2 by dividing the number of items (n) by the total number of items (N) and then multiplying by 100.



	EC	FS	GP	KZN	LP	MP	NC	NW	WP
2006	7.18	4.85	40.48	14.96	6.33	5.22	1.50	6.32	12.81
2008	7.29	4.74	40.76	15.95	5.29	5.19	1.55	6.30	13.01

Figure 4.7: Percentage distribution of items per province

The province with the highest number of patients that claimed according to the total database in both 2006 and 2008 was the Gauteng Province with 37.96% (n = 745 573) and 39.99% (n = 515 825) respectively (refer to Figure 4.5 & Table 4.5). The Kwazulu-Natal and Western Cape Province were, respectively, second and third with the number of patients that claimed according to the total database for the years 2006 and 2008. The province with the lowest number of patient claims according the total database in both 2006 and 2008 was the Northern Cape Province at 1.4% (n = 27 724) and 1.41% (n = 18 069) respectively (refer to Figure 4.5 & Table 4.5).

The number of prescriptions and number of items per year claimed, was the highest in the Gauteng Province representing 39.36% and 40.48% in 2006 versus 40.01% and 40.76% in 2008 according to the total database(refer to Table 4.5 & Figures 4.6 & 4.7). The number of prescriptions as well as number of items per year was second most claimed in Kwazulu-Natal Province for the study periods. The province with the third most number of prescriptions and items claimed was the Western Cape Province. The Northern Cape was the lowest of all the provinces that claimed for the study periods (Figures 4.6 & 4.7).

Gauteng Province had relatively more people residing there (Chapter 2.3.3) and it can be assumed that could be the reason why there were more members on this PBM database that were from the Gauteng Province. In contrast to the Gauteng Province, the Northern Cape Province had the lowest number of people residing there (Chapter 2.3.3), and the lowest number of patients that claimed according to this PBM database.

4.2.4. Analyses of Gauteng versus Northern Cape Province

This section represents the total data of the Gauteng and Northern Cape Province. The following table illustrates the characteristics of the Gauteng Province (GP) and the Northern Cape Province (NC).

Table 4.4: Number of patients, prescriptions and items in Gauteng Province and Northern Cape Province

	Total GP		**Total NC**	
Study period	**2006**	**2008**	**2006**	**2008**
Number of patients (N)	745 573	515 825	27 724	18 069
Female (n)	421 159	289 589	15 381	9 679
Male (n)	323 867	226 236	12 336	8 390
Unknown (n)	547	0	7	0
0<x≤12 (n)	107 293	59 507	4 184	2 021
12<x≤18 (n)	51 343	34 814	2 007	1 275
18<x≤40 (n)	227 777	143 115	7 644	4 449
40<x≤65 (n)	278 311	212 098	10 913	8 277
65 + (n)	80 849	66 291	2 976	2 047
Number of prescriptions (N)	3 630 346	2 848 491	137 499	111 010
Female (n)	2 180 136	1 712 205	81 936	64 319
Male (n)	1 448 149	1 136 286	55 550	46 691
Unknown (n)	2 061	0	13	0
0<x≤12 (n)	316 166	182 542	11 525	6 204
12<x≤18 (n)	142 875	103 696	5 073	3 825
18<x≤40 (n)	819 180	561 753	29 677	19 475
40<x≤65 (n)	1 626 663	1 351 433	67 040	60 313
65 + (n)	725 462	649 067	24 184	21 193
Number of items (N)	8 545 665	6 700 970	317 515	254 492
Female (n)	5 130 316	4 031 882	191 651	149 487
Male (n)	3 411 088	2 669 088	125 835	105 005
Unknown (n)	4 261	0	29	0
0<x≤12 (n)	788 619	440 310	27 492	14 598
12<x≤18 (n)	339 200	234 165	11 749	8 173
18<x≤40 (n)	1 820 082	1 207 581	65 313	41 425
40<x≤65 (n)	3 748 954	3 129 505	152 361	136 409
65 + (n)	1 848 810	1 689 409	60 600	53 887

From Table 4.1, it can be observed that the Gauteng Province had a higher number of patients, prescriptions and items than the Northern Cape Province for both 2006 and 2008. This is in accordance to a higher number of inhabitants in the Gauteng compared to the

Northern Cape (refer to paragraph 2.3.3), and subsequently a higher number of members on this PBM database would be from the Gauteng Province (Table 4.4).

The Gauteng and Northern Cape did not differ in a practically significant way with regard to the average number of prescriptions per patient for 2006 and 2008 (*d* = 0.01 for 2006 and *d* = 0.09 for 2008). The *d*-value for the average number of items per prescription between the Northern Cape and Gauteng Province was 0.03 in 2006 and 0.04 in 2008. These values were practically insignificant (refer to Tables A.3 to A.6, Appendix A).

4.2.4.1 Analysis based on the patients' gender between two provinces

The three gender groups for this analysis were: female, male and unknown. When the patient's gender was not indicated, the patient was classified in the category of unknown . Table 4.5 illustrates the percentage that each gender represented for the specific period. The prevalence for each gender was calculated from Table 4.4 by dividing the number of patients, prescriptions and items (n) by the total number of patients, prescriptions and items (N) for the study periods and then multiplying by 100.

Table 4.5: Percentage distribution based on gender in the Northern Cape Province and Gauteng Province

		Percentage of gender in total database (%)			
Provinces		GP		NC	
Year		2006	2008	2006	2008
Patients	Female	56.49	56.14	55.48	53.57
	Male	43.44	43.86	44.50	46.43
	Unknown	0.07	0	0.03	0
Prescriptions	Female	60.05	60.11	59.59	57.94
	Male	39.89	39.89	40.40	42.06
	Unknown	0.057	0	0.01	0
Items	Female	60.03	60.17	60.36	58.74
	Male	39.92	39.83	39.63	41.26
	Unknown	0.05	0	0.01	0

4.2.4.1.1 Female patients

According to the total database the female patients in the Gauteng and Northern Cape claimed more often than their male counterparts. Females from both Gauteng and the Northern Cape claimed more prescriptions and items than their male counter parts (Table 4.5).

The number of prescriptions did not differ practically significantly between the Northern Cape and Gauteng (d = 0.006 in 2006 & d = 0.02 in 2008). In both 2006 and 2008, there were no difference of practical significance between the Northern Cape and Gauteng province (refer to Tables A.3 to A.6, Appendix A).

4.2.4.1.2 Male patients

Males subsequently represented the smaller portion of the number of patients, prescriptions and items on the total database for both provinces (refer to Table 4.5).

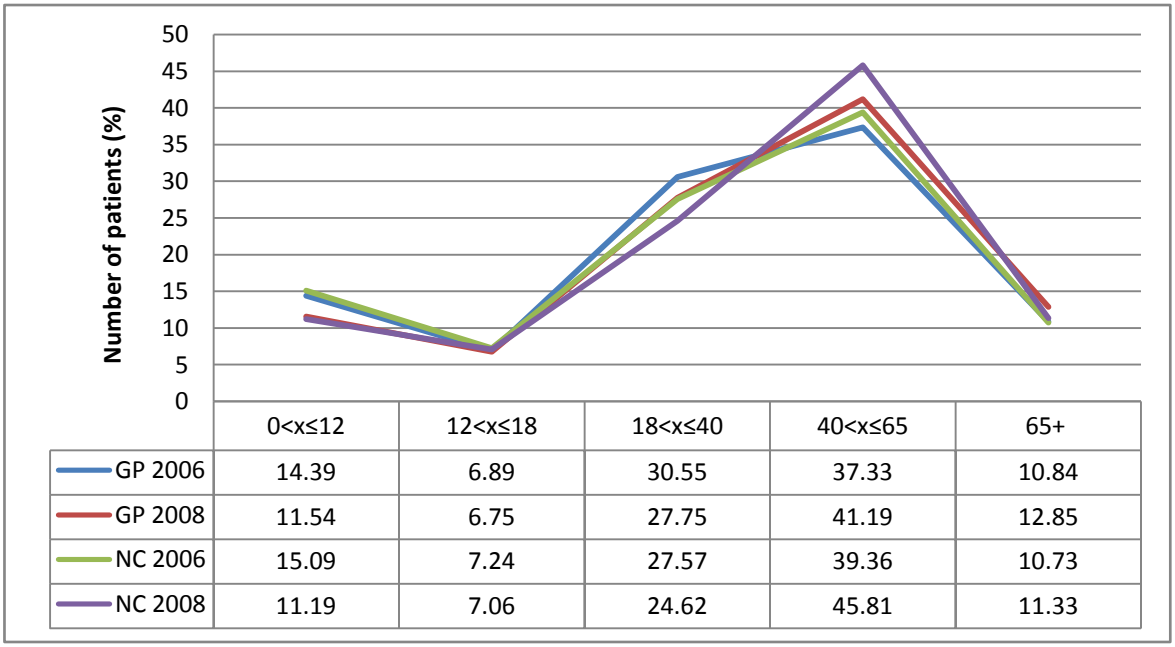
Difference in the average number of prescriptions per male patient showed no practical significance between the Northern Cape and Gauteng Province during 2006 (d = 0.005) and 2008 (d = 0.09). There was also no practically significant difference for the number of items per prescriptions between the two provinces in 2006 (d = 0.06) and 2008 (d = 0.07) (refer to Tables A.3 to A.6, Appendix A).

4.2.4.1.3 Unknown gender category

This category represented a small proportion of the data in the Northern Cape as well as in Gauteng Province. This group was merely part of the two provinces for 2006 and not for 2008, because all the claims had a gender status in 2008.

4.2.4.2 Analyses based on the patient's age: Northern Cape versus Gauteng Province

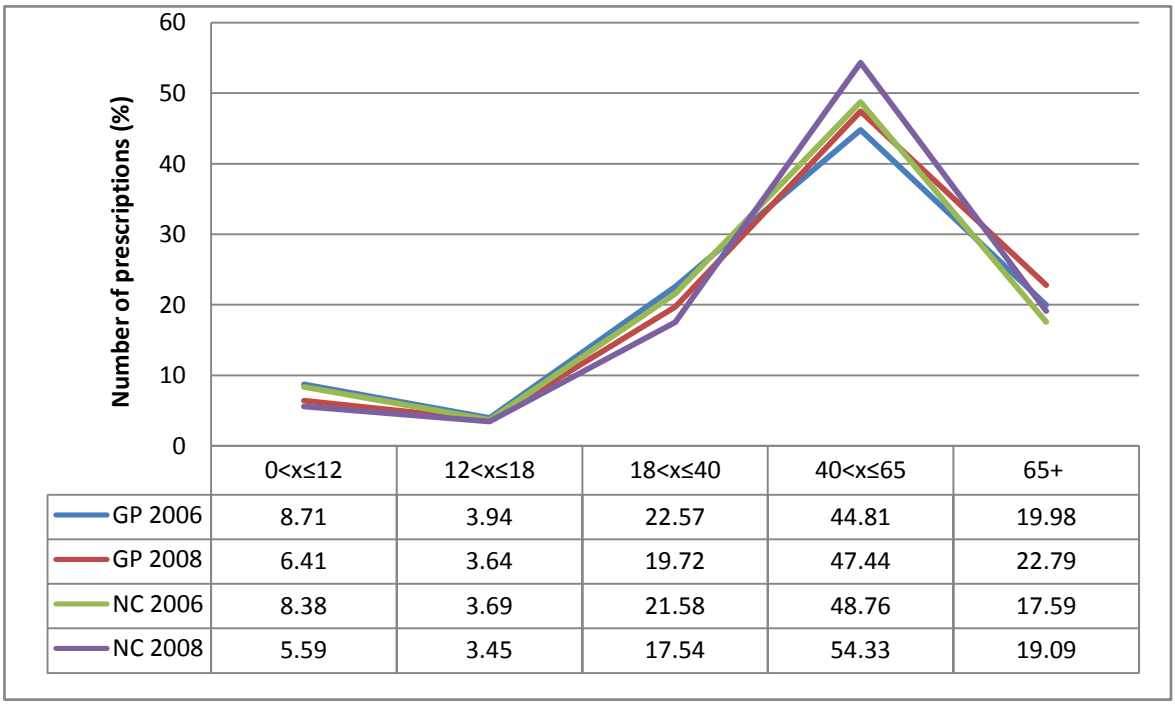
The analyses were done according to different age groups of the patients. In section 4.2.2 the different age groups are illustrated. Figure 4.8 illustrates the percentage distribution of the age groups in each province for the years 2006 and 2008. The prevalence for each age group was calculated from Table 4.4 by dividing the number of patients (n) by the total number of patients (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	14.39	6.89	30.55	37.33	10.84
GP 2008	11.54	6.75	27.75	41.19	12.85
NC 2006	15.09	7.24	27.57	39.36	10.73
NC 2008	11.19	7.06	24.62	45.81	11.33

Figure 4.8: Percentage distribution of the age groups in each province

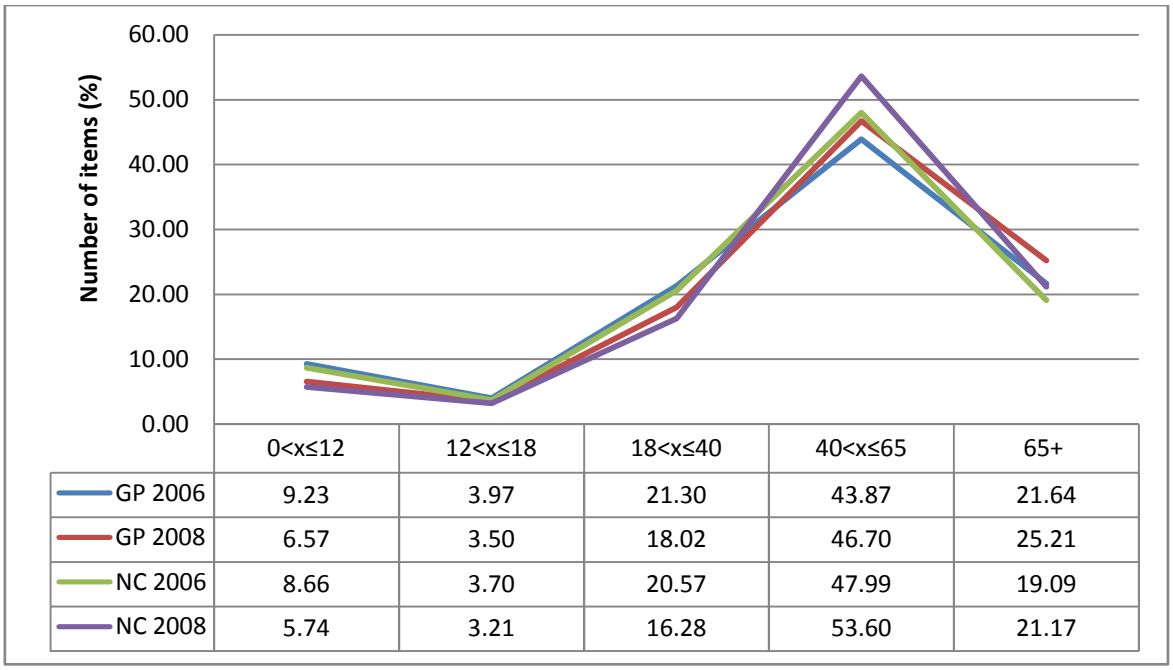
The following Figure 4.9 illustrated the percentage of prescriptions that were claimed by each age group for the years 2006 and 2008. The prevalence for each age group was calculated from Table 4.4 by dividing the number of prescriptions (n) by the total number of prescriptions (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	8.71	3.94	22.57	44.81	19.98
GP 2008	6.41	3.64	19.72	47.44	22.79
NC 2006	8.38	3.69	21.58	48.76	17.59
NC 2008	5.59	3.45	17.54	54.33	19.09

Figure 4.9: Percentage distribution of prescriptions in different age groups from two provinces

The following Figure 4.10 illustrates the percentage of items claimed for each age group. The prevalence for each age group was calculated from Table 4.4 by dividing the number of items (n) by the total number of items (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	9.23	3.97	21.30	43.87	21.64
GP 2008	6.57	3.50	18.02	46.70	25.21
NC 2006	8.66	3.70	20.57	47.99	19.09
NC 2008	5.74	3.21	16.28	53.60	21.17

Figure 4.10: Percentage distribution of items in different age groups from each province

Discussions on Figures 4.8, 4.9 and 4.10 follow in sections 4.2.4.2.1 to 4.2.4.2.5.

4.2.4.2.1 Age group 1

Age group 1 had the second lowest number of patients, prescriptions and items claimed in both provinces during 2006 and 2008 (Figure 4.8). The Gauteng and Northern Cape Province showed a decrease in the number of patients, prescriptions and items in age group 1 from 2006 to 2008.

In accordance with the higher number of patients in the Gauteng, the number of prescriptions and number of items claimed in this province were higher than the number of patients, prescriptions and items in Northern Cape Province (refer to Tables A.7 to A.9, Appendix A).

This higher number of items and prescriptions were, however, not practically significant (e.g. *d*-values) (refer to Tables A.3 to A.6, Appendix A).

4.2.4.2.2 Age group 2

According to Figures 4.8 to 4.10, age group 2 had the lowest number of patients, prescriptions and items claimed in 2006 and 2008. This applied to both provinces. The trends for the number of patients, prescriptions and items were relatively similar for the two

provinces during the two years. The Gauteng Province had a higher prevalence for patients, prescriptions and items claimed than the Northern Cape Province (refer to Tables A.7 to A.9, Appendix A).

The difference between the average number of prescriptions per patient in the Gauteng and the Northern Cape Province was not of practical significance. In 2006 and 2008, the average number of items per prescription did not differ enough between the Northern Cape and Gauteng for it to be practically significant (Tables A.3 to A.6, Appendix A).

4.2.4.2.3 Age group 3

Age group 3 had the second most patients and prescriptions that were claimed in the two provinces for both 2006 and 2008. There was a decrease in the percentage of patients, prescriptions and items in the Northern Cape and Gauteng Province from 2006 to 2008 (refer to Figure 4.8 to 4.10).

The *d*-values for the average number of prescriptions per patient and the average number of items per prescription were below 0.2. This means that the differences between the two provinces were not practically significant (refer to Tables A.3 to A.6, Appendix A).

4.2.4.2.4 Age group 4

Age group 4 had the highest number of patient, prescriptions and items claimed for 2006 and 2008 in the two provinces. This age group demonstrated an increase in claims during 2006 to 2008 according to Figures 4.8 to 4.10.

This age group had the highest prevalence for the number of patients, number of prescription and number of items in the Gauteng and Northern Cape provinces (refer to Tables A.7 to A.9, Appendix A).

The average number of prescriptions per patient revealed a small difference between the Northern Cape and Gauteng Province in 2008. The average number of items per prescriptions was not practically significant between the two provinces for both years (refer to Tables A.3 to A.6, Appendix A).

4.2.4.2.5 Age group 5

Approximately one in every ten patients that claimed prescriptions in the Northern Cape and Gauteng, were older than 65 years (Figures 4.8 to 4.10). This age group represented the second largest prevalence in the Gauteng and Northern Cape Province for both 2006 and 2008 (refer to Tables A.7 to A.9, Appendix A).

The *d*-values for the average number of prescriptions per patient and the average number of items per prescriptions were very small for both years. Given that the *d*-values were small, there was no practical significance between the Gauteng and Northern Cape Province (refer to Tables A.3 to A.6, Appendix A).

4.3 ANALYSIS OF THE BENZODIAZEPINES

The basic characteristics of the number of patients, prescriptions and items for 2006 and 2008 are indicated in Table 4.6.

Table 4.6: An overview of prescribing patterns of benzodiazepines for 2006 and 2008

	GENDER			**AGE (YEARS)**					**PRESCRIBERS**		
	Female	Male	Unknown	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+	GMP	Other	Psychiatrist
Number of patients											
N_{2006} = 142 462	95 844	46 539	79	745	1 776	33 438	73 545	32 958	-	-	-
N_{2008} = 102 758	69 304	33 454	-	466	1 211	19 934	54 333	26 814	-	-	-
Number of prescriptions											
N_{2006} = 402 903	279 733	122 977	193	985	2 187	54 331	195 387	150 013	333 128	49 643	20 132
N_{2008} = 324 747	226 935	97 812	-	645	1 613	35 207	154 814	132 468	265 463	41 071	18 210
Number of items											
N_{2006} = 424 907	295 492	129 220	195	1 017	2 248	56 468	206 350	158 824	350 507	51 980	22 420
N_{2008} = 343 563	240 374	103 189	-	688	1 651	36 857	164 138	140 229	279 926	43 257	20 377
Average number of prescriptions per patient											
2006 (2.83±3.26)	2.92±3.33	2.64±3.10	2.44±2.88	1.32±1.45	1.23±0.86	1.62±1.65	2.66±3.08	4.55±4.17	2.75±3.18	2.26±2.46	3.01±3.14
2008 (3.16±3.58)	3.27±3.66	2.92±3.39	-	1.38±1.58	1.33±1.19	1.77±2.00	2.85±3.29	4.94±4.36	3.06±3.48	2.54±2.76	3.46±3.55
Average number of items per prescriptions											
2006 (1.05±0.24)	1.06±0.24	1.05±0.23	1.01±0.10	1.03±0.21	1.03±0.18	1.04±0.20	1.06±0.24	1.06±0.25	1.05±0.23	1.05±0.22	1.11±0.35
2008 (1.06±0.24)	1.06±0.25	1.05±0.24	-	1.07±0.25	1.02±0.15	1.05±0.22	1.06±0.25	1.06±0.24	1.06±0.24	1.05±0.23	1.12±0.34

The benzodiazepine data represented 7.25% (n = 142 462) patients in 2006 compared to 7.97% (n = 102 758) patients in 2008 of the total database, signifying an increase of 0.72% (refer to Tables 4.6 & B.1, Appendix B). This means that nearly one patient out of every thirteen patients claimed benzodiazepine for the two years. In 2006 and 2008, 4.37% (n = 402 903) and 4.56% (n = 343 563) benzodiazepine prescriptions were claimed according to the total database. The number of benzodiazepine items that were claimed was 2.01% (n = 424 907) in 2006 and 2.09% (n = 343 563) in 2008 (refer to Table 4.6 & Table B.1, Appendix B). This means that of all the medicine items claimed, only one in every fifty medicine items was for a benzodiazepine.

The above-mentioned results indicated that the usage of benzodiazepines had increased from 2006 to 2008 although the number of benzodiazepine patients, benzodiazepine prescriptions and benzodiazepine items had decreased. The higher usage of benzodiazepines could be due to an increase of anxiety and insomnia caused by escalating crime rates (refer to paragraph 2.8).

The majority of prescriptions for benzodiazepines were prescribed by general medical practitioners (GMP), in 2006, 82.68% (n = 333 128) and 81.75% (n = 265 463) in 2008. The number of prescriptions prescribed by other practitioners and psychiatrists, was lower than the number of prescriptions prescribed by the general medical practitioners. The benzodiazepine items were also prescribed more often by general medical practitioners, 82.49% (n = 350 507) in 2006 and 81.48% (n = 279 926) in 2008 (Table 4.6 & A.16, Appendix A). This was comparable with the literature (refer to paragraph 2.8.11).

The difference between the average number of prescriptions per patient of the total database and the benzodiazepine data was 0.3 in 2006 and 0.34 in 2008. This indicated a small effect size for the difference between the two data sets (d = 0.2) (refer to Tables A.12 & A.13, Appendix A). The dissimilarity between the d-value of the average number of items per prescription on the total database and benzodiazepine data was 0.85 in 2006 and 0.84 in 2008 (refer to Tables A.14 & A.15, Appendix A). This difference between the average number of items per prescriptions was practically significant. The large difference is because benzodiazepines are mostly prescribed as a mono-therapy.

The difference in the average number of benzodiazepine prescriptions per patient and the average number of benzodiazepine items per prescription between the prescribers was not practically significant (refer to Table A.17, Appendix A).

4.3.1 Analysis based on days between refills of benzodiazepines

The following figure illustrates the number of days supplied for benzodiazepines. The time periods for days between refills were illustrated in section 3.7.6. The percentage of days between refills was calculated from Table B.3 (Appendix B) by dividing the number of items per time period (n) by the total number of items per time period (N) and then multiplying by 100.

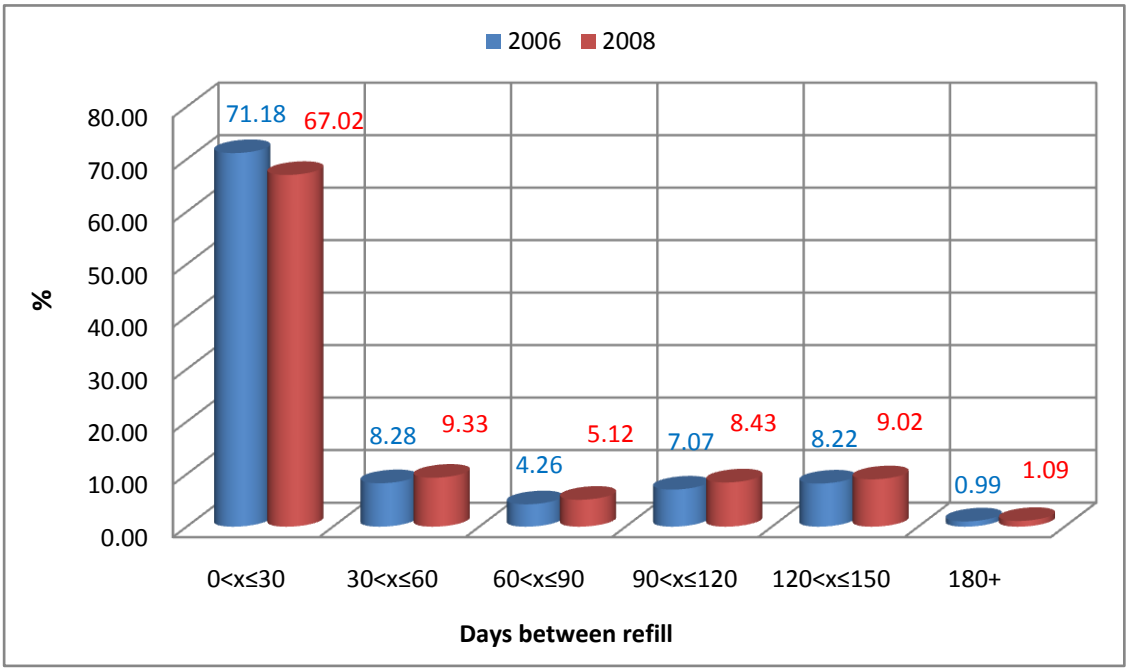


Figure 4.11: Percentage days between refills of the total number of benzodiazepine items

From Figure 4.11 it can be gathered that the majority (i.e., 71.18% in 2006 & 67.02% in 2008) of prescriptions claimed for benzodiazepines contained a number of items for a treatment period of 30 days or below. From 2006 to 2008, however, the percentage of prescriptions and items prescribed for longer prescription periods increased. The prescriptions claimed for longer than 30 days represented in total approximately 30% of all claims for benzodiazepines. In 2006 and 2008 the least benzodiazepines were given for 180 days and longer (Figure 4.11).

4.3.2 Analysis based on the gender of the patients whom claimed benzodiazepines

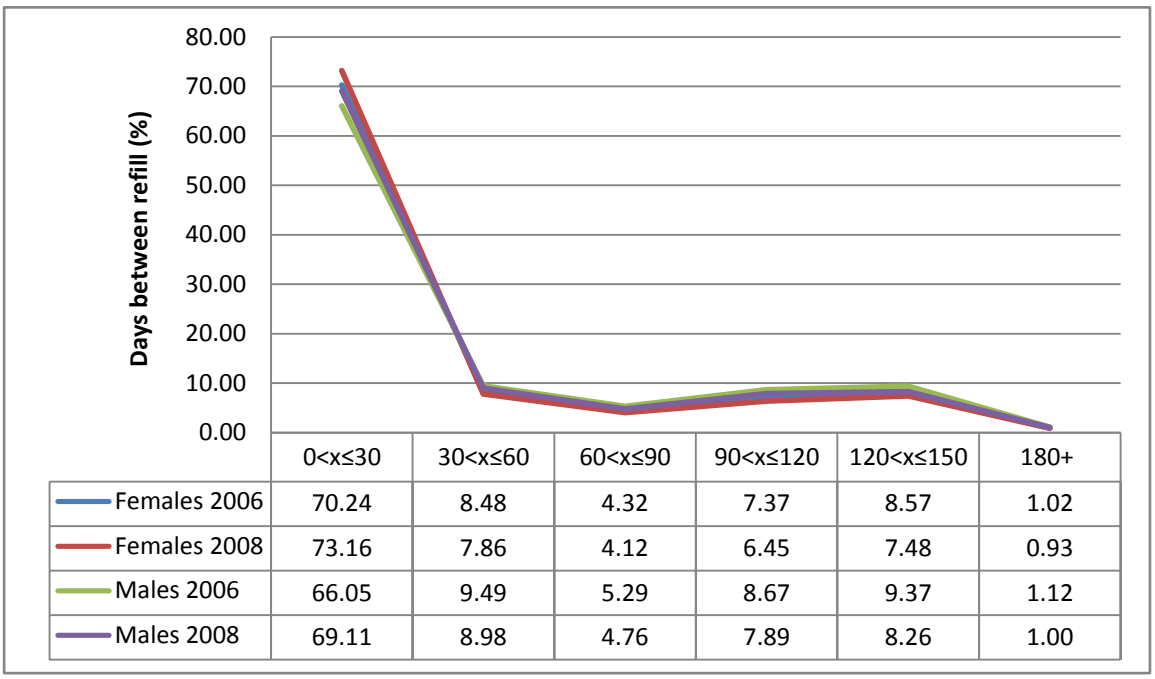
The gender was divided into three groups for the analysis, namely: female, male and unknown. The unknown category was used when the patient's gender was not indicated. Table 4.7 illustrates the percentage distribution represented by each gender group. The prevalence for each gender was calculated from Table 4.6 by dividing the number of patients that claimed benzodiazepine, benzodiazepine prescriptions and benzodiazepine items (n) by

the total number of patients that claimed benzodiazepine, benzodiazepine prescriptions and benzodiazepine items (N) for the study periods and then multiplying by 100.

Table 4.7: Percentage distribution of male and female patient who claimed benzodiazepines

		Percentage of gender of total benzodiazepine data (%)	
Year		2006	2008
Patients	Female	67.28	67.44
	Male	32.67	32.56
	Unknown	0.06	-
Prescriptions	Female	69.43	69.88
	Male	30.52	30.12
	Unknown	0.05	-
Items	Female	69.54	69.96
	Male	30.41	30.04
	Unknown	0.05	-

The following figure illustrates the percentage of days between refills presented by the females and males. The different days between refill time periods can be seen in section 3.7.6. The percentage of days between refills per gender was calculated from Table B.2 (Appendix B) by dividing the number of items per time period (n) by the total number of items per time period (N) and then multiplying by 100.



	0<x≤30	30<x≤60	60<x≤90	90<x≤120	120<x≤150	180+
Females 2006	70.24	8.48	4.32	7.37	8.57	1.02
Females 2008	73.16	7.86	4.12	6.45	7.48	0.93
Males 2006	66.05	9.49	5.29	8.67	9.37	1.12
Males 2008	69.11	8.98	4.76	7.89	8.26	1.00

Figure 4.12: Percentage days between refills of the different genders that claimed benzodiazepines items for 2006 and 2008

4.3.2.1 Female patients

Females that claimed benzodiazepine represented 67.28% (n = 95 844) of the total number of patients in the study population in 2006, and 67.44% (n = 69 304) in 2008. In 2006 and 2008 benzodiazepine prescriptions claimed by females represented 69.43% (n = 279 733) and 69.88% (n = 226 935) of the total benzodiazepine prescriptions. Benzodiazepine items claimed by the female gender represented 69.54% (n = 295 492) and 69.96% of all benzodiazepine items claimed respectively for 2006 and 2008 (n = 240 374) (refer to Tables 4.6 & 4.7, appendix A). To conclude, of all benzodiazepine items claimed respectively for 2006 and 2008, two thirds of all the patients who claimed benzodiazepine were female. This was similar to what was found in the literature (refer to paragraph 2.7.11).

The prevalence of the patients who claimed benzodiazepines for 2006 was 8.61% and for 2008 it was 9.52%. This means that nearly one in every fifteen female patients on the total database claimed benzodiazepine during the study periods. The prevalence of the benzodiazepine prescriptions was 5.05% in 2006 and 5.30% in 2008. In 2006 and 2008, the prevalence of benzodiazepine items represented 2.33% and 2.43% of the total data (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per female patient per year was 2.92±3.33 in 2006 compared to 3.27±3.66 in 2008. The average number of items per prescription claimed for female patients was 1.06±0.24 in 2006 and 1.06±0.25 in 2008. The *d*-value (0.096 & 0) for the difference in the time periods of average number of

benzodiazepine prescriptions per patient and average number of items per prescription did not differ in a practically significant way (refer to Tables A.10 & A.11, Appendix A).

The *d*–value for the average number of benzodiazepine prescriptions per patient for the year 2006 was 0.32 and it was 0.36 for 2008 between the benzodiazepine data and total database. The average number of benzodiazepine prescriptions per patient had a small effect size difference between the benzodiazepine data and the total database prescriptions per patient (refer to Tables A.12 & A.13, Appendix A). The average number of benzodiazepine items per prescriptions had a large effect size (d = 0.81 in 2006 and d = 0.79 in 2008). This indicated that the difference between the average number of items per prescriptions between the total database and benzodiazepine data was practically significant (refer to Tables A.14 & A.15, Appendix A).

Benzodiazepines were prescribed for a shorter time period to females than to their counterpart males. In 2008 the benzodiazepines were prescribed for a shorter time period to females than in 2006. Most of the benzodiazepines were prescribed for than 30 days and below (70.24% in 2006 and 73.16% in 2008). Only a few times were benzodiazepines prescribed for longer than 180 days (refer to Figure 4.12)

4.3.2.2 Male patients

Male patients represented a smaller portion of all patients on the benzodiazepine data than female patients. Males represented 32.67% (n = 46 539) in 2006 and 32.55% (n = 33 454) in 2008. In 2006, 30.52% (n = 122 977) of all benzodiazepine prescriptions were claimed by males, versus 30.12% (n = 97 812) in 2008. The number of benzodiazepine items claimed by males, was 30.41% (n = 129 220) in 2006 and 30.04% (n = 103 189) in 2008 (refer to Tables 4.6 & 4.7). This result with regard to males corresponded with results from the literature (refer to paragraph 2.8.11).

Male patients who received benzodiazepines represented 5.48% in 2006 and 5.98% in 2008 of all male patients on the database. This means that one in every eighteen male patients claimed benzodiazepines according to the total database during the study period. In 2006 and 2008 the prevalence of benzodiazepine prescriptions claimed by male patients on the total database was 3.35% and 3.45% of all the prescriptions claimed by male patients. The prevalence for benzodiazepine items claimed by male patients was 1.54% in 2006 and 1.58% in 2008 of all the items on the total database claimed by male patients (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per male patient was 2.64±3.10 in 2006 and 2.92±3.39 in 2008. The average number of benzodiazepine items per prescription

claimed by the male gender was 1.05±0.23 in 2006 and 1.05±0.24. There was no practically significant difference between the average number of benzodiazepine prescriptions per patient and the average number of benzodiazepine items per prescription for the two years (d = 0.083 & 0) (refer to Tables A.10 & A.11, Appendix A).

The practical significance was small between the average number of prescription per patient and the claims on the total database, and the average number of benzodiazepine prescriptions per patient according to the benzodiazepine data (*d* = 0.3 in 2006 & *d* = 0.34 in 2008) (refer to Tables A.12 & A.13, Appendix A). However, the average number of benzodiazepine items per prescription according to the benzodiazepine data and the average number of items per prescription according to the total database differed practically significantly (*d* = 0.85 in 2006 & *d* = 0.83 in 2008) (refer to Tables A.14 & A.15, Appendix A).

The days between refill was longer for male patients who claimed benzodiazepines than female patients. Similar to females, the days between refill for the prescribed benzodiazepines were longer in 2006 than in 2008. Only a small number of benzodiazepines were prescribed for longer than 180 days for both study periods (refer to Figure 4.12).

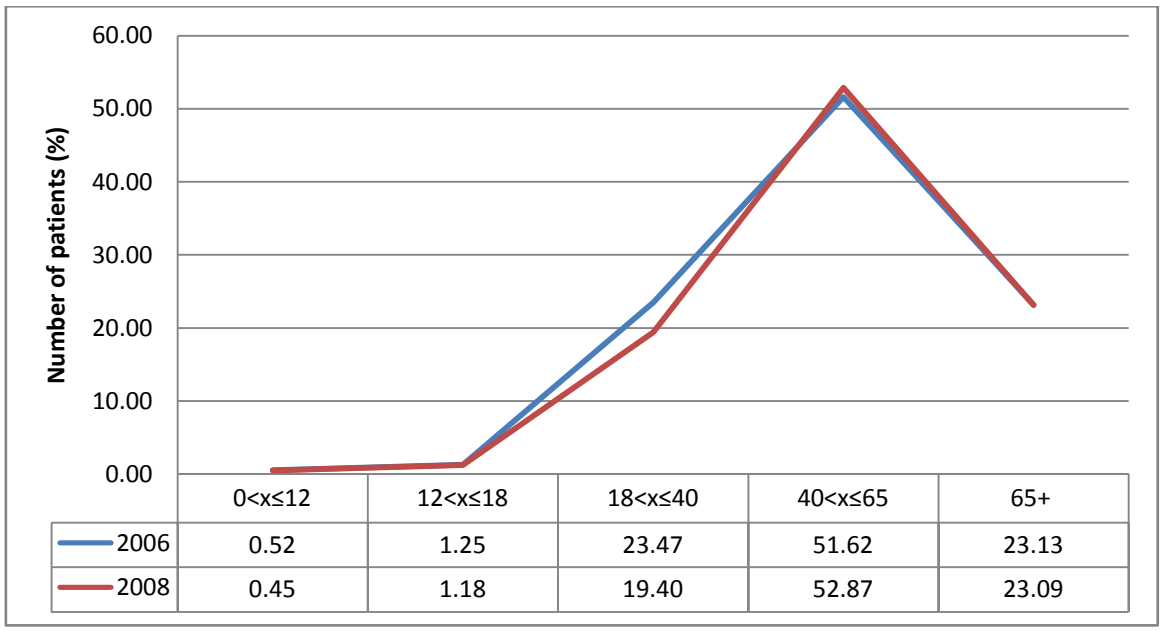
4.3.2.3 Unknown patients

This category represented a small portion of the benzodiazepine data. This category was only part of the benzodiazepine data for 2006 and not for 2008, because all the claims had a gender status in 2008. Unknown patients represented 0.05% (n = 193) of all benzodiazepine prescriptions in 2006. The number of items claimed by the unknown category was 0.05% (n = 195) in 2006.

The average number of prescriptions per patient was 2.44±2.88 and the average number of items per prescription was 1.01±0.1.

4.3.3 Analysis based on the patient's age of those that used benzodiazepines

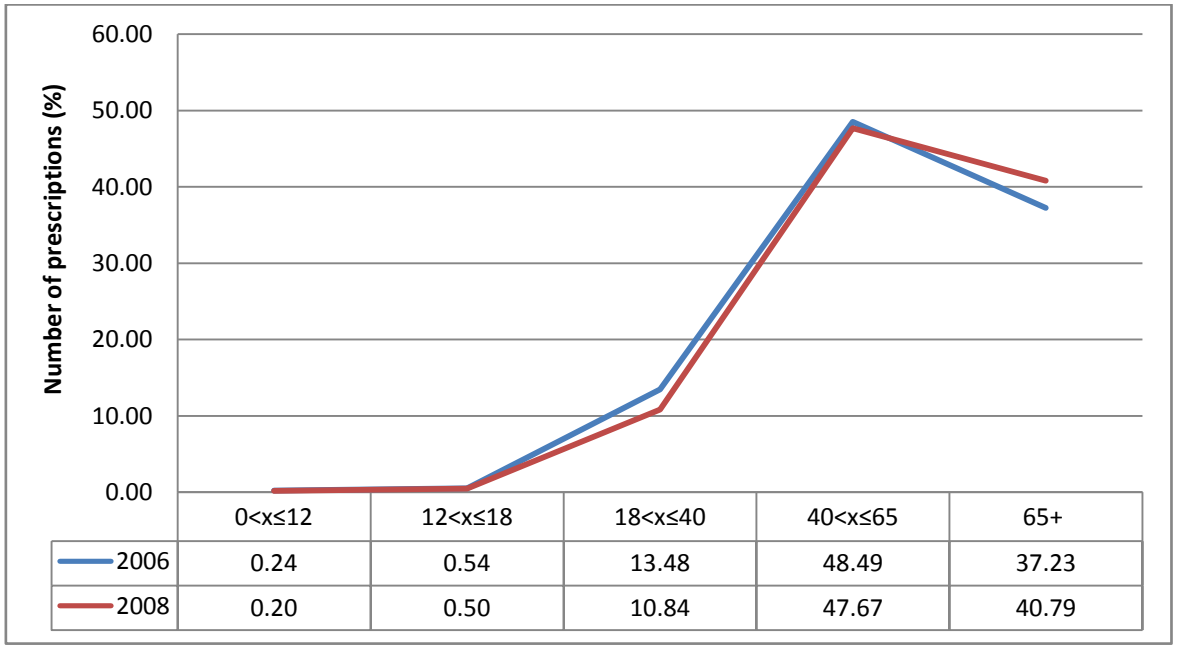
The analyses were done according to different age groups of the patients (refer to paragraph 4.2.2). Figure 4.13 illustrates the percentage of patients who claimed benzodiazepine according to age group. The prevalence for each age group was calculated from Table 4.6 by dividing the number of patients that claimed benzodiazepine (n) by the total number of patients on the benzodiazepine data (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2006	0.52	1.25	23.47	51.62	23.13
2008	0.45	1.18	19.40	52.87	23.09

Figure 4.13: Prevalence distribution of the different age groups of those who used benzodiazepine

The following figure (4.14) illustrates the percentage of benzodiazepine prescriptions that were claimed by each age group for the years 2006 and 2008. The prevalence for each age group was calculated from Table 4.6 by dividing the number of benzodiazepine prescriptions (n) by the total number of prescriptions on the benzodiazepine data (N) for the study periods and then multiplying by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2006	0.24	0.54	13.48	48.49	37.23
2008	0.20	0.50	10.84	47.67	40.79

Figure 4.14: The percentage distribution of benzodiazepine prescriptions claimed by each age group.

The following figure (4.15) illustrates the percentage of items that each age group claimed. The prevalence for each age group was calculated from Table 4.6 by dividing the number of benzodiazepine prescriptions (n) by the total number of prescriptions on the benzodiazepine data (N) for the study periods and then multiplying by 100.

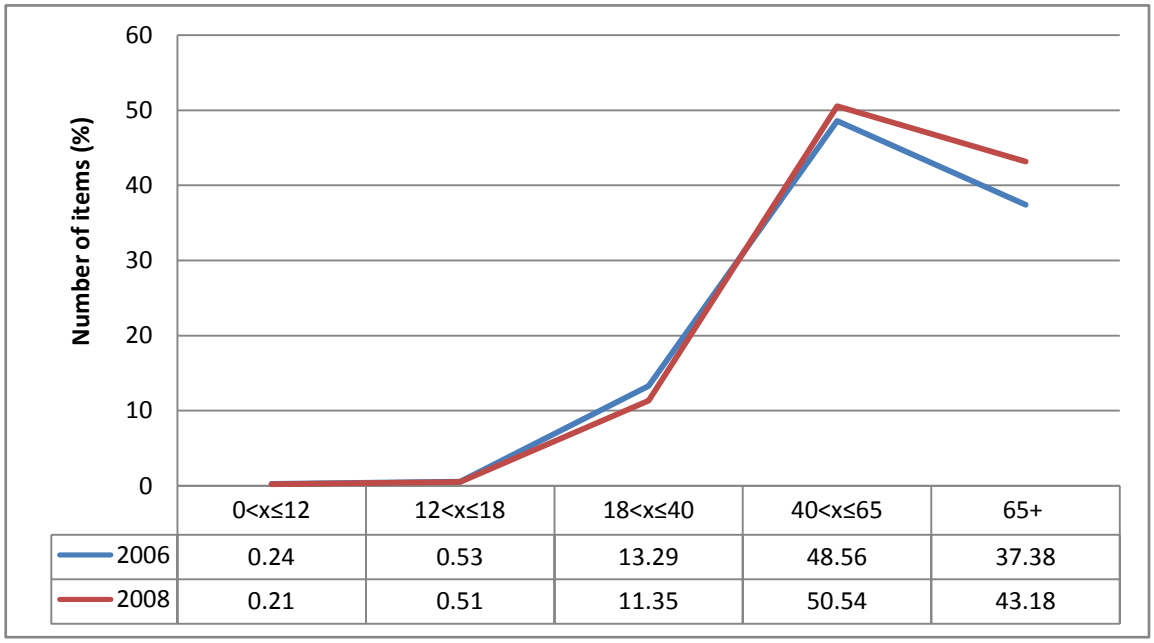


Figure 4.15: The percentage of benzodiazepine items claimed by each age group.

The following table illustrates the percentage of days between dates of supply of each age group for 2006 and 2008. The percentage of days between refills per age group was calculated from Table B.2 (Appendix B) by dividing the number of items per time period (n) by the total number of items per time period (N). The total obtained was multiplied by 100.

Table 4.8: Number of days supplied according to age groups.

		Age groups				
Number of days supply	**Year**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
0<x≤30	2006	94.39%	94.87%	88.46%	73.88%	47.81%
	2008	94.48%	93.56%	85.66%	71.51%	46.06%
30<x≤60	2006	1.91%	3.11%	5.49%	8.23%	11.34%
	2008	1.02%	2.80%	6.38%	8.89%	12.28%
60<x≤90	2006	0.51%	0.78%	2.05%	4.15%	6.79%
	2008	0.61%	1.36%	2.64%	4.73%	7.56%
90<x≤120	2006	1.66%	0.78%	2.55%	6.41%	13.08%
	2008	1.02%	1.36%	3.27%	7.21%	14.15%
120<x≤150	2006	0.89%	0.47%	1.37%	6.55%	18.62%
	2008	2.04%	0.83%	1.81%	6.84%	17.81%
180 +	2006	0.64%	0.00%	0.07%	0.78%	2.36%
	2008	0.82%	0.08%	0.23%	0.81%	2.14%

Table 4.8 shows that benzodiazepines duration of use increased with increasing age.

Figures 4.13, 4.14, 4.15 and Table 4.8 will be discussed in sections 4.3.3.1 to 4.3.3.5.

4.3.3.1 Age group 1

Patients from age group 1 represented 0.52% (n = 745) in 2006 and 0.45% (n = 466) in 2008 of all the patients who claimed benzodiazepines (Figure 4.13 & Table 4.8). Patients between birth and 12 years accounted for 0.26% and 0.31% of all benzodiazepines claimed by them in 2006 and 2008 according to the total database (refer to Table B.1, Appendix B). The percentage of benzodiazepine prescriptions claimed by this age group for 2006 was 0.24% (n = 985) and 0.20% (n = 645) for 2008 (Figure 4.14). In 2006 and 2008 was the prevalence 0.12% and 0.14% for benzodiazepine prescriptions claimed according to the total database (refer to Table B.1). The number of benzodiazepine items represented 0.24% (n = 1 017) and 0.21% (n = 688) of the total number of benzodiazepine items for 2006 and 2008 respectively (Figure 4.22). The prevalence of benzodiazepine items was 0.05% in 2006 and 0.06% in 2008 of all items on the total database (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per patient between the ages of 0 to 12 years was 1.32±1.45 in 2006 and 1.38±1.58 in 2008. Based on Table A.10 (Appendix A), there was no practically significant difference in the average number of prescriptions per patient between these two years. The difference between the total database and the benzodiazepine study population with regard to the average number of prescriptions per patient, showed *d*-values of 0.53 in 2006 and 0.52 in 2008. This indicates a medium effect size (refer to Tables A.12 & A.13, Appendix A). The average number of items per prescription per year was 2.47±1.34 in 2006 and 2.40±1.34 in 2008 for this group. The *d*-value was 0.05 which means that there was not a practical significant difference between the two years, but there was a practical significant difference between the average number of items per prescription per year from the total database and the average number of benzodiazepine items per prescription from the benzodiazepine data. The effect size between the difference of the total data and benzodiazepine data's number of items per prescription was relatively large (d= 1.08 in 2006 & d = 0.99 in 2008) (refer to Tables A.11, A.13 & A.14, Appendix A).

Most prescriptions (i.e., 94.39% in 2006 & 94.48% in 2008) claimed for patients aged birth to 12 years, were for a period of below 30 days (refer to Table 4.8).

4.3.3.2 Age group 2

According to Figure 4.13, only 1.25% (n = 1 776) and 1.18% (n = 1 211) indicated the percentage of patients (between the ages of 12 and 18 years) that claimed benzodiazepines

in 2006 and 2008. Age group 2 represented 1.28% in 2006 and 1.30% in 2008 of all the patients who claimed benzodiazepines according to the total database (refer to Table B.1, Appendix B). The number of benzodiazepine prescriptions claimed by this group, represented 0.54% (n = 2 186) in 2006 and 0.50% (n = 1 613) in 2008 respectively (Figure 4.14). The number of benzodiazepine prescriptions accounted for 0.58% of all benzodiazepines claimed by this age group according the total database in 2006 and 0.60% of those in 2008 (refer to Table B.1, Appendix B). The number of benzodiazepine items claimed for patients between the ages of 12 and 18 years, was 0.53% (n = 2 248) in 2006 and 0.51% (1 651) in 2008 (Figure 4.15). The prevalence was 0.25% in 2006 and 0.27% in 2008 for benzodiazepine items claimed according to the total database (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per patient for this group was 2.72±2.86 in 2006 and 2.89±3.12 in 2008. The average number of benzodiazepine items per prescription for patients between the ages of 12 and 18 years was 2.34±1.33 in 2006 and 2.25±1.31 in 2008. The *d*-values for the average number of benzodiazepine prescriptions per patient and the average number of benzodiazepine items per prescription indicated 0.055 and 0.068, respectively (refer to Tables A.10 & A.11, Appendix A), indicating a insignificant difference for practical reasons.

The *d*-values were 0.52 in 2006 and 0.5 in 2008 for the difference between the average number of prescriptions per patient per year and the average number of benzodiazepine prescriptions per patient. This indicated a medium effect size (refer to Tables A.12 & A.13, Appendix). The effect size between the average number of benzodiazepine items and average number of items per prescription was large (d = 0.99 in 2006 & d = 0.94 in 2008). The difference in the average number of items per prescription and the average number of benzodiazepine items per prescription, can therefore be regarded as practically significant (refer to Tables A.14 & A.15, Appendix A).

Patients that belonged to this age group had most of their prescriptions for benzodiazepine prescribed for a period of 30 days (94.87% in 2006 & 93.56% in 2008) (Table 4.8).

4.3.3.3 Age group 3

Patients in age group 3 represented 23.47% (n = 33 438) in 2006 of all patients who received benzodiazepines and in 2008 it was 19.40% (n = 19 934) (Figure 4.13). The prevalence was 5.75% in 2006 and 5.86% in 2008 for patients who claimed benzodiazepines in this age group according to the total database (refer to Table B.1, Appendix B). The number of benzodiazepine prescriptions between the years of 18 to 40 was 13.48% (n = 54 331) in 2006 and 10.84% (n = 35 207) in 2008 (Figure 4.14). Prescriptions for these patients

accounted for 2.66% in 2006 and 2.64% in 2008 for all benzodiazepine prescriptions claimed according to the total database (refer to Table B.1, Appendix B). The number of benzodiazepine items represented 13.29% (n = 55 468) and 11.25% (n = 36 857) for 2006 and 2008 (Figure 4.15). The prevalence of benzodiazepine items claimed from the total database for 2006 and 2008 indicated 1.27% and 1.29% (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per patient for 2006 and 2008 was 3.52±4.32 and 3.92±4.67. The difference between the two years was not practically significant (refer to Table A.10, Appendix A). The *d*-values between the average number of prescriptions and average number of benzodiazepine prescriptions per patient were 0.44 in 2006 and 0.46 in 2008. This implicates a medium effect size. The average number of benzodiazepine items per prescription for this group was 2.18±1.31 and 2.14±1.30. The *d*-value (0.031) illustrated that the difference between 2006 and 2008 was practically insignificant (refer to Table A.11, Appendix A). The number of items per prescription per year differed practically significantly from the average number of benzodiazepine items per prescription per year (*d* = 0.87 in 2006 & *d* = 0.84 in 2008) (refer to Tables A.14 & A.15, Appendix A).

The majority of these patients were given benzodiazepines for a period of 30 days (88.46% in 2006 & 85.66%) (refer to Table 4.8).

4.3.3.4 Age group 4

The number of patients in this group represented 51.62% (n = 73 545) in 2006 and (n =54 333) in 2008 of the total number of patients who received benzodiazepines (Figure 4.13). The patients, who claimed benzodiazepine that belonged to this age group, represented 9.93% in 2006 and 10.18% in 2008 of all the patients in this age group that claimed according to the total database (refer to Table B.1, Appendix B). The total number of benzodiazepine prescriptions claimed by this group was 48.49% (n = 195 387) in 2006 and 47.67% (n = 154 814) in 2008 (Figure 4.14). The benzodiazepine prescriptions had a prevalence of 4.78% in 2006 and 4.62% in 2008, claimed according to the total database (refer to Table B.1, Appendix B). The total number of benzodiazepine items claimed for patients in age group 4 represented 48.56% (n = 206 350) in 2006 and 50.54% (n = 164 138) in 2008 (Figure 4.15). The prevalence for benzodiazepine items, claimed according to the total database, among this age group for 2006 and 2008 was 2.24% and 2.14% (refer to Table B.1, Appendix B). The results above corresponded with the results according to literature (section 2.7.11).

The average number of benzodiazepine prescriptions per patient per year was 5.52±6.78 in 2006 and 6.29±7.18 in 2008. The *d*-value (0.11) was practically insignificant for average

number of benzodiazepine prescriptions per patient per year (refer to Table A.10, Appendix A). The difference between the average number of prescriptions per patient and the average number of benzodiazepine prescriptions per patient had a medium effect size (*d* = 0.42 in 2006 *d* = 0.48 in 2008) (refer to Tables A.12 & A.13, Appendix A). In 2006 and 2008 the average number of benzodiazepine items per prescription amounted to 8.58±9.46 and 9.89±10.03. The *d*-value (0.0197) for the difference between two years was of not practical significance (refer to Table A.11, Appendix A). The average number of items per prescription and the average number of benzodiazepine item per prescription differed practically significantly (the *d*-values were larger than 0.8) (refer to Tables A.14 & A.15, Appendix A).

Almost a quarter of the patients of this age group received their benzodiazepines for the time period of 30 days (refer to Table 4.8). This was relatively less than the previous three age groups.

4.3.3.5 Age group 5

In 2006 and 2008, the number of patients that claimed benzodiazepines was 23.13% (n = 32 958) and 26.09% (n = 26 814) (Table 4.13). Almost one in every seven patients older than 65 years claimed benzodiazepines according to the total database (refer to Table B.1, Appendix B). The number of benzodiazepine prescriptions claimed by the group older than 65 years represented 37.23% (n = 150 013) in 2006 and 40.67% (n = 132 468) in 2008 (Figure 4.14). The prevalence for benzodiazepine prescriptions claimed on the total database was 7.91% in 2006 and 7.74% in 2008 (refer to Table B.1, Appendix B). The number of items represented 37.38% (n = 158 824) and 43.18% (n = 140 229) of the total number of items claimed in 2006 and 2008 respectively. The number of benzodiazepine items claimed by this age group represented 3.47% in 2006 and 3.31% in 2008 of all benzodiazepine items claimed on the total database (refer to Table B.1, Appendix B).

The average number of benzodiazepine prescriptions per patient per year was 8.58±9.46 in 2006 and 9.89±10.03 in 2008. The *d*-value (0.13) was not practically significant for the difference between 2006 and 2008 (refer to Table A.10, Appendix A). A medium effect size was noticeable from Tables A.12 and A.13 (Appendix A) between the average number of prescription and average number of benzodiazepine prescriptions per patient in 2006 and 2008. The average number of benzodiazepine items per prescription was 2.41±1.80 and 2.48±1.87. The *d*-value (0.0197) was practically insignificant for the difference between the two years (refer to Table A.11, Appendix A). In 2006 and 2008 the *d*-value for the average number of items per prescriptions and average number of benzodiazepine items per prescriptions came to 0.75 in 2006 and 0.76 in 2008. The difference between these values presented a large effect size which means the difference was practically significant (refer to Tables A.14 & A.15, Appendix A).

In this age group less than half of the patients that claimed benzodiazepines received their benzodiazepines for 30 days (47.81% in 2006 versus 46.06% in 2008). In 2006, 18.62% of the patients that claimed benzodiazepines in this age group received their benzodiazepines for 150 days and in 2008 it was 17.81% (Table 4.8).

4.3.4 Analysis of the usage of benzodiazepines in the Gauteng and Northern Cape Province

In this section, the prescribing patterns of benzodiazepines in two provinces in 2006 and 2008 are described. Tables 4.9 and 4.10 provide an overview of the provinces' prescribing patterns of benzodiazepines for the two years.

Table 4.9: Prescribing patterns of benzodiazepine in the Gauteng Province for 2006 and 2008

	GENDER			AGE (YEARS)					PRESCRIBERS		
	Female	**Male**	**Unknown**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**	**GMP**	**Other**	**Psychiatrist**
Number of patients											
n_{2006} = 59 209	39 809	19 365	35	305	733	14 761	30 393	13 017	-	-	-
n_{2008} = 43 713	29 445	14 268	0	192	521	9 102	23 206	10 692	-	-	-
Number of prescriptions											
n_{2006} = 173 723	120 069	53 571	83	391	915	25 401	87 448	59 567	136 827	26 330	10 566
n_{2008} = 145 148	101 299	43 849	0	268	718	17 587	73 114	53 461	112 731	22 447	9 969
Number of items											
n_{2006} = 184 500	127 570	56 845	85	397	949	26 636	93 167	63 351	144 970	27 687	11 843
n_{2008} = 155 044	108 358	46 686	0	294	732	18 596	78 353	57 069	119 844	23 867	11 332
Average number of prescriptions per patient											
2006 (2.93±3.32)	3.02±3.37	2.77±3.21		1.29±1.22	1.25±0.86	1.72±1.81	2.88±3.26	4.58±4.13	2.83±3.20	2.31±2.47	3.01±3.11
2008 (3.32±3.66)	3.44±3.74	3.07±3.48		1.40±1.72	1.38±1.27	1.93±2.23	3.15±3.52	5±4.34	3.18±3.54	2.65±2.84	3.44±3.51
Average number of items per prescriptions											
2006 (1.06±0.25)	1.06±0.25	1.06±0.25		1.01±0.11	1.04±0.21	1.05±0.22	1.07±0.26	1.06±0.26	1.06±0.25	1.05±0.24	1.12±0.35
2008 (1.07±0.26)	1.07±0.27	1.06±0.26		1.10±0.30	1.02±0.14	1.06±0.24	1.07±0.27	1.07±0.26	1.06±0.26	1.06±0.26	1.14±0.36

Table 4.10: Prescribing patterns of benzodiazepine in the Northern Cape Province for 2006 and 2008

	GENDER			AGE (YEARS)					PRESCRIBERS		
	Female	**Male**	**Unknown**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**	**GMP**	**Other**	**Psychiatrist**
Number of patients											
n_{2006} = 2 485	1 684	801	0	15	28	593	1 369	480	-	-	-
n_{2008} = 1 719	1 162	557	0	18	25	324	979	373	-	-	-
Number of prescriptions											
n_{2006} = 6 354	4 355	1 999	13	32	30	936	3 268	2 088	6 079	216	59
n_{2008} = 4 768	3 254	1 514	0	26	29	544	2 412	1 757	4 550	165	53
Number of items											
n_{2006} = 6 665	4 574	2 091	0	32	30	957	3 428	2 218	6 378	224	63
n_{2008} = 5 027	3 416	1 611	0	33	34	562	2 543	1 855	4 793	174	60
Average number of prescriptions per patient											
2006 (2.56±3)	2.59±3.07	2.50±2.86		2.13±3.44	1.07±0.26	1.58±1.68	2.39±2.65	4.35±4.28	2.55±2.99	1.98±2.53	1.6±0.96
2008 (2.77±3.34)	2.80±3.42	2.72±3.18	-	1.44±1.42	1.16±0.47	1.68±2.76	2.46±2.89	4.71±4.20	2.76±3.34	2.12±2.41	2.12±1.54
Average number of items per prescriptions											
2006 (1.05±0.22)	1.05±0.22	1.05±0.21		1.0±0.0	1.0±0.0	1.02±0.14	1.05±0.22	1.06±0.24	1.05±0.22	1.04±0.19	1.07±0.25
2008 (1.05±0.23)	1.05±0.22	1.06±0.24	-	1.27±0.45	1.17±0.38	1.03±0.18	1.05±0.23	1.06±0.23	1.05±0.23	1.06±0.23	1.13±0.34

The number of patients that claimed benzodiazepines in the Northern Cape (NC) was lower than the number of patients that claimed benzodiazepines in the Gauteng (GP). However, the percentage of patients that claimed benzodiazepines in each province was almost equivalent for 2006 (GP = 7.91% versus NC = 8.96%) and 2008 (GP = 8.47% versus NC = 9.51%) (refer to Table A.30, Appendix A). The percentages of benzodiazepine prescriptions claimed per province were 4.79% (n = 173 723) in Gauteng compared to 4.62% (n = 6 354) in the Northern Cape for 2006, and 5.10% (n = 145 148) in Gauteng versus 4.30% (n = 4 768) in the Northern Cape for 2008. Thus the difference between the two provinces for 2006 and 2008 was relatively small (refer to Table A.31, Appendix A). The percentage of benzodiazepine items claimed per province Gauteng was 2.16% (n = 184 500) for 2006 and it was 2.31% (n = 155 044) for 2008. In the Northern Cape it was 2.10% (n = 6 665) in 2006 and 1.98% (n = 5 027) in 2008 (refer to Table A.32, Appendix A).

General medical practitioners prescribed most of the benzodiazepine prescriptions in both NC and GP (refer to Table A.18, appendix A). In the Northern Cape the benzodiazepine prescriptions prescribed by the general medical practitioners represented 95.67% (n = 6 079) in 2006 and 95.43% (n = 4 550) in 2008. The general medical practitioners in the Gauteng prescribed 78.76% (n = 136 827) in 2006 and 77.67% (n = 112 731) in 2008 of benzodiazepine prescriptions. The number of benzodiazepine prescriptions prescribed by other prescribers was higher in the Gauteng than the Northern Cape Province (15.16% in GP for 2006 versus 3.40% in NC for 2006 & 15.47% of GP versus 3.46% of NC in 2008). The number of benzodiazepine prescriptions prescribed by psychiatrists and claimed in the Northern Cape, was only 0.93% (n = 59) in 2006 and 1.11% (n =53) in 2008. The percentage of benzodiazepine items per prescriptions prescribed by the different prescribers was similar to the number of benzodiazepine prescriptions in the Gauteng and Northern Cape for both years (refer to Table A.18, Appendix A).

The Gauteng and Northern Cape Province had a small practical insignificant difference between the average number of benzodiazepine prescriptions per patient for 2006 and 2008 (d = 0.11 for 2006 and d = 0.15 for 2008) (refer to Tables A.23 & A.24, Appendix A). The difference between the two provinces' average numbers of benzodiazepine items per prescriptions was practical insignificant for both years (refer to Tables A.25 & A.26, Appendix A).

The difference between the average numbers of benzodiazepine prescriptions per patient of the different prescribers was practically insignificant for both years (refer to Tables A.19 to A.21, appendix A). The Gauteng and Northern Cape did differ with regard to the average number of benzodiazepine prescriptions per patient prescribed by psychiatrists (refer to Table A.22, appendix A). The dissimilarity between the two provinces gave only a medium

effect. This means that there were relatively more benzodiazepine prescriptions prescribed to the patients by psychiatrists in the Gauteng than in the Northern Cape Province.

4.3.4.1 Analysis based on the gender of the patients who claimed benzodiazepines

The investigation of the gender was conducted by dividing the gender group into three groups, namely: female, male and unknown. In 2006, the gender of a number of patients, prescriptions and items were not specified and these were placed under the category of unknown. Table 4.26 illustrates the percentage of benzodiazepine claims stratified by gender for the Gauteng and Northern Cape Province during study period. The prevalence for each gender was calculated from Table 4.9 and 4.10 by dividing the number of patients that claimed benzodiazepine, benzodiazepine prescriptions and benzodiazepine items (n) by the total number of patients that claimed benzodiazepine, benzodiazepine prescriptions and benzodiazepine items (N) in the Gauteng and Northern Cape Province for the study periods and then multiplied by 100.

Table 4.11: Percentage distribution of gender groups that claimed benzodiazepines in the Gauteng and Northern Cape Province for 2006 and 2008.

		Percentage of gender in total database (%) *			
Provinces		GP		NC	
Year		2006	2008	2006	2008
Patients	Female	67.24	67.36	67.77	67.60
	Male	32.71	32.64	32.23	32.40
	Unknown	0.06	-	-	-
Prescriptions	Female	69.12	69.79	68.54	68.25
	Male	30.84	30.21	31.46	31.75
	Unknown	0.05	-	0.2	-
Items	Female	69.14	69.89	68.63	67.95
	Male	30.81	30.11	31.37	32.05
	Unknown	0.05	-	-	-

4.3.4.1.1 Female patients

The percentage of benzodiazepine claims by the female patients demonstrated a similar trend in Northern Cape Province, as compared to Gauteng Province. More females patients

received benzodiazepines in 2006 and 2008 compared to male counterparts. Almost one in every ten females in the Gauteng Province (9.45% in 2006 versus 10.17% in 2008) and Northern Cape (10.95% in 2006 versus 12.01% in 2008) claimed benzodiazepines per year (refer to Table A.30, Appendix A). The percentage of patients that claimed benzodiazepine per province according to the total data of each province was almost the same for the Gauteng and Northern Cape during 2006 and 2008 (refer to Table A.30, Appendix A). The number of benzodiazepine prescriptions and number of benzodiazepine items were both more often claimed by the females than males in Gauteng and Northern Cape Province according to the total data per province (Table 4.11). In 2006 was the percentage of benzodiazepine prescriptions claimed per province was 5.51% (n_{GP} = 120 069) and 5.32% (n_{NC} = 4 355) and in 2008 it was 5.92% (n_{GP} = 101 299) and 5.06% (n_{NC} = 3 254) (Table A.31). The benzodiazepine items that were claimed in these two provinces were 2.49% (n_{GP} = 127 570) and 2.69% (n_{NC} = 108 358) in 2006 and 2.39% (n_{GP} = 4 574) and 2.29% (n_{NC} = 3 416) in 2008 (Table A.32). These two provinces had relatively similar percentages of benzodiazepine items per province.

The average number of benzodiazepine prescriptions per patient per year had a relatively small practical significance between the Northern Cape and Gauteng for both years (*d* = 0.13 in 2006 & *d* = 0.17 in 2008) (refer to Tables A.23 & A.24, Appendix A). There was no practical significance for the difference in the average number of benzodiazepine items per prescription between the Northern Cape and Gauteng province in 2006 and 2008 (refer to Table A.25 & A.26, Appendix A).

4.3.4.1.2 Male patients

Male patients that claimed benzodiazepines represented a smaller percentage than the female patients that claimed benzodiazepine for both the Northern Cape and Gauteng Province for the years 2006 and 2008. The prevalence of the number of patients that claimed benzodiazepine per province calculated 5.97% (n = 19 365) in 2006 and 6.31% (n = 14 268) in 2008 for Gauteng Province (refer to Table A.30, Appendix A). The prevalence of the number of patients that claimed benzodiazepine per province was relatively the same for Northern Cape (n = 801 in 2006 & n = 557 in 2008) (refer to Table A.30, Appendix A). The percentage of benzodiazepine prescriptions and benzodiazepine items claimed was lower for the males in the two provinces during the two years (Tables 4.9 & 4.10). The prevalence of benzodiazepine prescriptions and items per province did not differ much between the two provinces (refer to Tables A.31 & A.32, Appendix A).

The difference in the average number of benzodiazepine prescriptions per male patient per year was not practical insignificant between the Northern Cape and Gauteng Province for 2006 and 2008 (refer to Tables A.23 & A.24, Appendix A). The difference in the average

number of benzodiazepine items per prescription between the two provinces for 2006 and 2008 was practically insignificant (refer to Tables A.25 & A.26, Appendix A).

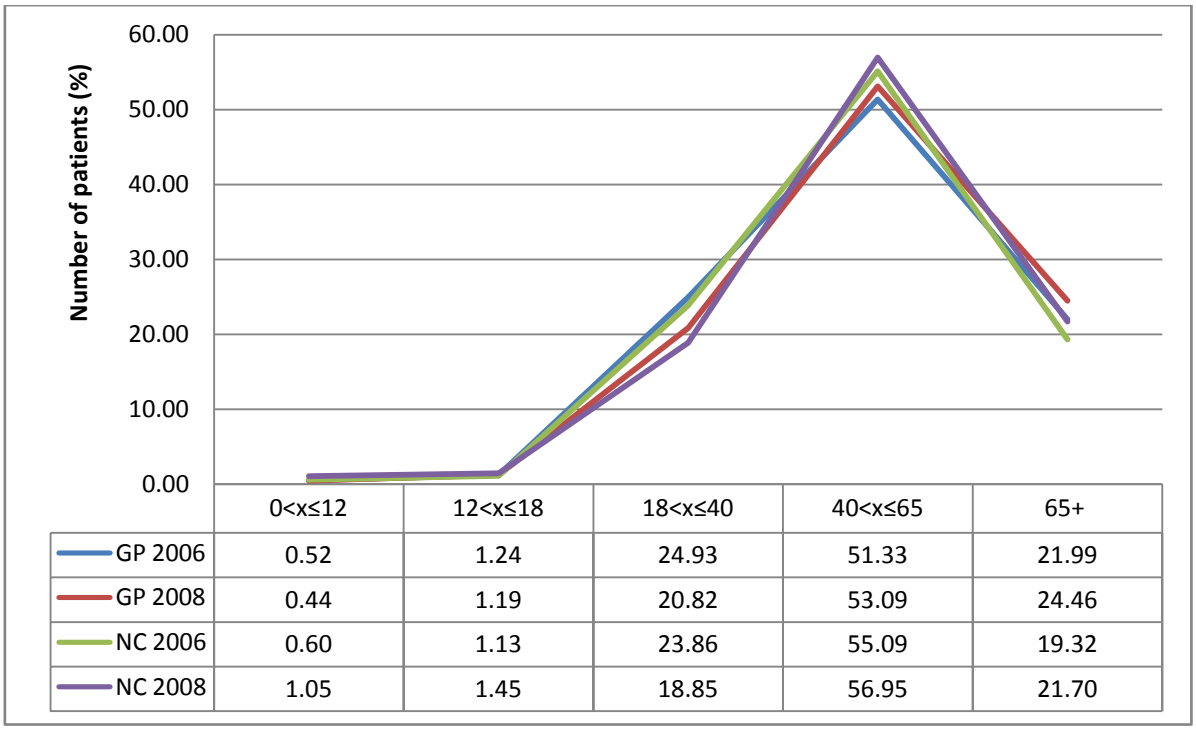
4.3.4.1.3 Unknown patients

The gender status of only 0.06% of patients that received benzodiazepine in the Gauteng Province had not been recorded on the database (refer to Tables 4.9 & 4.10). In 2006 the number of benzodiazepine prescriptions came to only 0.05% in the Gauteng and 0.2% in the Northern Cape province.

4.3.4.2 Analysis based on the patients' age of those who used benzodiazepines

The analyses of the groups were done according to different age groups of the patients that claimed benzodiazepine for 2006 and 2008 (refer to section 4.2.2).

Figure 4.16 illustrates the percentage of patients who claimed benzodiazepine in each age group in the two provinces during 2006 and 2008. The prevalence for each age group was calculated from Tables 4.9 and 4.10 by dividing the number of patients that claimed benzodiazepine (n) by the total number of patients that claimed benzodiazepine (N) in the Gauteng and Northern Cape Province for the study periods and then multiplied by 100.

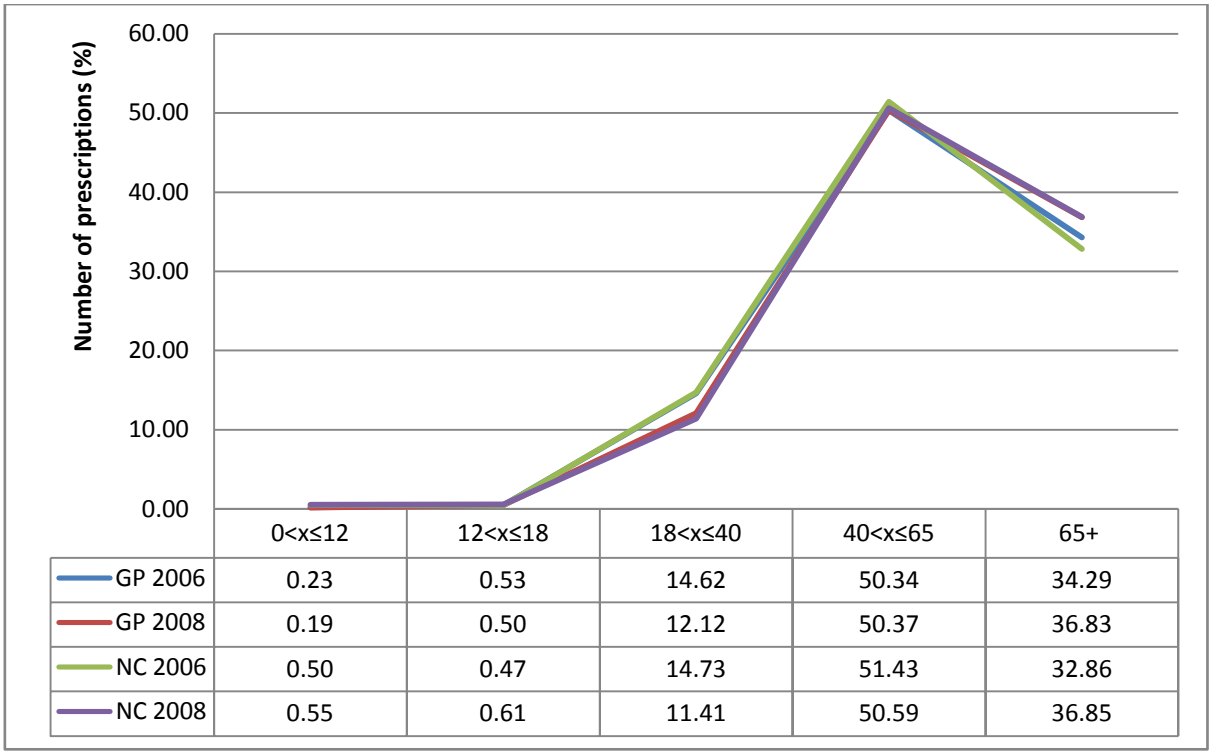


	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	0.52	1.24	24.93	51.33	21.99
GP 2008	0.44	1.19	20.82	53.09	24.46
NC 2006	0.60	1.13	23.86	55.09	19.32
NC 2008	1.05	1.45	18.85	56.95	21.70

Figure 4.16: Prevalence distribution of the different age groups indicating those who used benzodiazepine

The following figure (4.18) illustrates the percentage of benzodiazepine prescriptions that were claimed by each age group for the years 2006 and 2008. The prevalence for each age

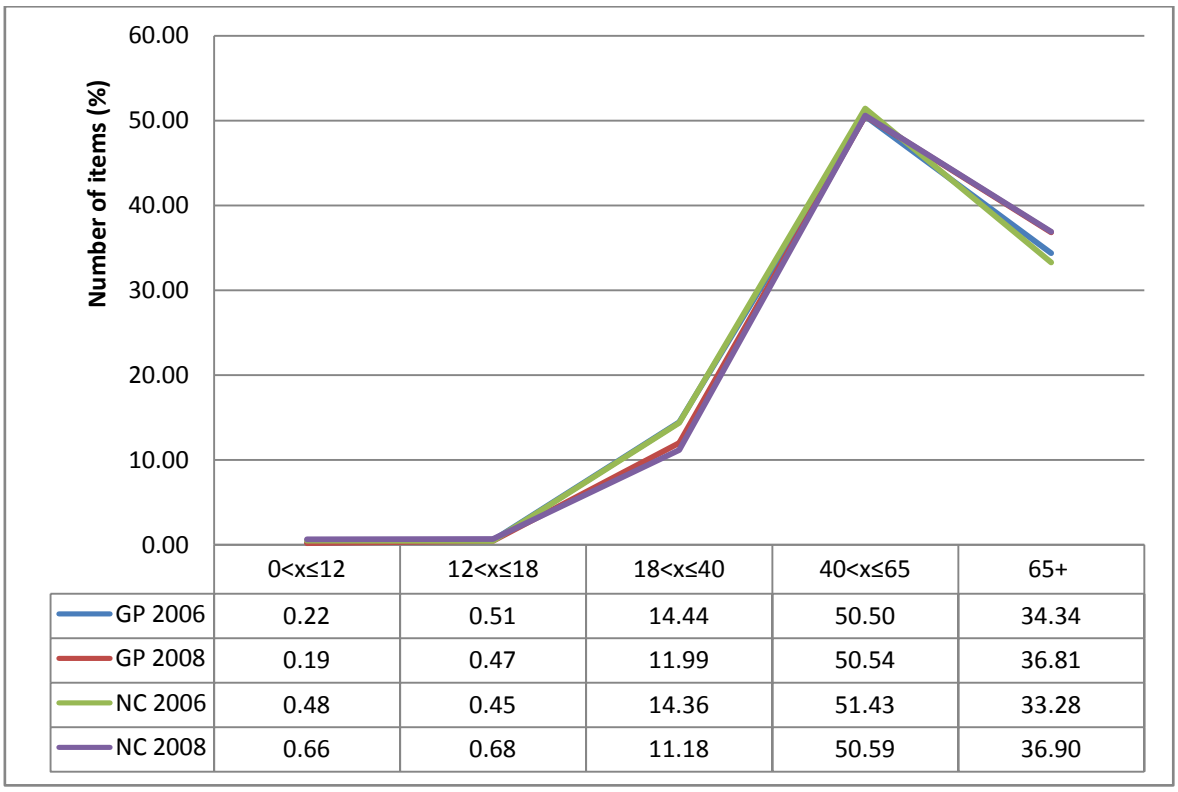
group was calculated from Table 4.9 and 4.10 by dividing the number of benzodiazepine prescriptions (n) by the total benzodiazepine prescriptions (N) in the Gauteng and Northern Cape Province for the study periods and then multiplied by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	0.23	0.53	14.62	50.34	34.29
GP 2008	0.19	0.50	12.12	50.37	36.83
NC 2006	0.50	0.47	14.73	51.43	32.86
NC 2008	0.55	0.61	11.41	50.59	36.85

Figure 4.17: The percentage distribution of benzodiazepine prescriptions claimed by each age group.

The following figure (4.18) illustrates the percentage of benzodiazepines items that each age group claimed in 2006 and 2008 from the two provinces. The prevalence for each age group was calculated from Tables 4.9 and 4.10 by dividing the number of benzodiazepine items (n) by the total benzodiazepine items (N) in the Gauteng and Northern Cape Province for the study periods and then multiplied by 100.



	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP 2006	0.22	0.51	14.44	50.50	34.34
GP 2008	0.19	0.47	11.99	50.54	36.81
NC 2006	0.48	0.45	14.36	51.43	33.28
NC 2008	0.66	0.68	11.18	50.59	36.90

Figure 4.18: The percentage distribution of benzodiazepine items claimed by each age group.

Figures 4.16, 4.17 and 4.18 will now be discussed in the followings sections of the age groups.

4.3.4.2.1 Age group 1

The number of patients in age group 1 claimed the lowest number of benzodiazepines for the Northern Cape and Gauteng for both years. There was a decrease in the number of patients that claimed benzodiazepines in the Northern Cape from 2006 to 2008 (Tables 4.9, 4.10 & Figure 4.16). The prevalence of these two provinces' patients that claimed benzodiazepine was also relatively low in comparison with the total number of patients that claimed benzodiazepine (refer to Table A.27, Appendix A). The Gauteng and Northern Cape Province also displayed reasonably equivalent percentages of benzodiazepine claimed per total of patients of each province for both years (refer to Table A.30, Appendix A). The percentage of benzodiazepine prescriptions and benzodiazepine items were also the least for this age in both provinces for both years (Figures 4.17 & 4.18). The prevalence of the number of benzodiazepine prescriptions and benzodiazepine items were relatively low for the two provinces compared to the total benzodiazepine data per province (refer to Tables A.28 & A.29, Appendix A). In 2006 and 2008, the percentages of benzodiazepine prescriptions and benzodiazepine items claimed from the total number of prescriptions and items of each province were relatively alike for the Gauteng and Northern Cape Province (refer to Tables A.31 & A.32, Appendix A).

The difference in the average number of benzodiazepine prescriptions per patient per year between the two provinces was small and thus practically insignificant for 2006 and 2008 (refer to Tables A.23 & A.24, Appendix A). In 2006 the *d*-value for the average number of benzodiazepine items per prescription was practically insignificant, and for 2008 the difference between the provinces was relatively small and thus practically insignificant (refer to Tables A.25 & A.26, Appendix A).

4.3.4.2.2 Age group 2

This age group of patients had the second lowest number of claims for benzodiazepines in both provinces in 2006 and 2008 (Tables 4.9, 4.10 & Figure 4.16). The prevalence of the number of patients per province that claimed benzodiazepines was relatively small for both provinces (refer to Tables A.27 & Table A.30, Appendix A). The number of benzodiazepine prescriptions and benzodiazepine items was also relatively small for both provinces (Tables 4.9 & 4.10). The prevalence of the benzodiazepine prescriptions and benzodiazepine items in the Gauteng and Northern Cape Province was small compared to the total benzodiazepine data (refer to Tables A.28 & A.29, Appendix A). Gauteng and Northern Cape Province had almost an equivalent percentage of benzodiazepine prescriptions and items per total prescriptions and items per province during both years (refer to Tables A.31 & A.32, Appendix A).

The difference between the two provinces' average number of benzodiazepine prescriptions per patient was 0.21 for 2006 and was 0.17 in 2008 (refer to Tables A.23 & A.24, Appendix A). This difference had only a small effect size and was therefore not practically significant. In 2006 the difference in the average number of benzodiazepine items per prescription in both provinces was relatively small ($d \leq 0.2$) (refer to Table A.25, Appendix A). The difference between the two provinces in terms of average number of benzodiazepine items per prescription for 2008, showed a medium effect size and could be considered as almost being of practical significance (refer to Table A.26, Appendix A).

4.3.4.2.3 Age group 3

The patients of this age group that claimed benzodiazepines showed a decrease from 2006 to 2008 in both the Gauteng and Northern Cape Province (Tables 4.9, 4.10 & Figure 4.16). Almost one in every ten patients that claimed benzodiazepines was from the Gauteng Province (refer to Table A.27, appendix A). In 2006 the percentage of benzodiazepine claimed per province was 6.48% (n_{GP} = 14 761) versus 7.76% (n_{NC} = 593) and in 2008 it was 6.36% (n_{GP} = 9 102) versus 7.28% (n_{NC} = 324) (refer to Table A.30, appendix A). The two provinces showed a decrease in the number of benzodiazepine prescriptions and items from 2006 to 2008 (Tables 4.9, 4.10 & Figures 4.17, 4.18). The prevalence of the number of benzodiazepine prescriptions and items for 2006 and 2008 from the total benzodiazepine

data was higher in the Gauteng than in the Northern Cape (refer to Tables A.28 & A.29, Appendix A). The percentage of benzodiazepine prescriptions and items per total data of each province did not differ much between the two provinces (refer to Tables A.31 & A.32, Appendix A).

The *d*-values for the average number of benzodiazepine prescriptions per patient between the two provinces for the two years were practically insignificant for calculated *d*-values (refer to Tables A.23 & A.24, Appendix A). The difference in the average number of benzodiazepine items per prescription in the Gauteng and Northern Cape Province showed a relatively small effect size for 2006 as well as 2008 (refer to Tables A.25 & A.26, Appendix A).

4.3.4.2.4 Age group 4

This age group had the highest number of patients that claimed benzodiazepines in both provinces for 2006 and 2008 (Tables 4.9, 4.10 & Figure 4.16). Almost one in every five patients that claimed benzodiazepine was from the Gauteng (refer to Table A.27, Appendix A). The number of patients per province that claimed benzodiazepines in the Gauteng was 10.92% (n = 30 393) in 2006 and 10.94% (n = 23 206) in 2008 of all patients in the Gauteng (refer to Table A.30, Appendix A). The percentage of patients in the Northern Cape Province that claimed benzodiazepines in 2006 was 12.55% (n_{2006} = 1 369) and 11.83% in 2008 (n_{2008} = 979) (refer to Table A.30, Appendix A). This was relatively similar to the Gauteng Province. Approximately one in every two benzodiazepine prescriptions and items that were claimed was for this age group (Figures 4.17 & 4.18). The Gauteng showed a prevalence between 21.7% and 24.13% during the two years for the number of benzodiazepine prescriptions and benzodiazepine items claimed from the total number of benzodiazepine prescriptions and items on the benzodiazepine data (refer to Tables A.28 & A.29, Appendix A). In 2006 and 2008 the percentages of benzodiazepine prescriptions and items in the Northern Cape Province were relatively similar compared to the Gauteng Province's percentage of benzodiazepine prescriptions and benzodiazepine items claimed from the total number of prescription and items per province (refer to Tables A.31 & A.32, Appendix A).

The *d*-value calculated for the difference in the number of benzodiazepine prescriptions and items per patient claimed per year in the Gauteng and Northern Cape showed a small effect size that was practically insignificant (refer to Tables A.23, A.24, A.25 & A.26, Appendix A).

4.3.4.2.5 Age group 5

The number of patients (older than 65 years) that claimed benzodiazepines in the Gauteng and Northern Cape Province increased from 2006 to 2008 (refer to Tables 4.9, 4.10 & Figure 4.16). Almost one in every six patients that claimed benzodiazepine in Gauteng (16.10% in

2006 & 16.13% in 2008) and Northern Cape Province were (16.13% in 2006 & 18.22% in 2008) older than 65 years old (refer to Table A.30, Appendix A). This age group represented approximately 35% of benzodiazepine prescriptions and items claimed according to the total benzodiazepine data claimed in the Gauteng and Northern Cape during 2006 and 2008 (Figures 4.17 & 4.18). The benzodiazepine prescriptions that were claimed in these two provinces were 8.21% (n_{GP} = 59 567) versus 8.24% (n_{NC} = 53 461) in 2006 and 8.63% (n_{GP} = 2 088) versus 8.29% (n_{NC} = 1 757) in 2008 (refer to Table A.31, Appendix A). The prevalence of the number of benzodiazepine prescriptions and items increased from 2006 to 2008 in both provinces (refer to Tables A.28 & A.29, Appendix A). The percentage of benzodiazepine items claimed per province was almost the same for the Gauteng and Northern Cape during 2006 and 2008 (refer to Table A.32, Appendix A).

The difference in average number of benzodiazepine prescriptions per patient, as well as the average number of items per prescription between the two provinces, was practically insignificant for the study periods (refer to Table A.23, A.24, A.25 & A.26, Appendix A).

4.3.5 Analysis based on active ingredient

Nineteen different active ingredients were claimed during 2006 and 2008 (refer to Table B.3, Appendix B). Figure 4.19 illustrates the percentage of active ingredients claimed during 2006 and 2008.

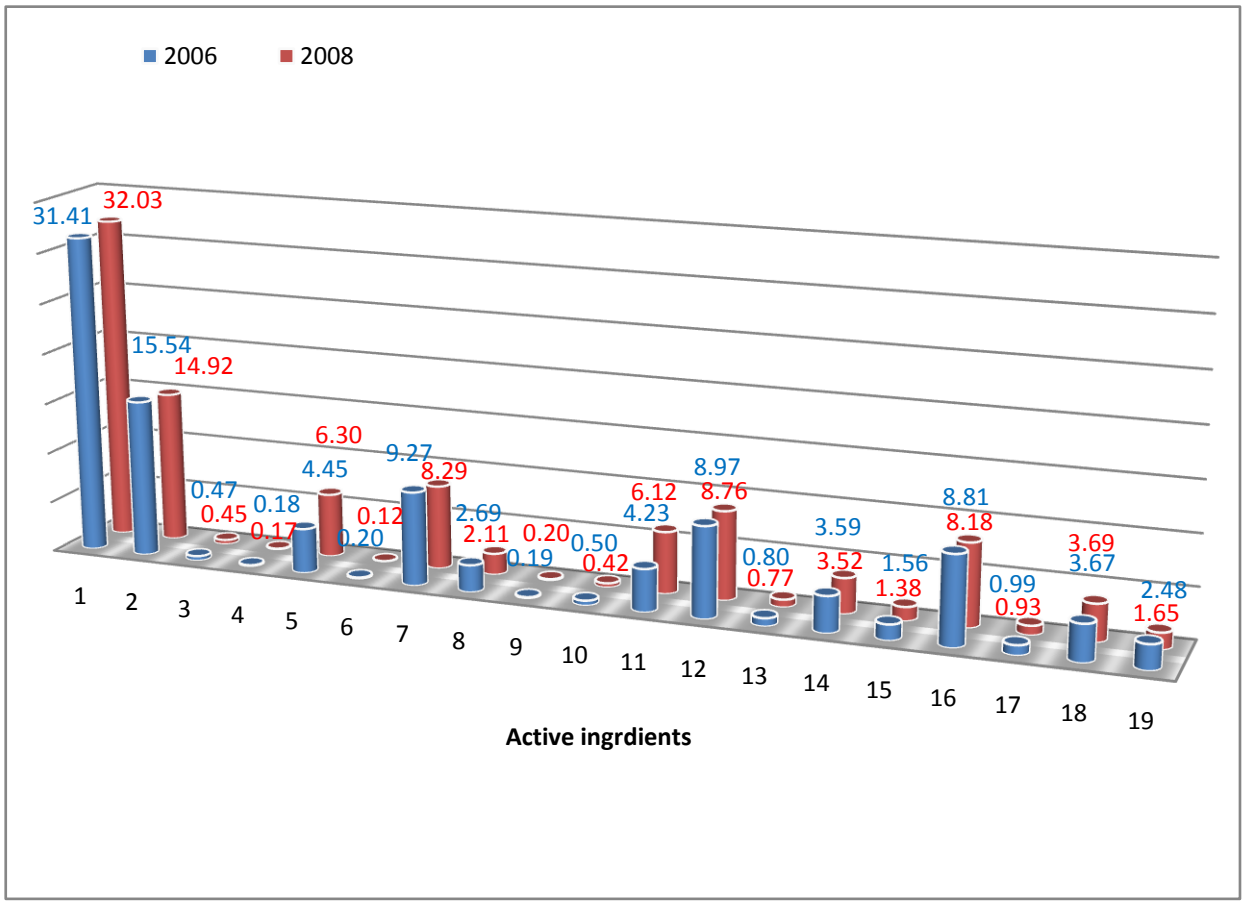


Figure 4.19: Percentage distribution of the benzodiazepines according to the active ingredient.

Table 4.12 summarises the number of days between refills of the active ingredients for 2006 and 2008.

Table 4.12: Number of days between supply of the active ingredients

		Percentage of days between refills of the different age groups (%)											
	Number of days	0<x≤30 days		30<x≤60 days		60<x≤90 days		90<x≤120 days		120<x≤150 days		180 + days	
	Study period	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008
Active ingredients	Alprazolam	71.96	67.17	9.03	10.49	4.42	5.64	7.04	8.54	6.78	7.48	0.77	0.69
	Bromazepam	65.36	58.95	8.97	10.03	5.27	6.11	8.89	11.53	10.31	12.16	1.20	1.23
	Brotizolam	48.38	44.30	12.09	9.87	6.32	6.33	12.82	15.95	18.23	21.27	2.17	2.28
	Chlordiazepoxide	70.03	65.73	9.09	11.74	7.07	3.76	4.71	7.98	8.42	9.86	0.67	0.94
	Clobazam	71.50	69.41	10.70	10.52	4.75	5.01	6.39	7.06	5.98	6.92	0.68	1.09
	Clorazepate	41.97	37.50	11.40	11.25	5.18	5.00	11.92	11.25	27.46	32.50	2.07	2.50
	Diazepam	93.03	92.00	2.83	2.73	1.16	1.32	1.43	1.79	1.40	1.89	0.15	0.27
	Flunitrazepam	55.73	48.97	11.15	12.42	7.01	6.95	11.09	13.86	14.02	16.55	1.01	1.25
	Flurazepam	47.51	41.46	13.57	12.20	6.33	9.15	14.03	12.20	15.84	19.51	2.71	5.49
	Ketazolam	76.05	78.24	9.12	6.20	2.81	3.03	4.51	5.48	6.61	6.05	0.90	1.01
	Loprazolam	54.19	53.96	11.30	11.73	6.29	6.55	12.20	11.96	14.10	13.37	1.92	2.45
	Lorazepam	67.03	64.82	7.48	8.12	4.12	4.64	6.98	7.34	12.31	12.80	2.08	2.29
	Lormetazepam	53.88	48.76	13.47	10.25	5.23	8.35	10.95	10.40	14.34	19.47	2.13	2.78
	Midazolam	74.15	70.48	7.45	8.52	3.65	3.42	6.96	7.82	6.91	8.40	0.88	1.37
	Nitrazepam	61.56	51.01	9.48	8.02	5.00	5.66	9.44	11.91	12.58	19.17	1.94	4.22
	Oxazepam	57.72	54.32	11.12	13.15	5.63	7.25	10.60	12.25	13.65	12.28	1.28	0.76
	Prazepam	57.60	54.49	12.17	11.19	5.75	7.50	9.59	9.29	13.50	15.10	1.40	2.43
	Temazepam	64.67	58.09	9.17	10.31	5.26	5.47	8.87	9.81	10.72	14.04	1.31	2.28
	Triazolam	40.00	34.66	9.98	13.05	7.19	11.41	13.99	18.62	25.10	20.97	3.75	1.28

The active ingredient that was claimed the most, was alprazolam with 31.41% (n = 133 471) in 2006 and 32.03% (n = 110 028) in 2008 (refer to Figure 4.19 & Table B.2, Appendix B). Bromazepam was claimed second most of all the active ingredients, at 15.54% (n = 66 042) in 2006 and 14.92% (n = 51 275) in 2008. In 2006, diazepam was claimed third most with 9.27% (n = 39 406) but in 2008 it was fourth with 8.29% (n =28 468). Lorazepam was claimed fourth most of all the prescribed benzodiazepines in 2006 with 8.97% (n = 38 117) and third most in 2008 with 8.76% (n = 30 083) (refer to Figure 4.19 & Table B.2, Appendix B).

The two most often prescribed benzodiazepines of the benzodiazepine data, may be used for the prescription of anxiety (refer to section 2.7.3). The four most often claimed benzodiazepines, with the exception of diazepam, were all intermediate working agents (refer to section 2.7.4).

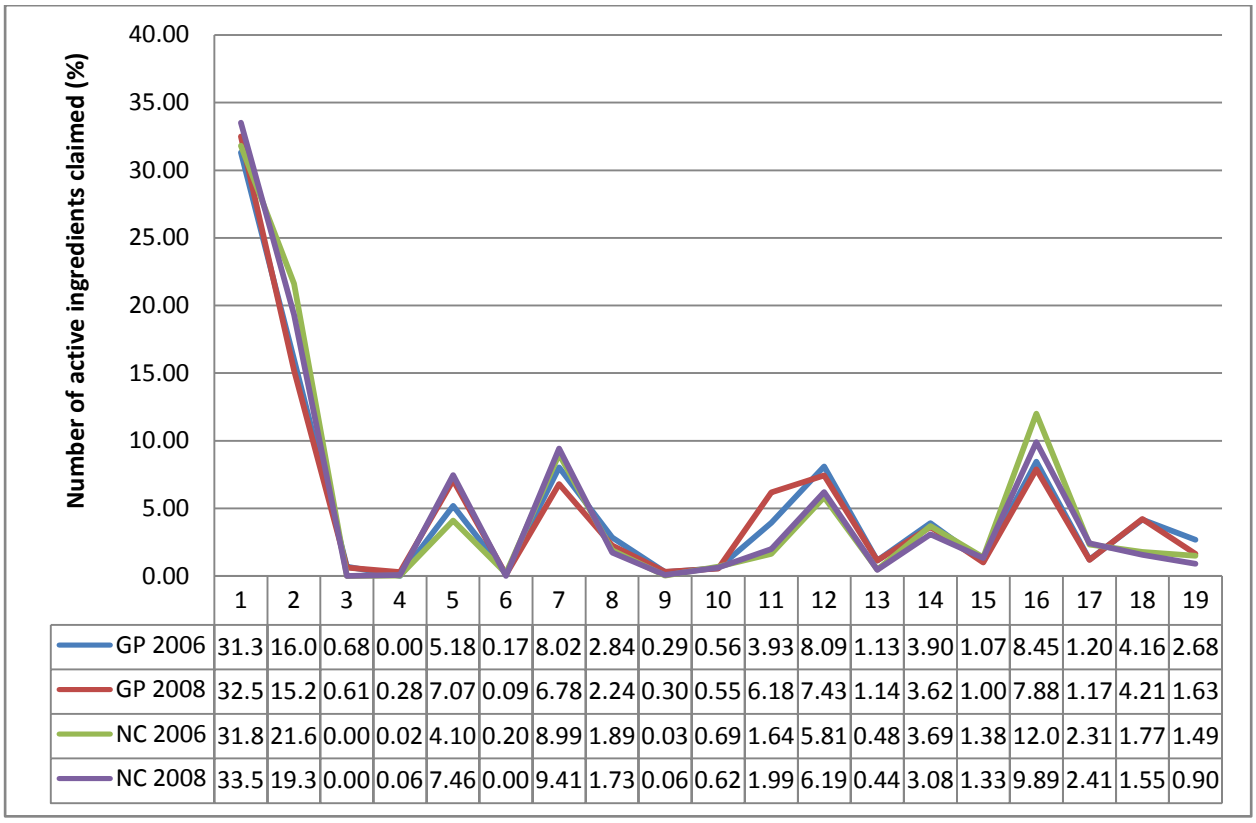
The benzodiazepines were mostly claimed for females. In most cases females claimed more than two thirds of the benzodiazepines (refer to Table B.3, Appendix B). This result was comparable with the literature according to which females had the tendency of claiming more benzodiazepines than their male counterparts (refer to section 2.7.11).

Longo & Johnson (2000:2121) for example, showed that in America alprazolam, diazepam and lorazepam were mostly claimed. In another study in South Africa, (Kairuz & Truter, 2007:305) indicated that diazepam and alprazolam were mostly claimed (refer to chapter 2.7.11).

The number of days between refills for active ingredients illustrated a decrease for 30 days and illustrated an increase for the time periods of more than 30 days. These trends can be viewed as reason for concern because this means that prescribers were prescribing benzodiazepines for longer time periods than a month at a time. The effect of using benzodiazepines for longer than a month can be seen in section 2.8.8. Diazepam was the benzodiazepine that was given the highest percentage within 30 days (93.03% in 2006 & 92% in 2008). The benzodiazepine that was received the least often for 30 days, was triazolam (40% in 2006 & 34.66% in 2008). Clorazepate was given the second least of the benzodiazepines that were given for 30 days (Table 4.12). The number of days between refills was relatively small for the prescriptions given between 60 and 120 days (Table 4.12). Triazolam (25.10%) and clorazepate (27.46%) was the benzodiazepine that was given the most often for 150 days in 2006 and in 2008 and it included clorazepate with 32.50% and brotizolam with 21.27%. The number of times that a prescription was written for a time period of 180 days was the highest for triazolam (3.75%) and flurazepam (2.71%) in 2006. In 2008 it was the highest for flurazepam (2.71%) and nitrazepam (4.22%) (Table 4.12).

4.3.5.1 Analysis of benzodiazepines based on active ingredients, stratified by province

In the Gauteng province all nineteen of the active ingredients were claimed in both years. In the Northern Cape, eighteen of the nineteen active ingredients were claimed in 2006 compared to the seventeen in 2008. Figure 4.21 illustrates the percentage active ingredient represented in the two provinces (refer to Tables B.4 & B.5, Appendix B).



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
GP 2006	31.3	16.0	0.68	0.00	5.18	0.17	8.02	2.84	0.29	0.56	3.93	8.09	1.13	3.90	1.07	8.45	1.20	4.16	2.68
GP 2008	32.5	15.2	0.61	0.28	7.07	0.09	6.78	2.24	0.30	0.55	6.18	7.43	1.14	3.62	1.00	7.88	1.17	4.21	1.63
NC 2006	31.8	21.6	0.00	0.02	4.10	0.20	8.99	1.89	0.03	0.69	1.64	5.81	0.48	3.69	1.38	12.0	2.31	1.77	1.49
NC 2008	33.5	19.3	0.00	0.06	7.46	0.00	9.41	1.73	0.06	0.62	1.99	6.19	0.44	3.08	1.33	9.89	2.41	1.55	0.90

Figure 4.20: Prescribing patterns of the different active ingredients in the Gauteng and Northern Cape provinces

In 2006 and 2008, alprazolam was the most often claimed benzodiazepine with 31.82% (n = 57 827) and 32.58% (n = 50 518) in Gauteng (refer to Figure 4.20 & Table B.4, B.5, Appendix B). The Northern Cape Province had similar trends as Gauteng with alprazolam that was claimed 31.82% in 2006 and 33.56% in 2008 (Figure 4.20 & Table B.5, Appendix B). Bromazepam was claimed second most, in Gauteng by 16.01% (n =29 544) in 2006 and 15.25% (n = 23 640) in 2008 (refer to Figure 4.21 & Table B.4, Appendix B), and in the Northern Cape Province with 21.64% (n = 1 442) in 2006 and 19.34% (n = 972) in 2008 (refer to Figure 4.20 & Table B.5, Appendix B). The benzodiazepine that was claimed third most often was oxazepam with 8.45% (n =15 583) versus 12.08% (n = 805) in 2006, and 7.88% (n = 12 225) versus 9.89% (n = 497) in 2008 in the Gauteng Province and Northern Cape Province respectively (refer to Figure 4.20, Tables B.4 & B.5, Appendix B). Diazepam was claimed fourth most in the Northern Cape, but

was fifth in Gauteng for both years. Lorazepam was claimed fourth most in Gauteng and fifth most in the Northern Cape Province (refer to Figure 4.20, Tables B.4 & B.5, Appendix B).

The five most often prescribed benzodiazepines on the database, may be used for the treatment of anxiety (refer to section 2.8.3). These benzodiazepines (five benzodiazepines) were all intermediate working except diazepam that had long acting working mechanism and oxazepam that had short acting working mechanism (section 2.8.4). Benzodiazepines that had a longer working mechanism were less likely to cause benzodiazepine dependence (section 2.8.8).

The benzodiazepine that was claimed the least in the Northern Cape was chlordiazepoxide with 0.02% (n = 1) in 2006 and 0.06% (n = 3) in 2008. The benzodiazepine that was claimed the least in the Gauteng Province was clorazepate with 0.17% (n = 308) in 2006 and 0.09% (n = 137) in 2008 (Figure 4.20, Tables B.4 & B.5, Appendix B).

The number of active ingredients claimed in the Gauteng, was claimed more often by females than males. The Northern Cape Province had similar trends as Gauteng, where the females claimed relatively more benzodiazepines than the males. According to the literature the females also claimed more benzodiazepines than their male counterparts (section 2.8.11).

4.3.6 Analysis based on trade names

In 2006, a total of ninety-seven trade name benzodiazepines were claimed and in 2008 it was ninety-five. Table 4.13 illustrates the ten benzodiazepines that were claimed the most often during 2006 and 2008. Prevalence was calculated from Table B.7 (Appendix B) with the formula of: n/N x 100.

Table 4.13: The top ten most claimed benzodiazepines for 2006 and 2008, based on trade names

	Top 10 most claimed benzodiazepines					
	2006			2008		
Rank	**Trade name**	**n**	**Prevalence (%)**	**Trade name**	**n**	**Prevalence (%)**
1	Adco-Alzam® 0.5 mg	33 377	7.86	Adco-Alzam® 0.5 mg	27 178	7.91
2	Sandoz Bromazepam® 3 mg	23 682	5.57	Sandoz Bromazepam® 6 mg	16 017	4.66
3	Adco-Alzam® 0.25 mg	20 455	4.81	Adco-Alzam® 0.25 mg	15 569	4.53
4	Dormonoct® 2 mg	17 960	4.23	Brazepam® 3 mg	14 542	4.23
5	Azor® 0.5 mg	16 866	3.97	Urbanol® 10 mg	12 670	3.69
6	Brazepam® 3 mg	15 290	3.60	Azor® 0.5 mg	11 419	3.32
7	Tranqipam® 1 mg	13 664	3.22	Tranqipam® 1 mg	10 827	3.15
8	Pax® 5 mg	12 812	3.02	Paxadorm® 5 mg	10 341	3.01
9	Purata® 30 mg	12 546	2.95	Pax® 10 mg	9 730	2.83
10	Normison® 20 mg	12 186	2.87	Zopax® 0.5 mg	9 695	2.82

The benzodiazepine that was claimed most often during 2006 and 2008 was Adco-Alzam® 0.5 mg with 7.86% (n = 33 377) in 2006 versus 7.91% (n = 27 178) in 2008 (Table 4.13). Almost one of every twelve benzodiazepines that were claimed was for Adco-Alzam® 0.5 mg (Table 4.13). Sandoz Bromazepam® 3 mg was claimed second most of all benzodiazepines for 2006 with 5.57% (n = 23 682) and Sandoz Bromazepam® 6 mg was second most for 2008 with 4.66% (n = 16 017) (Table 4.13). In 2006 and 2008 Adco-Alzam® 0.25 mg was the benzodiazepine that was claimed third most of all benzodiazepines with 4.81% (n_{2006} = 20 455) and 4.53% (n_{2008} = 15 569) (Table 4.13). Dormonoct® 2 mg was claimed fourth most in 2006 and Brazepam® 3 mg was claimed fourth most in 2008. Azor® 0.5 mg and Urbanol® 10 mg were respectively claimed fifth most for 2006 and 2008 of all benzodiazepines (Table 4.13).

The trade names that were prescribed for longer than 180 days at a time on the benzodiazepine data, may be prescribed for insomnia (refer to section 2.7.3 & Table B.10, Appendix B). The trade name products that were mostly prescribed for longer than six months were Tranqipam® 2.5 mg in 2006 and Dalmadorm® 30 mg in 2008. In 2006, Halcion® 0.25 mg was claimed second most of benzodiazepines that were prescribed for longer than 180 days and Tranqipam® 1 mg third most of the benzodiazepines that were prescribed for longer than 180 days (refer to Table B.10, Appendix B). The benzodiazepines that were received for longer than the time period of 180 days, were Sandoz Nitrazepam® 5 mg second most and Mogadon® 5 mg was

third most for 2008. Dalmadorm® 15 mg and Noctamid 1 mg were the fourth most prescribed trade name products for longer than 180 days (Table B.10). The percentage of days between refills for the time period of longer than 180 days was fifth for Loramet® 2 mg in 2006 and Tranqipam® in 2008 of all benzodiazepines that were prescribed in the benzodiazepine data.

4.3.6.1 Analyses of benzodiazepines based on trade names: Gauteng versus Northern Cape Province

Patients in the Gauteng Province claimed ninety-two of the ninety-seven trade name products on the benzodiazepine data versus the Northern Cape's seventy-seven for 2006. The total number of benzodiazepines that were claimed in the Gauteng was ninety and in the Northern Cape it was seventy-three of the ninety-five on the benzodiazepine data for 2008.

Table 4.14 displays the ten benzodiazepines that were claimed the most often in the Gauteng Province during the two years. Prevalence was calculated from Table B.8 (Appendix B) with the formula of: n/N x 100

Table 4.14: The top ten most claimed benzodiazepines in the Gauteng for 2006 and 2008

	Top 10 most claimed benzodiazepines in the Gauteng					
	2006			**2008**		
Rank	**Trade name**	**n**	**Prevalence (%)**	**Trade name**	**n**	**Prevalence (%)**
1	Adco-Alzam® 0.5 mg	13 294	7.21	Adco-Alzam® 0.5 mg	11 719	7.56
2	Sandoz Bromazepam® 3 mg	10 356	5.61	Dormicum® 7.5 mg	9 581	6.18
3	Adco-Alzam® 0.25 mg	8 036	4.36	Sandoz Bromazepam® 3 mg	6 941	4.48
4	Azor® 3 mg	7 657	4.15	Urbanol® 10 mg	6 476	4.18
5	Dormonoct® 2 mg	7 260	3.93	Adco-Alzam® 0.25 mg	6 402	4.13
6	Normison® 20 mg	6 206	3.36	Brazepam® 3 mg	5 935	3.83
7	Purata® 30 mg	6 128	3.32	Azor® 0.5 mg	5 763	3.72
8	Sandoz Bromazepam® 6 mg	5 850	3.17	Pax® 10 mg	5 168	3.33
9	Brazepam® 3 mg	5 837	3.16	Xanor® SR 0.5mg	4 677	3.02
10	Urbanol® 10 mg	5 781	3.13	Sandoz Bromazepam® 6 mg	4 666	3.01

The benzodiazepine claimed mostly in the Gauteng Province for 2006 and 2008, was Adco-Alzam® 0.5 mg at 7.21% (n= 13 294) and 7.56% (n = 11 719) respectively (Table 4.14). Sandoz Bromazepam® 3 mg was claimed second most of all the benzodiazepines for 2006 (n = 10 356)

and third most for 2008 (n = 6 941) in the Gauteng Province (Table 4.14). In 2008, Dormicum® was claimed second most, representing 6.18% (n = 9 581) of all benzodiazepines claimed in the Gauteng Province. Adco-Alzam® 0.25 mg represented the third most benzodiazepine claims for 2006 with 4.36% (n = 8 036) and fifth most for 2008 with 4.13% (n = 6 402) of all the benzodiazepines in the Gauteng (Table 4.14). In 2006 Azor® 3 mg and in 2008 Urbanol® 10 mg were claimed the fourth most of all the benzodiazepines in the Gauteng. The benzodiazepine that was claimed fifth most in the Gauteng province for 2006 was Dormonoct® 2 mg (Table 4.14).

In Table 4.15 the ten benzodiazepines that were claimed the most often in the Northern Cape for 2006 and 2008 were displayed. Prevalence was calculated from Table B.9 (Appendix B) with the formula of: n/N x 100.

Table 4.15: The top ten most claimed benzodiazepines in the Northern Cape in 2006 and 2008

	Top 10 most claimed benzodiazepines in the Northern Cape					
	2006			**2008**		
Rank	**Trade name**	**n**	**Prevalence (%)**	**Trade name**	**n**	**Prevalence (%)**
1	Brazepam® 3mg	679	10.19	Brazepam® 3mg	487	9.69
2	Azor® 0.5mg	664	9.96	Azor® 0.5mg	379	7.54
3	Azor® 0.25mg	465	6.98	Bromazepam® 6mg	322	6.41
4	Bromazepam® 6mg	445	6.68	Azor® 0.25mg	318	6.33
5	Purata® 15mg	310	4.65	Zopax® 0.5mg	280	5.57
6	Purata® 30mg	249	3.74	Urbanol® 10mg	273	5.43
7	Pax® 5mg	249	3.74	Pax® 5mg	205	4.08
8	Urbanol® 10mg	225	3.38	Adco-Alzam® 0.5mg	200	3.98
9	Dormicum® 15mg	220	3.30	Purata® 15mg	141	2.80
10	Zopax® 0.5mg	2.18	3.27	Dormicum® 15mg	138	2.75

Nearly one of every ten benzodiazepines claimed in the Northern Cape was for Brazepam® 3 mg during 2006 and 2008 (10.19% in 2006 & 9.69% in 2008) (Table 4.15). Azor® 0.5 mg was claimed second most in the Northern Cape at 9.96% (n = 664) in 2006 and 7.54% (n = 379) in 2008 (Table 4.15). Azor® 0.25 mg was claimed third most in 2006 with 6.98% (n = 465) and fourth most in 2008 with 6.33% (n = 318) (Table 4.15). Bromazepam® 6 mg, the benzodiazepine that was claimed third most of all benzodiazepines in 2008 with 6.41% (n = 322) and fourth most in the 2006 with 6.68% (n = 445) in the Northern Cape Province (Table 4.15). There were two different benzodiazepines that were claimed fifth most in the Northern Cape, namely Purata® 15 mg for 2006 and Zopax® 0.5 mg for 2008 (Table 4.15).

4.4 CONCLUSION

The total database was analysed according to the study periods. The gender that claimed most often according to this PBM was examined. The different age groups were investigated to determine which age group claimed the most often according to the total database. The prescribing patterns in the different provinces were determined and the prescribing patterns of the Gauteng and Northern Cape Province were subjected to analyses.

Subsequent to the total database the benzodiazepine data were analysed. The prescribing patterns of benzodiazepines were examined with the focus on geographical area in South Africa. The differences between prescribing patterns of the various age groups and genders were investigated. The number of days between refills was also investigated.

4.5 CHAPTER SUMMARY

In this chapter the results of the empirical investigation were illustrated. The focus was on different variables such as gender, various age groups, prescribing patterns, days between refills and provinces.

Chapter 5 will present conclusions regarding the results that were found in this chapter and will also give recommendations for future studies.

CHAPTER 5

CONCLUSION AND RECOMMENDATION

5.1 INTRODUCTION

The conclusion of this study was based on the results of the literature review and the empirical investigation. Recommendations for future studies will be made according to the results and conclusions from this study.

5.2 CONCLUSIONS

The following conclusions were based on the specific research objectives in chapter 1 (section 1.3.2.1).

5.2.1 Conclusions based on the literature review

The first specific objective was to describe and define the terms of urbanisation, crime, insomnia and anxiety.

Through the literature urbanisation, crime, insomnia and anxiety were defined and described. Urbanisation was defined as the process of repositioning the population from the rural areas towards the urban areas (Van Jaarsveld, 1985:5) (refer to paragraph 2.3.1). Different definitions of urbanisation were found from different sources. The different trends of urbanisation for previous years as well as for years to come were described according to countries worldwide (refer to paragraph 2.3.2). The trends for the different continents were illustrated, America was the most urbanised and Africa was the least urbanised of the four continents (refer to paragraph 2.3.2). Urbanisation in South Africa was discussed and special mention was made of the two provinces Gauteng and Northern Cape Province (refer to paragraph 2.3.3). The Gauteng Province was unquestionably more urbanised compared to the Northern Cape Province (refer to paragraph 2.3.3).

Crime was defined as an evil or injurious act that breaks the law and is liable to public prosecution and punishment (Kennedy, 1990:1; OED; 2010a) (refer to paragraph 2.4.1). The background on crime was then articulated and it was found that in South Africa there were only a few people who had not yet been exposed to or a victim of a crime (notice paragraph 2.4.2). The different factors (race, age, citizenship, location, education and lifestyle) that have an effect on crime were mentioned (refer to paragraph 2.4.3). The prevalence of crime worldwide as well as in South Africa was discussed in paragraph 2.4.3. South Africa's homicide rate (i.e., 37.3) appeared to be larger than the homicide rate in other countries (i.e., 7.6), including United States. On the other hand South Africa's homicide rate was the same as countries such as

Venezuela and Brazil (refer to paragraph 2.4.4). The difference between the Gauteng and Northern Cape Province was relatively large when looking at the number of trio crimes and the general percentage of the crime rate. Per capita the crime rate was approximately the same for the two provinces (refer to paragraph 2.4.4).

Anxiety can be described a distressing, unpleasant emotional state of nervousness (Porter and Beers, 2006:1672) (refer to paragraph 2.5.1). The different types of anxiety disorders namely: generalised anxiety disorder, panic disorder, obsessive-compulsive disorder, phobic disorder and dissociative disorder were discussed (refer to paragraph 2.5.2). The causes of anxiety, such as urbanisation and accompanying crime events as well as stress, were also examined (refer to paragraph 2.5.2). The differences in prevalence were discussed in paragraph 2.5.3. The prevalence of anxiety disorders in South Africa corresponded with that in other countries (refer to paragraph 2.5.3). The prevalence of anxiety disorders in the Northern Cape and Gauteng indicated similarities (refer to paragraph 2.5.3).

Insomnia was defined as the difficulty a person has to fall to asleep or remain asleep, intermittent wakefulness during night or waking up too early (refer to paragraph 2.6.1). The different aspects that may lead to insomnia were discussed in the background section (refer to paragraph 2.6.2). Insomnia can either be treated by lifestyle changes or medicine (refer to paragraph 2.6.3). The prevalence of insomnia in different countries was discussed, even though the author could not find any statistics about the prevalence of insomnia in South Africa (refer to paragraph 2.6.4).

The second specific objective was to establish the relationship between the geographical area, crime and urbanisation globally.

The geographical area referred to the different countries worldwide. Table 1.1 indicated the different countries and their population density which indicated their level of urbanisation. According to Louw and Bekker, (1996:10) high density and lack of space in urban areas would be inclined to result in conflict and violence (notice paragraph 2.4.1). The crime rate in urbanised areas would accordingly be expected to be higher, but literature on countries world wide did not confirm this fact (table: 1.1). The United Kingdom, for example, displayed a relatively high population density but a relatively low homicide rate. On the other hand Trinidad and Tobago showed a high population density and a high homicide rate.

The third specific objective was to determine the relationship between geographical areas, crime and urbanisation, as applicable to South Africa.

The geographical area referred to the two provinces in South Africa, the Gauteng Province and the Northern Cape Province. The Gauteng Province showed to be more densely urbanised

than the Northern Cape Province (refer to paragraph 2.4.4) (notice paragraph 2.4.1). Urbanisation results in high density and lack of space and could in turn cause frictions that could lead to conflict and violence (Louw & Bekker, 1996:10). Crime may consequently be higher in urban areas. This statement could apply to the Gauteng Province and Northern Cape Province where Gauteng had a higher homicide rate than Northern Cape (South Africa statistics, 1998:51). Gauteng is more densely populated province of the two. The per capita calculations for correlating crime rates did, however, not indicate noteworthy differences.

The fourth specific objective was to depict from the literature the relationship between crime, urbanisation and anxiety and insomnia.

In the second and third specific objectives the relationship between urbanisation and crime was investigated. Crime as such causes stress and fear (Craig *et al*., 1995:1332). These two components are part of the psychological component of anxiety (refer to paragraph 2.5.2). In the wake of urbanisation anxiety can be expected to follow (Table 2.4). Insomnia is one of the symptoms of anxiety. Insomnia is also a result of stress. In paragraph 2.2 an illustration of the relationship between urbanisation, crime, anxiety and insomnia was given. Each one of these could lead to the other one and in this way a relationship between these was confirmed.

The fifth specific objective was to describe and define benzodiazepines.

Benzodiazepines have been classified in various ways. Benzodiazepines were classified either as central nervous system drugs or as sedative hypnotic and anxiolytic or as hypnotic and sedative drugs (Charney *et al.,* 2006; Snyman, 2009:13a; Trevor & Way, 2009:271).

In the background section the structure of benzodiazepines was discussed and also the classification system (refer to paragraph 2.7.1). Benzodiazepines' mechanism of action is mediated by enhancement of the activity of gamma-aminobutyric acid, a major inhibitory neurotransmitter in the brain (Rossiter, 2010:474; Stahl, 2010:102) (refer to paragraph 2.7.2). The different trade names of benzodiazepines were mentioned in section 2.7.3 and also the indications of benzodiazepines. The different indications of benzodiazepines were anxiety, insomnia, conversion disorders, convulsions, management of alcohol withdrawal, muscle spasm, pre-anaesthetic and chest pain (notice paragraph 2.7.3).

The benzodiazepines were then arranged into the different groups according to their half-life elimination. The different groups were ultra short-acting, short-acting, intermediate-acting and long-acting (notice paragraph 2.7.4). The following contra-indications were discussed in section 2.7.5: myasthenia gravis, respiratory disorders, pregnancy and hepatic diseases.
The side-effects of benzodiazepine were divided into two groups, *i.e.* the more frequently observed side-effects and the infrequently observed side-effects. The frequent side-effects were drowsiness, impaired judgement, diminished motor skill and confusion and the infrequent

side-effects were depression, nausea, vomiting, constipation, skin rashes, weight gain (refer to paragraph 2.7.6). In Table 2.7 (refer to paragraph 2.7.7) the different drug interactions that could occur in combination with benzodiazepines were illustrated. The drug interactions differed according to the different drugs. Some drugs increased the sedation of benzodiazepines and others delayed the onset of the effects of benzodiazepines.

Dependence was divided into two types, *i.e.* the physical and the physiological (refer to paragraph 2.7.8). The physiological dependence had another component namely psychological. Patients have a 50% chance of being developing dependence related to benzodiazepines after a year of usage of benzodiazepines (Rossiter, 2010:475). When patients are depended and attempt to discontinue the treatment of benzodiazepines, they experience withdrawal symptoms. The steps for avoiding and treating withdrawal symptoms were described in paragraph 2.7.9.

The law on schedule 5 and 6 substances was discussed and the fact that benzodiazepines may be dispense only if the patient has a prescription (2.7.10).

According to the literature review general practitioners were more likely to prescribe benzodiazepines in developing countries than already developed countries. Females were more likely to receive prescriptions for benzodiazepines than males. An increase in the number of prescriptions per patient with increasing age could be detected (notice paragraph 2.7.11). The usage of benzodiazepines was different in each country. In some countries diazepam was claimed the most and in others lorazepam or temazepam. Benzodiazepines that had hypnotic effect were claimed more often than benzodiazepines with anxiolytic effect (2.7.12).

5.2.2 Conclusions based on the empirical investigation

The first objective was to determine the age and gender of patients in comparison to the total set of data.

In sections 4.2.1 and 4.2.2, the following results regarding age and gender of patients that claimed from the total database could be observed:

Female patients represented 55.77% in 2006 and 55.23% in 2008 of the total number of patients on the total database. Their counterparts, male patients, represented a smaller number of patients on the total database. The female gender claimed the most prescriptions according to the database with 59.91% in 2006 and 59.95% in 2008. The total number of items claimed from the female gender for 2006 was 60.15% and 60.18% (Table 4.2). The male patients would understandably claim lower percentages of prescriptions as well as items.

The number of patients between the years of 12 and 18 was the age group that claimed the smallest number of prescriptions and items on the total database. The number of patients between the age of 40 and 65 years represented the highest percentage of claims reflected in the total database (37.69% in 2006 & 41.36% in 2008) (Figure 4.2). The total number of prescriptions and items claimed by age group 4 for the study periods was the highest of all the age groups that claimed according the total database. The number of patients between birth and 12 years claimed the second lowest number of prescription and number of items. The number of prescriptions and number of items were claimed second most by age group 5 (patients older than 65 years).

The number of patients between the ages of 40 and 65 years represented the highest percentage of claims on the total database versus the patients between 12 and 18 years that represented the lowest number of claims.

The second objective was to determine the prescribing patterns in the different provinces in South Africa according to the total set of data.

The province with the highest number of patient claims as reflected the total database in both 2006 and 2008 was the Gauteng Province with 37.96% (n = 745 573) and 39.99% (n =515 825) respectively. The Kwazulu-Natal and Western Cape Provinces were, respectively, second and third with the number of patients that claimed as recorded in the total database for the years 2006 and 2008. The province with the smallest number of patient claims in both 2006 and 2008 was the Northern Cape Province at 1.4% (n = 27 724) and 1.41% (n = 18 069) respectively (refer to section 4.2.3).

The number of prescriptions and number of items per year claimed according to the total database, were the highest in the Gauteng Province representing 39.86% and 40.48% in 2006 versus 40% and 40.76% in 2008. The second highest number of prescriptions and items claimed per year were claimed by Kwazulu-Natal Province for the study periods. The province with the third most number of claims for prescriptions and items according to the total database was the Western Cape Province. As reflected in the total database and in comparison with all the provinces that submitted claims, the province presenting with the lowest number of claims for prescriptions and items was the Northern Cape. The Northern Cape had the least number of claimed prescriptions and items. This held true for both study periods (refer to section 4.2.3).

The results above derived from information captured in the total database and according to these results it can be concluded that the Gauteng Province represented the highest percentage of claims and the Northern Cape Province represented the smallest percentage of claims.

The third objective was to determine the prescribing patterns in the Gauteng Province and Northern Cape Province with regard to the gender and age according to the total set of data.

Female patients in the Gauteng and Northern Cape submitted more claims than their male counterparts. Females from both Gauteng and Northern Cape claimed more prescriptions and items than their male counter parts. Males subsequently represented the smaller portion of the number of patients, prescriptions and items on the total database for both provinces (refer to section 4.2.3.1).

Age group 2 had the smallest number of patients, prescriptions and items claimed in 2006 and 2008 and this applied to both provinces. Age group 4 had the most patients as well as prescriptions and item claims for 2006 and 2008 in the two provinces. The patients older than 65 years represented the second largest prevalence for the number of prescriptions and items claimed in both Gauteng and Northern Cape and for both 2006 and 2008. The number of patients between birth and 12 years claimed second lowest number of prescriptions and number of items (refer to section 4.2.3.2)

With regard to age groups it can be concluded that the number of patients between the age of 40 and 65 years represented the highest percentage of claims in both Northern Cape and Gauteng versus the patients between 12 and 18 years that represented the smallest number of claims for both Northern Cape and Gauteng.

The fourth objective was to determine the prescribing patterns of benzodiazepine in the Gauteng Province and the Northern Cape Province with regard to benzodiazepine data on the total database.

The number of patients that claimed benzodiazepines in the Northern Cape (NC) was lower than the number of patients that claimed benzodiazepines in the Gauteng (GP). However, the percentage of patients that claimed benzodiazepines in Gauteng (7.91% in 2006 & 8.47% in 2008) and Northern Cape Province (8.96% & 9.51%) corresponded to a great extent. The percentages of benzodiazepine prescriptions claimed per province were 4.79% (n = 173 723) in Gauteng compared to 4.62% (n = 6 354) in the Northern Cape for 2006, and 5.10% (n = 145 148) in Gauteng versus 4.30% (n = 4 768) in the Northern Cape for 2008. The percentage of benzodiazepine items claimed per province was 2.16% (n = 184 500) for 2006 and 2.31% (n = 155 044) for 2008 in Gauteng and in the Northern Cape it was 2.10% (n = 6 665) in 2006 and 1.98% (n = 5 027) in 2008 (refer to section 4.3.4).

The percentage of benzodiazepine claims by the female patients demonstrated a similar trend in Northern Cape and Gauteng. More females patients received benzodiazepines in 2006 and 2008 compared to their counterpart males. Almost one in every ten females in the Gauteng

Province (9.45% in 2006 versus 10.17% in 2008) and Northern Cape (10.95% in 2006 versus 12.01% in 2008) claimed benzodiazepines per year (refer to section 4.3.4.1).

The prevalence of the number of male patients that claimed benzodiazepine per province was 5.97% (n = 19 365) in 2006 and 6.31% (n = 14 268) in 2008 for Gauteng Province. The prevalence of the number of male patients that claimed benzodiazepine per province for Northern Cape was 6.49% in 2006 and 6.64% in 2008. Both of the provinces, Gauteng and Northern Cape, had relatively similar prevalences for the number of male patients that claimed benzodiazepines. The prevalence of benzodiazepine prescriptions and items per province did not differ much between the two provinces (refer to section 4.3.4.1).

Age group 1 presented with the smallest number of patients that submitted benzodiazepine claims for both the Northern Cape and Gauteng and for both years. The number of patients from this age group and that claimed benzodiazepines in the Northern Cape had higher percentage of claims in 2008 than in 2006. The prevalence of these two provinces' patients from this age group that claimed benzodiazepine per province also presented as low in comparison with the total number of patients that claimed benzodiazepine. Gauteng and Northern Cape also showed equivalent percentages with regard to the number of benzodiazepine claims per province for both years for this age group. The percentages of benzodiazepine prescriptions and benzodiazepine items were also the lowest for this age in both provinces for both years. The prevalence of the number of benzodiazepine prescriptions and benzodiazepine items per province was low for the two provinces compared to the total benzodiazepine data per province. In 2006 and 2008, the percentages of benzodiazepine prescriptions and benzodiazepine items claimed were much alike for both provinces (refer to section 4.3.4.2).

Age group 4 had the highest number of patients that claimed benzodiazepines in both provinces for 2006 and 2008. The number of patients per province that claimed benzodiazepines in Gauteng was 10.92% (n = 30 393) in 2006 and 10.94% (n = 23 206) in 2008 of all patients in Gauteng. The percentage of patients per province that claimed benzodiazepines in the Northern Cape was similar to that of Gauteng (12.55% & 11.83%). In 2006 and 2008 the percentage of benzodiazepine prescriptions and items in Northern Cape was in comparison similar to Gauteng's percentage (refer to section 4.3.4.2).

In 2006 and 2008, alprazolam was more often claimed than other benzodiazepine items in the Gauteng. The Northern Cape Province had similar trends as Gauteng with alprazolam that was claimed more often than other benzodiazepines. Bromazepam was claimed second most in both Gauteng and the Northern Cape. The benzodiazepine that was claimed third most in Gauteng and Northern Cape was oxazepam. Diazepam was claimed fourth most in the

Northern Cape, but was fifth most in Gauteng for both years. Lorazepam was claimed fourth most in Gauteng and fifth most in the Northern Cape (refer to section 4.3.5.1).

The benzodiazepine that was claimed the least often in the Northern Cape was chlordiazepoxide and the benzodiazepine that was claimed the least frequently in Gauteng was clorazepate (refer to section 4.3.5).

The number of active ingredients claimed in the Gauteng Province and Northern Cape Province, was claimed more by females than males (refer to section 4.3.5.1).

The benzodiazepine claimed most frequently in the Gauteng Province for 2006 and 2008, was Adco-Alzam® 0.5 mg. The benzodiazepine claimed most often in the Northern Cape was Brazepam® 3 mg during 2006 and 2008. Sandoz Bromazepam® 3 mg was claimed second most of all the benzodiazepines for 2006 and third most for 2008 in the Gauteng Province. Azor® 0.5 mg was claimed second most in the Northern Cape for the study periods (refer to section 4.3.6.1).

In 2008, Dormicum® was claimed second most of all benzodiazepines claimed in the Gauteng Province. Adco-Alzam® 0.25 mg represented the third most benzodiazepine claims for 2006 and fifth most for 2008 of all the benzodiazepines claimed in Gauteng. In 2006 Azor® 3 mg and in 2008 Urbanol® 10 mg were claimed the fourth most in Gauteng. The benzodiazepine that was claimed fifth most in the Gauteng Province for 2006 was Dormonoct® 2 mg (refer to section 4.3.6.1).

Azor® 0.25 mg was claimed third most in 2006 and fourth most in 2008. Bromazepam® 6 mg, was the benzodiazepine that was claimed third most of all benzodiazepines in 2008 and fourth most in the 2006 in the Northern Cape Province. There were two different benzodiazepines that were claimed fifth most in the Northern Cape, Purata® 15 mg for 2006 and Zopax® 0.5 mg for 2008 (refer to section 4.3.6.1).

The difference in the average number of benzodiazepine prescriptions per patient in the Gauteng Province and the Northern Cape Province for male as well as female patients, patients and across all age groups was practically insignificant (refer to section 4.3.4.1). The difference in the average number of benzodiazepine items per prescription in the Gauteng Province and Northern Cape Province was practically insignificant for male patients, female patients and across all age groups (refer to section 4.3.4.1).

There were no significant differences between the prescribing patterns for benzodiazepines in the two provinces.

The fifth objective was to determine the prescribing patterns of benzodiazepines amongst the different genders groups with regard to benzodiazepine data on database.

Females that claimed benzodiazepine represented 67.28% of the total number of patients in the study population in 2006, and 67.44% in 2008. In 2006 and 2008 benzodiazepine prescriptions claimed by females represented 69.43% and 69.88% of the total benzodiazepine prescriptions. Benzodiazepine items claimed by the female gender represented 69.54% and 69.96% of all benzodiazepine items claimed respectively for 2006 and 2008. To conclude, of all benzodiazepine items claimed respectively for 2006 and 2008, two thirds of all the patients whom claimed benzodiazepine were female. As can be expected the male patients presented with lower percentages than the females with regard to benzodiazepine claims (refer to section 4.3.4.1).

The active ingredients relevant to benzodiazepine were mostly claimed for females. In most cases females claimed more than two thirds of the active ingredients. This result correlated with findings according to the available literature as such findings also indicated that females claimed more than males (refer to section 4.3.4.1).

The six objective was to determine prescribing patterns of benzodiazepines amongst the different gender groups with regard to benzodiazepine data on the total database.

Patients from age group 1 represented only 0.52% in 2006 and 0.45% in 2008 of all the patients who claimed benzodiazepines. This age group 1 claimed the lowest number of benzodiazepine prescriptions and benzodiazepine items for 2006 and 2008. The percentage of patients (between the ages of 12 and 18 years) was only 1.25% (2006) and 1.18% (2008). This age group 2 claimed the second lowest number of benzodiazepine prescriptions and benzodiazepine items for 2006 and 2008. The number of patients aged 40 to 65 years represented 51.62% in 2006 and 52.87% in 2008 of the total number of patients who received benzodiazepines. Age group 4 claimed the highest number of benzodiazepine prescriptions and benzodiazepine items for 2006 and 2008. In 2006 and 2008, the number of patients older than 65 years that claimed benzodiazepines could be calculated as 23.13% and 26.09%. The number of benzodiazepine prescriptions and benzodiazepine items were claimed second most by patients older than 65 years (refer to section 4.3.4.2).

The difference between the total database and the benzodiazepine study population with regard to the average number of prescriptions per patient, showed *d*-values of medium effect. There was a practical significant difference between the average number of items per prescription per year from the total database and the average number of benzodiazepine items per prescription from the benzodiazepine data. The effect size between the difference of the total data and

benzodiazepine data's number of items per prescription was large. This was because benzodiazepines were mostly prescribed as a mono-therapy (refer to section 4.3.4.2).

The seventh objective was to determine the days between refills of the benzodiazepine prescriptions with regard to benzodiazepine data on database.

The majority of prescriptions claimed for benzodiazepines was for the treatment period of 30 days or shorter. From 2006 to 2008, there was an increase in the percentage of prescriptions and items prescribed for longer prescription periods. In 2006 and 2008, the lowest number of benzodiazepines appeared as prescribed for 180 days and longer (refer to section 4.3.1).

Benzodiazepines were prescribed for a shorter time period for females than their males counterpart. In 2006 the benzodiazepines prescribed indicated a longer time period for females than in 2008. Most of the benzodiazepines, for both female and male patients, were prescribed for shorter than 30 days. Very few prescriptions for benzodiazepines, for both male and female patients, were prescribed for longer than 180 days (refer section 4.3.2).

Most prescriptions (i.e., 94.39%) were claimed for a period of shorter than 30 days for patients aged from birth to 12 years. Patients between 12 and 18 years and 18 and 40 years claimed mostly the prescribed benzodiazepines for a period of 30 days. Almost three quarters of the patients between the ages of 40 and 65 years received their benzodiazepines for the time period of 30 days. In patients older than 65 years fewer than half of the patients that claimed benzodiazepines received their benzodiazepines for 30 days (47.81% in 2006 versus 46.06% in 2008). In 2006, 18.62% of the benzodiazepine patients in this age group received their benzodiazepines for 150 days and in 2008 it was 17.81% (refer to section 4.3.3).

The number of days between refills for active ingredients illustrated a decrease for 30 day periods and illustrated an increase for the time periods more than 30 days. These trends can be viewed as reason for concern because this means that prescribers were prescribing benzodiazepines for longer time periods than a month. Diazepam was the benzodiazepine that was given the highest percentage within 30 days (93.03% in 2006 & 92% in 2008). The benzodiazepine that was received the least often for 30 days, was Triazolam. Clorazepate indicated the second lowest of the benzodiazepines that were prescribed in 30 day interval group. Prescriptions issued for time periods of 60 and 120 days occurred less frequently. Triazolam and clorazepate were the benzodiazepines that were prescribed the most frequently for 150 days in 2006 and in 2008 prescriptions, clorazepate and brotizolam indicated the highest number. In the event of prescriptions issued for 180 days the highest number was recorded for 2006 in triazolam and flurazepam. In 2008 the highest number was flurazepam and nitrazepam (refer to section 4.3.5).

The trade name products that were mostly prescribed for longer than six months were Tranqipam® 2.5 mg in 2006 and Dalmadorm® 30 mg in 2008. In 2006, Halcion® 0.25 mg was claimed second most of benzodiazepines that were prescribed for longer than 180 days and Tranqipam 1 mg third most of the benzodiazepines that were prescribed for longer than 180 days. The benzodiazepines that exceed the time period of 180 days, were Sandoz Nitrazepam® 5 mg (second most frequently) and Mogadon® 5 mg (third most frequently) in 2008. Dalmadorm® 15 mg and Noctamid 1 mg were the fourth most often prescribed trade name products for longer than 180 days (refer section 4.3.6).

According to the results above it can be concluded that there were no important differences between the number of days between refills for the different genders. The days between refills had increased with the increasing of age of the patients.

The eighth objective was to determine prescribing patterns of benzodiazepines by the general medical practitioner, specialists and other practitioners with regard to benzodiazepine data on the database.

The majority of prescriptions for benzodiazepines were prescribed by general medical practitioners, *i.e.* in 2006, 82.68% (n = 333 128) and 82.49% (n = 265 463) in 2008. The number of prescriptions that was prescribed by other practitioners and psychiatrists, was lower than the number of prescriptions prescribed by the general medical practitioners. The number of benzodiazepine items were also prescribed more often by general medical practitioners than other prescribers, 81.75% (n = 350 507) in 2006 and 81.48% (n =279 926) in 2008 (refer to section 4.3).

General practitioners prescribed most of the benzodiazepine prescriptions in both Northern Cape and Gauteng. In the Northern Cape benzodiazepine prescriptions prescribed by the general medical practitioners represented 95.67% (n = 6 079) in 2006 and 95.43% (n = 4 550) in 2008. The general medical practitioners in Gauteng prescribed 78.76% (n = 136 827) in 2006 and 77.67% (n = 112 731) in 2008 of benzodiazepine prescriptions. The number of benzodiazepine prescriptions prescribed by other prescribers was higher in Gauteng than in the Northern Cape Province. The number of benzodiazepine prescriptions that were prescribed by psychiatrists and claimed in the Northern Cape, indicated only 0.93% in 2006 and 1.11% in 2008 (refer to section 4.3.4).

Gauteng and Northern Cape did differ with regard to the average number of benzodiazepine prescriptions per patient prescribed by psychiatrists. The dissimilarity between the two provinces rendered only a medium effect. This means that there were more benzodiazepine prescriptions were prescribed to the patients by psychiatrists in the Gauteng than in the Northern Cape Province (refer to section 4.3.4).

5.3 RECOMMENDATIONS

The following recommendations for further research can be made at the completion of this study:

- Studies on of the prevalence of insomnia in South Africa should be conducted.
- The benzodiazepine dependence in patients older than 40 years and who resides in South Africa should be investigated.
- The prescribing patterns of benzodiazepines in other province in South Africa and other factors that might have an effect on the prescribing patterns should be subjected to further research.
- The investigation of the prescribing patterns of prescribers according to which dependence may developed, should be investigated.
- The off-label prescribing of benzodiazepines should be examined.

5.4 CHAPTER SUMMARY

In this chapter the conclusions were discussed according to the specific research objectives. This chapter also made recommendations from this study for further studies.

BIBLIOGRAPHY

ALTBEKER, A. 2007. A country at war with itself: South Africa's crisis of crime. Johannesburg: Jonathan Ball Publishers, 160 p.

ASHTON, H. 2005. The diagnosis and management of benzodiazepine dependence. *Current opinion in psychiatry*, 18:249-255. http://www.tenyek-tevhitek.hu/ashtoncurrent.pdf Date of access: 14 Apr. 2009.

BANERJEE, A. 2003. Medical statistics made clear. London: Royal Society of Medicine Press. 137 p.

BEAUREGARD, R.A. 2009. The suburbanization of New York: is the world's greatest city just another town. *International journal of urban & regional research*, 33(2):580-581. Available: Academic Search Premier.

BENDTSEN, P., HENSING, G., MCKENZIE, L. & STRIDSMAN, A.K. 1999. Prescribing benzodiazepines: a critical incident study of a physician dilemma. *Journal of social science and medicine*, 49:459-467. Available: ScienceDirect.

BLAND, M. 2000. An introduction to medical statistics. 3rd ed. Oxford: Oxford University Press. 405 p.

BORCHARDT, M. 1999. Review of clinical pharmacology and use of the benzodiazepines. *Journal of perianesthesia nursing,* 14(2):65-72. Available: ScienceDirect.

BOYD, C.P., KOSTANSKI, M., GULLONE, E. & OLLENDICK, T.H. 2000. Prevalence of anxiety and depression in Australian adolescents: comparisons with worldwide data. *Journal of genetic psychology*, 161(4):479-492. Available: Academic Search Premier.

BRENNAN-GALVIN, E. 2002. Crime and violence in an urbanizing world. *Journal of international affairs*, 56(1):123-145. Available: Academic Search Premier.

BURGER, J. 2009. Worrying trends. *Institute for security studies*, 30:3-11. Available: SA ePublications.

BUVINIC, M. & MORRISON, A.R. 2000. Living in a more violent world. *Foreign policy*, 118:58-72. Available: Academic Search Premier.

CHARNEY, D.S., MIHIC, S.J. & HARRIS, R.A. 2006. Hypnotics and sedatives. (*In* Brunton L.L., Lazo J.S & Parker K.L *eds*: Goodman & Gillman's The Pharmacological Basis of Therapeutics, 11th ed). http://www.accessmedicine.com/content.aspx?aID=938422. Date of access: 29 Mar. 2010.

COHEN, J. 1988. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, N.J: Erlbaum. 567p.

COSTA, J.A. 1999. Introduction: the implications for public health of controls on the benzodiazepines. *European neuropsychopharmacology journal*, 9(Supplement6):391-392. Available: ScienceDirect.

COUNCIL FOR MEDICAL SCHEMES. 2010. Registered medical schemes in South Africa. http://www.medicalschemes.com/Consumer_Assistance/RegSchemes.aspx Date of access: 15 Sep. 2010.

CRAIG, K.J., BROWN, K.J. & BAUM, A. 1995. Environmental factors in the etiology of anxiety. (*In* Bloom F.E. & Kupper D.J., *eds*. Psychopharmacology: the fourth generation of progress. New York: Raven Press. p.1325–1334).

DE LAS CUEVAS, C., SANZ, E. & DE LA FUENTE, J. 2003. Benzodiazepines: more "behavioural" addiction than dependence. *Psychopharmacology*, 167(3):297-303. Available: Academic Search Premier.

DEPARTMENT of Health and Children Dublin see IRELAND. 2002.

DILLMAN, D. A. 1979. Residential preferences, quality of life, and the population turnaround. *American journal agricultural and economics*, 61(5):960-966. Available: Business Source premier.

DEMOMBYNES, G. & OZLER, B. 2005. Crime and local inequality in South Africa. *Journal of development economics*, 76(2):1-63. Available: ScienceDirect.

DU PLESSIS, A. & LOUW, A. 2005. Crime and prevention in South Africa: 10 years on. www.iss.co.za/uploads/WORLDCRIMCONFAUG05.PDF. Date of access: 22 Jun. 2009.

EGAN, M., WOLFSON, C., MORIDE, Y. & MONETTE, J. 2000. Do patient factors alter the relationship between physician characteristics and use of long-acting benzodiazepines. *Journal of clinical epidemiology*, 53(11):1181-1187. Available: ScienceDirect.

EPILEPSY SOUTH AFRICA. 2008. Facts about epilepsy. http://www.epilepsy.org.za/facts/index.php Date of access: 3 Mar. 2009.

ERWIN, W.G. 1991. The definition of drug utilization review: statement of issues. *Clinical pharmacology & therapeutics*, 50(5):596-599. Available: MEDLINE.

GRAY, A. 2005. Insomnia in the elderly: is an evidence-based approach possible? *South African family practice journal*, 47(3):31-36. Available: Africa-Wide Information.

GROENEWEGEN, P.P., LEUFKENS, H.G., SPREEUWENBERG, P. & WORM, W. 1999. Neighbourhood characteristics and use of benzodiazepines in the Netherlands. *Social science & medicine*, 48(12):1701-1711. Available: ScienceDirect.

GUO, J.J., GIBSON, J.T., HANCOCK, G.R. & BARKER, K.N. 1995. Retrospective drug utilization review and the behaviour of medical aid prescribers: an empirical marginal analysis. *Clinical therapeutics,* 17(6):1174-1187. Available: ScienceDirect.

HARVEY, S. & DAVID, Z. 2009. Insomnia. *Insomnia (A.D.A.M),* (27):1-8. Available: Health source – consumer edition. Date of access: 6 Apr. 2009.

HEATHER, N., BOWIE, A., ASHTON, H., McAVOY, B., SPENCER, I., BRODIE, J. & GIDDINGS, D. 2004. Randomised controlled trial of two brief interventions against long-term benzodiazepine use: outcome of intervention. *Addiction research and theory*, 12(2):141-154. Available: Academic Search Premier.

HERMAN, A.A., STEIN, D.J., SEEDAT, S., HEERINGA, S.G., MOOMAL, H. & WILLIAMS, D.R. 2009. The South African stress and health (SASH) study: 12-month and lifetime prevalence of common mental disorders. *South African medical journal*, 99(5):339-344. Available: SA ePublications.

HOWLEY, P. 2009. Attitudes towards compact city living: towards a greater understanding of residential behaviour. *Land use policy,* 26(3):792-798. Available: ScienceDirect.

HPCSA (Health Professions Council of South Africa). 2010. All health care professionals. http://www.hpcsa.co.za/home_all_health.php Date of access: 11 August 2010.

HUFFMAN, J.C. & STERN, T. A. 2003. The use of benzodiazepines in the treatment of chest pain: a review of the literature. *Journal of emergency medicine*, 25(4):427-437. Available: ScienceDirect.

INESTA, A. 1992. Drug utilization in community pharmacy. *Journal of clinical pharmacy and therapeutics*, 17(6):353-355. Available: Academic Search Premier.

IRELAND. Department of Health and Children Dublin. 2002. Report of the Benzodiazepine Committee. http://www.dohc.ie/publications/pdf/benzo1.pdf. Date of access: 3 Mar. 2009.

ISS (Institute for Security Studies). 2005. Crime statistic per province. http://www.iss.co.za/pgcontent.php?UID=13096 Date of access: 6 May 2010.

JANEWAY, D. 2009. An integrated approach to the diagnosis and treatment of anxiety within the practice of cardiology. *Cardiology in review*, 17(1):36-43. http://xa.yimg.com/kq/groups/14600825/1449663735/name/Anxiety+Within+the+Practice+of+Cardiology.pdf Date of access: 15 Jul. 2009.

JUDD, F.K., JACKSON, H.J., KOMITI, A., MURRAY, G., HODGINS, G. & FRASER, C. 2002. High prevalence disorders in urban and rural communities. *Australian and New Zealand journal of psychiatry*, 36(1):104:113. Available: Academic Search Premier.

KAIRUZ, T.E. & TRUTER, I. 2007. A descriptive study of anxiolytic and hypnotic prescribing according to age and sex. *International journal of pharmacy practice*, 15:301-306. Date of access: 25 Aug. 2009.

KAMEL, N.S. & GAMMACK, J.K. 2006. Insomnia in the elderly: cause, approach, and treatment. *The American journal of medicine*, 119(6):463-469. Available: ScienceDirect.

KENNEDY, L.W. 1990. On the borders of crime: conflict management and criminology. London: Longman. 153 p.

KRAKOW, B., JOHNSTON, L., MELENDREZ, D., HOLLIFIELD, M., WARNER, T.D., CHAVEZ-KENNEDY, D. & HERLAN, M.J. 2001. An open-label trial of evidence-based cognitive behavior therapy for nightmares and insomnia in crime victims with PTSD. *American journal for psychiatry,* 158:2043-2047. http://ajp.psychiatryonline.org/cgi/reprint/158/12/2043 Date of access: 16 Oct. 2009

KROENKE, K., STRINE, T.W., SPITZER, R.L., WILLIAMS, J.B.W., BERRY, J.T. & MOKDAD, A.H. 2009. The PHQ-8 as a measure of current depression in the general population. *Journal of affective disorders*, 114(1):163-173. Available: ScienceDirect.

LADER, M.H. 1999. Limitations on the use of benzodiazepines in anxiety and insomnia: are they justified? *European neuropsychopharmacology journal*, 9(6):399-405. Available: ScienceDirect.

LEETMAA, K & TAMMARU, T. 2007. Suburbanization in countries in transition: destinations of suburbanizers in the Tallinn metropolitan area. *Journal of environment & planning*, 89(2):126-146. Available: Academic Search Premier.

LONGO, L.P. & JOHNSON, B. 2000. Addiction: Part 1. Benzodiazepines: side effects, abuse risk and alternatives. *American family physician journal*, 61:2121-2128. Available: CINAHL.

LOUW, A. & BEKKER, S. 1996. Cities Under siege: urban violence in South, Central and West Africa. University of Natal: Indicator Press. 92 p.

MCC (MEDICINE CONTROL COUNCIL). 2010. Medicine and related substances act 101 of 1965. http://www.mccza.com/dynamism/default_dynamic.asp?grpID=26&doc=dynamic_generated_page.asp&categID=142&groupID=26 Date of access: 13 Sep 2010.

MCKERNAN, R.M, ROSAHL, T.W., REYNOLDS, D.S., SUR, C., WAFFORD, K.A., ATACK, J.R., FARRAR, S., MYERS, J., COOK, G., FERRIS, P., GARRETT, L., BRISTOW, L., MARSHALL, G., MACAULAY, A., BROWN, N., HOWELL, O., MOORE, K.W., CARLING, R.W., STREET, L.J., CASTRO, J.L., RAGAN, C.I., DAWSON, G.R. & WHITING, P.J. 2000. Sedative but not anxiolytic properties of benzodiazepines are mediated by the $GABA_A$ receptor α_1 subtype. *Nature neuroscience*, 3(6):587-592. Available: Academic Search Premier.

MIESZKOWSKI, P. & MILLS, E. S. 1993. The causes of metropolitan suburbanization. *Journal of economic perspectives*, 7(3):135-147. Available: Business Source Premier.

MOCH, S. 2009. A perspective on anxiolytics. *South Africa pharmaceutical journal*, 76(7):20-24. Available: Africa-Wide Information.

MOCH, S. 2010. Sleepless in South Africa: insomnia is not just a night-time problem. *South Africa pharmaceutical journal*, 77(7):18-26. Available: Africa-Wide Information.

MORIN, C.M., LEBLANC, M., DALEY, M., GREGOIRE, J.P & MERETTE, C. 2006. Epidemiology of insomnia: prevalence, self-help treatments, consultations and determinants of help-seeking behaviours. *Sleep medicine*, 7(2):123-130. Available: ScienceDirect.

MURIS, P., DU PLESSIS, M. & LOXTON, H. 2008. Orgins of common fears in South African children. *Journal of anxiety disorders*, 22(8):1510-1515. Available: ScienceDirect.

NAUDE, W., ROSSOUW, S. & KRUGELL, W. 2009. The non-monetary quality of city life in South Africa. *Habitat international*, 33:319-326. Available: ScienceDirect.

NCI ***see*** UNITED STATES. NATIONAL CANCER INSTITUTE. 2009.

NEUTEL, C.I. 2005. The epidemiology of long-term benzodiazepine use. *International review of psychiatry*, 17(3):189-197. Available: Academic Search Premier.

NOMOYI, C. 2000. The incidence of violent crime in the rural areas in South Africa: a challenge to indigenous institutions. *Acta Criminologica*, 13(1):66-71. Available: SA ePublications.

NORMAN, T. R., ELLEN, S. R. & BURROWS, G. D. 1997. Benzodiazepines in anxiety disorders: managing therapeutics and dependence. *Medical journal of Australia*, 167(9):490-495. Available: MEDLINE.

OED (Oxford English Dictionary). 2010a. Crime. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 22 Jun 2009.

OED (Oxford English Dictionary). 2010b. Dependence. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 29 Mar. 2010.

OED (Oxford English Dictionary). 2010c. Patient. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 10 Mar. 2010.

OED (Oxford English Dictionary). 2010d. Metropolitan. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 12 Aug. 2009.

OED (Oxford English Dictionary). 2010e. Psychiatrist. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 10 Mar. 2010.

OED (Oxford English Dictionary). 2010f. Urbanization. Oxford: At the Clarendon Press. Available: http://dictionary.oed.com/cgi/entry Date of access: 22 Jun 2009.

OHAYON, M.M. 2002. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep medicine reviews*, 6(2):97-111. Available: ScienceDirect.

PARRY, C.D.H., PLUDDEMANN, A., LOUW, A. & LEGGETT, T. 2004. The 3-metros study of drugs and crime in South Africa: findings and policy implications. *The American journal of drugs and alcohol abuse*, 30(1):167-185. Available: Academic Research Premier.

PEREZ, G.G. & TUDOR, R. 1993. A post-marketing surveillance survey on the use of dipotassium clorazepate in clinical practice in the Philippines. *Current medical research and opinion,* 13(3):175-186. http://www.ncbi.nlm.nih.gov/pubmed/8222745 Date of access: 1 Sep 2009.

PHAROAH, R. 2009. Who is at risk. *Institute for security studies*, 182:1-16. Available: SA ePublications.

POPULATION REFERENCE BUREAU. 2009. World population data sheet: density. http://www.prb.org/Datafinder/Topic/Bar.aspx?sort=v&order=d&variable=132 Date of access: 25 May 2010.

PORTER, R.S. & BEERS, M.H. 2006. Depressive disorders. (*In* Jones, T.V., Kaplan, J. L., Berkwits, M., *eds*. The Merck manual of diagnosis and therapy. 18th ed. New York: Whitehouse Station. p. 1672-1678.).

QUIGLEY, P.A. 2001. Public health dimensions of benzodiazepine regulation. *Critical public health,* 11(4):331-339. Available: Academic Research Premier.

QUIGLEY, P., USHER, C., BENNETT, K. & FEELY, J. 2006. Socioeconomic influences on benzodiazepine consumption in an Irish region. *European addiction research*, 12(3):145-150. Available: Academic Research Premier.

RICHARDS, C. 2005. When counting sheep does not help: the growing incidence of sleep disorders. *Business trends*, 10(9):611-614. Available: ScienceDirect.

ROBERTSON, J. R. & TREASURE, W. 1996. Benzodiazepine abuse: nature and extent of the problem. *CNS drugs*, 2:137-146. Available: Academic Research Premier.

ROGERS, A., PILGRIM, D., BRENNAN, S., SULAIMAN, I., WATSON, G. & CHEW-GRAHAM, C. 2007. Prescribing benzodiazepines in general practice: a new view of an old problem. *Health journal*, 11(2):181-198. http://hea.sagepub.com/content/11/2/181.full.pdf+html Date of access: 8 Jun. 2009.

ROSSITER, D. 2010. Anxiolytics. South African medicines formulary. 9th ed. Cape Town: Health and Medical Publishing Group of the South African Medical Association, 639p.

SAS INSTITUTE INC. 2010. SAS for Windows 9.1.3.

SERRADELL, J., BJORNSON, D.C. & HARTZEM, A.G. 1987. Drug utilization study methodologies: national and international perspectives. *Drug intelligence and clinical pharmacy*, 21(12):994:1001. Available: CINAHL.

SJÖQVIST, F. & BIRKETT, D. 2003. Chapter 10. drug utilization. (*In* World Health Organization., *ed*. Introduction to drug utilization research. World Health Organization. p. 76-84.).

SMITH, A.J., SKETRIS, I., COOKE, C., GARDNER, D., KISELY, S. & TETT, S.E. 2008. A comparison of benzodiazepine and related drug use in Nova Scotia and Australia. *The Canadian journal of psychiatry*, 53(8):545-552. Available: Academic Research Premier.

SNYMAN, J.R. ed. 2009. Central nervous system. *Monthly index of medical specialties*, 49(3):394.

SOUMERAI, S.B. & LIPTON, H.L. 1995. Computer-based drug-utilization review – risks, benefit, or boondoggle. *The New England journal of medicine,* 332(24):1641-1645.

SOUTH AFRICA. 1997. Medicine and related substances control amendment act. *Government gazette*, 18505:42. http://www.bhfglobal.com/files/Medicines%20and%20Related%20Substances%20Control%20Act%20101%20of%201965.pdf Date of access: 2 Aug 2010

SOUTH AFRICA. 2003. Medicines and related Substances Act 101 of 1965 after amended by the Medicines and Related Substances Control Amendment Act (Act 90 of 1997). PSSA pharmacy law compendium, Vol. 1, service issue 1 as at 30 June 2003.

SRISURAPANONT, M., GARNER, P., CRITCHLEY, J. & WONGPAKARAN, N. 2005. Benzodiazepine prescribing behaviour and attitudes: a survey among general practitioners practicing in northern Thailand. *BioMed Central family practice*, 6:27-31. Available: MEDLINE.

STAHL, S.M. 2010. Stahl's illustrated anxiety, stress, and PTSD. New York: Cambridge University Press, 190p.

STATISTICS SOUTH AFRICA. 2006. Migration and urbanisation in South Africa. Available: www.statssa.gov.za Date of access: 12 May 2010.

STATISTICS SOUTH AFRICA. 2007. Community Survey. Available: http://www.statssa.gov.za/Publications/CS2007Basic/CS2007Basic.pdf Date of access: 12 May 2010.

STATISTICS SOUTH AFRICA. 2006. Population Census 2004: Northern Cape. www.statssa.gov.za Date of access: 12 Feb. 2009.

STATISTICS SOUTH AFRICA. 1999. Victims of crime survey 1998. www.statssa.gov.za Date of access: 24 Feb 2009.

STEIN, D.J., SEEDAT, S., HERMAN, A., MOOMAL, H., HEERINGA, S.G., KESSLER, R.C & WILLIAMS, D.R. 2008. Lifetime prevalence of psychiatric disorders in South Africa. *The British journal of psychiatry*, 192(2):112-117. Available: MEDLINE.

STEYN, H.S. 2009. Manual for determination of effect size indices and practical significance. Potchefstroom: Statistical Consultation Services, NWU. http://www.puk.ac.za/opencms/export/PUK/html/fakulteite/natuur/skd/handleiding_e.html Date of access: 19 Jul. 2010.

STRAKER, G., MENDELSOHN, M., MOOSA, F. & TUDIN, P. 1996. Violent political contexts and the emotional concerns of townships youth. *Child development*, 67(1):46-54. Available: Academic Research Premier.

SWEETMAN, S.C. 2010. Martindale: the complete drug reference. London: Pharmaceutical Press. http://www.puk.ac.za:2535/mc/martindale/current/7000-a6-k.htm Date of access: 22 Mar. 2010.

TAKETOMO, C.K., HODDING, J.H. & KRAUS, D.M. 2000. Pediatric dosage handbook. 7th ed. Cleveland: Lexi-Comp. 1458p.

TIERNEY, L.M., MCPHEE, S.J. & PAPADAKIS, M.A. 2005. Current medical diagnosis & treatment. 44th ed. New York: McGraw Hill. 1887p.

TREVOR, A.J. & WAY, W.L. 2009. Sedative-hypnotic drugs. (*In* Katzung, B.G., Masters, S.B. & Trevor, A.J., *eds*. Basic & Clinical Pharmacology. 11th ed. New York: McGraw Hill. p. 371-386.).

TRUTER, I. 1994. A drug utilization study to establish norms for rational and cost-effective use of medicine. University of Port Elizabeth. (Thesis – M.Sc.) 329 p.

TU, K., MAMDANI, M.M., HUX, J.E. & TU, J. 2001. Progressive trends in the prevalence of benzodiazepine prescribing in older people in Ontario, Canada. *Journal of American geriatrics society*, 49(10):1341-1345. Available: Academic Research Premier.

UNITED NATIONS. Department of Economics and Social Affairs. 2007. World urbanization prospects 2007 review. 230p. http://www.un.org/esa/population/publications/wup2007/2007WUP_Highlights_web.pdf Date of access: 4 Mar. 2010.

UNITED NATIONS POPULATION FUND. 2007. State of world population: unleashing the potential of urban growth. http://www.un.org/partnerships/Docs/UNFPA_State%20of%20the%20World%20Report%202007.pdf Date of access: 04 Mar. 2010.

UNITED STATES. National Cancer Institute. 2009. Overview of cancer prevalence statistics. http://www.srab.cancer.gov/prevalence/ Date of access: 13 Oct. 2010.

VAN JAARSVELD, F. A. 1985. Verstedeliking in Suid-Afrika. Pretoria: Universiteit van Pretoria. 190 p.

WANING, B & MONTAGNE, M. 2001. Pharmacoepidemiology principles and practice. New York: McGraw-Hill. 205 p.

WILSON, J.F. 2008. In the clinic: insomnia. *Annals of internal medicine*, 148(1):131-146. Available: Academic Search Premier.

WILSON, S. & NUTT, D. 2008. Insomnia: guide to diagnosis and choice of treatment. *Prescriber,* 16(22):29-40. http://onlinelibrary.wiley.com/doi/10.1002/psb.227/pdf Date of access: 23 Jul. 2009.

WHO (WORLD HEALTH ORGANIZATION). 1993. World health statistics annual 1992. Geneva. 463 p.

WHO (WORLD HEALTH ORGANIZATION). 2003. Introduction to drug utilisation research. http://www.who.int/medicines/areas/quality_safety/safety_efficacy/utilization/en/index.html Date of access: 5 May 2010.

WHO (WORLD HEALTH ORGANIZATION). 2009. Epilepsy. http://www.who.int/mediacentre/factsheets Date of access: 2 Mar. 2009.

WHO (WORLD HEALTH ORGANIZATION). 2010. What do we mean by “sex” and “gender”. http://www.who.int/gender/whatisgender/en/ Date of access: 19 Jul. 2010.

YORK, P. 2002. The design of dosage forms. (*In* Aulton, M.E., *ed*. Pharmaceutics: the science of dosage form design. 2nd ed. Spain: Elsevier. p. 1-3.).

ZIKMUND, W.G., BABIN, B.J., CARR, J.C. & GRIFFIN, M. 2010. Business research methods. 8th ed. Mason, OH: South-Western. 674 p.

APPENDIX A

APPENDIX A

Table A.1: The *d*-value for the difference between the average number of prescriptions per patient

Average number of prescriptions per patient								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
N_{2006}	4.70±6.15	4.98±6.52	4.33±5.62	2.88±2.96	2.72±2.86	3.52±4.32	5.52±6.78	8.58±9.46
N_{2008}	5.52±6.87	5.88±7.27	5.05±6.27	3.01±3.13	2.89±3.12	3.92±4.67	6.29±7.18	9.89±10.03
d-value	0.12	0.12	0.12	0.042	0.055	0.086	0.11	0.13

(refer to formula in section 3.6.2.3)

Table A.2: The *d*-value for the difference between the average number of items per prescription

Average number of items per prescription								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
N_{2006}	2.37±1.55	2.29±1.52	2.29±1.46	2.47±1.34	2.34±1.33	2.18±1.31	2.25±1.47	2.41±1.80
N_{2008}	2.43±1.64	2.31±1.58	2.31±1.52	2.40±1.34	2.25±1.31	2.14±1.30	2.28±1.52	2.48±1.87
d-value	0.037	0.013	0.013	0.05	0.068	0.031	0.0197	0.037

(refer to formula in section 3.6.2.3)

Table A.3: The *d*-value of the average number of prescriptions per patient between the Northern Cape and Gauteng province for 2006

Average number of prescriptions per patient for 2006								
		Gender		Age Categories				
	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP	4.87±6.18	5.18±6.56	4.47±5.62	2.95±3.01	2.78±2.92	3.60±4.25	5.84±6.85	8.97±9.46
NC	4.96±6.30	5.33±6.70	4.50±5.74	2.76±2.79	2.53±2.58	3.88±4.78	6.14±7.18	8.13±8.81
d-value	0.01	0.02	0.005	0.06	0.09	0.06	0.04	0.09

(refer to formula in section 3.6.2.3)

Table A.4: The *d*-value of the average number of prescriptions per patient between the Northern Cape and Gauteng province for 2008

Average number of prescriptions per patient for 2008								
		Gender		Age Categories				
	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP	5.52±6.78	5.91±7.21	5.02±6.15	3.07±3.19	2.98±3.25	3.93±4.64	6.37±7.21	9.79±9.76
NC	6.14±7.00	6.65±7.58	5.57±6.23	3.07±3.10	3±3.27	4.38±5.17	7.29±7.39	10.35±9.62
d-value	0.09	0.1	0.09	0	0.006	0.09	0.12	0.06

(refer to formula in section 3.6.2.3)

Table A.5: The *d*-value of the average number of items per prescriptions between the Northern Cape and Gauteng province for 2006

Average number of items per prescription 2006								
		Gender		Age Categories				
	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP	2.35±1.55	2.35±1.58	2.36±1.50	2.49±1.36	2.37±1.36	2.22±2.30	2.30±1.51	2.55±1.91
NC	2.31±1.50	2.34±1.55	2.27±1.43	2.39±1.27	2.32±1.32	2.20±1.38	2.27±1.49	2.51±1.75
d-value	0.03	0.006	0.06	0.07	0.04	0.009	0.02	0.02

(refer to formula in section 3.6.2.3)

Table A.6: The *d*-value of the average number of items per prescriptions between the Northern Cape and Gauteng province for 2008

Average number of items per prescription 2008								
		Gender		Age Categories				
	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
GP	2.35±1.60	2.35±1.64	2.35±1.55	2.41±1.35	2.26±1.32	2.15±1.32	2.32±1.56	2.6±1.96
NC	2.29±1.49	2.32±1.55	2.25±1.41	2.35±1.27	2.14±1.26	2.13±1.29	2.26±1.43	2.54±1.86
d-value	0.04	0.02	0.07	0.04	0.09	0.02	0.04	0.03

(refer to formula in section 3.6.2.3)

Table A.7 – The percentage of distribution of the number of patients in the Northern Cape and Gauteng from the total database for 2006 and 2008

	Age groups (years)					
	Year	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
Number of patients (N_{2006} = 1 964 381; N_{2008} = 1 290 017)						
Patients in GP (n)	2006	107 293	51 343	227 777	278 311	80 849
	2008	59 507	34 814	143 115	212 098	66 291
Patients in NC (n)	2006	4 184	2 007	7 644	10 913	2 976
	2008	2 021	1 275	4 449	8 277	2 047
Prevalence GP (n/N x 100)	2006	5.46%	2.61%	11.60%	14.17%	4.12%
	2008	4.61%	2.70%	11.09%	16.44%	5.14%
Prevalence NC (n/N x 100)	2006	0.21%	0.10%	0.39%	0.56%	0.15%
	2008	0.16%	0.10%	0.34%	0.64%	0.16%

Table A.8 - The percentage of distribution of the number of prescriptions in the Northern Cape and Gauteng from the total database for 2006 and 2008

	Age groups (years)					
	Year	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
Number of prescriptions (N_{2006} = 9 223 281; N_{2008} = 7 120 035)						
Prescriptions in GP (n)	2006	316 166	142 875	819 179	1 626 660	725 461
	2008	182 542	103 696	561 753	1 351 433	649 067
Prescriptions in NC (n)	2006	11 525	5 073	29 677	67 039	24 184
	2008	6 204	3 825	19 475	60 313	21 193
Prevalence GP (n/N x 100)	2006	3.43	1.55	8.88	17.64	7.87
	2008	0.16	1.46	7.89	18.98	9.12
Prevalence NC (n/N x 100)	2006	0.12	0.06	0.32	0.73	0.26
	2008	0.09	0.05	0.27	0.85	0.30

Table A.9 – The percentage of distribution of the number of items in the Northern Cape and Gauteng province from the total database for 2006and 2008

	Age groups (years)					
	Year	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
Number of items (N_{2006} = 21113422; N_{2008} = 16439253)						
Items in GP (n)	2006	788 619	339 200	1 820 082	3 748 954	1 848 810
	2008	440 310	234 165	1 207 581	3 129 505	1 689 409
Items in NC (n)	2006	27 492	11 749	65 313	152 361	60 600
	2008	14 598	8 173	41 425	136 409	53 887
Prevalence GP (n/N x 100)	2006	3.74	1.61	8.62	17.76	8.76
	2008	2.68	1.42	7.35	19.04	10.28
Prevalence NC (n/N x 100)	2006	0.13	0.06	0.31	0.72	0.29
	2008	0.09	0.05	0.25	0.83	0.33

Table A.10: The *d*-value between the average number of benzodiazepine prescriptions per patient for 2006 and 2008

Average number of benzodiazepine prescription per patient								
		Gender		**Age Categories**				
Year	**Total**	**Female**	**Male**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
N_{2006}	2.83±3.26	2.92±3.33	2.64±3.10	1.32±1.45	1.23±0.86	1.62±1.65	2.66±3.08	4.55±4.17
N_{2008}	3.16±3.58	3.27±3.66	2.92±3.39	1.38±1.58	1.33±1.19	1.77±2.00	2.85±3.29	4.94±4.36
d-value	0.092	0.096	0.083	0.038	0.084	0.075	0.058	0.9

(refer to formula in section 3.6.2.3)

Table A.11: The *d*-value between the average number of benzodiazepine items per prescription for 2006 and 2008

Average number of benzodiazepines items per prescription								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
N_{2006}	1.05±0.24	1.06±0.24	1.05±0.23	1.03±0.21	1.03±0.18	1.04±0.20	1.06±0.24	1.06±0.25
N_{2008}	1.06±0.24	1.06±0.25	1.05±0.24	1.07±0.25	1.02±0.15	1.05±0.22	1.06±0.25	1.06±0.24
d-value	0.042	0	0	0.16	0.056	0.046	0	0

(refer to formula in section 3.6.2.3)

Table A.12: The *d*-value between the average number of benzodiazepine prescription per patient of the total data and the benzodiazepine data for 2006

Average number of benzodiazepine prescriptions per patient for 2006								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
n_{2006}	4.70±6.15	4.98±6.52	4.33±5.62	2.88±2.96	2.72±2.86	3.52±4.32	5.52±6.78	8.58±9.46
n_{2006}	2.83±3.26	2.92±3.33	2.64±3.10	1.32±1.45	1.23±0.86	1.62±1.65	2.66±3.08	4.55±4.17
d-value	0.3	0.32	0.3	0.53	0.52	0.44	0.42	0.43

(refer to formula in section 3.6.2.3)

Table A.13: The *d*-value between the average number of benzodiazepine prescription per patient of the total data and the benzodiazepine data for 2008

Average number of benzodiazepine prescriptions per patient in 2008								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
n_{2008}	5.52±6.87	5.88±7.27	5.05±6.27	3.01±3.13	2.89±3.12	3.92±4.67	6.29±7.18	9.89±10.03
n_{2008}	3.16±3.58	3.27±3.66	2.92±3.39	1.38±1.58	1.33±1.19	1.77±2.00	2.85±3.29	4.94±4.36
d-value	0.34	0.36	0.34	0.52	0.5	0.46	0.48	0.49

(refer to formula in section 3.6.2.3)

Table A.14: The *d*-value between the average number of benzodiazepine items per prescription of the total data and the benzodiazepine data for 2006

Average number of benzodiazepine items per prescription								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
n_{2006}	2.37±1.55	2.29±1.52	2.29±1.46	2.47±1.34	2.34±1.33	2.18±1.31	2.25±1.47	2.41±1.80
n_{2006}	1.05±0.24	1.06±0.24	1.05±0.23	1.03±0.18	1.03±0.18	1.04±0.20	1.06±0.24	1.06±0.25
d-value	0.85	0.81	0.85	1.08	0.99	0.87	0.81	0.75

(refer to formula in section 3.6.2.3)

Table A.15: The *d*-value between the average number of benzodiazepine items per prescription of the total data and the benzodiazepine data for 2008

Average number of benzodiazepine items per prescription								
		Gender		Age Categories				
Year	**Total**	**Female**	**Male**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
n_{2008}	2.43±1.64	2.31±1.58	2.31±1.52	2.40±1.34	2.25±1.31	2.14±1.30	2.28±1.52	2.48±1.87
n_{2008}	1.06±0.24	1.06±0.25	1.05±0.24	1.07±0.25	1.02±0.15	1.05±0.22	1.06±0.25	1.06±0.24
d-value	0.84	0.79	0.83	0.99	0.94	0.84	0.81	0.76

(refer to formula in section 3.6.2.3)

Table A.16: Percentage of benzodiazepine prescriptions prescribed by each practitioner

				Prevalence (n/N x 100)		
	GMP	Other	Psychiatrist	GMP	Other	Psychiatrist
Number of prescriptions						
N_{2006} = 402 903	333 128	49 643	20 132	82.68%	12.32%	5.00%
N_{2008} = 324 744	265 463	41 071	18 210	82.49%	12.23%	5.28%
Number of items						
N_{2006} = 424 907	350 507	51 980	22 420	81.75%	12.65%	5.61%
N_{2008} = 343 560	279 926	43 257	20 377	81.48%	12.59%	7.28%

Table A.17: The *d*-value between the different prescribers for 2006 and 2008

Practitioner	**2006**	**2008**	**Practitioner**	**2006**	**2008**	**Practitioner**	**2006**	**2008**
GMP	2.75±3.18	3.06±3.48	GMP	2.75±3.18	3.06±3.48	Psychiatrist	3.01±3.14	3.46±3.55
Psychiatrist	3.01±3.14	3.46±3.55	Other	2.26±2.46	2.54±2.76	Other	2.26±2.46	2.54±2.76
d-value	0.08	0.11		0.15	0.15		0.24	0.26

(refer to formula in section 3.6.2.3)

Table A.18: Percentage of benzodiazepine prescriptions prescribed by each practitioner in the Gauteng and Northern Cape Province

					Prevalence (n/N x 100)		
		GMP	Other	Psychiatrist	GMP	Other	Psychiatrist
	Number of prescriptions						
GP	N_{2006} = 173 723	136 827	26 330	10 566	78.76%	15.16%	6.08%
	N_{2008} = 145 147	112 731	22 447	99 69	77.67%	15.47%	6.87%
NC	N_{2006} = 6 354	6 079	216	59	95.67%	3.40%	0.93%
	N_{2008} = 4 768	4 550	165	53	95.43%	3.46%	1.11%
	Number of items						
GP	N_{2006} = 184 500	144 970	27 687	11 843	78.57%	15.01%	6.42%
	N_{2008} = 155 043	119 844	23 867	11 332	77.30%	15.39%	7.31%
NC	N_{2006} = 6665	6 378	224	63	95.69%	3.36%	0.95%
	N_{2008} = 5 027	4 793	174	60	95.35%	3.46%	1.19%

Table A.19: The *d*-value of the average number of prescriptions per patient between general practitioners and other practitioners for 2006 and 2008

Provinces	Gauteng		Northern Cape	
Practitioner	2006	2008	2006	2008
GMP	2.83±3.20	3.18±3.54	2.55±2.99	2.76±3.34
Other	2.31±2.47	2.65±2.84	1.98±2.53	2.12±2.41
d-value	0.16	0.15	0.19	0.19

(refer to formula in section 3.6.2.3)

Table A.20: The *d*-value of the average number of prescriptions per patient between general practitioners and psychiatrists for 2006 and 2008

Provinces	Gauteng		Northern Cape	
Year	2006	2008	2006	2008
GMP	2.83±3.20	3.18±3.54	2.55±2.99	2.76±3.34
Psychiatrist	3.01±3.11	3.44±3.51	1.6±0.96	2.12±1.54
d-value	0.056	0.07	0.32	0.19

(refer to formula in section 3.6.2.3)

Table A.21: The *d*-value of the average number of prescriptions per patient between psychiatrist and other practitioners for 2006 and 2008

Provinces	**Gauteng**		**Northern Cape**	
Year	**2006**	**2008**	**2006**	**2008**
Psychiatrist	3.01±3.11	3.44±3.51	1.6±0.96	2.12±1.54
Other	2.31±2.47	2.65±2.84	1.98±2.53	2.12±2.41
d-value	0.23	0.23	0.15	0

(refer to formula in section 3.6.2.3)

Table A.22: The *d*-value between the average number of prescriptions per patient prescribed by practitioners in two provinces

	2006			**2008**		
	GMP	**Other**	**Psychiatrist**	**GMP**	**Other**	**Psychiatrist**
GP	2.83±3.20	2.31±2.47	3.01±3.11	3.18±3.54	2.65±2.84	3.44±3.51
NC	2.55±2.99	1.98±2.53	1.6±0.96	2.76±3.34	2.12±2.41	2.12±1.54
d-value	0.09	0.13	0.45	0.12	0.19	0.38

(refer to formula in section 3.6.2.3)

Table A.23: The d-values of the average number of benzodiazepine prescriptions per patient between two provinces in 2006

Average number of benzodiazepine prescriptions per patient in the Northern Cape and Gauteng for 2006								
		Gender		**Age Categories**				
Year	**Total**	**Female**	**Male**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
2006	2.93±3.32	3.02±3.37	2.77±3.21	1.29±1.22	1.25±0.86	1.72±1.81	2.88±3.26	4.58±4.13
2006	2.56±3	2.59±3.07	2.50±2.86	2.13±3.44	1.07±0.26	1.58±1.68	2.39±2.65	4.35±4.28
d-value	0.11	0.13	0.08	0.24	0.21	0.08	0.15	0.05

(refer to formula in section 3.6.2.3)

Table A.24: The d-values of the average number of benzodiazepine prescriptions per patient between two provinces in 2008

Average number of benzodiazepine prescriptions per patient in the Northern Cape and Gauteng for 2008								
		Gender		**Age Categories**				
Year	**Total**	**Female**	**Male**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
2008	3.32±3.66	3.44±3.74	3.07±3.48	1.40±1.72	1.38±1.27	1.93±2.23	3.15±3.52	5±4.34
2008	2.77±3.34	2.80±3.42	2.72±3.18	1.44±1.42	1.16±0.47	1.68±2.76	2.46±2.89	4.71±4.20
d-value	0.15	0.17	0.1	0.02	0.17	0.09	0.2	0.067

(refer to formula in section 3.6.2.3)

Table A.25: The d-values of the average number of benzodiazepine items per prescription between two provinces in 2006

Average number of benzodiazepine items per prescription in the Northern Cape and Gauteng for 2006								
		Gender		**Age Categories**				
Year	**Total**	**Female**	**Male**	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
2006	1.06±0.25	1.06±0.25	1.06±0.25	1.01±0.11	1.04±0.21	1.05±0.22	1.07±0.26	1.06±0.26
2006	1.05±0.22	1.05±0.22	1.05±0.21	1.0±0.0	1.0±0.0	1.02±0.14	1.05±0.22	1.06±0.24
d-value	0.04	0.04	0.04	0.09	0.19	0.14	0.077	0.0

(refer to formula in section 3.6.2.3)

Table A.26: The d-values of the average number of benzodiazepine items per prescription between two provinces in 2008

Average number of benzodiazepine items per prescription in the Northern Cape and Gauteng for 2008								
		Gender		Age Categories				
Year	Total	Female	Male	0<x≤12	12<x≤18	18<x≤40	40<x≤65	65+
2008	1.07±0.26	1.07±0.27	1.06±0.26	1.10±0.30	1.02±0.14	1.06±0.24	1.07±0.27	1.07±0.26
2008	1.05±0.23	1.05±0.22	1.06±0.24	1.27±0.45	1.17±0.38	1.03±0.18	1.05±0.23	1.06±0.23
d-value	0.08	0.07	0	0.38	0.4	0.13	0.07	0.04

(refer to formula in section 3.6.2.3)

Table A.27: The percentage of distribution of the number of benzodiazepine patients in the Northern Cape and Gauteng that claimed from the total data for 2006 and 2008

	Age groups (years)					
	Year	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
Number of patients (N_{2006} = 142 462; N_{2008} = 102 758)						
	2006	305	733	14 761	30 393	13 017
Patients in GP (n)	2008	192	521	9 102	23 206	10 692
	2006	15	28	593	1 369	480
Patients in NC (n)	2008	18	25	324	979	373
	2006	0.21%	0.51%	10.36%	21.33%	9.14%
Prevalence GP (n/N x 100)	2008	0.19%	0.51%	8.86%	22.58%	10.41%
	2006	0.01%	0.02%	0.42%	0.96%	0.34%
Prevalence NC (n/N x 100)	2008	0.02%	0.02%	0.32%	0.95%	0.36%

Table A.28: The percentage of distribution of the number of benzodiazepine prescriptions in Northern Cape and Gauteng that claimed from the total data for 2006 and 2008

	Age groups (years)					
	Year	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
Number of prescriptions (N_{2006} = 402 903; N_{2008} = 324 747)						
Prescriptions in GP (n)	2006	391	915	25 401	87 448	59 567
	2008	268	718	17 587	73 114	53 461
Prescriptions in NC (n)	2006	32	30	936	3 268	2 088
	2008	26	29	544	2 412	1 757
Prevalence GP (n/N)	2006	0.10%	0.23%	6.30%	21.70%	14.78%
	2008	0.08%	0.22%	5.42%	22.51%	16.46%
Prevalence NC (n/N)	2006	0.01%	0.01%	0.23%	0.81%	0.52%
	2008	0.01%	0.01%	0.17%	0.74%	0.54%

Table A.29: The percentage of distribution of the number of benzodiazepine prescriptions in Northern Cape and Gauteng that claimed from the total data for 2006 and 2008

	Age groups (years)					
	Year	**0<x≤12**	**12<x≤18**	**18<x≤40**	**40<x≤65**	**65+**
Number of items (N_{2006} = 424 907; N_{2008} = 343 563)						
Items in GP (n)	2006	397	949	26 636	93 167	63 351
	2008	294	732	18 596	78 353	57 069
Items in NC (n)	2006	32	30	957	3 428	2 218
	2008	33	34	562	2543	1855
Prevalence GP (n/N)	2006	0.09%	0.22%	6.27%	21.93%	14.91%
	2008	0.09%	0.23%	5.73%	24.13%	17.57%
Prevalence NC (n/N)	2006	0.01%	0.01%	0.23%	0.81%	0.52%
	2008	0.01%	0.01%	0.17%	0.78%	0.57%

Table A.30: The percentage of benzodiazepines claimed per province during 2006 and 2008

	Total patients in GP (N)		Total patients in NC (N)		Benzodiazepine patients in GP (n)		Benzodiazepine patients in NC (n)		Prevalence of GP in % (n/N)		Prevalence of NC in % (n/N)	
Year	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**	**2006**	**2008**
Total	745 573	515 825	27 724	18 069	59 209	43 713	2 485	1 719	7.91	8.47	8.96	9.51
Female	421 159	289 589	15 381	9 679	39 809	29 445	1 684	1 162	9.45	10.17	10.95	12.01
Male	323 867	226 236	12 336	8 390	19 365	14 268	801	557	5.97	6.31	6.49	6.64
0<x≤12	107 293	59 507	4 184	2 021	305	192	15	18	0.28	0.32	0.36	0.89
12<x≤18	51 343	34 814	2 007	1 275	733	521	28	25	1.42	1.50	1.40	1.96
18<x≤40	227 777	143 115	7 644	4 449	14 761	9 102	593	324	6.48	6.36	7.76	7.28
40<x≤65	278 311	212 098	10 913	8 277	30 393	23 206	1 369	979	10.92	10.94	12.55	11.83
65 +	80 849	66 291	2 976	2 047	13 017	10 692	480	373	16.10	16.13	16.13	18.22

Table A.31: The percentage of benzodiazepines prescriptions claimed per province during 2006 and 2008

	Total prescriptions in GP (N)		Total prescription in NC (N)		Benzodiazepine prescriptions in GP (n)		Benzodiazepine prescriptions in NC (n)		Prevalence of GP in % (n/N)		Prevalence of NC in % (n/N)	
Year	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008
Total	3 630 346	2 848 495	137 499	111 010	173 723	145 148	6 354	4 768	4.79	5.10	4.62	4.30
Female	2 180 136	1 712 207	819 36	64 319	120 069	101 299	4 355	3 254	5.51	5.92	5.32	5.06
Male	1 448 149	1 136 292	55 550	46 692	53 571	43 849	1 999	1 514	3.70	3.86	3.60	3.24
0<x≤12	316 166	182 542	11 525	6 204	392	268	32	26	0.12	0.15	0.28	0.42
12<x≤18	142 875	103 696	5 073	3 825	915	718	30	29	0.64	0.69	0.59	0.76
18<x≤40	819 179	561 753	29 677	19 475	25 401	17 587	936	544	3.10	3.13	3.15	2.79
40<x≤65	1 626 660	1 351 433	67 039	60 313	87 448	73 114	3 268	2 412	5.38	5.41	4.87	4.00
65 +	725 461	649 067	24 184	21 193	59 567	53 461	2 088	1 757	8.21	8.24	8.63	8.29

Table A.32: The percentage of benzodiazepines items claimed per province during 2006 and 2008

	Total items in GP (N)		Total items in NC (N)		Benzodiazepine items in GP (n)		Benzodiazepine items in NC (n)		Prevalence of GP in % (n/N)		Prevalence of NC in % (n/N)	
Year	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008
Total	8 545 665	6 700 970	317 515	254 492	184 500	155 044	6 665	5 027	2.16	2.31	2.10	1.98
Female	5 130 316	4 031 882	191 651	149 487	127 570	108 358	4 574	3 416	2.49	2.69	2.39	2.29
Male	3 411 088	2 669 088	125 835	105 005	56 845	46 686	2 091	1 611	1.67	1.75	1.66	1.53
0<x≤12	788 619	440 310	27 492	14 598	397	294	32	33	0.05	0.07	0.12	0.23
12<x≤18	339 200	234 165	11 749	8 173	949	732	30	34	0.28	0.31	0.26	0.42
18<x≤40	1 820 082	1 207 581	65 313	41 425	26 636	18 596	957	562	1.46	1.54	1.47	1.36
40<x≤65	3 748 954	3 129 505	152 361	136 409	93 167	78 353	3 428	2 543	2.49	2.50	2.25	1.86
65 +	1 848 810	1 689 409	60 600	53 887	63 351	57 069	2 218	1 855	3.43	3.38	3.66	3.44

APPENDIX B

APPENDIX B

Table B.1: Prescribing patterns of benzodiazepine in 2006 and 2008

		Benzodiazepines (n_{2006})	Benzodiazepines (n_{2008})	Total data (N_{2006})	Total data (N_{2008})	Prevalence (n/N)	Prevalence (n/N)
	Number of patient	142 462	102 758	1 964 381	1 290 017	7.25%	7.97%
Gender	Female	95 844	69 304	1 113 427	728 051	8.61%	9.52%
	Male	46 539	33 454	849 635	561 966	5.48%	5.95%
	Unknown			1 319			
Age groups (years)	0<x≤12	745	466	282 549	150 400	0.26%	0.31%
	12<x≤18	1 776	1 211	138 935	92 923	1.28%	1.30%
	18<x≤40	33 438	19 934	581 406	340 115	5.75%	5.86%
	40<x≤65	73 545	54 333	740 455	533 493	9.93%	10.18%
	65 +	32 958	26 814	221 036	173 086	14.91%	15.49%
	Number of prescriptions	402 903	324 747	9 223 230	712 003	4.37%	4.56%
Gender	Female	279 733	226 935	5 543 056	4 281 971	5.05%	5.30%
	Male	122 977	97 812	3 675 209	2 838 064	3.35%	3.45%
	Unknown	193		4 965		3.89%	
Age groups (years)	0<x≤12	985	645	812 794	453 226	0.12%	0.14%
	12<x≤18	2 187	1 613	377 446	268 047	0.58%	0.60%
	18<x≤40	54 331	35 207	2 045 313	1 333 911	2.66%	2.64%
	40<x≤65	195 387	154 814	4 090 499	3 353 768	4.78%	4.62%
	65 +	150 013	132 468	1 897 178	1 711 083	7.91%	7.74%
	Number of items	424 907	343 563	21 113 422	16 439 253	2.01%	2.09%
Gender	Female	295 492	240 374	5 336 203	9 893 928	5.54%	2.43%
	Male	129 220	103 189	3 565 331	6545325	3.62%	1.58%
	Unknown	195		4 814		4.05%	
Age groups (years)	0<x≤12	1 017	688	2 005 107	1 085 511	0.05%	0.06%
	12<x≤18	2 248	1 651	882 991	602 822	0.25%	0.27%
	18<x≤40	56 468	36 857	4 449 232	2 855 035	1.27%	1.29%
	40<x≤65	206 350	164 138	9 197 629	7 658 730	2.24%	2.14%
	65 +	158 824	140 229	4 578 463	4 237 155	3.47%	3.31%

Table B.2: Number of days supplied of benzodiazepine items

	Days supplied	Year	Total (N)	Female (n)	Male (n)	Unknown (n)	0<x≤12 (n)	12<x≤18 (n)	18<x≤40 (n)	40<x≤65 (n)	65+ (n)
Total days supply	0<x≤30	2006	124 752	83 684	41 009	59	741	1 832	35 490	66 241	20 448
		2008	90 343	61 003	29 340	0	462	1 235	20 968	49 711	17 967
	30<x≤60	2006	14 508	10 097	4 405	6	15	60	2 203	7 380	4 850
		2008	12 572	8 761	3 811	0	5	37	1 562	6 178	4 790
	60<x≤90	2006	7 464	5 149	2 309	6	4	15	824	3 719	2 902
		2008	6 908	4 889	2 019	0	3	18	647	3 291	2 949
	90<x≤120	2006	12 394	8 776	3 613	5	13	15	1 024	5 746	5 596
		2008	11 359	8 009	3 350	0	5	18	801	5 015	5 520
	120<x≤150	2006	14 406	10 205	4 195	6	7	9	551	5 875	7 964
		2008	12 162	8 657	3 505	0	10	11	444	4 752	6 945
	180 +	2006	1 742	1 221	520	1	5	0	28	701	1 008
		2008	1 463	1 035	428	0	4	1	56	568	834

Table B.3: Prescribing patterns of benzodiazepines according to the active ingredient

Rank		Number of benzodiazepine items					Prevalence of		
		Years	Total	Female	Male	Un-known	Individual /Total	Females	Males
	Total benzodiazepines	2006	424 907	295 492	129 220	195			
		2008	343 563	240 374	103 189				
1	Alprazolam	2006	133 471	95 500	37 889	82	31.41%	71.55%	28.39%
		2008	110 028	78 981	31 047	0	32.03%	71.78%	28.22%
2	Bromazepam	2006	66 042	47 376	18 633	33	15.54%	71.74%	28.21%
		2008	51 275	37 040	14 235	0	14.92%	72.24%	27.76%
3	Brotizolam	2006	1 995	1 263	732	0	0.47%	63.31%	36.69%
		2008	1 562	1 041	521	0	0.45%	66.65%	33.36%
4	Chlordiazepoxide	2006	765	467	298	0	0.18%	61.05%	38.95%
		2008	567	351	216	0	0.17%	61.91%	38.1%
5	Clobazam	2006	18 925	13 085	5 838	2	4.45%	69.14%	30.85%
		2008	21 660	14 954	6 706	0	6.30%	69.04%	30.96%
6	Clorazepate	2006	871	508	363	0	0.20%	58.32%	41.68%
		2008	402	225	177	0	0.12%	55.97%	44.03%
7	Diazepam	2006	39 406	25 183	14 200	23	9.27%	63.91%	36.04%
		2008	28 468	17 801	10 667	0	8.29%	62.53%	37.47%
8	Flunitrazepam	2006	11 412	7 039	4 372	1	2.69%	61.68%	38.31%
		2008	7 244	4 486	2 758	0	2.11%	61.93%	38.07%
9	Flurazepam	2006	801	533	268	0	0.19%	66.54%	33.46%
		2008	685	409	276	0	0.20%	59.71%	40.29%
10	Ketazolam	2006	2 125	1 396	724	5	0.50%	65.69%	34.07%
		2008	1 454	1 015	439	0	0.42%	69.81%	30.19%
11	Loprazolam	2006	17 960	11 641	6 319	0	4.23%	64.82%	35.18%
		2008	21 030	13 716	8 528	0	6.12%	65.22%	40.55%
12	Lorazepam	2006	38 117	26 722	11 381	14	8.97%	70.11%	29.86%
		2008	30 083	21 555	8 528	0	8.76%	71.65%	28.35%
13	Lormetazepam	2006	3 388	2 441	947	0	0.80%	72.05%	27.95%
		2008	2 657	1 901	756	0	0.77%	71.55%	28.45%
14	Midazolam	2006	15 241	9 326	5 914	1	3.59%	61.19%	38.80%
		2008	12 109	7 392	4 717	0	3.52%	61.05%	38.96%
15	Nitrazepam	2006	6 626	4 549	2 076	1	1.56%	68.65%	31.33%
		2008	4 727	3 325	1 402	0	1.38%	70.34%	29.66%
16	Oxazepam	2006	37 415	28 023	9 366	26	8.81%	74.90%	25.03%
		2008	28 094	21 474	6 620	0	8.18%	76.44%	23.56%
17	Prazepam	2006	4 194	2 876	1 318	0	0.99%	68.57%	31.43%
		2008	3 183	2 202	981	0	0.93%	69.18%	30.82%
18	Temazepam	2006	15 615	10 675	4 933	7	3.67%	68.36%	31.59%
		2008	12 672	8 840	3 832	0	3.69%	69.76%	30.24%
19	Triazolam	2006	10 538	6 889	3 649	0	2.48%	65.37%	34.63%
		2008	5 663	3 666	1 997	0	1.65%	64.74%	35.26%

The prevalence was calculated by the formula of: n/N x 100. n is the different active ingredients (individual) or genders and N is the total number of benzodiazepines

Table B.4: Prescribing patterns of benzodiazepines according to the active ingredient in the Gauteng Province

		Number of benzodiazepine items					Prevalence of		
Rank		Years	Total	Female	Male	Unknown	Individual /Total	Females	Males
	Total Benzodiazepines	2006	184 500						
		2008	155 044						
1	Alprazolam	2006	57 827	41 008	16 772	47	31.34%	70.92%	29%
		2008	50 518	36 369	14 149	0	32.58%	71.99%	28.01%
2	Bromazepam	2006	29 544	21 190	8 341	13	16.01%	71.72%	28.23%
		2008	23 640	17 115	6 525	0	15.25%	72.4%	27.6%
3	Brotizolam	2006	1 251	755	496	0	0.68%	60.35%	39.66%
		2008	945	604	341	0	0.61%	63.92%	36.09%
4	Chlordiazepoxide	2006	553	332	221	0	0.30%	60.04%	39.96%
		2008	428	268	160	0	0.28%	62.62%	37.38%
5	Clobazam	2006	9 565	6 700	2 863	2	5.18%	70.05%	29.93%
		2008	10 958	7 575	3 383	0	7.07%	69.13%	30.87%
6	Clorazepate	2006	308	184	124	0	0.17%	59.74%	40.26%
		2008	137	82	55	0	0.09%	59.85%	40.15%
7	Diazepam	2006	14 796	9 543	5 249	4	8.02%	64.5%	35.48%
		2008	10 517	6 482	4 035	0	6.78%	61.63%	38.37%
8	Flunitrazepam	2006	5 249	3 156	2 093	0	2.84%	60.13%	39.87%
		2008	3 472	2 083	1 389	0	2.24%	59.99%	40.01%
9	Flurazepam	2006	533	363	170	0	0.29%	68.11%	31.9%
		2008	470	294	176	0	0.30%	62.55%	37.45%
10	Ketazolam	2006	1 038	648	385	5	0.56%	62.43%	37.09%
		2008	847	554	293	0	0.55%	65.41%	34.59%
11	Loprazolam	2006	7 260	4 682	2 578	0	3.93%	64.49%	35.51%
		2008	9 581	6 208	3 373	0	6.18%	64.8%	35.21%
12	Lorazepam	2006	14 926	10 293	4 632	1	8.09%	68.96%	31.03%
		2008	11 513	8 156	3 357	0	7.43%	70.84%	29.16%
13	Lormetazepam	2006	2 087	1 464	623	0	1.13%	70.15%	29.85%
		2008	1 773	1 273	500	0	1.14%	71.8%	28.2%
14	Midazolam	2006	7187	4 358	2 828	1	3.90%	60.64%	39.35%
		2008	5 607	3 471	2 136	0	3.62%	61.91%	38.1%

The prevalence was calculated by the formula of: n/N x 100. n is the different active ingredients (individual) or genders and N is the total number of benzodiazepines

Table B.4: Prescribing patterns of benzodiazepines according to the active ingredient in the Gauteng Province (continued)

		Years	Total	Female	Male	Un-known	Active ingredient /Total	Females	Males
15	Nitrazepam	2006	1 972	1 342	630	0	1.07%	68.05%	31.95%
		2008	1 549	1 130	419	0	1.00%	72.95%	27.05%
16	Oxazepam	2006	15 583	11 605	3 973	5	8.45%	74.47%	25.5%
		2008	12 225	9 242	2 983	0	7.88%	75.6%	24.4%
17	Prazepam	2006	2 205	1 548	657	0	1.20%	70.2%	29.8%
		2008	1 807	1 319	488	0	1.17%	72.99%	27.01%
18	Temazepam	2006	7 676	5 192	2 477	7	4.16%	67.64%	32.27%
		2008	6 527	4 508	2 019	0	4.21%	69.07%	30.93%
19	Triazolam	2006	4 940	3 207	1 733	0	2.68%	64.92%	35.08%
		2008	2 530	1 625	905	0	1.63%	64.23%	35.77%

The prevalence was calculated by the formula of: n/N x 100. n is the different active ingredients or genders and N is the total number of benzodiazepines

Table B.5: Prescribing patterns of benzodiazepines according to the active ingredient in the Northern Cape Province for 2006 and 2008

			Number items (n)			Prevalence of		
Rank		Years	Total	Female	Male	Individual/total	Females	Males
	Total Benzodiazepine	2006	6 665					
		2008	5 027					
1	Alprazolam	2006	2 121	1 581	540	31.82%	74.54	25.46
		2008	1 687	1 199	488	33.56%	71.07	28.93
2	Bromazepam	2006	1 442	999	443	21.64%	69.28	30.72
		2008	972	655	317	19.34%	67.39	32.61
3	Chlordiazepoxide	2006	1	1	0	0.02%	100	0
		2008	3	0	3	0.06%	0	100
4	Clobazam	2006	273	177	96	4.10%	64.84	35.17
		2008	375	216	159	7.46%	57.6	42.4
5	Clorazepate	2006	13	11	2	0.20%	84.62	15.39
6	Diazepam	2006	599	362	237	8.99%	60.43	39.57
		2008	473	307	166	9.41%	64.91	35.1
7	Flunitrazepam	2006	126	84	42	1.89%	66.67	33.3
		2008	87	52	35	1.73%	59.77	40.23
8	Flurazepam	2006	2	0	2	0.03%	0	100
		2008	3	3	0	0.06%	100	0
9	Ketazolam	2006	46	26	20	0.69%	56.52	43.48
		2008	31	29	2	0.62%	93.55	6.45
10	Loprazolam	2006	109	69	40	1.64%	63.30	36.7
		2008	100	67	33	1.99%	67	33
11	Lorazepam	2006	387	252	135	5.81%	65.12	34.88
		2008	311	212	99	6.19%	68.17	31.83
12	Lormetazepam	2006	32	18	14	0.48%	56.25	43.75
		2008	22	7	15	0.44%	31.82	68.18
13	Midazolam	2006	246	157	89	3.69%	63.82	36.18
		2008	155	104	51	3.08%	67.1	32.9
14	Nitrazepam	2006	92	50	42	1.38%	54.35	45.65
		2008	67	36	31	1.33%	53.73	46.27
15	Oxazepam	2006	805	588	217	12.08%	73.04	26.96
		2008	497	387	110	9.89%	77.87	22.13
16	Prazepam	2006	154	71	83	2.31%	46.10	53.9
		2008	121	85	36	2.41%	70.25	29.75
17	Temazepam	2006	118	60	58	1.77%	50.85	49.15
		2008	78	17	61	1.55%	21.8	78.21
18	Triazolam	2006	99	68	31	1.49%	68.69	31.31
		2008	45	40	5	0.90%	88.89	11.11

The prevalence was calculated by the formula of: n/N x 100. n is the different active ingredients (individual) or genders and N is the total number of benzodiazepines

Table B.6: Number of days supplied according to active ingredients for 2006 and 2008

Days supplied	0<x≤30		30<x≤60		60<x≤90		90<x≤120		120<x≤150		180+	
Years	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008	2006	2008
Alprazolam	42 274	31072	5304	4 853	2 595	2 610	4 133	3 949	3 983	3 459	455	319
Bromazepam	15 615	9 960	2 143	1 695	1 259	1 032	2 124	1 948	2 462	2 054	286	208
Brotizolam	268	175	67	39	35	25	71	63	101	84	12	9
Chlordiazepoxide	208	140	27	25	21	8	14	17	25	21	2	2
Clobazam	6 267	6 488	938	983	416	468	560	660	524	647	60	102
Clorazepate	81	30	22	9	10	4	23	9	53	26	4	2
Diazepam	26 297	17 990	799	534	328	259	405	350	397	370	41	52
Flunitrazepam	1 995	1 021	399	259	251	145	397	289	502	345	36	26
Flurazepam	105	68	30	20	14	15	31	20	35	32	6	9
Ketazolam	759	543	91	43	28	21	45	38	66	42	9	7
Loprazolam	2 998	3 552	625	772	348	431	675	787	780	880	106	161
Lorazepam	8 586	6 352	958	796	528	455	894	719	1 577	1 254	267	224
Lormetazepam	556	333	139	70	54	57	113	71	148	133	22	19
Midazolam	5 117	3 508	514	424	252	170	480	389	477	418	61	68
Nitrazepam	1 331	604	205	95	108	67	204	141	272	227	42	50
Oxazepam	6 899	5 167	1 329	1 251	673	690	1 267	1 165	1 632	1 168	153	72
Prazepam	781	516	165	106	78	71	130	88	183	143	19	23
Temazepam	3 697	2 338	524	415	301	220	507	395	613	565	75	92
Triazolam	918	486	229	183	165	160	321	261	576	294	86	18

Table B.7: Prevalence of benzodiazepines according to the trade name for 2006 and 2008

Trade names	Number of items (n)		Prevalence (n/N)	
Years	2006	2008	2006	2008
Total Benzodiazepine	424 907	343 563		
Adco-Alzam® 0.25 mg	20 455	15 569	4.81%	4.53%
Adco-Alzam® 0.5 mg	33 377	27 178	7.86%	7.91%
Adco-Alzam® 1 mg	8 847	7 733	2.08%	2.25%
Arem® 5 mg	5 612	4 398	1.32%	1.28%
Ativan® 0.5 mg	973	735	0.23%	0.21%
Ativan® 1 mg	6 275	4 811	1.48%	1.40%
Ativan® 2.5 mg	2 435	1 953	0.57%	0.57%
Ativan® 4 mg/ml inj	206	177	0.05%	0.05%
Ativan® SL 1 mg	6 258	5 960	1.47%	1.73%
Azor® 0.25 mg	10 092	7 121	2.38%	2.07%
Azor® 0.5 mg	16 866	11 419	3.97%	3.32%
Azor® 1 mg	3 890	3 273	0.92%	0.95%
Benzopin® 2 mg	18	0	0.00%	0.00%
Benzopin® 5 mg	57	0	0.01%	0.00%
Betapam® 5 mg	11 273	6 500	2.65%	1.89%
Brazepam® 3 mg	15 290	14 542	3.60%	4.23%
Brazepam® 6 mg	7 526	7 045	1.77%	2.05%
Bromaze® 3 mg	1 802	76	0.42%	0.02%
Bramaze® 6 mg	1 637	1 125	0.39%	0.33%
Calmpose® 2 ml inj	1	61	0.00%	0.02%
CPL ALNCE Alprazolam® 0.25 mg	60	22	0.01%	0.01%
CPL ALNCE Alprazolam® 0.5 mg	60	255	0.01%	0.07%
Dalmadorm® 15 mg	299	430	0.07%	0.13%
Dalmadorm® 30 mg	502	3 183	0.12%	0.93%
Demetrin® 10 mg	4 194	66	0.99%	0.02%
Diazepam® 10 mg/2 ml inj	115	8 500	0.03%	2.47%
Dormicum® 15 mg	10 490	171	2.47%	0.05%
Dormicum® 15 mg/3 ml	353	10	0.08%	0.00%
Dormicum® 50 mg/10 ml inj	19	817	0.00%	0.24%
Dormicum® 5 mg/5 ml	1 150	2 554	0.27%	0.74%
Dormicum® 7.5 mg	3 166	21 030	0.75%	6.12%
Dormonoct® 2 mg	17 960	369	4.23%	0.11%
Halcion® 0.125 mg	164	133	0.04%	0.04%
Halcion® 0.25 mg	10 374	5 530	2.44%	1.61%
Hypnor® 1 mg	279	637	0.07%	0.19%
Lendormin® 0.25 mg	1 995	1 562	0.47%	0.45%
Lexotan® 3 mg	4 214	3 112	0.99%	0.91%
Lexotan® 6 mg	892	700	0.21%	0.20%
Librium® 25 mg	765	567	0.18%	0.17%
Loramet® 0.5 mg	162	109	0.04%	0.03%
Loramet® 1 mg	535	525	0.13%	0.15%
Loramet® 2 mg	1 924	1 495	0.45%	0.44%
Medopam® 10 mg	1	3	0.00%	0.00%
Medopam® 15 mg	2	1	0.00%	0.00%
Merck-Alaprazolam® 0.25 mg	427	553	0.10%	0.16%
Merck-Alaprazolam® 0.5 mg	601	666	0.14%	0.19%
Merck-Alaprazolam® 1 mg	233	358	0.05%	0.10%
Micro Diazepam® 10 mg/2 ml	8	23	0.00%	0.01%

Table B.7: Prevalence of benzodiazepines according to the trade name for 2006 and 2008 (continued)

Micro Midazolam® 5 mg/5 ml inj	1	1	0.00%	0.00%
Midacum® 15 mg/3 ml inj	5	6	0.00%	0.00%
Midacum® 5 mg/1 ml inj	34	3	0.01%	0.00%
Midanium® 15 mg/3 ml inj	23	46	0.01%	0.01%
Mogadon® 5 mg	185	1	0.04%	0.00%
Noctamid® 1 mg	767	111	0.18%	0.03%
Normison® 10 mg	3 429	528	0.81%	0.15%
Normison® 20 mg	12 186	2 942	2.87%	0.86%
Pax® 10 mg	6 429	9 730	1.51%	2.83%
Pax® 10 mg/2 ml inj	258	6 092	0.06%	1.77%
Pax® 5 mg	12 812	211	3.02%	0.06%
Paxadorm® 5 mg	153	10 341	0.04%	3.01%
Purata® 10 mg	7 642	2	1.80%	0.00%
Purata® 15 mg	11 178	6 203	2.63%	1.81%
Purata® 30 mg	12 546	8 179	2.95%	2.38%
Rohypnol® 1 mg	1 343	8 008	0.32%	2.33%
Sandoz Bromazepam® 3 mg	23 682	677	5.57%	0.20%
Sandoz Bromazepam® 6 mg	10 999	16 017	2.59%	4.66%
Sandoz Diazepam® 2 mg	509	8 658	0.12%	2.52%
Sandoz Diazepam® 5 mg	1 990	408	0.47%	0.12%
Sandoz Flunitraz® 1 mg	9 790	792	2.30%	0.23%
Sandoz Nitrazepam® 5 mg	676	5 930	0.16%	1.73%
Sandoz Oxazepam® 15 mg	1 286	216	0.30%	0.06%
Sandoz Oxazepam® 30 mg	1 184	1 104	0.28%	0.32%
Scripto-pam® 5 mg	1	1 185	0.00%	0.34%
Serepax® 10 mg	915	887	0.22%	0.26%
Serepax® 15 mg	1 616	1 462	0.38%	0.43%
Serepax® 30 mg	1 045	1 062	0.25%	0.31%
Solatran® 15 mg	2 125	1 454	0.50%	0.42%
Tranject® 2 ml inj	484	207	0.11%	0.06%
Tranqipam® 1 mg	13 664	10 827	3.22%	3.15%
Tranqipam® 2.5 mg	8 306	5 620	1.95%	1.64%
Tranxene® 15 mg	871	402	0.20%	0.12%
Urbanol® 10 mg	11 543	12 670	2.72%	3.69%
Urbanol® 5 mg	7 382	8 990	1.74%	2.62%
Valium® 10 mg	1 102	760	0.26%	0.22%
Valium® 10 mg/2 ml inj	1 138	629	0.27%	0.18%
Valium® 2 mg	460	386	0.11%	0.11%
Valium® 5 mg	2 751	1 684	0.65%	0.49%
Xanor® 0.25 mg	3 732	2 890	0.88%	0.84%
Xanor® 0.5 mg	4 887	4 236	1.15%	1.23%
Xanor® 1 mg	735	782	0.17%	0.23%
Xanor® 2 mg	148	87	0.03%	0.03%
Xanor® 0.5 mg	10 562	9 214	2.49%	2.68%
Xanor® SR 1 mg	2 355	1 969	0.55%	0.57%
Xanor® SR 2 mg	165	162	0.04%	0.05%
Zopax® 0.25 mg	4 563	4 642	1.07%	1.35%
Zopax® 0.5 mg	9 022	9 695	2.12%	2.82%
Zopax® 1 mg	2 394	2 398	0.56%	0.70%

Table B.8: Prevalence of benzodiazepines according to the trade name in the Gauteng province during 2006 and 2008

	Number of items		Prevalence in GP (n/N)	
Year	2006	2008	2006	2008
Total benzodiazepines in GP	184 500	155 044		
Adco-Alzam® 0.25 mg	8 036	6 402	4.36%	4.13%
Adco-Alzam® 0.5 mg	13 294	11 719	7.21%	7.56%
Adco-Alzam® 1 mg	4 374	4 113	2.37%	2.65%
Arem® 5 mg	1 633	1 403	0.89%	0.90%
Ativan® 0.5 mg	515	387	0.28%	0.25%
Ativan® 1 mg	2 823	2 137	1.53%	1.38%
Ativan® 2.5 mg	1 184	916	0.64%	0.59%
Ativan® 4 mg/ml inj	80	41	0.04%	0.03%
Ativan® SL 1 mg	2 480	2 531	1.34%	1.63%
Azor® 0.25 mg	4 499	3 337	2.44%	2.15%
Azor® 0.5 mg	7 657	5 763	4.15%	3.72%
Azor® 1 mg	2 059	2 015	1.12%	1.30%
Benzopin® 2 mg	4	0	0.00%	0.00%
Benzopin® 5 mg	20	0	0.01%	0.00%
Betapam® 5 mg	4 091	2 170	2.22%	1.40%
Brazepam® 3 mg	5 837	5 935	3.16%	3.83%
Brazepam® 6 mg	3 442	3 322	1.87%	2.14%
Bromaze® 3 mg	452	9	0.24%	0.01%
Bramaze® 6 mg	380	426	0.21%	0.27%
Calmpose® 2 ml inj	1	6	0.00%	0.00%
CPL ALNCE Alprazolam® 0.25 mg	28	2	0.02%	0.00%
CPL ALNCE Alprazolam® 0.5 mg	19	186	0.01%	0.12%
Dalmadorm® 15 mg	197	284	0.11%	0.18%
Dalmadorm® 30 mg	336	1 807	0.18%	1.17%
Demetrin® 10 mg	2 205	25	1.20%	0.02%
Diazepam® 10 mg/2 ml inj	35	4 069	0.02%	2.62%
Dormicum® 15 mg	4 985	85	2.70%	0.05%
Dormicum® 15 mg/3 ml	241	1	0.13%	0.00%
Dormicum® 50 mg/10 ml inj	12	293	0.01%	0.19%
Dormicum® 5 mg/5 ml	467	1 125	0.25%	0.73%
Dormicum® 7.5 mg	1 473	9 581	0.80%	6.18%
Dormonoct® 2 mg	7 260	175	3.93%	0.11%
Halcion® 0.125 mg	67	78	0.04%	0.05%
Halcion® 0.25 mg	4 873	2 452	2.64%	1.58%
Hypnor® 1 mg	92	322	0.05%	0.21%
Lendormin® 0.25 mg	1 251	945	0.68%	0.61%
Lexotan® 3 mg	2 624	1 882	1.42%	1.21%
Lexotan® 6 mg	603	459	0.33%	0.30%
Librium® 25 mg	553	428	0.30%	0.28%
Loramet® 0.5 mg	65	94	0.04%	0.06%
Loramet® 1 mg	337	361	0.18%	0.23%
Loramet® 2 mg	1 313	1 086	0.71%	0.70%
Medopam® 15 mg	2	2	0.00%	0.00%
Merck-Alaprazolam® 0.25 mg	85	166	0.05%	0.11%
Merck-Alaprazolam® 0.5 mg	149	232	0.08%	0.15%
Merck-Alaprazolam® 1 mg	67	164	0.04%	0.11%

Table B.8: Prevalence of benzodiazepines according to the trade name in the Gauteng province during 2006 and 2008 (continued)

Midacum® 5 mg/1 ml inj	4	2	0.00%	0.00%
Midanium® 15 mg/3 ml inj	5	33	0.00%	0.02%
Mogadon® 5 mg	83	1	0.04%	0.00%
Noctamid® 1 mg	372	61	0.20%	0.04%
Normison® 10 mg	1 470	232	0.80%	0.15%
Normison® 20 mg	6 206	1 359	3.36%	0.88%
Pax® 10 mg	2 598	5 168	1.41%	3.33%
Pax® 10 mg/2 ml inj	30	2 463	0.02%	1.59%
Pax® 5 mg	4 173	47	2.26%	0.03%
Paxadorm® 5 mg	20	3 442	0.01%	2.22%
Purata® 10 mg	3 220	2 703	1.75%	1.74%
Purata® 15 mg	3 409	2 487	1.85%	1.60%
Purata® 30 mg	6 128	4 073	3.32%	2.63%
Rohypnol® 1 mg	859	394	0.47%	0.25%
Sandoz Bromazepam® 3 mg	10 356	6 941	5.61%	4.48%
Sandoz Bromazepam® 6 mg	5 850	4 666	3.17%	3.01%
Sandoz Diazepam® 2 mg	191	101	0.10%	0.07%
Sandoz Diazepam® 5 mg	677	261	0.37%	0.17%
Sandoz Flunitraz® 1 mg	4 298	2 756	2.33%	1.78%
Sandoz Nitrazepam® 5 mg	236	85	0.13%	0.05%
Sandoz Oxazepam® 15 mg	289	365	0.16%	0.24%
Sandoz Oxazepam® 30 mg	547	625	0.30%	0.40%
Serepax® 10 mg	524	524	0.28%	0.34%
Serepax® 15 mg	762	709	0.41%	0.46%
Serepax® 30 mg	702	737	0.38%	0.48%
Solatran® 15 mg	1 038	847	0.56%	0.55%
Tranject® 2 ml inj	251	25	0.14%	0.02%
Tranqipam® 1 mg	4 433	3 204	2.40%	2.07%
Tranqipam® 2.5 mg	3 411	2 297	1.85%	1.48%
Tranxene® 15 mg	308	137	0.17%	0.09%
Urbanol® 10 mg	5 781	6 476	3.13%	4.18%
Urbanol® 5 mg	3 784	4 482	2.05%	2.89%
Valium® 10 mg	476	382	0.26%	0.25%
Valium® 10 mg/2 ml inj	626	266	0.34%	0.17%
Valium® 2 mg	262	186	0.14%	0.12%
Valium® 5 mg	1 361	972	0.74%	0.63%
Xanor® 0.25 mg	2 334	1 777	1.27%	1.15%
Xanor® 0.5 mg	2 855	2 364	1.55%	1.52%
Xanor® 1 mg	484	524	0.26%	0.34%
Xanor® 2 mg	114	71	0.06%	0.05%
Xanor® 0.5 mg	5 421	4 677	2.94%	3.02%
Xanor® SR 1 mg	1 201	1 072	0.65%	0.69%
Xanor® SR 2 mg	108	75	0.06%	0.05%
Zopax® 0.25 mg	1 361	1 646	0.74%	1.06%
Zopax® 0.5 mg	2 836	3 343	1.54%	2.16%
Zopax® 1 mg	846	1 050	0.46%	0.68%

Table B.9: Prevalence of benzodiazepines according to the trade name in the Northern Cape Province during 2006 and 2008

	Benzodiazepines in NC		Prevalence in NC (n/N)	
Year	2006	2008	2006	2008
Total benzodiazepine	6 665	5 027		
Adco-Alzam® 0.25 mg	144	70	2.16%	1.39%
Adco-Alzam® 0.5 mg	201	200	3.02%	3.98%
Adco-Alzam® 1 mg	39	49	0.59%	0.97%
Arem® 5 mg	81	54	1.22%	1.07%
Ativan® 0.5 mg	7	5	0.11%	0.10%
Ativan® 1 mg	32	27	0.48%	0.54%
Ativan® 2.5 mg	17	14	0.26%	0.28%
Ativan® 4 mg/ml inj	2	3	0.03%	0.06%
Ativan® SL 1 mg	124	123	1.86%	2.45%
Azor® 0.25 mg	465	318	6.98%	6.33%
Azor® 0.5 mg	664	379	9.96%	7.54%
Azor® 1 mg	45	32	0.68%	0.64%
Benzopin® 2 mg	1	0	0.02%	0.00%
Benzopin® 5 mg	204	99	3.06%	1.97%
Betapam® 5 mg	679	487	10.19%	9.69%
Brazepam® 3 mg	445	322	6.68%	6.41%
Brazepam® 6 mg	23	2	0.35%	0.04%
Bromaze® 3 mg	50	32	0.75%	0.64%
Bramaze® 6 mg	4	1	0.06%	0.02%
Dalmadorm® 30 mg	2	3	0.03%	0.06%
Demetrin® 10 mg	154	121	2.31%	2.41%
Diazepam® 10 mg/2 ml inj	29	6	0.44%	0.12%
Dormicum® 15 mg	220	138	3.30%	2.75%
Dormicum® 15 mg/3 ml	8	11	0.12%	0.22%
Dormicum® 5 mg/5 ml	8	6	0.12%	0.12%
Dormicum® 7.5 mg	10	100	0.15%	1.99%
Dormonoct® 2 mg	109	24	1.64%	0.48%
Hypnor® 1 mg	99	45	1.49%	0.90%
Lendormin® 0.25 mg	1	1	0.02%	0.02%
Lexotan® 3 mg	43	15	0.65%	0.30%
Lexotan® 6 mg	14	1	0.21%	0.02%
Librium® 25 mg	1	3	0.02%	0.06%
Loramet® 0.5 mg	0	3	0.00%	0.06%
Loramet® 1 mg	2	16	0.03%	0.32%
Merck-Alaprazolam® 0.25 mg	5	3	0.08%	0.06%
Merck-Alaprazolam® 0.5 mg	9	9	0.14%	0.18%
Merck-Alaprazolam® 1 mg	2	0	0.03%	0.00%

Table B.9: Prevalence of benzodiazepines according to the trade name in the Northern Cape Province during 2006 and 2008 (continued)

Mogadon® 5 mg	7	13	0.11%	0.26%
Noctamid® 1 mg	30	3	0.45%	0.06%
Normison® 10 mg	34	20	0.51%	0.40%
Normison® 20 mg	84	58	1.26%	1.15%
Pax® 10 mg	49	73	0.74%	1.45%
Pax® 10 mg/2 ml inj	2	3	0.03%	0.06%
Pax® 5 mg	249	205	3.74%	4.08%
Purata® 10 mg	142	114	2.13%	2.27%
Purata® 15 mg	310	141	4.65%	2.80%
Purata® 30 mg	249	137	3.74%	2.73%
Rohypnol® 1 mg	9	1	0.14%	0.02%
Sandoz Bromazepam® 3 mg	140	67	2.10%	1.33%
Sandoz Bromazepam® 6 mg	48	46	0.72%	0.92%
Sandoz Diazepam® 2 mg	2	5	0.03%	0.10%
Sandoz Diazepam® 5 mg	16	6	0.24%	0.12%
Sandoz Flunitraz® 1 mg	116	85	1.74%	1.69%
Sandoz Nitrazepam® 5 mg	4	0	0.06%	0.00%
Sandoz Oxazepam® 15 mg	33	25	0.50%	0.50%
Sandoz Oxazepam® 30 mg	24	21	0.36%	0.42%
Serepax® 10 mg	2	3	0.03%	0.06%
Serepax® 15 mg	43	39	0.65%	0.78%
Serepax® 30 mg	2	17	0.03%	0.34%
Solatran® 15 mg	46	31	0.69%	0.62%
Tranject® 2 ml inj	17	28	0.26%	0.56%
Tranqipam® 1 mg	114	85	1.71%	1.69%
Tranqipam® 2.5 mg	91	54	1.37%	1.07%
Tranxene® 15 mg	13	0	0.20%	0.00%
Urbanol® 10 mg	225	273	3.38%	5.43%
Urbanol® 5 mg	48	102	0.72%	2.03%
Valium® 10 mg	3	2	0.05%	0.04%
Valium® 10 mg/2 ml inj	2	1	0.03%	0.02%
Valium® 2 mg	25	21	0.38%	0.42%
Xanor® 0.25 mg	41	38	0.62%	0.76%
Xanor® 0.5 mg	35	74	0.53%	1.47%
Xanor® 1 mg	1	9	0.02%	0.18%
Xanor® 0.5 mg	73	45	1.10%	0.90%
Xanor® SR 1 mg	21	5	0.32%	0.10%
Xanor® SR 2 mg	1	0	0.02%	0.00%
Zopax® 0.25 mg	116	131	1.74%	2.61%
Zopax® 0.5 mg	218	280	3.27%	5.57%
Zopax® 1 mg	37	44	0.56%	0.88%

Table B.10: The percentage of benzodiazepines (ten with the highest percentage) that was prescribed for longer than 180 days for 2006 and 2008

2006		
Trade name	**Number of items**	**Prevalence of each trade name (%)**
Tranqipam® 2.5 mg	77	4.04
Halcion® 0.25 mg	86	3.85
Tranqipam® 1 mg	130	3.60
Dalmadorm® 15 mg	3	3.06
Loramet® 2 mg	16	2.94
Ativan® 2.5 mg	19	2.57
Dalmadorm® 30 mg	3	2.44
Sandoz Bromazepam® 6 mg	70	2.42
Arem® 5 mg	39	2.22
Lendormin® 0.25 mg	12	2.17
2008		
Dalmadorm® 30 mg	7	7.07
Sandoz Nitrazepam® 5 mg	3	6.52
Mogadon® 5 mg	1	4.55
Noctamid® 1 mg	5	4.42
Tranqipam® 1 mg	116	4.33
Arem® 5 mg	45	4.13
Xanor® 1 mg	10	4.03
Tranqipam® 2.5 mg	43	3.87
Loramet® 2 mg	12	3.79
Xanor® SR 2 mg	2	3.70

The prevalence was calculated by the formula of: n/N x 100. n is the different active ingredients or genders and N is the total number of benzodiazepines